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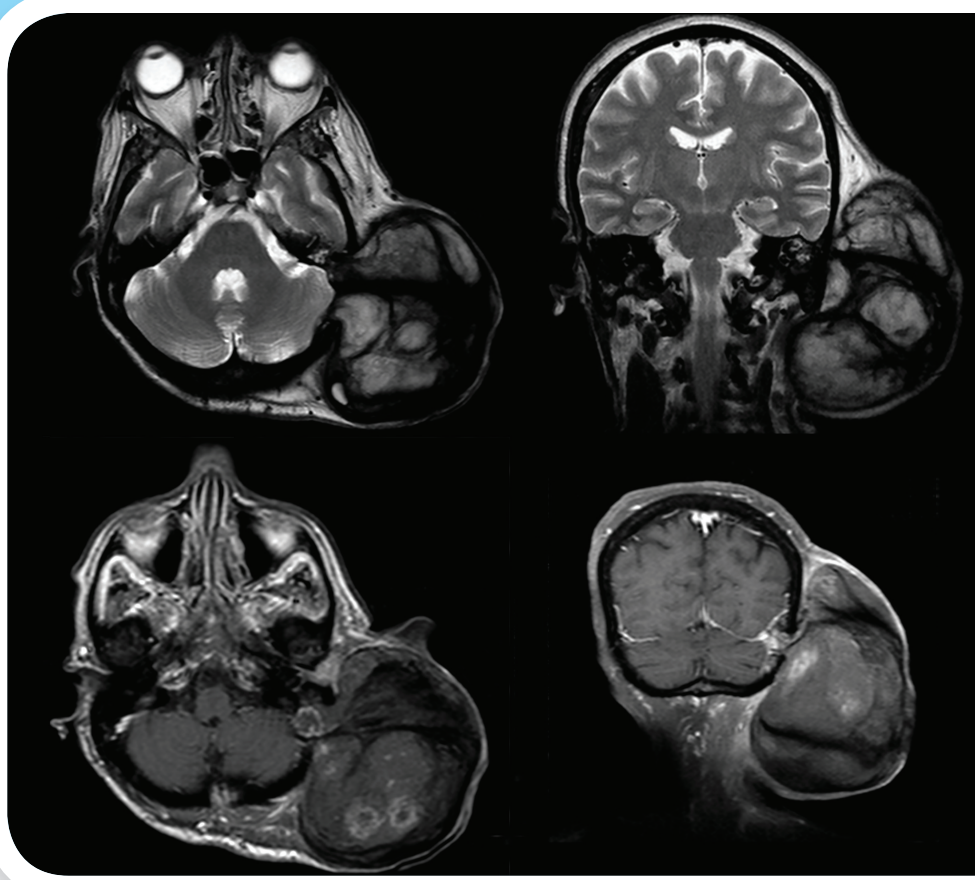

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Hydrodynamic Considerations VII: Impact of a 6 years of Ongoing Training Program on the Handling of External Ventricular Drainage

Considerações hidrodinâmicas VII: Impacto de 6 anos um programa de educação continuada no manuseio de drenagem ventricular externa

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Abstract

Introduction A new culture of care in the use of external ventricular drainage (EVD) systems at neurological intensive units (neuro-ICUs) and operating rooms (ORs) has been gaining popular since the past decade. In neurosurgical units of developed countries, the application of such operational standards has significantly reduced infection rates to below 5%. The present work reports the results of 6 years of experience of an ongoing training program held by the Discipline of Neurosurgery at Fundação Faculdade Regional de Medicina – FUNFARME –, in the municipality of São José do Rio Preto, state of São Paulo, Brazil.

Methods The design of the project was discussed and agreed among staff involved in infection control, neurosurgery, and nursing. The purposes of the project were met, and the entire hospital neuro-NICU nursing staff and neurosurgical residents (which comprises the materials to be handled and the techniques to insert the ventricular catheter) were trained.

Results A total of 992 implantations were included in the study; the sample, which was composed of 56% of female patients and 44% of males patients, had an average age of 53 years (range: 8 to 88 years), and underwent EVD for a median of 5 days (range: 1 to 24 days). From a historical percentage of infection $>$ 20%, the following cumulative

Keywords
- EVD infections
- EVD
- control of EVD infections
- training program on EVD infections

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infection rates were observed from 2013 to August 2019 respectively: 22.85%, 26.01%, 13.34,% 13.75%, 11.04%, 7.17%, and 12.21%.

Conclusion On average, the rates of infection decreased progressively throughout the years. However, infection started to increase again as the program was unfortunately partially abandoned by the neurosurgical team. Its efficacy is dependent on the willingness to participate of each individual in the neurosurgical staff.

Resumo

Introdução Uma nova cultura de cuidados na utilização de sistemas de drenagem ventricular externa (DVE) em unidades de terapia intensiva neurocirúrgicas (UTINs) e salas de operação (SOs) tornou-se popular desde a última década. Em unidades neurocirúrgicas de países desenvolvidos, a aplicação de tais padrões operacionais reduziu significativamente as taxas de infecção para menos de 5%. Este trabalho relata os resultados de 6 anos de experiência com um programa de educação continuada oferecido pela Disciplina de Neurocirurgia da Fundação Faculdade Regional de Medicina (FUNFARME) de São José do Rio Preto, São Paulo, Brasil.

Métodos O desenho do projeto foi discutido e acordado entre o pessoal de controle de infecção, neurocirúrgico e enfermagem. Foram realizados os objetivos do projeto, bem como o treinamento (que envolve os materiais a serem manipulados e as técnicas de inserção do cateter ventricular)de toda equipe de enfermagem da UTIN do hospital e dos residentes de neurocirurgia.

Resultados Um total de 992 implantes foram incluídos no estudo; a amostra, composta de 56% de pacientes do sexo feminino e de 44% do sexo masculino, tinha uma média de idade de 53 anos (variação:8 a 88 anos), e se submeteu a DVE por uma média de 5 dias (variação: 1 a 24 dias). De uma porcentagem histórica de infecção acima de 20%, as seguintes taxas cumulativas ocorreram de 2013 a agosto de 2019, respectivamente: 22,85%, 26,01%, 13,34%, 13,75%, 11,04%, 7,17%, e 12,21%.

Conclusão As taxas de infecção diminuíram progressivamente ao longo dos anos. No entanto, a infecção voltou a aumentar, pois o programa, infelizmente, foi parcialmente abandonado pela equipe neurocirúrgica. A sua eficácia depende da disposição de participar de cada indivíduo da equipe neurocirúrgica.

Palavras-chave
- infecções por DVE
- DVE
- controle de infecções por DVE
- programa educacional sobre infecção por DVE

Introduction

One of the most frequent neurosurgical procedures performed worldwide in neurological intensive care units (neuro-ICUs) is the implantation of an external ventricular drainage (EVD) system as a temporary relief for intracranial hypertension due to different pathologies, including head injuries, expansive lesions, spontaneous subarachnoid hemorrhage, and intraventricular hemorrhage, among others. However, EVDs are directly connected to the ventricular system of the patient; they work hydraulically, and patients submitted to EVDs are in a coma state, and are frequently handled while in bed or transported for repeated computed tomography (CT) scans, and, therefore totally dependent upon the cautious employed in handling the EVDs. Infection and EVD revisions have long been a matter of concern in neurosurgical units because mishandling may result in significant morbidity and even mortality if not treated appropriately. The reported incidence of EVD infections in the literature show variable rates ranging from 2% to as high as 30%.[1–3]

Throughout the past decade, a new culture of care in the use of EVD systems at neuro-ICUs and operating rooms (ORs) became increasingly popular. It essentially proposes the *training* of all teams involved, imposing discipline and zero tolerance to breaches of the stablished norms for EVD insertion and handling. In neurosurgical units of developing countries, the application of such operational standards has significantly reduced infection rates to below 5%.[4,5] The objective of the present paper is to describe a six-year experience with EVD systems at Fundação Faculdade Regional de Medicina (FUNFARME), a public university in Brazil.

Materials and Methods

A training program was gradually implemented. Stage I: conducted throughout April 2013, with the definition of the following principles: 1) standardization of the use of EVD systems to reduce the incidence of infections; we adapted the protocol developed by Korinek et al.[4] to our

reality, keeping its essential characteristics: total trichotomy; rigorous disinfection of the scalp (twice); standardization of antibiotic therapy (if any); manipulations by nursing staff strongly discouraged; tubing washing ban due to accumulated blood; access to the cerebrospinal fluid (CSF) restricted and, if it was the case, it was performed only by the resident neurosurgeon; handling the patient only after closing all the clamps, including during transportation for imaging exams; changing bed linen; changing the position and handling by physiotherapists; and coming or returning from the operating room. 2. Standardization of EVD systems; we used the concept of drainage developed by Tronnier et al.,[1] which comprises a series of preventable mechanisms that should be available in an optimum EVD system, such as adequate fixation of the ventricular-catheter component in the scalp to avoid up and down movements once the catheter has been implanted in the ventricles; adequate diameters of the orifices and the catheter tube for CSF drainage (which, unlike hydrocephalus in an elective patient, has a high protein content and red-blood-cell count), which contained a ventricular catheter connector with the drainage without tapering (that is, a connector with the same internal diameter as the ventricular catheter, as it is an important site for occlusion, and at the same time not possible to detect such blockage after implantation); absence of three-way taps near the patient's head, as a possible route of contamination; the system that does not allow accidental disconnections, that is, that does have bonded luer-lock connections. The program was followed by the Committee for the Control of Hospital Infections (Comissão de Controle de Infecção Hospitalar, CCIH, in Porutguese), and the Department of Neurosurgery at FUNFARME. The management group was aware that the chances of success of the training relied on the adherence of the people involved.

Stage II: it took place during the month of May 2013, with awareness and training of nursing, intensivists, and the CCIH and neurosurgery personnel. Thus, 360 nurses and technicians and 15 residents in neurosurgery were initially exposed to the training program. Neurosurgical residents were given the frontal bone insertion of the catheter as the anatomic site (Kocher point), angulations, depth of insertion, techniques to determine distances by tomography, hydraulics applied in EVD systems, possible sources of complications; the methods of prevention and handling of EVD systems were reviewed for junior neurosurgical residents. In June 2013, the CCIH stablished the protocol for care of EVD systems, which became the standard at FUNFARME for this surgical procedure, and involved care during the insertion of the catheter, care regarding the dressing, care for the patient with an EVD system, protocols for collection of CSF through the EVD system, emptying of the collection bag, administration of intrathecal antibiotic therapy, patient transportation for imaging exams, and removal of the EVD system. Procedures for each action were computerized and made available electronically; the EVD system chosen was the one that best matched the concepts by Tronnier et al.[1] and Korinek et al.[4] Posters were hung in the ORs for follow-up by everyone involved (►**Figs. 1** and **2**). All measures were implemented within the deadlines, and the project started on

Fig. 1

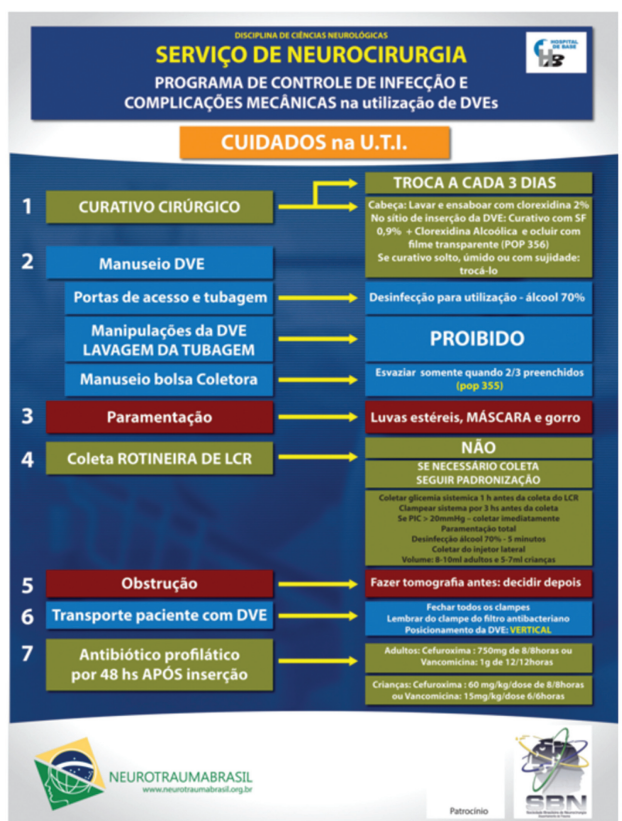

Fig. 2

July 1st, 2013. We began woth an infection rate higher than 20%. The data on infection were obtained from the CCIH, and were monitored by a nurse specialized in neurosurgical procedures (CS). In the following years, the protocol was changed according to the acquired experience as well as the number of interventions (understood as the number of repeated training sessions for the nursing personnel). The indications for insertion of an EVD system were any pathology causing acute hydrocephalus. The approach was defined as right frontal (Kocher point) unless another location was indicated.

Results

The first 18 months of the program comprised the learning curve.

From July 1st, 2013 to June 30th, 2014, 115 EVD systems were implanted. A total of 9 patients (8.7%) underwent revision or replacement of a previous EVD system, making the total of 106 patients (56.3% of men amd 43,.7% of women) with a new EVD system inserted. The indications for the implantation are summarized on ►**Table 1**. The major contributing pathologies for the insertion of EVD systems were hemorrhagic stroke, subarachnoid hemorrhage, and head Injury (75% of the total). A total of 11.3% of the total sample had intraventricular hemorrhage (not shown on ►**Table 1**). Among them, 8 patients were had hemorrhagic stroke, which means that blood dissected into the ventricles of 26.7% of them. The projected approach to the ventricles (Kocher's point) was accomplished in 98% of the patients. The number of days with the EVD system implanted ranged from 1 to 24 days. The Average age of the sample was of 46.5 ± 24.2 years, ranging from 4 to 88 years. The average standard deviation, and minimum and maximum of days with the EVD system imolanted are shown on ►**Table 1** according to the pathology.

Effect of the Training

Infection rates – The Learning Curve

The infection rate seemed erratic throughout the first months; the percentual of infection (represented by the black line) was related to the number of implanted EVD systems throughout a specific month, but there was also a relationship with the accomplished patients' check lists. Interventions (repeated training sessions) were scheduled for June 2014, but we moved in up to March. During the following two months, the protocol was observed in the majority of patients, and there was a significative drop on infection rate. A new intervention occurred six months later, and the same situation was observed. It became clear that frequent training interventions were necessary to achieve lower infection rates.

The Following Years

►**Fig. 4**

The number of EVD systems implanted remained stable throughout the years, except for 2017, in which 240 units were implanted. In total, 992 EVD systems were implanted.

After adapting the frequency of the training interventions and conitnuing with the training program, infection rates dropped from 26.01% in 2014 to 13.34% in 2015, and gradually decreased to 7.7% in 2018. There was an unexpected trend towards a rise in 2019. Query as to a possible cause led us to the information of discontinuation, with junior residents no longer exposed to the training program (►**Fig. 5**).

Discussion

The implantation of EVD systems is a common, temporary and valuable tool against several disorders of the central nervous system which cause transient CSF absorptive deficits. Placement of an EVD system may be beneficial, since even small volumes of CSF can significantly lower ICP; it may provide clearance of hemorrhage from a ventricle[6] to control intracranial hypertension and provide a chance for ICP stabilization and further patient treatment. However, EVD systems directly connect the ventricular system to the outside world; they work based on hydraulic principles, and patients are usually unconscious. Therefore, patients are essentially dependent on the care dedicated to them. Beyond the mechanical problems caused by the handling of EVD systems,[1] infection is the utmost concern of a neurosurgeon.

The handling of EVD systems followed a few different rationales throughout the past 40 years. Mayhall et al.[7]

Table 1

Pathology	Number of patients	Average	Standard deviation	Days (minimum)	Days (maximum)
Head Injury	20	4.25	2.92	1	11
Subarachnoid hemorrhage	26	6.15	3.89	1	15
Hemorrhagic stroke	30	5.67	3.4	1	11
Tumors	9	2.88	0.92	2	4
Infection	7	8.6	7.5	2	24
Hidrocephalus	4	4.5	1	4	6
Ischemic stroke	2	4.5	2.12	3	6
Uncommon vascular lesions	3	9	5.5	4	15

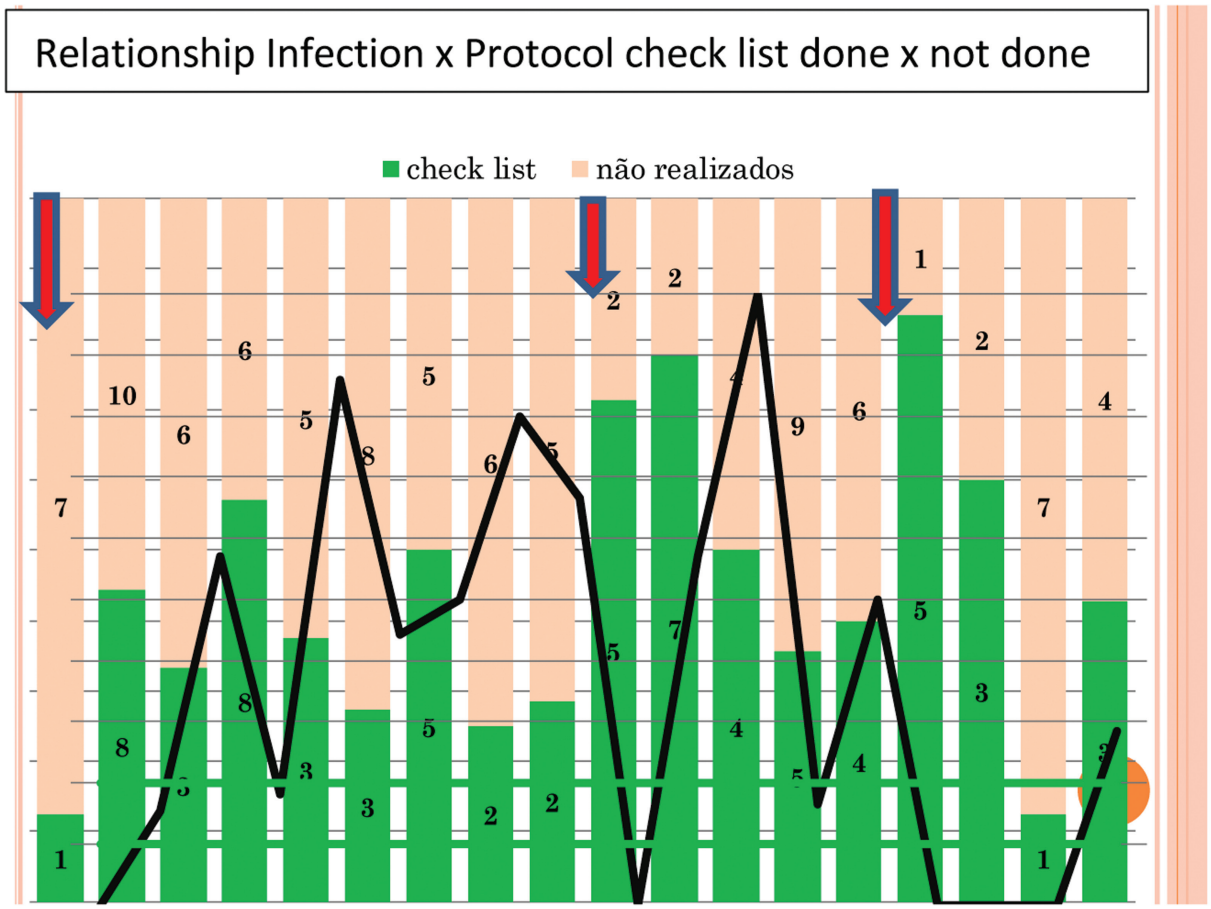

Fig. 3 The red arrows indicate training interventions. The black lines indicate infection rates. The bars indicate the months, starting in July 2013 and finishing in December 2014. The green bars indicate the check list items accomplished each month. The pink bars indicate check list items not accomplished each month.

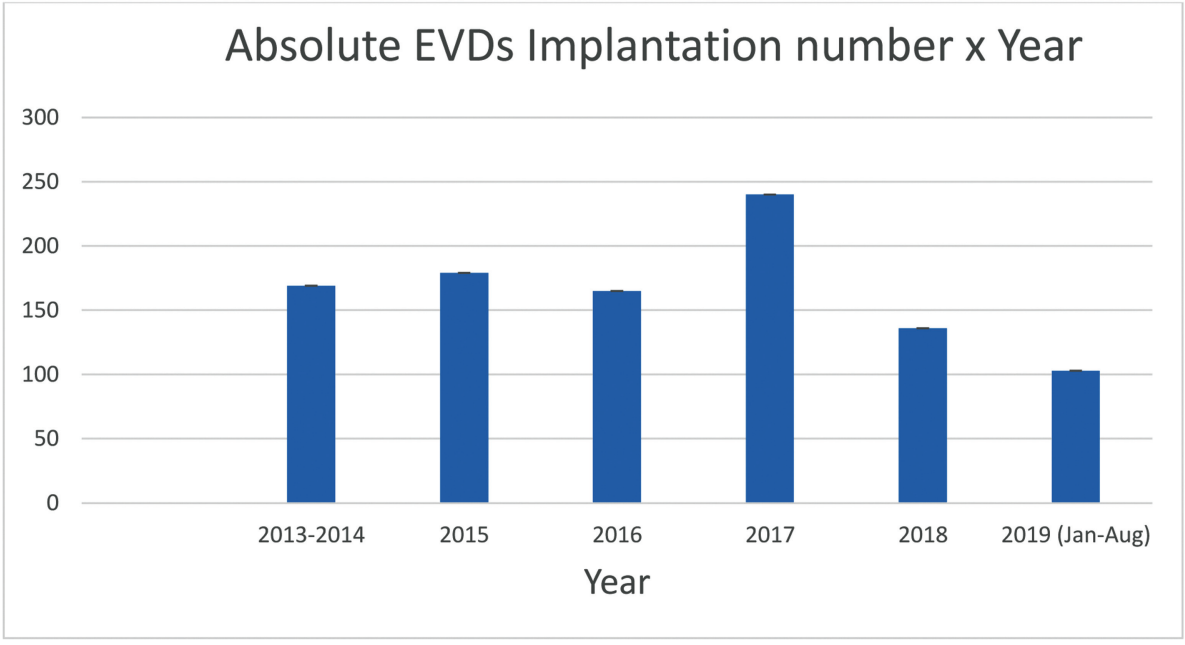

Fig. 4 Yearly rate of EVD implantation.

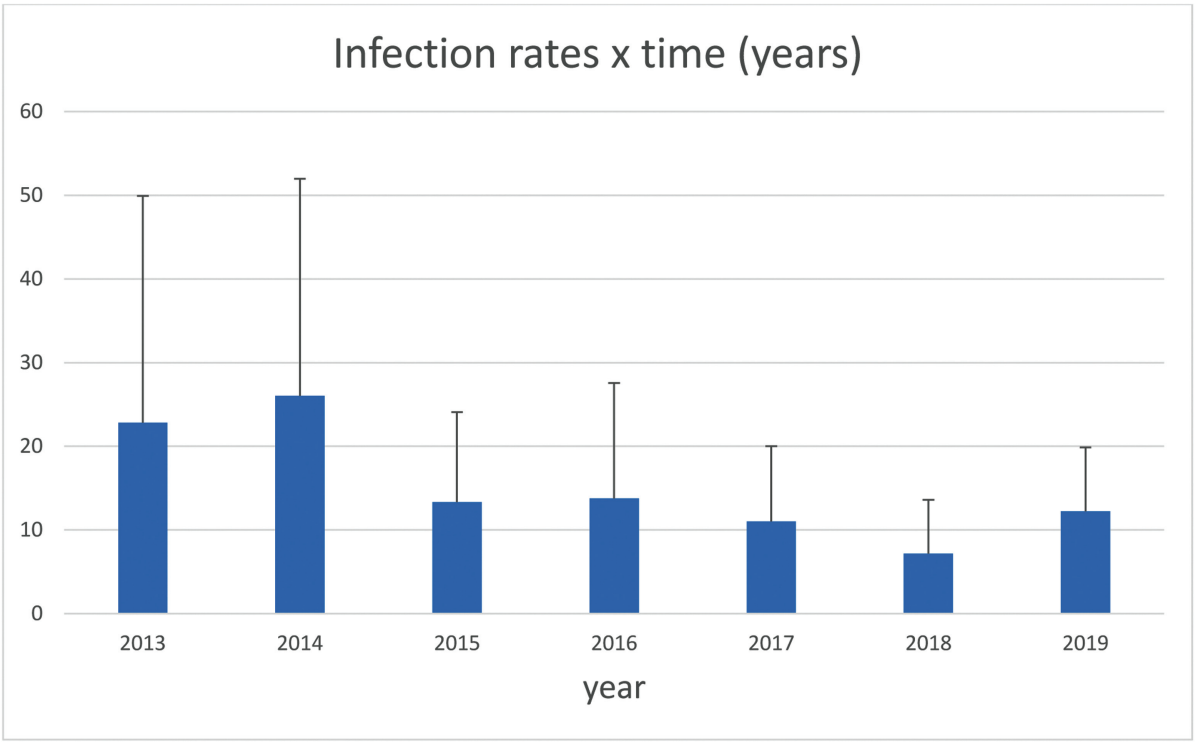

Fig. 5 Yearly rate of infection.

(1984), conducted a study involving 172 consecutive neurosurgical patients over a 2-year period, to determine the incidence, risk factors, and clinical characteristics of the infections. This was perhaps the first publication which established or suggested an applied methodology with the objective of controlling infections from EVD systems. The authors[7] concluded that "if monitoring is required for more than five days, the catheter should be removed and inserted at a different site." It basically stablished a conduct for everyone, and only 12 years later, Holloway et al.[8] published a new study demonstrating exactly the inverse, that is, "based on these data, it is recommended that ventriculostomy catheters for intracranial pressure monitoring be removed as quickly as possible, and in circumstances in which prolonged monitoring is required, there appears to be no benefit from catheter exchange." Interestingly, both protocols came from the same institution, the Medical College of Virginia, Richmond, United States. Wong et al.,[9] Mahé et al.,[10] and Lo et al.,[11] among other authors, conducted similar studies and reached the same conclusion. Thus, at the turn of the millennium, there was a new way to manage EVD systems, but the rates of infection were still high. In 2005, Korinek et al.[4] were one of the first group of authors to call attention to a training program aiming to decrease infection rates. A written protocol for the insertion of EVD systems, nursing and surveillance was implemented and applied in 175 patients. Protocol violations were monitored. The results were outstanding; the incidence of patient-related ventriculitis decreased from 12,2% to 5,7%. More importantly, "During the study period, the only statistically significant risk factors for infection were CSF leak and protocol violations", and the authors concluded that "EVD can be left safely, as long as needed, provided that meticulous care is taken for EVD insertion and nursing. EVD duration seems to have no effect on infection incidence." Thus, Korinek et al.[4] proposed new standards for EVD care in NICUs. Honda et al.,[12] in an eight-year study period, described a decrease by more than three-quarters after the implementation of multiple interventions. In Brazil, Camacho et al.[5] were probably the first group to apply such concepts. They published a series of 194 procedures, corresponding to 1,217 catheters;day. "EVD-related infection rates were reduced from 9.5% to 4.8% per patient, from 8.8% to 4.4% per procedure, and the incidence density dropped from 14.0 to 6.9 infections per 1,000 catheters-day". They concluded that "educational intervention proved to be a useful tool in reducing these rates and showed also impact on mortality." Flint et al.[13] also applied the same rationale and followed infection rates based on CSF cultures. The rate of positive CSF cultures decreased from 9.8% at baseline (14 out of 143; 11.43 per 1,000 catheter-days) to 0;8% (1 out of 119; 0.79 per 1,000 catheter-days) in the EVD infection control period. Thus, the introduction of an evidence-based infection-control protocol was associated with a dramatic reduction in the risk of EVD infection. If ventricular hemorrhage is taken into account, EVD systems have an even higher mechanical and propension for blockage and infection.[14]

Conclusion

The present study was performed in a tertiary hospital, where there is a 14-bed neuro-ICU which is insufficient to

meet the demand of the neurosurgical department. In this unit, the personnel is obviously more specialized than those in the remaining units. Ideally, this fact should have been taken into account before we started the study, and we should have only considered the neurosurgical unit to avoid bias. Another consideration is the high rotation of nurses in the neuro-ICU, that is, nurses were moved from one sector to another quite frequently, and a quarterly training program was held after 18 months of the study. However, even considering patients from all ICUs, one can observe on ►**Fig. 5** that the infection rates dropped throughout the years. Thus, the infection rates can be controlled at major public hospitals, and the data herein shown can be even improved if a long-term prevention program policy is implemented. Unfortunately, in a query with neurosurgical residents, we found out that the training program for them was interrupted. Certainly there is a social and economic impact to the institution when protocols are broken. Such an interruption will certainly affect the infection rates, as already demonstrated in ►**Fig. 5**. The implementation of a training program to decrease infection rates in a public environment is a time-consuming and difficult task, but it can be done with the commitment of the nursing staff and neurosurgical team. The infections rates observed with our training project were among the lowest in the country. The results of the present study are in agreement with those of the aforementioned studies. The present study contributed to a high-level decision to return with the training program.

Conflict of Interests

The authors have no conflict of interests to declare.

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Role of Ommaya Reservoir Placement in Hydrocephalus Management following Aneurysmal Subarachnoid Hemorrhage, an Initial Experience

Papel da colocação do reservatório de Ommaya no tratamento da hidrocefalia após hemorragia subaracnoidea aneurismática, uma experiência inicial

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Abstract

Introduction Weaning from external ventricular drainage (EVD) of cerebrospinal fluid (CSF) in hydrocephalus induced by aneurismal subarachnoid hemorrhage (SAH) had been proposed either through the rapid, gradual or intermittent approaches. There are no uniform guidelines for it. Given this, we planned to study the comparative outcome between EVD drainage with intermittent clamping versus EDV followed by Ommaya reservoir.

Material and Methods The present retrograde observational study was conducted from July 2018 to March 2021 in the department of neurosurgery with 67 patients who developed hydrocephalus following SAH after aneurysm rupture. We divided the patients into two groups. Group 1 had only EVD placed for CSF drainage with intermittent clamping before the placement of the ventriculoperitoneal (VP) shunt, and, in group 2, an Ommaya reservoir was placed after EVD before the shunt.

Result There were 38 patients in group 1 and 29 in group 2. They were age-matched, with a mild male predominance in group 1. Shunt dependency was significantly reduced in group 2 patients ($p = 0.011$), along with reduced length of stay in ICU ($p = 0{,}001$) and length of stay in Hospital ($p = 0.019$). We found improved Glasgow outcome score in group 2 patients ($p = 0.006$) together with reduced incidence of infarct ($p = 0.0095$).

Conclusion We may infer from the present study that continuous drainage through EVD, initially, in hydrocephalus induced by SAH following aneurysm rupture, increases cerebral perfusion pressure (CPP) and decreases intracranial pressure (ICP) leading to

Keywords
- shunt dependent hydrocephalus
- subarachnoid hemorrhage
- aneurysm rupture
- continuous and intermittent drainage
- external ventricular drainage
- Ommaya

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decreased infarct rate and intermittent drainage through Ommaya following EVD reservoir, decreases shunt dependency, reduces ICU and hospital stay, with improved Glasgow outcome score on follow-up, but these findings need to be validated in a prospective randomized control trial.

Resumo

Introdução O desmame da drenagem ventricular externa (DVE) do líquido cefalorraquidiano (LCR) na hidrocefalia induzida por hemorragia subaracnóidea aneurismática (HSA) foi proposto pelas abordagens rápida, gradual ou intermitente. Não há diretrizes uniformes para isso. Diante disso, planejamos estudar o resultado comparativo entre drenagem DVE com pinçamento intermitente versus DVE seguido de reservatório de Ommaya.

Materiais e métodos O presente estudo observacional retrógrado foi realizado de julho de 2018 a março de 2021 no departamento de neurocirurgia com 67 pacientes que desenvolveram hidrocefalia após HSA consequente de ruptura de aneurisma. Dividimos os pacientes em dois grupos. O grupo 1 teve apenas DVE colocado para drenagem do líquor com pinçamento intermitente antes da colocação da derivação ventrículo-peritoneal (VP) e, no grupo 2, um reservatório de Ommaya foi colocado após a DVE antes da derivação.

Resultado Havia 38 pacientes no grupo 1 e 29 no grupo 2. Eles eram pareados por idade, com leve predominância do sexo masculino no grupo 1. A dependência de shunt foi significativamente reduzida nos pacientes do grupo 2 ($p = 0{,}011$), juntamente com menor tempo de internação na UTI ($p = 0{,}001$) e tempo de permanência no Hospital ($p = 0{,}019$). Encontramos melhora no escore de Glasgow nos pacientes do grupo 2 ($p = 0{,}006$) juntamente com redução da incidência de infarto ($p = 0{,}0095$).

Conclusão Podemos inferir do presente estudo que a drenagem contínua por DVE, inicialmente, na hidrocefalia induzida por HSA após ruptura de aneurisma, aumenta a pressão de perfusão cerebral (PPC) e diminui a pressão intracraniana (PIC) levando à diminuição da taxa de infarto e drenagem intermitente por Ommaya após DVE reservatório, diminui a dependência do shunt, reduz a permanência na UTI e no hospital, com melhora do escore de Glasgow no acompanhamento, mas esses achados precisam ser validados em um estudo prospectivo randomizado de controle.

Palavras-chave
- hidrocefalia dependente de derivação
- hemorragia subaracnoide
- ruptura de aneurisma
- drenagem contínua e intermitente
- drenagem ventricular externa
- Ommaya

Introduction

Hydrocephalus develops in between 6 and 60% of cases following subarachnoid hemorrhage (SAH).[1] Most often, hydrocephalus responds to cisternostomy while performing aneurysmal clipping and by putting external ventricular drainage (EVD) during surgery and postoperatively. Similarly, EVD is placed before coiling, when the endovascular procedure is planned or following it if hydrocephalus persists. In between 40 and 50% of these patients, removing EVD leads to ventriculomegaly and clinical deterioration due to which ventriculoperitoneal shunt needs to be placed. Continuous drainage through EVD has the inherent risk of developing infection (between 0 and 45% of the cases), tube blockage, intracranial hemorrhage, etc.[2] There is growing evidence emphasizing intermittent and slow drainage of CSF leading to lesser chances of EVD-related complications. Replacement of EVD by Ommaya reservoir has been found to reduce chances of infection in different studies.[3,4] Some studies have reported reduced shunt dependency in hydrocephalus following SAH when CSF is drained intermittently and gradually when compared with continuous drainage and fast weaning.[5] Few studies suggested a reduction in the rate of complications associated with intermittent EVD drainage and decreased number of ventriculoperitoneal shunts required in it.[6] There are conflicting reports that these findings in other studies are associated with increased risk of vasospasm, no difference in shunt dependency, and outcome following intermittent CSF drainage when compared with continuous CSF drainage. Therefore, we tried to evaluate the efficacy of Ommaya reservoir placement in such cases in reducing shunt dependency as well the length of stay in hospital and the functional outcome on follow-up.

Material and Methods

Ethical clearance for the present study was obtained from the institution. We have adhered to the Institutional and Departmental Ethical Guidelines while working on the present

study and during its final submission with institutional ethical clearance (no. IEC/2021/355). Detailed written informed consent was obtained at the time of admission in the hospital from the patients, next of kin, or guardian for the use of their data for teaching and clinical research purposes.

The present study was conducted between July 2018 and March 2021in the department of Neurosurgery at our institute. In this period, 250 cases of ruptured aneurysms were treated, out of which 67 cases were included in the study as they were presenting with hydrocephalus. In the present study, we included the patients who developed hydrocephalus following ruptured aneurysm with intracranial bleeding (subarachnoid, intraventricular, etc.) and required EVD. The primary objective of the present study was to assess the reduction in the requirement of ventriculoperitoneal shunt following Ommaya reservoir placement after failed EVD and the second objective was to assess the reduction in duration of stay in ICU and hospital together with any improvement in Glasgow outcome score on follow-up in this group of patients.

Clinical information was obtained from the medical charts of the patients. The following data were collected: age, gender, Glasgow Coma Scale (GCS) score at the time of admission, Hunt and Hess grade, Fischer score on computed tomography (CT), duration of EVD placement, complications associated with EVD, Ommaya reservoir placement, history of CSF drainage, Glasgow outcome score at follow-up, and comorbidities, including obstructive lung diseases (i.e., asthma and chronic obstructive pulmonary disease), coronary artery diseases, heart failure, stroke, diabetes, cirrhosis, chronic kidney disease, hemodialysis, and metastases.

Radiological findings on NCCT head as Fischer grade of subarachnoid haemorrhage (SAH), Evan's index, periventricular lusency were noted from medical records of the patients. Preoperative aneurysm configuration, postoperative obliteration of aneurysm, vasospasm were noted from DSA findings as observed in records available.

The following laboratory data were collected preoperatively and postoperatively: routine blood investigations, CSF routine microscopy sent at regular intervals and associated CBC findings, CSF culture, and sensitivity report of CSF.

Ommaya reservoir was placed 2.5 cm lateral and 1 cm in front of the coronal suture by making an elliptical incision and placing a burr hole within the scalp. Ommaya reservoir tapping was done with number 16 scalp vein with its tubings and kept under sterile transparent dressings.

EVD Management Protocol

We placed EVD in cases with hydrocephalus following aneurysmal SAH and to open it intermittently to drain from 50 to 100 ml depending on ICP measurement of >20 cm or lower. We performed continuous drainage through EVD after the aneurysms were secured by either endovascular coiling or microsurgical clipping. Once the patient started improving postoperatively, we gradually weaned off the patient from EVD by intermittently opening the EVD. Meanwhile, we strictly monitored any drop in GCS and rise in blood pressure to look for features of raised ICP. Trial of weaning from EVD was given every 48 hours in patients with Hunt and Hess grades 1 and 2 and 72 hours in grades 3and 4, so that multiple trials of tube clamping can be made to ensure removal of EVD at the appropriate time. During these repeated trials, few patients had hardware complications as frequent blockage, infections, etc, for which it was replaced by Ommaya reservoir. Placement of Ommaya reservoir act as a conduit for intermittent CSF drainage and antibiotics installation, which helped us in decreasing intracranial infection and in performing a gradual and intermittent EVD drainage.

Once the Ommaya reservoir was placed, we used to assess the requirement of tapping CSF through it depending on the GCS status of the patient which was bserved and charted in critical care sheet at regular interval. In patients for whom more frequent drainage was required through the scalp vein set (>3 or 4 times/day) regularly for 4 or 5 days as we used to wait for CSF sample to become sterile and replace it with VP shunt. Once the patient's GCS improved and became stable, we assessed the need for continuation of Ommaya reservoir by reducing tapping of CSF through it. Initially, it was done 3-4 times at a 24-hour interval, followed by draining CSF through it at 48 hours twice and then 72 hourly twice, if the patient remained stable while this Ommaya reservoir was taken out. It was challenging to measure opening CSF pressure or measure ICP regularly through different monitoring devices and it was not done in all patients included in the study, but we rely more on clinical parameters as repeat measures of GCS, Blood pressure, pulse rate, and respiratory rate, O2 saturation as reflective of increased intracranial pressure.

Ommaya reservoir was preferred as it reduces external hardware-related risks of getting infected, blocked, pullout, etc, and helps better patient mobilization with intermittent draining by the scalp vein set.

Indications for putting an Ommaya reservoir in the patients who were earlier having EVD for hydrocephalus following SAH after aneurysm rupture in the present study were:

1. Patients in whom cisternostomy was perfomed while performing microsurgical clipping required lesser Ommaya reservoir after external ventricular drainage. This requirement was least in patients in whom lamina terminalis and fenestration of Liliquist membrane was done simultaneously ($p = 0.002$).
2. Patients who could not be weaned from EVD drainage and who required some more time to assess for GCS to get stabilized.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD) and were compared using independent *t*-tests. Categorical variables were expressed as numbers (percentage) and compared using the chi-squared test or the Fisher exact test, as appropriate. Multiple logistic regression analysis was performed to identify the factors related to Ommaya reservoir placement. Factors with a *p-value* < 0.05

in the univariate analysis were entered into the stepwise logistic regression analysis. A two-tailed *p-value* < 0.05 was considered statistically significant. The significance of Ommaya reservoir placement and duration of ICU stay and of hospital stay was analyzed using single variable analysis of variance (ANOVA) test. Shunt dependency following Ommaya reservoir on follow-up was calculated from Kaplan–Miere curve and significance risk ratio for shunt dependency in absence of Ommaya was calculated from COX-Proportional hazard ratio.

Results

Patient in group 1 with EVD only has 39 patients and group 2 who required Ommaya after EVD has 28 patients. Both groups were age-group matched, with a slight male preponderance in group 1. Ommaya reservoir placement was significantly associated with high Fischer grade on CT and infarct on preoperative CT scan. It was not significantly associated with the location of the aneurysm or with the type of procedure (clipping versus coiling). (►**Table 1**)

Different risk factors were analysed which may have been responsible for continuation of Ommaya reservoir after taking out EVD as age, sex, procedure (clip vs. coil, vasospasm, infarction), CSF protein measured from day1-10, CSF findings suggesting CNS infection, Fischer grade, Hunt and Hess grade etc. On stepwise multiple regression analysis we found that Fischer grade on CT ($p = 0.0073$), CSF findings suggestive of infection (0.0071), and CSF protein as measured on 7th day of EVD insertion was significantly responsile for taking out EVD and replacing it by Ommaya reservoir. On comparative analysis, the receiver operator curve (ROC) showed the area under the curve of these factors as 0.932, with a positive predictive value of 0.88. (►**Table 2**)(►**Figure 1**)

Patients in whom cisternostomy was perfomed while performing microsurgical clipping required lesser Ommaya reservoir after external ventricular drainage. This requirement was least in patients in whom lamina terminalis and fenestration of Liliquist membrane was done simultaneously ($p = 0.002$). (►**Table 3**)

Supplementation with Ommaya reservoir placement after removal of EVD was more common in patients in whom no cisternostomy was performed as observed in patients who underwent endovascular coiling. (►**Table 4**)

Shunt dependency was less in patients in whom EVD was removed and replaced by Ommaya (19 of 29, 65.5%) when compared to patients in whom trial of Ommaya reservoir placement was not done after removal of EVD (3 of 38 patients, 7.8%). (►**Table 5**)

There was a significant decrease in the length of ICU stay in patients in whom Ommaya was placed (29.65 ± 7.26

Table 1 Demography and clinical features of patients with hydrocephalus with and without Ommaya

Variables	Group 1 (Hydrocephalus with EVD only) ($n = 38$)	Group 2 (Hydrocephalus with EVD followed by Ommaya) ($n = 29$)	*p-value*
Age (years old)	51.10 ± 10.83	50.63 ± 9.53	0.12
Gender (M/F)	10/19	21/17	
Location of the aneurysm	16	19	0.059
Anterior circulation	10	22	
Posterior circulation			
Hunt and hess grade			
< 3	8	14	0.12
> 3	30	15	
Fischer grade on CT			
1	–	–	0.003
2	5	6	
3	16	12	
4	17	11	
Infarct on CT head	32/38	15/29	0.0095
Procedure			
Microsurgical clipping	12	17	0.059
Coiling	21	17	
Spasmolysis			
Responded	9	17	0.056
Not responded	29	12	

Abbreviations: CT, computed tomography; EVD, external ventricular drainage; F, female; M, male.

Table 2 Risk factors predisposing placement of Ommaya reservoir following external ventricular drainage on multiple logistic regression analysis

Variable	Coefficient	Std. Error	Odds ratio	95%CI	Wald	*p-value*
Infection in EVD	2.82574	1.04901	16.8734	2.1591–131.8677	7.2561	0.0071
Duration of EVD	0.35785	0.13339	1.4303	1.1012–1.8576	7.1976	0.0073
Fischer grade on CT	−1.80728	0.81816	0.1641	0.0330–0.8157	4.8795	0.0272
Procedure (Clipping versus coiling)	1.58530	0.92061	4.8807	0.8032–29.6570	2.9653	0.0851
CSF opening pressure	1.07135	0.89699	2.9193	0.5032–16.9361	1.4266	0.2323
Constant	−5.97053	3.72866			2.5640	0.1093

Abbreviations: CI, confidence interval; CSF, cerebrospinal fluid; EVD, external ventricular drainage.

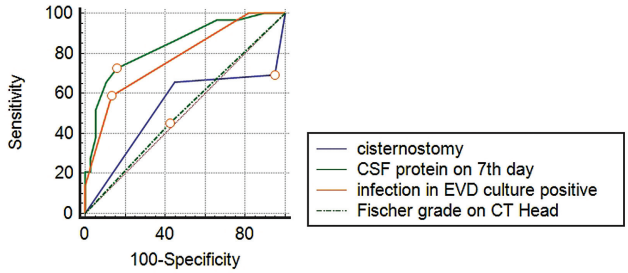

Fig. 1 Reciever operating curve (ROC) suggesting area under curve of 0.9 and predictive value of 0.88 of risk factors predisposing Ommaya placement.

versus 36.13 ± 4.80; $p = 0.001$); similarly, there was a significant decrease in the length of hospital stay (in days) in group 1 (39.63 ± 7.35 versus 44.86 ± 5.61; $p = 0.019$) (►**Figure 2**). One patient in group 1 and 2 patients in group 2 succumbed to death due to cardiac illnesses (►**Table 6**). On follow-up, there was a significant reduction in shunt dependency as observed on Kaplan-Miere survival curve analysis. Cox proportional hazard ratio for shunt dependency on not placing Ommaya reservoir had a coefficient of 1.244 with a 95% confidence interval (CI) (1.6026–7.5107), with a *p-value* of 0.0016. (►**Figure 3**)

Discussion

Patients who develop hydrocephalus following SAH have raised intracranial pressure ICP, leading to decreased perfusion pressure (PF). There may be other factors, such as infarct and edema due to vasospasm, leading to increased ICP and decreased PF. We come across a tricky situation when we put EVD for a prolonged time and it either stops draining due to blockage in the tube or gets infected with the patient developing meningitis and ventriculitis. Intermittent CSF drain through Ommaya reservoir helps us in reducing intracranial pressure and instilling antibiotics through it reduces meningitis, such findings are reported in other studies also.[2,4]

Intermittent drainage of CSF has a certain advantage over continuous drainage through EVD in terms of establishing a pressure gradient across the CSF drainage pathway, which helps in the healthy and early recovery of the natural CSF drainage pathway. There are studies in which the only cisternostomy had been performed without placement of

Table 3 Cisternostomy and Ommaya reservoir placement

Ommaya reservoir placement	Cisternostomy				
	Lamina terminalis opened	Liliquist membrane opened	Both cisterns opened	None	
Present	9 31.0% RT 81.8% CT 13.4% GT	0 0.0% RT 0.0% CT 0.0% GT	1 3.4% RT 5.3% CT 1.5% GT	19 65.5% RT 52.8% CT 28.4% GT	29 (43.3%)
Absent	2 5.3% RT 18.2% CT 3.0% GT	1 2.6% RT 100.0% CT 1.5% GT	18 47.4% RT 94.7% CT 26.9% GT	17 44.7% RT 47.2% CT 25.4% GT	38 (56.7%)
	11 (16.4%)	1 (1.5%)	19 (28.4%)	36 (53.7%)	67
		Chi-squared	19.927		
		DF	3		
		Significance level	$p = 0.0002$		

Abbreviations: RT, row total; CT, column total; GT, grand total, DF, degree of freedom.

Table 4 Ommaya reservoir placement and shunt dependency

Shunt-dependent	Ommaya reservoir placement		
	Present	Absent	
Present	10 34.5% RT 22.2% CT 14.9% GT	19 65.5% RT 86.4% CT 28.4% GT	29 (43.3%)
Absent	35 92.1% RT 77.8% CT 52.2% GT	3 7.9% RT 13.6% CT 4.5% GT	38 (56.7%)
	Chi-squared	24.394	
	DF	1	
	Significance level	$p < 0.0001$	

Abbreviations: RT, row total; CT, column total; GT, grand total, DF, degree of freedom.

Table 5 Ommaya reservoir placement and Glasgow outcome score at follow-up

Ommaya reservoir placement	Glasgow outcome score					
	1	2	3	4	5	
Present	0 0.0% RT 0.0% CT 0.0% GT	0 0.0% RT 0.0% CT 0.0% GT	7 24.1% RT 22.6% CT 10.4% GT	13 44.8% RT 59.1% CT 19.4% GT	9 31.0% RT 90.0% CT 13.4% GT	29 (43.3%)
Absent	1 2.6% RT 100.0% CT 1.5% GT	3 7.9% RT 100.0% CT 4.5% GT	24 63.2% RT 77.4% CT 35.8% GT	9 23.7% RT 40.9% CT 13.4% GT	1 2.6% RT 10.0% CT 1.5% GT	38 (56.7%)
	1 (1.5%)	3 (4.5%)	31 (46.3%)	22 (32.8%)	10 (14.9%)	67
				Chi-squared	19.594	
				DF	4	
				Significance level	$p = 0.0006$	
				Contingency coefficient	0.476	
				Chi-squared	19.594	

5-Resumption of normal life with minor neurological deficits; 4-moderately disabled patient independent in daily life; 3-Severely disabled patient dependent for daily work; 2-Neurovegetative state;1-Death.
Abbreviations: RT, row total; CT, column total; GT, grand total, DF, degree of freedom.

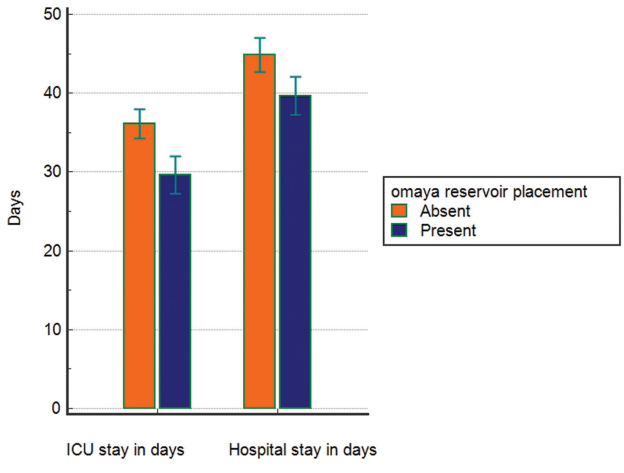

Fig. 2 ICU and hospital stay in patients who required Ommaya reservoir placement.

EVD with good effect, without the requirement of subsequent ventriculoperitoneal shunt.[7,8] In the present study, in which multiple cisterns (lamina terminalis cistern, the membrane of Liliquist, etc) were opened intraoperatively required. In the present study, patients in whom multiple cisterns (both lamina terminalis membrane of liliquist, etc.) were opened to release CSF require lesser number of EVD, Ommaya reservoir placement and were less shunt dependent when compared to patients in whom multiple cisternostomies were not performed. In the study by Komotar et al., in which they performed fenestration of the lamina terminalis, 14% the of patients with acute hydrocephalus following SAH required VP shunt, but in the study by Winkler et al. who had performed fenestration of the lamina terminalis and of the Liliquist membrane, 3.2% of the cases required VP shunt.[9,10] In both studies, EVD was not performed. These findings suggest early recovery of the drainage pathway if continuous CSF drainage is avoided through EVD.

Table 6 Outcome after Ommaya reservoir placement

		Group 2 with Ommaya ($n = 28$)	Group 1 without Ommaya ($n = 39$)	*p-value*
ICU stay		29.65 ± 7.26	36.13 ± 4.80	0.019
Hospital stay		39.63 ± 7.35	44.86 ± 5.61	0.011
Shunt independency		21	1	0.0006
Mortality		1	2	–

Abbreviation: ICU, intensive care unit.

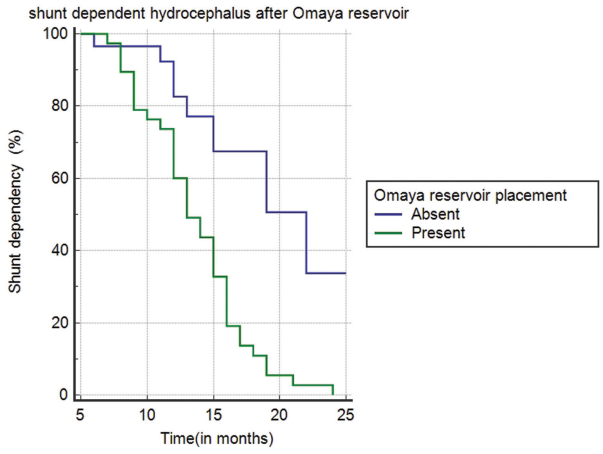

Fig. 3 Kaplan–Miere survival analysis curve revealing shunt dependency following Ommaya reservoir placement on follow-up.

Perhaps, intermittent drainage through the Ommaya pathway leads to the early establishment of the CSF pathway which leads to a reduction in the shunt dependency as has also been observed in our study.

Intermittent clamping reduces shunt dependency, but it requires careful patient monitoring and persistence, as observed in the study by Ascanio et al., in which they made multiple trials of EVD clamping before putting a shunt, which resulted in the decreased number of cases who were shunt dependent when compared with the study of Klopfenstein et al., who emphasized gradual weaning with a single clamp trial and reported a higher number of cases requiring VP shunt at the end.[5,11] Intermittent CSF drainage through the Ommaya reservoir works on the same principle and was also utilized in our cases, which gave us more time to wait for intracranial infections to subside following antibiotics installations and to try intermittently and gradually to observe for the avoidance of further external CSF drainage. It also resulted in the reduced number of shunt-dependent patients on follow-up in our study, when compared with intermittent EVD draining while weaning from continuous CSF drainage.

Increased risk of cerebral vasospasm and delayed ischemic neurological deficits have been reported in the study by Kim et al. and by Amato et al. where continuous drainage of CSF had been done for the treatment of hydrocephalus following SAH.[7,8] Olson et al. reported more complications and a higher incidence of vasospasm in the subgroup of patients with continuous CSF drainage and intermittent monitoring than in groups with intermittent CSF drainage with continuous monitoring.[12] In all three studies, although there was a higher rate of vasospasm in the continuous draining group, the difference reported was not statistically significant compared with the present study, which suggests reduced vasospasm resulting in decreased infarct observed in the group with Ommaya reservoir compared with the group only treated by EVD. The probable reason for this difference in intermittent drainage by the Ommaya group was associated with more chances of washout and drainage of blood degradation products, which are a formidable source of vasospasm, which is also reflected in lesser shunt dependency in this scenario. There are no exact guidelines for either continuous or intermittent drainage of CSF to decrease blood products in cisterns following SAH.[11–16]

Rao et al. had reported decreased ICU stay, hospital stay, and better Glasgow outcome score in the group with intermittent CSF drainage with rapid weaning.[14] Decreased ICU stay, hospital stay, and improved Glasgow outcome score on follow-up had been reported in the present study, similar to the study by Rao et al., but it differs from the study by Klopfenstein et al., who have reported decreased ICU and hospital stay, but an increased rate of shunt-dependent cases on follow-up.[11] Patients in whom EVD was inserted for CSF drainage and given lesser weaning trial by intermittent clamping of it have higher chances of being converted to VP shunt, as observed in the study by Klopfenstein et al.[11] (63% of the patients) when compared to more number of intermittent clamping trial of EVD before converting to shunt, as suggested in study by Rao et al.[14] and Olson et al.

In the studies by Klopfenstein et al. and by Olson et al., the subgroup of cases with rapid CSF drainage by EVD had a higher rate of tube clogging and shunt infection, similar to the present study.[11,13] We found high CSF protein content in the subgroup of patients with high blockage and infection. We preferred the Ommaya reservoir for intermittent drainage of CSF in patients in whom continuous drainage through EVD didn't work. In retrospect, we found better outcomes on the follow-up in these cases in which the Ommaya reservoir was placed.

Although we put Ommaya reservoir as a replacement for EVD, since it was not working, it helped our patients to achieve a better outcome. The main reason behind this may be the increased transcisternal pressure gradient and arachnoid granulations leading to faster recovery of CSF drainage pathway and less shunt dependence. Another proposition is that lower CSF pressure due to continuous drainage leads to reduced CSF secretion and decreased CSF pressure gradient

across the drainage pathway, leading to slower recovery and more shunt-dependent patients in these circumstances. The third reason for less VP shunt dependence with Ommaya reservoir was more attempts with intermittent drainage and lesser complications, such as blockage and infection, gave us more time to help the patient for the establishment of the natural CSF drainage pathway. Similar observations were made by Karimy et al. in his study.[17]

Conclusion

Continuous drainage through EVD helped initially in patients with hydrocephalus following SAH in decreasing ICP and increasing perfusion pressure leading to decreased infarct subsequently. Intermittent drainage through Ommaya in the later phase of CSF drainage probably helped in the maintenance of the CSF pressure gradient through the CSF drainage pathway, leading to decreased shunt dependency, and early recovery in ICU with decreased ICU and hospital stay. It appears from our study that patients developing hydrocephalus following SAH may be benefitted in a better way if CSF drainage is done continuously through EVD followed by intermittent CSF drainage by Ommaya reservoir; however, to validate these results, prospective randomized trials would be better.

Contribution of the Authors

Conceptualization, clinical work, data collection, data analysis, manuscript drafting and revision were done by Jha V. C. Data collection and analysis were done by Jha V. C, and Shahnawaz A. Data analysis and manuscript supervision were performed by Jha V. C, MSA and NJ. All authors have read and approved the final version of the manuscript. This manuscript has neither been presented as a whole nor part in any conference or scientific meeting. This article is neither published nor under consideration for publication anywhere else.

Conflict of Interests

The authors have no conflict of interests to declare.

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Traumatic Cervical Spinal Cord Injury: Correlation of Imaging Findings with Neurological Outcome

Lesão traumática da medula espinal cervical: Correlação de achados de imagem com laudo neurológico

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Abstract

Background Traumatic spinal cord injury (TSCI) is extremely costly to the global health system. Due to the significant frequency rate of traumatic cervical spinal cord injuries (TCSCI), the possible association between imaging findings and clinical outcome is not yet clear. In this study, we quantified maximum spinal cord compression and maximum cord swelling following TCSCI and determined the relevance of imaging findings to clinical outcome in patients.

Materials and Methods This retrospective cohort comprises 20 patients with TCSCIs (C3-C7), classified as complete, incomplete, and no SCI, who were treated at the Poursina Hospital, Iran, from 2018 to 2020, and underwent spinal surgery. Patients with penetrating injuries and multiple trauma were excluded. Imaging findings revealing spinal cord compression, swelling, and canal stenosis, based on the American Spinal Injury Association (ASIA) Impairment Scale (AIS) grades of patients from hospital admission (up to 48 hours after injury) and improvement of postoperative neurological symptoms (6–12 months) were evaluated.

Results Cord compression ($p = 0.05$) and cord swelling ($p = 0.02$) were significantly related to predictive neurological outcomes in all cases. Evaluation with AIS at hospital admission and at 6 to 12 months postoperatively showed significant correlation with fracture type ($p = 0.05$) and the longitudinal length of the intramedullary lesion (IML); $p = 0.01$, respectively.

Keywords
- traumatic cervical spinal cord injury
- imaging findings
- neurological outcome

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Conclusion According to the results obtained in this study, it may be concluded that there is a significant association between cervical spinal cord compression and swelling, and clinical outcomes in patients with complete, incomplete, and no SCI.

Resumo

IntroduçãoA lesão traumática da medula espinal (LTME) é extremamente onerosa para o sistema de saúde global. Devido à significativa taxa de frequência de lesões traumáticas da medula espinal cervical (TCSCI), a possível associação entre achados de imagem e evolução clínica ainda não está clara. Neste estudo, quantificamos a compressão medular máxima e o edema medular máximo após TCSCI e determinamos a relevância dos achados de imagem para o resultado clínico dos pacientes.

Materiais e métodos Esta coorte retrospectiva compreende 20 pacientes com TCSCIs (C3-C7), classificados como completos, incompletos e sem LME, que foram tratados no Hospital Poursina, Irã, de 2018 a 2020, e submetidos a cirurgia da coluna vertebral. Pacientes com lesões penetrantes e politraumatismos foram excluídos. Achados de imagem revelando compressão da medula espinhal, edema e estenose do canal, com base nos graus da American Spinal Injury Association (ASIA) Impairment Scale (AIS) de pacientes desde a admissão hospitalar (até 48 horas após a lesão) e melhora dos sintomas neurológicos pós-operatórios (6-12 meses) foram avaliados.

Resultados A compressão do cordão ($p \equiv 0,05$(e o edema do cordão ($p \equiv 0,02$) foram significativamente relacionados aos desfechos neurológicos preditivos em todos os casos. A avaliação com AIS na admissão hospitalar com 6 a 12 meses de pós-operatório mostrou correlação significativa com o tipo de fratura ($p \equiv 0,05$) e o comprimento longitudinal da lesão intramedular (IML); $p \equiv 0,01$, respectivamente.

Conclusão De acordo com os resultados obtidos neste estudo, pode-se concluir que existe uma associação significativa entre compressão e edema da medula espinal cervical e desfechos clínicos em pacientes com lesão medular completa, incompleta e sem lesão medular.

Palavras-chave
- lesão traumática da medula espinal cervical
- achados de imagem
- laudo neurológico

Introduction

Traumatic spinal cord injury (TSCI) is a catastrophic burden on the global health system;[1] it is classified as complete or incomplete injuries with a wide range of neurological outcomes that affect the functions associated with exact diagnostic and prognostic information.[2] In involved patients, the cervical region is responsible for 49% of spinal cord injuries (SCI) that result in real motor, sensory, and autonomic dysfunction below the level of injury.[3]

Handling of cervical spinal cord injury situations is performed by imaging and reliable physical, neurological, and electrophysiological examinations. The American Spinal Injury Association (ASIA) Impairment Scale (AIS) grades are the key neurological assessments to classify the severity of SCI patients. The AIS assessment results are highly sensitive for evaluation of expected short-, intermediate-, and long-term neurological outcomes. It also provides a better insight into the complete rehabilitation process for health care professionals.[4,5]

Plain radiography, computed tomography (CT) scan, and magnetic resonance imaging (MRI) are the imaging methods used to show spinal canal diameters and cord alteration in acute, sub-acute, and chronic SCI.[4] Midsagittal CT scan images allow characterization of the fracture and lesion structure (hemorrhage and edema) at the focal spinal cord injury site as well as representation of canal diameter changes.[6,7] External compression on the spinal cord and internal structures by MRI is the best method. Midsagittal T2-weighted images can help mainly with spinal cord lesion quality and quantity evaluation to characterize injury structures.[8–10]

Several studies have been conducted to evaluate the relationship between MRI quantitative parameters and short-term neurologic outcomes. Preservations showed that maximum spinal cord compression (MSCC) could be the cornerstone in determining the severity of neurologic impairment such that initiating correct rehabilitation therapies and prevention of persistent injury is necessary and to predict the long-term outcome as accurately as possible.[11–14]

Even so, because of the large heterogeneity among SCI patients due to injury mechanisms, lesion patterns, cervical degenerative diseases, type of spine fractures, and therapeutic approach, prediction of the possible association between clinical and imaging findings as sufficiently accurate markers of long-term neurologic outcomes has not been established. Additionally, clinical studies for traumatic cervical spinal cord injuries (TCSCI) and follow-up are fraught with several

complicating factors. They comprise imaging procedures that accurately neurologically examine patients. In this study, we intend to associate imaging quality with fracture type, maximum osseous canal compromise (MCC), spinal cord compression, swelling, and intramedullary lesion (IML) length, with the aim of predicting postoperative neurological improvement in traumatic cervical spinal cord injury patients with follow-up at 6 to 12 months.

Materials and Methods

In this retrospective cohort study, 20 patients with TCSCI treated at the Poursina Hospital, Iran, from 2018 to 2020, based on the National Spinal Cord Injury Registry of Iran (NSCIR-IR) database were assessed. The study was approved by the local ethical committee and the ethical code (IR.GUMS.REC.1398.529) was received.

The imaging was done for all cases with a single device. For CT scans, the HITACHI 16-slice (Hitachi Ltd., Chiyoda, Japan) scanner was used, and for MRI the Philips 1 Tesla (Koninklijke Philips N.V., Amsterdam, Netherlands) was used.

Imaging evaluation was performed twice by two neurosurgeon observers at different time points at a picture archiving and communication system (PACS) station. At the time of the assessments, the observers were blinded for clinical and neurological data.

We extracted patients' essential demographic features and clinical information from their electronic medical records; the collected data was organized in ►**Table 1**.

Inclusion and Exclusion Criteria

The inclusion criteria were patients aged from 15 to 70 years. Only those with preoperative MRI and CT scans were enrolled. All cases were operated up to 48 hours after trauma.

Table 1 Imaging parameters and evaluation

Imaging parameters	Evaluation
Type of fracture	A0 classification system
MCC (%)	(1-di/dm)*100 if dm = (da + db)/2
MSCC (%)	(1-di/dm)*100 if dm = (da + db)/2
MCS (%)	(ds/dm−1)*100 if dm = (da + db)/2
Longitudinal length of the IML (mm)	Length of the hyperintense signal in the spinal cord on T2 weighted MRI views

Abbreviations: IML, intramedullary lesion; MCC, maximum osseous canal compromise; MCS, maximum cord swelling; MSCC, maximum spinal cord compression.

The exclusion criteria were penetrating thoracolumbar spinal cord injury, multiple trauma, severe head trauma (Glasgow coma score < 13), spinal shock after trauma, severe chest weakness, hemodynamic instability due to hemorrhage of abdomen/retroperitoneal space, pelvic fracture, presence of fracture in more than three long bones, complete spinal injury, chronic severe degenerative lesions identified through CT scan and MRI, and low-quality imaging with inaccurate measurements.

Imaging Parameters

The type of fractures was determined based on the AOSpine Trauma Classification system.[15]

The MCC was measured based on CT scan mid-sagittal images. The other variables were evaluated following T2-weighted mid-sagittal images; they can be defined, briefly, as:

- MCC is determined by splitting the anteroposterior canal diameter at the affected zone (Di) by the average

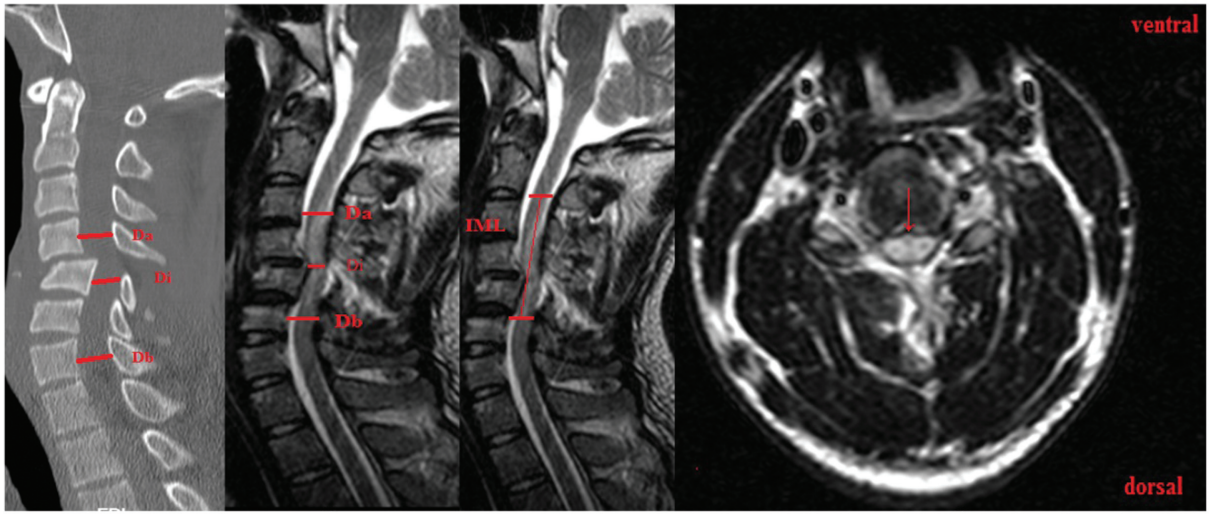

Fig. 1 (a) midsagittal CT scan, (b) and (c) midsagittal T2-weighted, (d) axial T2-weighted obtained from 24 years old man with acute TCSCI at C4-C5 level (AIS grade C). (Da) anteroposterior spinal cord diameter at 1 vertebral level above; (Db) anteroposterior spinal cord diameter at 1 vertebral level below; (Di) anteroposterior spinal cord diameter at injury site; IML: rostrocaudal length of intramedullary hyperintensity at the injury site. Arrow in axial T2-weighted displayed intramedullary hyperintensity and cord compression in the affected zone.

Table 2 Patients characteristics

Number of patients	20	
Gender, female/male	0/20	
Age (mean, SD, year)	44.7 ± 15.4 years	
Occupation	**(n)**	**%**
Reconstruction workers	5	25
Farmer	4	20
Employee	4	20
Shopkeeper	2	10
Engineer	2	10
Others	3	15
Trauma mechanism		
Fall	12	60
Accident	8	40
Others	0	
Smoking/alcohol consumption	4/7	
Background diseases		
None	10	50
Coronary artery disease	3	15
Hepatic disease	1	5
Covid-19	4	20
Renal disease	2	10
Injury level		
C3	2	10
C4	6	30
C5	8	40
C6	2	10
C7	2	10
Fracture classification		
A0	3	15
A1	1	5
A2	1	5
A3	7	35
A4	2	10
C	5	25
Treatment (no [%])		
Surgical anterior approach	20	100

of the normal canal diameter size within 1 vertebral level above (Da) and below (Db).

- MSCC is determined by splitting the anteroposterior canal diameter at the affected zone (Di) by the average of the normal canal diameter size within 1 vertebral level above (Da) and below (Db).
- Maximum cord swelling (MCS) is determined by the maximum swollen (Ds) anteroposterior spinal cord diameter at the affected zone and within 1 vertebral level above (Da) or below (Db).

Table 3 Patients' AIS grade at hospital admission and at 6 to 12 months follow-up

AIS grade	AIS-A	AIS-B	AIS-C	AIS-D	AIS-E	*p*-value
AIS grade at admission (no [%])	1	5	4	7	3	0.01
AIS grade follow-up 6–12 months (no [%])	1	2	3	6	9	

Abbreviations: AIS, American spinal injury association impairment scale.

- Longitudinal length of IML, which is the rostrocaudal length of intramedullary changes. (►**Figure 1**)

Neurological Assessment

Clinical examinations for neurological symptoms were done according to the AIS score system. Baseline AIS grading was done up to 48 hours after patients' admission at the hospital, presurgery. Long-term follow-up (6–12 months) of neurological evaluations postsurgery were performed by neurosurgeons through scheduled visits at the hospital clinic.

Statistical Analysis

Data analysis was done with the Statistical Package Social Sciences (SPSS, IBM Corp. Armonk, NY, USA) software, version 21.0. The utilized tests were the Kolmogorov-Smirnov test, paired sample T-test, Pearson correlation coefficient, Spearman test, and independent sample T-test. All *p*-values lower than 0.05 were considered statistically significant.

Results

All 20 cases were male subjects, and the mean age was 45.5 ± 15.1 years. The treatment performed in all patients was an anterior surgical approach. Falling (60%) and vehicle accidents (40%) were the main causes of trauma in these patients. None of these patients underwent steroid therapy. As might be expected, more than half of the patients included had an incomplete injury with AIS grades C and D, and the most numerous neurological levels of injury (NLI) were C4-C5. The list of comorbidities evaluated in this study is present in ►**Table 2**. Incomplete burst fractures (35%) and type C fractures (translocation) (25%) were the most common among patients.

The initial and follow-up AIS scores are shown in ►**Table 3**; there was a significant difference between them ($p = 0.01$).

Mean MCC on the initial MRI ranged from 39 to 9% for AIS scores A to E (►**Fig. 2a**). Mean MSCC on the initial MRI ranged from 45 to 7% for AIS scores A to E (►**Fig. 2b**). Mean MSC on the initial MRI ranged from 32 to 13% for AIS scores A to E (►**Fig. 2c**). Mean IML on the initial MRI ranged from 58 to 23 mm for AIS scores A to E (►**Fig. 2d**).[16]

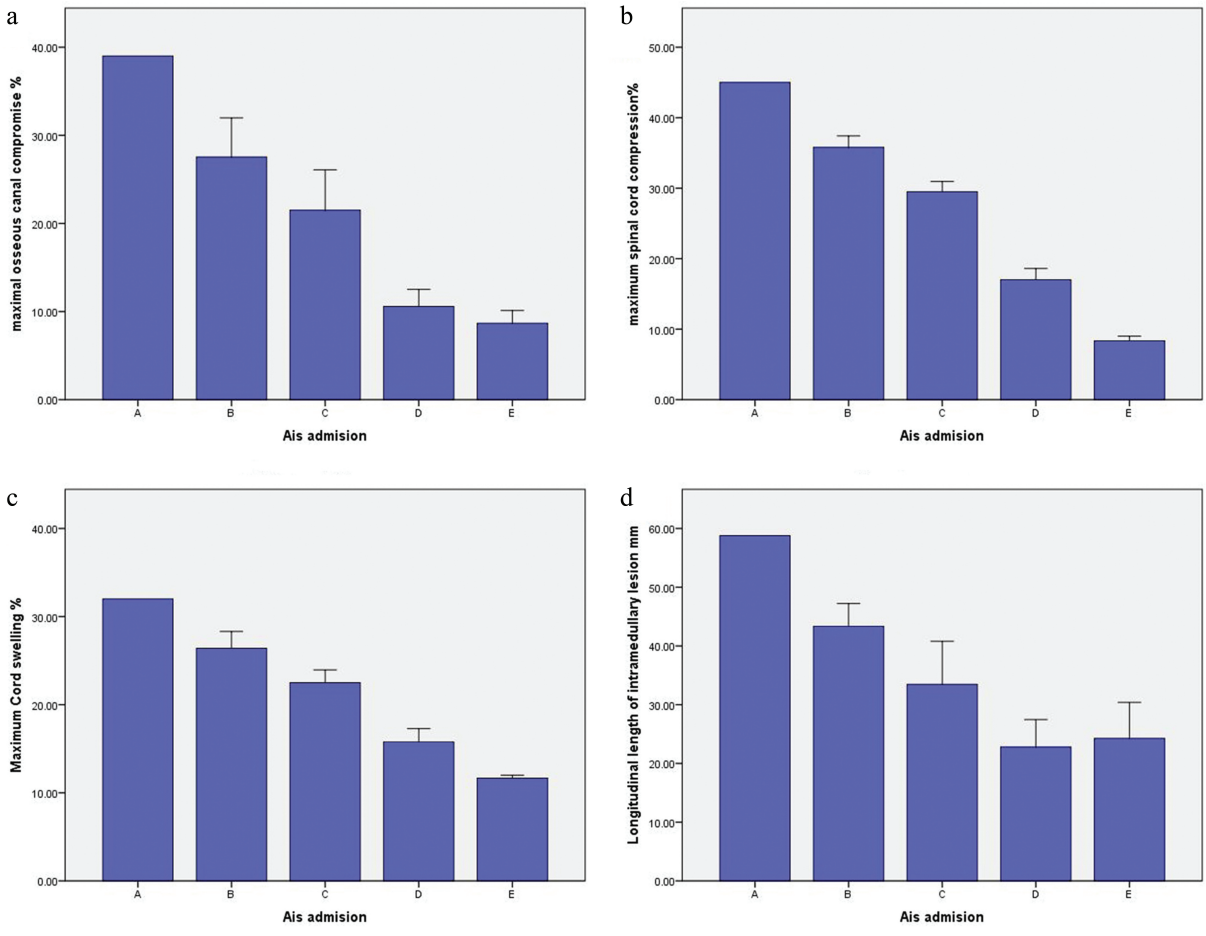

Fig. 2 (a) Mean MCC on the initial MRI for each AIS grade; (b) MSCC on the initial MRI for each AIS grade; (c) MCS in the initial MRI for each AIS grade; (d) longitudinal length of the IML for each AIS grade. Error bars indicate standard deviation (SD).

Table 4 Correlation of AIS with imaging findings

Parameters	AIS at admission	*p*-value	AIS at follow-up	*p*-value
CT maximum osseous canal compromise	0.790	0.001	0.713	0.001
MSCC	0.925	0.001	0.870	0.001
MCS	0.880	0.001	0.793	0.001
Longitudinal length of IML	0.666	0.01	0.629	0.03
Fracture type	0.606	0.05	0.615	0.05

Abbreviations: AIS, American spinal injury association impairment scale; CT, computed tomography; IML, intramedullary lesion; MCC, maximum canal compromise; MCS, maximum cord swelling; MSCC, maximum spinal cord compression.

In this study, the correlation between AIS at admission and follow-up with imaging parameters were assessed and the results are present in ►**Table 4**. Imaging findings had a significant correlation with patients' neurological outcome, which was evaluated based on the AIS test.

According to the data present in ►**Table 5**, the MCC ($p = 0.74$) and longitudinal length of IML ($p = 0.24$) were not significantly related to the improvement in patients. Conversely, maximum spinal cord compression ($p = 0.05$), and maximum cord swelling ($p = 0.02$) had a significant association with patient improvement.

Discussion

In this study, we assessed the relationship between imaging quantitative features with improvement of postoperative neurological symptoms (according to AIS) in patients with TCSCI without prior neurodegenerative diseases. This study's findings demonstrate that the presence of greater cord compression and swelling is a prognostic factor to predict the long-term neurological outcomes in patients under surgery.

Considering that most of the cervical spinal cord injuries are incomplete, the cause/mechanism of the SCI and

Table 5 The association of patient improvement with imaging findings

Quantitative parameters	Improvement (*p*-value)
CT MCC	0.74
Maximum spinal cord compression	0.05
Maximum cord swelling	0.02
Longitudinal length of IML	0.24

Abbreviations: CT, computed tomography; IML, intramedullary lesion; MCC, maximum osseous canal compromise; MCS, maximum cord swelling; MSCC, maximum spinal cord compression.

rehabilitation outcomes should not be conflated. In a study by Kiwerski, it was reported that the cause of the injury impacts the level of the spinal cord lesion. Moreover, the incidence of injuries from a flexion mechanism is more prevalent.[17] According to some studies, the highest leading cause of SCI in younger patients followed by motor vehicle accidents, sports, trauma, suicide attempts, and acts of violence was occurring. Falling was significantly the cause of TSCI in older patients (62.3%)[18]. In this study, TSCI was associated with cervical spinal cord lesion, caused by falls in 60% of cases, of whom 26% were construction workers, and 13% were farmers. However, patients with significant MSCC and MCS, as well as severe functional impairment, were more prevalent in motor vehicle accidents.

In this study, we found that falling was the main cause of TSCI in patients, which could be related to the work opportunities in the north of Iran, predominantly farming and reconstruction. Another study[19], which evaluated age, gender, BMI, and administration of steroids, determined that these items did not correlate with neurological outcomes and AIS follow-up. In our study, we found that the prevalence of TSCI is more common in male patients; however, the effect of administration of steroids was not evaluated in this study because the protocol prescribes the same treatment for all patients based on internal guidelines.

The first clinical evidence was presented by Firoz Miyanji et al.[9] who reported a significant correlation between AIS follow-up was 7.3 months (range, 1–35 months) evaluation with intramedullary hemorrhage and cord swelling at the time of injury. Furthermore, they suggested that the extent of MSCC is more reliable than the presence of canal stenosis for predicting the neurological outcomes after SCI. In our study, as shown in ►**Fig. 2**, we demonstrated that MSCC and MCS had a great relation with neurological outcomes. Patients with AIS grades A and B had MSCC and MCS over 38 and 28%, respectively. Additionally, in the present study, we evaluated the correlation of fracture type and the longitudinal length of IML with neurological outcomes in all patients. Patients with AIS grades A, B, and C usually had worsened fracture type and extensive IML. However, patients with AIS grades D and E mostly had milder fracture types and mild IML lesions. Sometimes, transitional fractures could be seen in patients with AIS grades D and E. It should be mentioned that transitional fractures could be treated by surgical approach. Low-grade transitional fractures in patients without significant degenerative SCIs could not lead to the neurological deficit in patients.

Another study by Rutges et al.[20] demonstrated an increase in vertical length of spinal cord edema in the first 48 hours after SCI, followed by a gradual decrease in the 3 weeks after injury. The MCC and MSCC reported in these studies range from 22 to 62% and 23 to 58%, respectively, for complete injuries, and from 14 to 38% and 20 to 52%, respectively, for incomplete injuries. [9,13,16]. All cases included in this study required emergency surgical treatment; therefore, follow-up regarding cord swelling was not possible for these patients. However, the qualitative assessment of T2 images from patients after 6 months showed no sign of cord swelling.

A Canadian study by Oichi T et al.[21] demonstrated that preexisting severe cervical cord compression is an independent risk factor for severe paralysis once patients develop traumatic CSCI without bone injury. Preexisting severe cervical cord compression could interference with patients' AIS score and imaging quantitative evaluations. In the current study, we investigated imaging parameters on patients without preexisting severe cervical cord compression with bone injury. The obtained results confirmed the relationship of traumatic spinal cord compression with neurological deficits.

Finally, H. Francis Farhadi[22] assessed the sensitivity and specificity of MRI parameters by including MCC, maximum spinal cord compression (MSCC), the longitudinal length of the IML, with the Brain and Spinal Injury Center (BASIC) score, and a novel derived Combined Axial and Sagittal Score (CASS). Both BASIC and IML were stronger predictors of AIS conversion when compared with MCC and MSCC ($p = 0.0002$ and $p = 0.04$). In the present study, as shown in ►**Table 4**, we found that IML was correlated with AIS at admission and follow-up 6 to 12 months postoperatively. However, we showed, in ►**Table 5**, that the patients' improvement had no significant relationship with those factors. Additionally, AIS-C and -D patients had the best neurologic improvement. We suggest that other studies are required to corroborate these results. Another limitation of our study is the small sample size per AIS grade, especially the AIS-A group ($n = 1$).

Conclusion

According to the obtained results, it may be concluded that there is a significant association between clinical and functional outcomes with spinal cord compression and cord swelling in TSCI patients. Hence, these are applicable variables to predict the final outcomes in patients with mild to acute cervical spinal cord injury. However, studies with a larger sample population and longer follow-up times are required to attain more reliable results.

Conflict of Interests

The authors have no conflict of interests to declare.

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Risk Factors for Malfunction of Ventriculoperitoneal Shunts Performed by Medical Residents in Children: An Exploratory Study

Fatores de risco para disfunção de derivações ventrículo-peritoneais realizadas por médicos residentes em crianças: Estudo exploratório

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Abstract

Introduction Ventriculoperitoneal shunts (VPSs) are common neurosurgical procedures, and in educational centers, they are often performed by residents. However, shunts have high rates of malfunction due to obstruction and infection, especially in pediatric patients. Monitoring the outcomes of shunts performed by trainee neurosurgeons is important to incorporate optimal practices and avoid complications.

Methods In the present study, we analyzed the malfunction rates of VPSs performed in children by residents as well as the risk factors for shunt malfunction.

Results The study included 37 patients aged between 0 and 1.93 years old at the time of surgery. Congenital hydrocephalus was observed in 70.3% of the patients, while 29.7% showed acquired hydrocephalus. The malfunction rate was 54.1%, and the median time to dysfunction was 28 days. Infections occurred in 16.2% of the cases. Cerebrospinal fluid leukocyte number and glucose content sampled at the time of shunt insertion were significantly different between the groups ($p = 0.013$ and $p = 0.007$, respectively), but did not have a predictive value for shunt malfunction. In a multivariate analysis, the etiology of hydrocephalus (acquired) and the academic semester (1st) in which the surgery was performed were independently associated with lower shunt survival ($p = 0.009$ and $p = 0.026$, respectively).

Keywords
- ventriculoperitoneal shunts
- hydrocephalus
- shunt malfunction
- medical resident
- teaching hospital
- ventriculostomy

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Conclusion Ventriculoperitoneal shunts performed in children by medical residents were at a higher risk of malfunction depending on the etiology of hydrocephalus and the academic semester in which the surgery was performed.

Resumo

Introdução As derivações ventrículo-peritoneais (DVPs) são procedimentos neurocirúrgicos comuns e, em centros educacionais, muitas vezes são realizados por residentes. No entanto, os shunts apresentam altas taxas de mau funcionamento devido a obstrução e infecção, especialmente em pacientes pediátricos. O monitoramento dos resultados das válvulas realizadas por neurocirurgiões em treinamento é importante para incorporar as práticas ideais e evitar complicações.

Métodos No presente estudo, analisamos as taxas de mau funcionamento de DVPs realizados em crianças por residentes, assim como os fatores de risco para mau funcionamento da válvula.

Resultados O estudo incluiu 37 pacientes com idades entre 0 e 1,93 anos na época da cirurgia. Hidrocefalia congênita foi observada em 70,3% dos pacientes, enquanto 29,7% apresentaram hidrocefalia adquirida. A taxa de disfunção foi de 54,1% e o tempo médio para disfunção foi de 28 dias. Infecções ocorreram em 16,2% dos casos. O número de leucócitos do líquido cefalorraquidiano e o conteúdo de glicose coletados no momento da inserção da válvula foram significativamente diferentes entre os grupos ($p = 0,013$ e $p = 0,007$, respectivamente), mas não tiveram um valor preditivo para o mau funcionamento da válvula. Em uma análise multivariada, a etiologia da hidrocefalia (adquirida) e o semestre letivo (1°) em que a cirurgia foi realizada foram independentemente associados a menor sobrevida do shunt ($p = 0,009$ e $p = 0,026$, respectivamente).

Conclusão: Derivações ventrículo-peritoneais realizadas em crianças por médicos residentes apresentaram maior risco de mau funcionamento dependendo da etiologia da hidrocefalia e do semestre letivo no qual a cirurgia foi realizada.

Palavras-chave
- derivação ventrículo-peritoneal
- hidrocefalia
- disfunção de derivação ventrículo-peritoneal
- hospital de ensino
- ventriculostomia

Introduction

Hydrocephalus is an important cause of neurological disability and can accompany several other conditions, such as infections, neoplasms, cerebrovascular diseases, and trauma. Its prevalence is estimated to be of 85 per 100,000 individuals, while the prevalence is higher among children (88 per 100,000 individuals), especially due to congenital malformations and neonatal complications related to prematurity.[1]

The treatment of hydrocephalus is surgical, and even though endoscopic third ventriculostomy has yielded significant advances in the management of this condition (particularly in cases of obstructive hydrocephalus), ventriculoperitoneal shunts (VPSs) remain the most common treatment option.[2,3] Ventriculoperitoneal shunts are effective for most cases; however, the rates of VPS malfunction are very high, and can increase up to 84.5%.[4–6]

Several classifications depending on the site of the problem and on the presence of infection have been proposed to categorize VPS malfunctions.[7] Indeed, VPS malfunctions are associated with worse outcomes, and a single malfunction has a high predictive value for further malfunctions, necessitating several surgical procedures throughout the lifetime of the patient.[8] Thus, a thorough understanding of the risk factors for VPS malfunction is essential to optimize the clinical follow-up and surveillance and facilitate early detection of malfunction and, ultimately, provide better care and improved prognosis.

Although guidelines and recommendations for shunt implantation emphasize that the procedure should be performed by an experienced neurosurgeon,[9] shunt procedures are performed by residents at many centers, especially in teaching hospitals in low- and middle-income countries (LMICs), as well as in developed countries.[10] This dilemma between patient safety and surgical education has made it important to monitor the surgical results of procedures performed by trainee neurosurgeons. In the present study, we aimed to analyze the malfunction rates of VPSs performed in children by residents as well as the risk factors for shunt revision.

Methods

This was a retrospective cohort study of a case series of patients attending the Pediatric Neurosurgery Outpatient Clinic at the Hospital das Clínicas da Faculdade de Medicina de Botucatu of the Universidade Estdual de São Paulo, Botucatu, state of São Paulo, Brazil. This is a university hospital located in the center-west region of the state of

São Paulo in Brazil, and it is the referral center for up to 2 million patients in 68 cities. The study protocol was approved by the local Institutional Review Board.

Using electronic medical registries, we recovered the data of patients who had undergone VPS procedures at this center. The surgical procedures were performed by 2nd-year medical residents under the supervision of experienced staff. We included all children born between 2013 and 2018 who were diagnosed with hydrocephalus and were treated with VPS. The children were routinely followed up at 1, 3, 6, and 12 months postoperatively, and then annually. The exclusion criteria were surgeries performed by nonresident neurosurgeons, patients lost to follow-up, and previous endoscopic third ventriculostomy.

The independent variables were age at VPS insertion, previous use of an external ventricle drain (EVD), cause of hydrocephalus, the semester in which the scholar was at the time of the surgery (since medical residency begins every March, the 1st academic semester was defined as March to September, and the 2nd semester from October to February), and the cerebrospinal fluid (CSF) parameters from the intraoperative sampling. The primary outcome was shunt malfunction and time for its occurrence. The secondary outcome was the cause of malfunction (obstruction or infection) and the microorganisms isolated from the cases that presented with infections.

For the statistical analysis, the distribution of the data was assessed using the Kolmogorov-Smirnov test. Comparisons between groups were performed using the Mann-Whitney test. Correlations were tested using the Spearman test. The chi-squared and the Fisher exact tests were used to compare categorical data. Multivariate analysis with Cox regression curves was used to analyze shunt survival with adjustments for covariates. Receiver operating characteristic (ROC) curves were generated to identify the predictive values of CSF parameters on shunt revision. For all tests, the level of statistical significance was set at 5%. Statistical analyses were performed using IBM SPSS Statistics for MacBook, version 24 (IBM Corp., Armonk, NY, USA).

Results

We evaluated the data from 37 patients (21 boys and 16 girls) aged 3.57 ± 1.44 years old. The mean follow-up duration was of 765.05 days ($\sim$ 2 years). The age of the patients at the time of surgery ranged from 0 to 1.93 years old (median: 2 months old). In total, 59.5% of the surgeries ($n = 22$) were performed in the 1st academic semester. Six children (16.2%) had received a prior EVD. Among the cases of congenital hydrocephalus ($n = 26$; 70.3%), 21 were caused by malformations of the central nervous system (such as aqueduct stenosis and myelomeningocele), and 5 were related to congenital infections (toxoplasmosis and cytomegalovirus). Among the cases of acquired hydrocephalus ($n = 11$; 29.7%), 9 were caused by peri-intraventricular hemorrhage (PIVH) of prematurity, and 2 were attributed to neonatal meningitis.

Table 1 Causes of shunt malfunction

Malfunction mechanism	*n* (%)
Catheter obstruction	7 (35%)
Shunt infection	6 (30%)
Catheter misplacement	3 (15%)
Wound dehiscence	2 (10%)
CSF hyperdrainage	1 (5%)
Catheter migration	1 (5%)

Abbreviation: CSF, cerebrospinal fluid.
Among 37 patients, 20 required a shunt revision.

The overall rate of shunt revision was 54.1%, and the median time for revision was 28 days (interquartile range = 418.5 days). The most common causes of shunt revision were catheter obstruction and shunt infection (►**Table 1**). Most of the microorganisms related to infection belonged to the *Staphylococcus* genus (4 out of 6). The overall infection rate was 16.2%. There was no difference in the time for shunt review between cases requiring revision due to infectious and noninfectious causes (mean: 297.33 versus 278.3 days, respectively, $p = 0.494$). In the CSF parameter data collected at the time of ventricular catheterization, patients with acquired hydrocephalus had higher levels of leukocytes ($p = 0.013$) and lower levels of glucose ($p = 0.007$) than those with congenital hydrocephalus (►**Table 2**). The children with and without shunt revision showed no difference in median age at the time of shunt insertion (64.0 versus 65.0%, respectively; $p = 0.964$). Similarly, none of the CSF parameters were significantly different between patients who required shunt revision and those did not.

In the univariate analysis, the semester in which shunt insertion was performed was not associated with the rate of shunt revision: the rate was 63.6% for procedures performed

Table 2 Cerebrospinal fluid parameters according to the etiology of hydrocephalus

CSF parameter	Acquired hydrocephalus ($n = 11$)	Congenital hydrocephalus ($n = 26$)	*p-value*
Leukocytes (median [IQR])	2.00 (8.00]	0.0 (0.00]	0.013
Protein mg/dl (median [IQR])	87.00 (404.00]	63.0 (98.00]	0.201
Red cells (median [IQR])	12.0 (70.00]	5.0 (55.00]	0.586
Glucose mg/dl (mean $\pm$ SD)	26.81 ± 8.76	37.43 ± 10.68	0.007
Lactate mmol/L (mean $\pm$ SD)	2.33 ± 0.61	2.08 ± 1.00	0.529

Abbreviations: CSF, cerebrospinal fluid; IQR, interquartile range; SD, standard deviation.

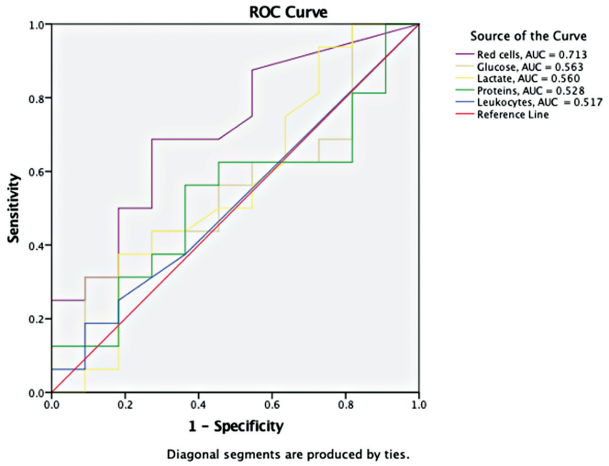

Fig. 1 Receiver operating characteristic curves for cerebrospinal fluid parameters. Red blood cells showed a higher area under the curve, but none of the parameters were statistically associated with the risk of shunt revision.

in the 1st semester and 40.0% for those performed in the 2nd semester ($p = 0.157$). All 6 patients who had previously received an EVD required shunt revision, while 45.2% of those without an EVD required shunt revision ($p = 0.022$). Similarly, the rate of shunt revision was higher among patients with acquired hydrocephalus than among those with congenital hydrocephalus (81.8 versus 42.3%; $p = 0.036$). Since the rate of previous EVD usage was higher among patients with acquired hydrocephalus (45.5 versus 3.8%; p = 0.005), further multivariate analysis was necessary for covariate adjustment.

The ROC curves of CSF parameters for predicting shunt revision did not yield significant cutoff values. For red blood cell count, the area under the curve (AUC) was 0.713 ($p = 0.064$). The other parameters had an AUC between 0.5 and 0.6 ($p > 0.6$), as shown in ►**Figure 1**.

In the Cox regression analysis with covariate adjustment, age at the time of surgery was not associated with a higher risk of shunt revision (Exp [B] = 0.998; 95% confidence interval [CI]: 0.994–1.002). However, the semester in which the surgery was performed showed a significant difference: surgeries performed in the 1st semester had a higher risk than those in the 2nd semester (odds ratio [OR] = 3.145; 95% CI: 1.149–8.612; $p = 0.026$). Patients with congenital hydrocephalus were also at a lower risk for shunt revision than those with acquired hydrocephalus (OR = 0.303; 95%CI: 0.124–0.741; $p = 0.009$). The differences are shown in ►**Figure 2**.

Discussion

Ventriculoperitoneal shunts are common neurosurgical procedures and one of the first surgical procedures learned by trainee neurosurgeons.[11] Despite the relatively easy technique, they carry non-negligible risks for complications. For pediatric patients, these risks are even higher, especially the risk of infection.[12] Therefore, close monitoring of the surgical results is of utmost importance for quality surveillance and improvement.

The rate of revision in our study was quite high (54.1%) and it was comparable to the higher rates reported in the literature.[13,14] Nevertheless, the infection rate (16.2%) was not as high. However, this finding must be analyzed with care, since we considered the first malfunction as the primary outcome. Patients who required a revision were at a higher risk of new subsequent revisions, since a single revision *per se* is recognized as an important risk factor for new revisions either due to obstruction or to infection.[15–18] Long-term follow-up assessments show that up to 84.5% of the patients

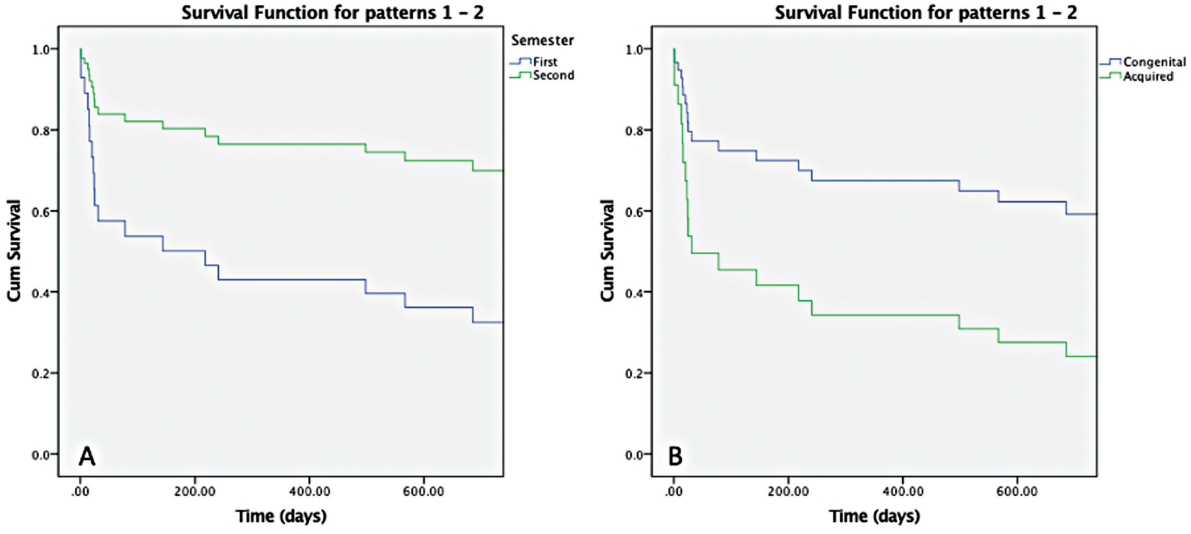

Fig. 2 Cumulative survivals of shunts performed in the 1st or 2nd semester (A, $p = 0.026$) and for cases of congenital or acquired hydrocephalus (B, $p = 0.009$). In all cases, most revisions occurred within the first 30 days. Shunts implanted in the 1st semester and in cases of acquired hydrocephalus had lower survival rates.

require at least 1 shunt revision, with high mortality rates directly associated with infection episodes.[5,8]

Regarding the causes of hydrocephalus, we found that most cases involved congenital etiologies and that the proportion of acquired diseases was lower. A multicenter study on VPS infections also reported a higher proportion of congenital malformations as the leading etiology.[17] In our study, the main cause of acquired hydrocephalus was prematurity-related peri-intraventricular hemorrhage, which may be the reason why some CSF parameters (leukocyte number and glucose levels) were different at the time of shunt insertion. However, these parameters were not significantly different between patients who underwent shunt revision and those who did not. The CSF parameters also could not predict shunt malfunction, even though the number of red cells showed a higher AUC, which is expected, because patients with peri-intraventricular hemorrhages have higher rates of shunt malfunction.[19] Studies with larger sample sizes could provide more insights into the role of CSF red cells in predicting shunt malfunction regardless of the etiology of hydrocephalus.

The use of EVDs was associated with acquired hydrocephalus, since peri-intraventricular hemorrhage and neonatal meningitis often require a temporary EVD. These patients most often required shunt revision, which is consistent with the literature: peri-intraventricular hemorrhage is an important risk factor for VPS malfunction. In addition, prematurity itself is another independent risk factor for VPS malfunction.[20] Therefore, premature children with peri-intraventricular hemorrhages should be closely monitored after shunt implantation, especially in the 1st postoperative month – when the infections and obstructions typically occur.

In our study, VPS implantation in the 1st academic semester was associated with a higher risk of revision, which indicates the effect of learning curves on the surgical outcomes of VPSs, as demonstrated previously.[21] Among the 20 cases of shunt malfunction, 5 (25%) could be attributed to low surgical experience (catheter misplacement and wound dehiscence). The "July effect" has been identified as an important factor related to complications of surgeries performed in the beginning of the training of new staff. Early resident transition may be responsible for this phenomenon. However, several studies have not demonstrated this finding, which could be attributed to good resident training with sufficient guidance and support.[22–25] When present, this effect is generally very small.[26,27] Nevertheless, these studies were conducted in high-income countries, and there is a lack of evidence regarding the equivalent "July effect" among neurosurgical trainees in low- and middle-income countries (LMICs). In this regard, a recent survey on the perceptions of LMIC neurosurgery residents of their educational programs highlighted concerns regarding inadequate exposure to subspecialties, exhausting work hours, and inconsistent supervision.[28] Additional studies are needed to evaluate the extent to which the lack of ideal supervision interferes with surgical outcomes, even though this was not the case in our setting.

Patient safety is of utmost importance, and all attempts should be made to accomplish it. However, balancing patient safety and the training of young surgeons is a constant challenge, especially in centers of academic education. Regarding VPSs, there is a clear dichotomy: the best practice guidelines advocate for these procedures to be performed by senior surgeons; however, most academic centers reserve these procedures for the early training years, given the high technical complexity of other neurosurgical procedures that should be acquired.

The limitations of our study included the small sample size and the lack of comparison with shunt procedures performed by graduate neurosurgeons. Studies addressing infection should have a strong series, especially if infection-related factors are considered in the analysis. Also, the demonstration of higher rates of complications related to the performing residents would demand a control group composed of graduate neurosurgeons. However, as an exploratory study, the present results may be an eye-opener for future Brazilian networks and multicenter collaborations aiming to both understand the learning curve of our residents and to implement best standardized practices throughout the country. In addition, since the primary outcome was the first shunt malfunction and the cases were subsequently censored, we did not evaluate the cumulative effect of a single shunt malfunction on repeated malfunctions and infections, which has been demonstrated in other studies. Moreover, long-term follow-up evaluations could provide additional data. Despite these limitations, our study reinforces the data on worse outcomes of VPSs performed in children with peri-intraventricular hemorrhage. Furthermore, our study adds new knowledge by demonstrating an equivalent "July effect" related to neurosurgery training for VPSs in children.

In conclusion, VPSs performed in children by medical residents were at a higher risk of malfunction, depending on the etiology of hydrocephalus and on the academic semester in which the surgery was performed.

Ethical Statement

The present retrospective study was approved by our institutional review board (IRB No. 2.533.607/2018). The parents of the patients signed informed consent forms.

Data Availability Statement

All data generated or analyzed during the present study can be retrieved upon request to the corresponding author.

Conflict of Interests:

The authors have no conflict of interests to declare.

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Neonate Brain Abscess by *Cronobacter spp*: A Powdered Infant Formula's Opportunistic Pathogen

Abscesso cerebral neonatal por Cronobacter spp: Um patógeno oportunista de fórmula láctea infantil

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Abstract

Cronobacter spp is an opportunistic pathogen that can cause severe neonatal infections, including septicemia, meningitis, and necrotizing enterocolitis. Over 90% of these infections outbreaks are associated with the increased consumption of powdered infant formula (PIF). We report the case of a male neonate born at term with adequate weight for gestational age, fed by breast milk and PIF. He was admitted to the ICU at 22 days old due to fever, irritability, impaired consciousness, and food intolerance. Investigation revealed an extensive abscess in the right frontoparietal region, that was surgically drained. The culture of the purulent material showed the growth of *Cronobacter spp*. Guided antibiotic was kept for 21 days. The patient presented a good clinical outcome, without neurological deficits. The microbiological powdered formula contamination by *Enterobacter sakazakii* (*Cronobacter spp*) can lead to a higher risk of severe infections in infants. Children may present sepsis, sensory alteration, and refractory seizures. An early brain image should be considered for symptomatic infants. The mortality rate ranges from 40 to 80%, and 74% of survivors have an adverse neurological outcome. From 1997–2013, there were reports of 6 outbreaks of *E. sakazakii* disease in Brazil. According to the World Health Organization (WHO), this disease is undernotified, and active foodborne surveillance systems are less than ideal. To better address this problem, in some countries, the notification is mandatory, and the adoption of stricter sanitary measures by regulatory agencies are proposed.

Keywords
- enterobacter sakazakii
- cronobacter spp.
- brain abscess
- powdered infant formula
- neonatal sepsis

Resumo

O *Cronobacter spp* é um patógeno oportunista que pode causar infecções neonatais graves, incluindo septicemia, meningite e enterocolite necrosante. Mais de 90% dessas infecções estão associadas ao aumento do consumo de fórmula infantil em pó (FIP). Relatamos o caso

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de um recém-nascido do sexo masculino, nascido a termo, com peso adequado para a idade gestacional, alimentado com leite materno e FIP. Ele foi internado na UTI com 22 dias de idade devido a febre, irritabilidade, comprometimento da consciência e intolerância alimentar. A investigação revelou abscesso extenso na região frontoparietal direita, que foi drenada cirurgicamente. A cultura do material purulento mostrou o crescimento de *Cronobacter spp*. Antibiótico guiado foi mantido por 21 dias. O paciente apresentou bom resultado clínico, sem déficits neurológicos. A contaminação microbiológica da fórmula em pó pela *Enterobacter sakazakii* (*Cronobacter spp*) pode levar a um risco aumentado de infecções graves neonatais. As crianças podem apresentar sepse, alterações sensoriais e crise convulsiva refratária. Uma imagem cerebral precoce deve ser considerada nestes pacientes. A taxa de mortalidade varia de 40 a 80%, e 74% dos sobreviventes têm um quadro neurológico sequelar. Entre 1997 e 2013, houve relatos de 6 surtos de *E. sakazakii* no Brasil. De acordo com a Organização Mundial de Saúde (OMS), esta doença está subnotificada e os sistemas de vigilância alimentar são insuficientes. Para resolver esse problema, em alguns países, a notificação é obrigatória e a adoção de medidas sanitárias mais rigorosas é exigida pelas agências reguladoras.

Palavras-chave
- enterobacter sakazakii
- cronobacter spp.
- abcesso cerebral
- fórmula láctea infantil em pó
- sepse neonatal

Introduction

Nowadays, the use of powdered infant formula (PIF) as a substitute to feed newborns is increasingly frequent. Although breastfeeding is the primary recommendation for adequate infantile nutrition, it is not always possible. The PIF is easily accessible; nevertheless, issues with the production and distribution of the formula have been associated with a higher risk of its contamination, and therefore of life-threatening foodborne diseases in infants.[1,2]

The first documented case of neonatal meningitis by the *Cronobacter* (previously named *Enterobacter sakazakii*) was in 1958.[3] But it was only in 1987 that the association of this bacteria as an important contaminator of commercial powdered formula was identified and emphasized.[4]

After that, many outbreaks happened around the world, and this pathogen emerged as a serious public health issue for the government and industries.[5–8] Since then, the World Health Organization (WHO) has published guidelines and promoted international conferences to address this issue and propose solutions.[7] Alongside with that, industries have invested their budget in developing ways to detect and prevent the contamination. In Brazil, some cases of *Cronobacter* infections were reported from 1997 to 2017, in different states, but the data on these cases is limited.[9,10]

These gram-negative bacteria are well-known for causing necrotizing enterocolitis, neonatal sepsis, and meningitis. In the central nervous system, besides meningitis, it can result in abscess formation, ventricle dilatation, and infarcts.[11] In addition, *Cronobacter* meningitis is the main cause of lethality, ~ 42% of infected newborns.[12]

Here we report a case of a neonate fed by PIF that evolved with a *Cronobacter* abscess, to highlight this issue for the neurosurgery community.

Case Report

Neonate, male, born at term with adequate weight for gestational age. The child used PIF as a complement to breastfeeding. He presented with fever and irritability when he was 22 days old and was admitted to the intensive care unit (ICU). The diagnosis of late-onset sepsis was established. He was treated with broad-spectrum antibiotics with an initial clinical improvement.

After 2 days, he presented again with fever, irritability, impaired consciousness, and food intolerance. Cerebrospinal fluid (CSF) analysis (►**Table 1**) revealed a neutrophilic pleocytosis consistent with meningitis. Further investigation with transcranial ultrasound (►**Fig. 1**) and brain magnetic resonance imaging (MRI) (►**Fig. 2**) revealed an extensive expansive lesion in the right fronto-parieto-occipital region suggestive of a brain abscess.

It was opted for surgical drainage and the material was sent to analysis. The culture of the purulent material (►**Fig. 3**) revealed the growth of *Cronobacter spp*. Guided antibiotic therapy was kept for 21 days, with ampicillin and gentamicin. The patient presented a good clinical outcome, without neurological deficits.

Discussion

Formulas are well-accepted alternatives for infant feeding when breastmilk is insufficient. However, microbiological powdered formulae contamination by the *Cronobacter spp* (formerly *Enterobacter sakazakii*) leading to a higher risk of severe infections in infants constitutes a major health issue, already alerted by the WHO.[7,9,11]

Although infection by the *Cronobacter spp.* can affect all ages,[13] the population at higher risk for invasive and

Table 1 Cerebrospinal Fluid Results

WBC 2900/mm^3	Neutrophils 70%
RBC 0/mm^3	Lymphocytes 20%
Protein 200mg/dl	Lactate 64mg/dl
Glucose 10mg/dl	Culture negative

Abbreviations: RBC, red blood cells; WBC, white blood cells.

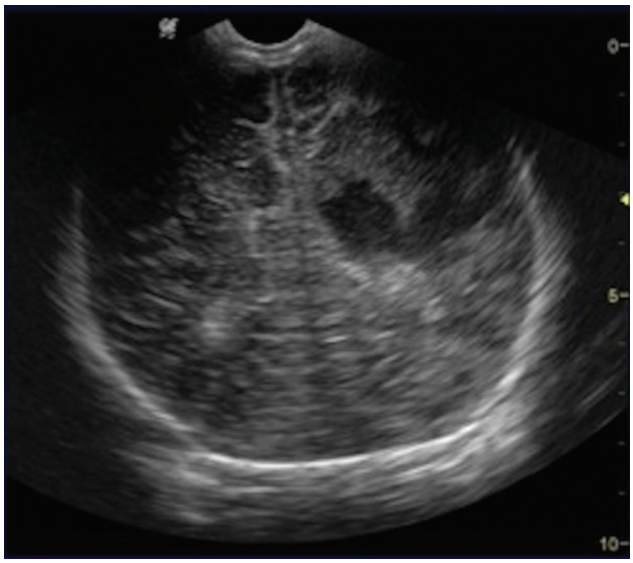

Fig. 1 Transfontanellar ultrasound with a coronal view showing a hypoechoic area at the right cerebral hemisphere.

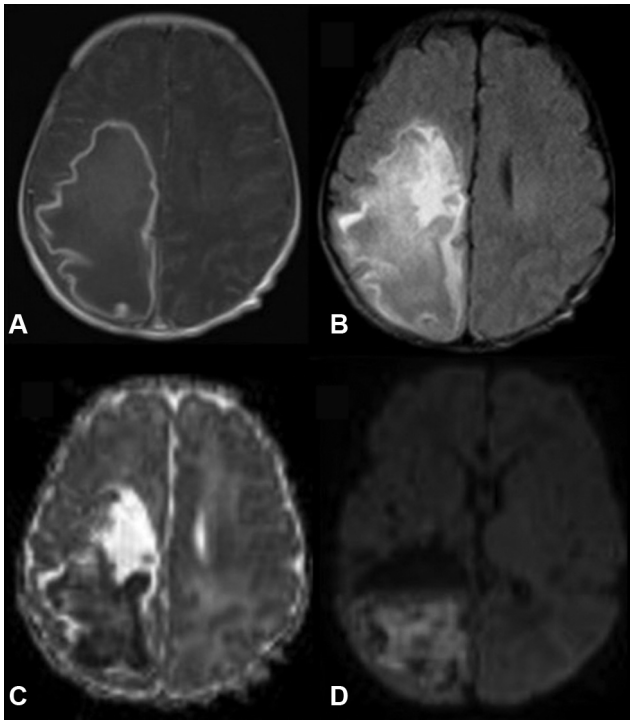

Fig. 2 MRI axial view: A. T1–weighted gadolinium enhanced B. Fluid-attenuated inversion recovery (FLAIR) C. Apparent diffusion coeficiente (ADC) D. Diffusion weighted imaging (DWI) revealing an extensive right fronto-parieto-occipital abscess.

life-threatening infections are low-birthweight infants, premature, immunodeficient and long-term hospitalizations.[11,14] These risk factors are supposed to be associated with an immature immune system and a low density of intestinal microflora predisposing the individual to more severe infections.[15] The pathogenesis of this infection is still poorly understood, nevertheless recently researchers proved the *C. sakazakii* can survive and multiply within the brain capillary endothelial cells in rats[16] and in human microglial

Fig. 3 Macroscopic aspect of purulent material surgically drained.

cells, and also, translocate trough the human brain microvascular endothelial cells.[17,18] This invasive process influences cytokine secretion and induces a severe brain inflammatory state.

Children may present typical signs of sepsis, sensory alteration, and refractory seizures. An early brain image should be considered for symptomatic infants. The mortality rate ranges from 40 to 80% of infected infants,[14,19] and 74% of survivors have an adverse neurological outcome.

From 1997 to 2013, there were reports of 6 outbreaks of *E. sakazakii* disease in Brazil. However, according to the WHO, this disease is undernotified and active foodborne surveillance systems are less than ideal. To better address this problem in some countries, the notification is mandatory and the adoption of stricter sanitary measures by regulatory agencies are proposed.

Powdered infant formula is not sterile, and contamination by opportunistic pathogens is a health issue. The formula contamination can happen in any sequence of the process: during the production, at the micronutrients addition after the pasteurization, and during the preparation of the formula.[20]

Prevention campaign for the divulgation of Food and Agriculture Organization (FAO)/WHO guidelines for hospitals and parents regarding PIF preparation should be done, especially to the vulnerable population (infants < 2 months old). Alongside that, modern procedures associated with technological innovations have been implemented to the continuous surveillance of the production of the formula .[21]

Conclusion

Cronobacter spp. is responsible for a severe infection of the central nervous system (CNS) of newborns. It frequently evolves to brain abscess and requires neurosurgical treatment. The main source for this infection is an infected infant powdered formula. It is crucial for the neurosurgeons, mostly the ones treating infants, to know the existence of this entity.

Conflict of Interests

The authors have no conflict of interests to declare.

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Insulectomy for Refractory Epilepsy: Case Series and Literature Review

Insulectomia para epilepsia refratária: Série de casos e revisão de literatura

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Abstract

Surgical resection of the insula (insulectomy) is a procedure used for brain lesions and for refractory epilepsy. It has a difficult surgical access and the need of a wide anatomical knowledge and preoperative planning. There are two types of surgical approaches aiming the exposure of the insular cortex: transsylvian and transcortical. The importance of insulectomies is the efficacy in providing a remarkable decrease in seizures. The objective of the present article is to document the results of a series of 10 patients submitted to insulectomies for refractory epilepsies and compare them with the results of other studies reported in the literature, as well as to describe the main nuances of the surgical approaches and their associated risks. In the new case series, all patients corresponded to preoperative Engel classification IV for; after a mean 2-year follow-up period, they corresponded to Engel classification II. A subtotal resection was performed in six patients, and the remaining four underwent a partial resection, most of them leading to temporary complications. The literature review endorsed the good outcomes of the casuistry. A critical analysis of the presented data reiterates the opinion of several authors that insulectomies are beneficial and safe for the patients. A broad anatomical knowledge of the insular region, preoperative planning (limits of resections), and the use of modern microsurgical techniques must be considered as

Keywords
- island of reil
- insular cortex
- refractory epilepsy
- resective procedures

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basic principles by neurosurgeons for the prevention of perioperative morbidities. Insulectomies are safe and effective, although they result in temporary postoperative complications, and provide highly satisfactory results in terms of seizure control.

Resumo

A ressecção cirúrgica da ínsula (insulectomia) é um procedimento utilizado para lesões cerebrais e epilepsia refratária. A ínsula possui um acesso cirúrgico difícil com necessidade de um amplo conhecimento anatômico com planejamento pré-operatório. Existem dois tipos de abordagens cirúrgicas que visam a exposição do córtex insular: transsilvianas e transcorticais. A importância das insulectomias é a eficácia em proporcionar uma diminuição das convulsões. O objetivo do presente artigo é documentar os resultados de uma série de 10 pacientes submetidos a insulectomias para epilepsia refratária e compará-los com os resultados de outros estudos relatados na literatura, além de descrever as principais nuances das abordagens cirúrgicas e os seus riscos associados. Na série de casos, todos os pacientes se enquadravam na classificação pré-operatória de Engel IV e, após um período médio de seguimento de 2 anos, eles se enquadravam na classificação de Engel II. Seis pacientes foram submetidos a uma ressecção subtotal e os quatro restantes a uma ressecção parcial, implicando, majoritariamente, em complicações temporárias. A revisão da literatura endossou os bons resultados da casuística. A análise crítica dos dados apresentados reitera a opinião de vários autores de que as insulectomias são benéficas e seguras para os pacientes. O amplo conhecimento anatômico da região insular, o planejamento pré-operatório (limites das ressecções) e a utilização de técnicas microcirúrgicas modernas devem ser considerados princípios básicos para a prevenção de morbidades perioperatórias. As insulectomias são seguras e eficazes conquanto resultem em complicações pós-operatórias temporárias e proporcionem resultados altamente satisfatórios no que diz respeito ao controle das convulsões.

Palavras-chave
- ilha de reil
- córtex insular
- epilepsia refratária
- procedimentos ressectivos

Introduction

Surgical resection of the insula (insulectomy) is a procedure used for brain lesions and for refractory epilepsy. However, performing this procedure requires a detailed anatomical knowledge of the insula and its surroundings, since its location corresponds to the only cortical region of the brain not visible on the dorsolateral surface of the cerebral hemispheres, which justifies its difficult surgical access and the need of excellent preoperative planning and surgical skills.[1,2]

There are two types of surgical techniques to approach the insular cortex and perform a total or partial insulectomy: transsylvian and transcortical. Both types of surgical techniques are also associated and combined with other resections of different anatomical locations when needed and, therefore, create different terminologies like operculoinsulectomy (operculum and insula), orbitoinsulectomy (pars orbitalis and insula), or insulectomy plus lobectomy (resection of a brain lobe, for example). In addition, these approaches to the insula are usually associated with good seizure control and acceptable morbidity; nevertheless, it also depends on the histology and location of the lesion.[3,4] Besides seizure control, a successful surgical procedure aims to provide a positive impact on quality of life.

The knowledge of the insular anatomy, its functions and the clinical presentation of the seizures arising from this location is important for the surgical treatment.

Anatomy of the Insula

The insula, also known as the fifth cerebral lobe, can be described as an external shield of a true brain bloc of anatomically well-defined structures, which is arranged, from lateral to medial, as follows: insular cortex, extreme capsule, claustrum, external capsule, lentiform nucleus, internal capsule, and thalamus.[5,6]

This lobe, unlike the others, is located in the depth of the lateral sulcus, totally covered by the temporal and frontoparietal opercula, which potentially makes the surgical access more difficult, since, to visualize it, it is necessary to dissect the sylvian fissure and retract the opercula or go transcortical. Only then, the characteristic triangular shape of the insula and the periinsular sulci, which are the anatomical landmarks that separate and distinguish it from the surrounding cortical areas, can be recognized (►**Fig. 1**).[1,7–9]

On the insular surface, there are three short gyri (anterior, middle, and posterior – divided by the anterior and precentral insular sulci), two long gyri (anterior and posterior – divided by the postcentral insular sulcus) and, very often, two additional gyri situated cranially, called transverse and accessory insular gyrus. The short and long gyri are separated from each other by the central insular sulcus (►**Fig. 1**), which divides the insula into two portions, anterior and posterior, which are connected, to the frontal and temporoparietal lobes, respectively. Finally, the insula is delimited by the anterior, superior, and inferior

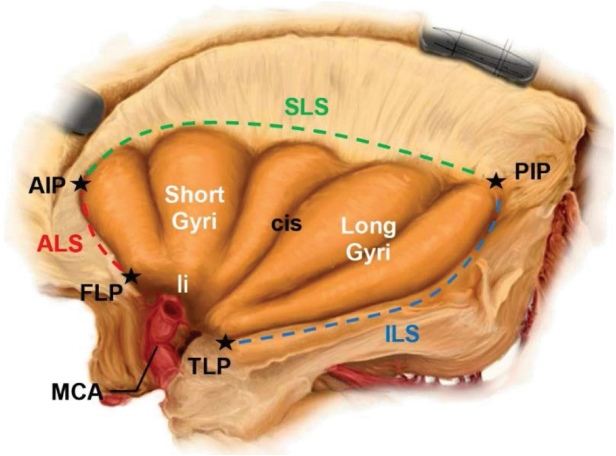

Fig. 1 Representative illustration of the insular cortex and its main anatomical landmarks; the short and long gyri (separated by the central insular sulcus); the anterior, superior, and inferior limiting sulci and, at the anterobasal portion of the insula, the region of the limen (where the sphenoidal segment of the middle cerebral artery bifurcates into M2). Abbreviations: AIP, anterior Insular point; ALS, anterior limiting sulcus; CIS, central Insular sulcus; FLP, frontal limen point; ILS, inferior limen sulcus; LI, limen insulae; MCA, middle cerebral artery; PIP, posterior Insular point; SLS, superior limiting sulcus; TLP, temporal limen point.

limiting sulci, which is also called periinsular sulcus or circular sulcus of the insula.[8,10,11]

Also considered an important anatomical landmark, located in the most anterobasal portion of the insula, is the limen, corresponding to the level at which the middle cerebral artery (MCA) bifurcates into the M2 branches, laterally to the anterior perforated substance (►**Fig. 2**).[8,10,11]

Vascularization of the Insula

The vascular supply to the insula comes from the MCA. The first segment of the MCA is referred to as sphenoidal, or M1, and arises from the ramification of the internal carotid artery (ICA) at the level of the anterior perforated substance, situated superiorly. The lenticulostriate arteries that arise

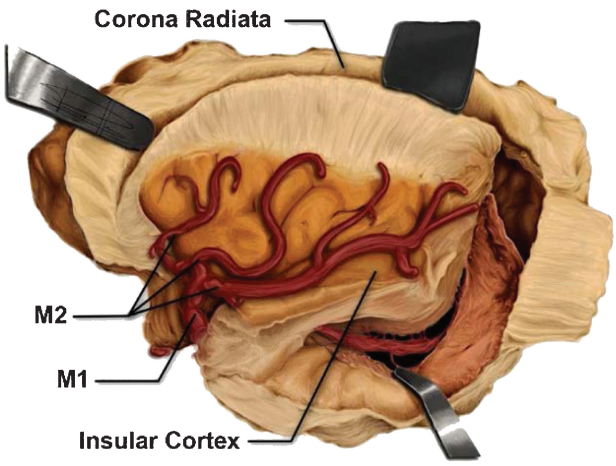

Fig. 2 Illustrative representation of the insular lobe and its adjacent structures, depicting the M1 and M2 branches of the middle cerebral artery (MCA). M1 = M_1 segment of MCA; M2 = M_2 segment of MCA. Source: Ribas et al.[11]

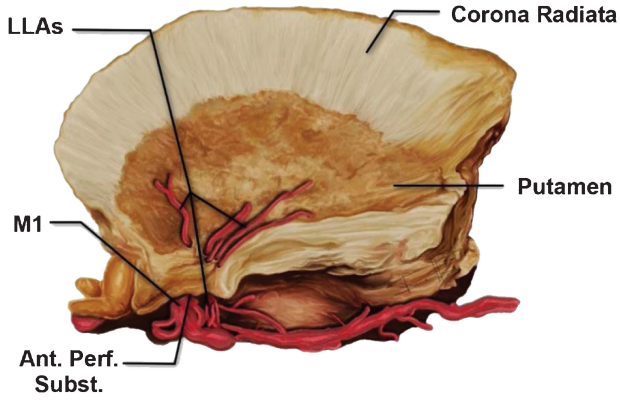

Fig. 3 Illustration representing a lateral view of lateral lenticulostriate arteries (arising from the sphenoidal segment of the middle cerebral artery) crossing the anterior perforated substance and later the lentiform nucleus, after resection, from medial to lateral, of the following structures: Insular cortex, extreme capsule, claustrum, and external capsule. Abbreviations: Ant.Perf.Subs., anterior perforated substance. Source: Ribas et al.[11]

at the M1 level are extremely important perforators that supply the basal ganglia and the internal capsule. These small arteries should be preserved during surgery at this location to avoid neurological deficits.[8,10]

At the level of the limen, the M1 (insular segment) branches into M2 segments, one superior and the other inferior, supplying the short and long gyri, respectively. The M2 segment is also important because the long perforating branches projecting superiorly and posteriorly irrigate the corona radiata and, therefore, should be preserved during surgery to prevent ischemic injury resulting in hemiparesis.[8,10,12–14]

The vascularization of the insula can be seen in more detail in ►**Figs. 2**, **3** and **4**.

Functions of the Insula

The function of the insula is not completely understood, probably because there are no isolated insular lesions to

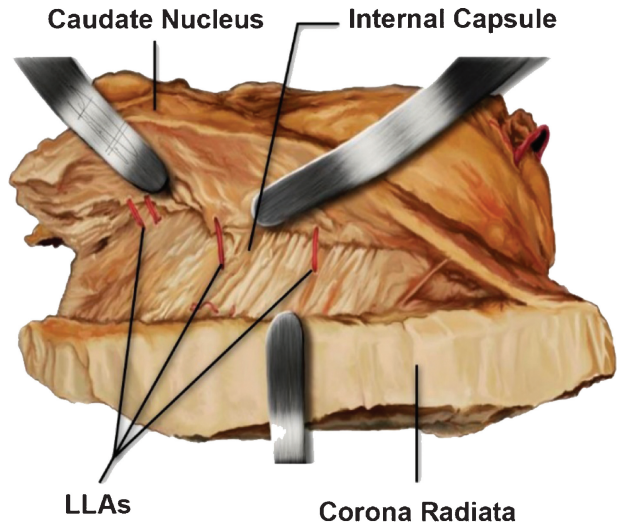

Fig. 4 Illustration representing a superior view of lateral lenticulostriate arteries crossing the internal capsule, with the caudate nucleus medially and, laterally, the internal capsule, after its resection through the sagittal plane. LLAs = lateral lenticulostriate arteries. Source: Ribas et al.[11]

better understand its neurological deficits.[15] However, there is consistent evidence that this lobe is involved in cognitive functions as well as in sensorimotor and socioemotional processing.

The insular functions related to sensorimotor processing are associated to visceral sensations, autonomic control, interoception, somatic, pain and auditory processing, and vestibular and chemosensory functions. The socioemotional processing functions are related to emotional experience, empathy, and risky decision-making. Finally, the cognitive functions are associated mainly to attention and speech.[8,9,15,16] In summary, the insula contributes to multiple cognitive and critical functions for human beings and is considered a part of the limbic cortex.

Connectivity

The insula has reciprocal connections with various regions of the brain. The most important insular networks are with the orbitofrontal, anterior cingulate, supplementary motor areas, the parietal and temporal cortex, as well as with subcortical structures, which explains its involvement in many cognitive functions.[9] These connections can be seen in ►**Fig. 5**, a reproduction of an image by Shelley et al.[17]

Semiology of Insular Epilepsies

Since the insula establishes several reciprocal connections with various cortical and subcortical areas of the brain, the semiology of seizures is characteristically heterogeneous, presenting many differences regarding the manifestation of symptoms and clinical signs. The most important types of seizure manifestation involve viscerosensory, somatosensory, olfactory, gustatory, auditory, and tonic clonic presentation, as well as changes in heartbeat pattern, vomiting, abnormal self-motor or hypermotor behaviors, and language disorders.[14,18,19]

By analyzing the presence and evolution of clinical symptoms that occur during the development of an ictal discharge inside the insular lobe, it is noted that seizures can arise from any part of the insula, therefore spreading to adjacent opercula regions.[18]

Historically, insular epilepsy has been and still is considered difficult to investigate; therefore, diagnosis, workup, and assessment can take a long time for these patients. Furthermore, insular epilepsy mimics symptoms of frontal and temporal seizures, as well as other types.[14,18,20,21] Because of this cluster of symptoms and signs, a thorough analysis and assessment is usually performed, especially regarding the history of the seizures and the auras, since insular and operculoinsular seizures with preserved consciousness are characteristically associated with asphyxia, painful sensations, and taste auras.[14,22]

Finally, when insular epilepsy is drug resistant, the resection of the epileptogenic area usually correlates with good to excellent seizure control over time. Also important is the use of invasive electroencephalography (EEG) monitoring when needed to better understand the size and right topography of the epileptogenic area and the seizure dissipation pattern. Therefore, the surgical resection is tailored for each patient and surgical approach performed.[14,18,23]

Methods

Study design and patients: Retrospective review of 10 patients submitted to either transsylvian or transcortical

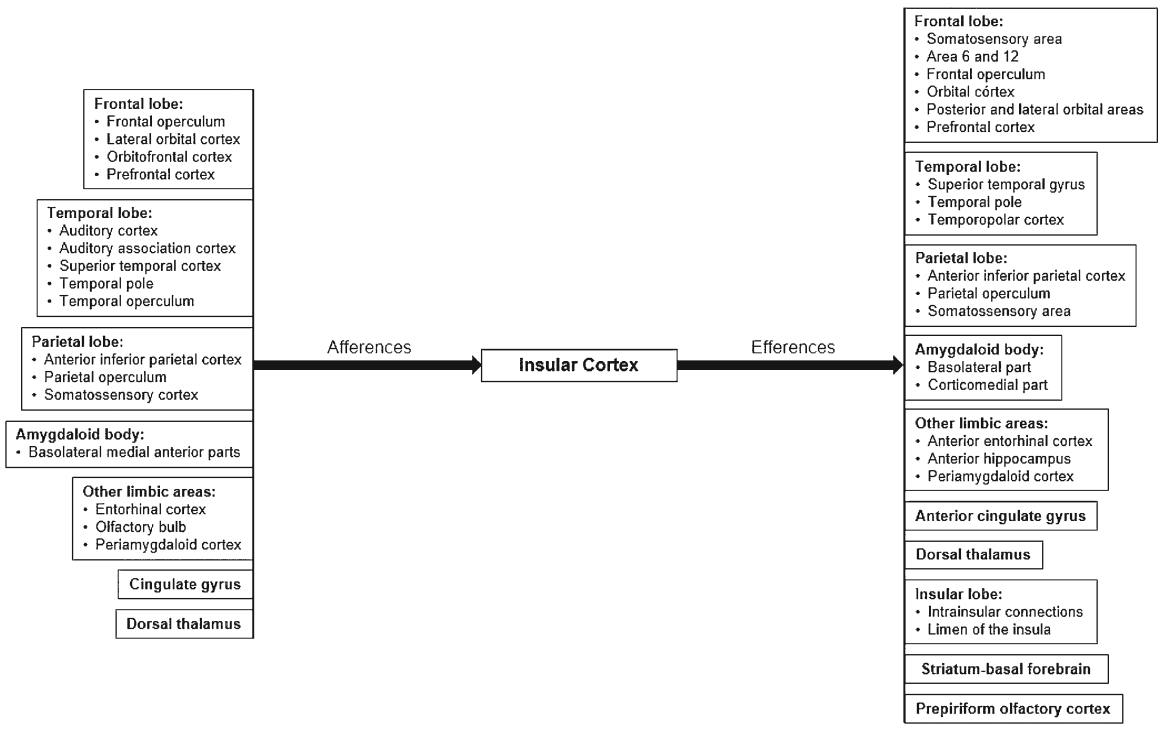

Fig. 5 Insular cortex connections with afferent and efferent projections. This image was reproduced from Shelley et al.[17]

insular resection procedures for refractory epilepsy for insular lesions. For all patients, medical history, semiology and frequency of the seizures, neurological status, magnetic resonance imaging (MRI) findings, and electrophysiological studies were recorded during the pre- and postoperative periods.

Preoperative procedure: All patients underwent preoperative epilepsy workup assessment. The anatomy and function of the insula were also described and reviewed in the context of the surgical approach description. These patients were operated on by the senior author of the present article.

Surgery and histopathology: For all procedures, intraoperative ultrasonography, neuronavigation, ultrasonic aspirator, and intraoperative neurophysiological monitoring (IONM) were used. Either a transsylvian approach for the left insula or a transcortical approach for the right insula was performed. Despite the approach utilized, tumor resection was performed aiming for gross total resection (GTR). Gross total resection was not feasible due to the high risk for neurological deficits. An extension of the resection was performed to remove the rim of the insular cortex or the epileptogenic surrounding area to achieve seizure control.

Follow-up

All patients were classified preoperatively according to the epilepsy classification by Engel and during the regular follow-ups (FUs). To describe the overall results, the last available outcome was used. Follow-up information regarding seizure reduction and neurological status was obtained from the regular outpatient appointments. The present study began in February 2014 and ended in August 2019. Patients were followed-up, on average, for 27 months.

Results

All 10 patients were right-handed and were left hemisphere-dominant. The mean age was 42.5 years old and there were 6 women and 4 men. The mean FU time was 27.2 months. All patients were Engel IV preoperatively and, after surgery, seven of them became Engel II regardless of the surgical approach, either transsylvian or transcortical, during the FU. Three patients during the study became Engel III (patients 1, 6, and 9). The baseline condition or anatomopathological diagnosis did not correlate with worse or better outcomes regarding seizure control. Regarding postoperative complications, there was a case with permanent hemiplegia in a patient with glioblastoma who died at 12 months of FU, a wound dehiscence with cerebrospinal fluid (CSF) fistula in the same patient, and another deceased patient at 13 months of FU also with a glioblastoma (►**Table 1**).

An awake transsylvian approach was the choice for six patients whose lesions were on the left hemisphere, whereas the transcortical approach was used for the remaining four patients whose lesions were on the right insula (three awake and one asleep). For 6 patients, a subtotal resection (STR) (between 90 and 95%) was performed, and for the remaining 4, a partial resection (PR) (< 90%) was achieved. Gross total resection (> 95%) was not achievable due to the high risk for

Table 1 Case series of Insulectomy

Case No.	Age (years old), gender	Race	Dominance	Preoperative (Engel class)	Pathology, side	Surgical approach	Resection	Postoperative (Engel class)	Complications	Follow-up and survival
1	55, F	Black	Left	IV	Glioblastoma, L	Transsylvian, awake	Partial	II	Permanent hemiplegia	Death after 12 mos
2	43, F	Black	Left	IV	Oligodendroglioma, L	Transsylvian, awake	Subtotal	II	—	19 mos
3	34, F	White	Left	IV	Grade II astrocytoma, R	Transcortical, sleep	Subtotal	II	—	22 mos
4	54, M	White	Left	IV	Oligodendroglioma, L	Transsylvian, awake	Partial	II	—	46 mos
5	19, F	Yellow	Left	IV	Cortical dysplasia, R	Transcortical, sleep	Subtotal	II	—	34 mos
6	53, M	White	Left	IV	Glioblastoma, L	Transsylvian, awake	Partial	II	—	Death after 13 mos
7	44, F	Black	Left	IV	Ganglioglioma, L	Transsylvian, awake	Subtotal	II	—	21 mos
8	32, M	White	Left	IV	Oligodendroglioma, L	Transsylvian, awake	Partial	II	—	11 mos
9	37, M	Black	Left	IV	Grade II astrocytoma, R	Transcortical, awake	Subtotal	II	CSF fistula	34 mos
10	54, F	White	Left	IV	Ganglioglioma, R	Transcortical, sleep	Subtotal	II	—	60 mos

Abbreviations: CSF, cerebrospinal fluid; F, female; L, left; M, male; mos, months; No, number; R, right.

neurological deficits. Seizure control was better for all patients except for the ones with glioblastomas, possibly due to the more aggressive behavior of the condition (►**Table 1**).

Discussion

From 2009 to 2017, 5 searched articles about insular epilepsy reported the results of 82 patients submitted to lesionectomies plus an insular approach aiming for seizure control (►**Table 2**). The results showed a significant improvement in seizure control after surgery in all studies. Von Lehe et al.[24] presented his results according to the ILAE (International League against Epilepsy) classification. They were able to show that 15 out of 24 patients were seizure free (ILAE 1), 4 patients were classified as ILAE 2 and 3; and the remaining 5 patients were class 5 postoperatively. The reported rate of complications was similar to that of our study, including hemiparesis, hemi hypoesthesia, and hemianopia as permanent complications, and hemiparesis and dysphasia as temporary complications. Intraoperative neurophysiological monitoring was used in 50% of the cases and there were no glioblastomas in this study.[24] Boucher et al.[25] did not classify their patients according to the seizure frequency after insulectomies; however, they described that the 18 patients analyzed presented a general improvement regarding epilepsy control. In this study, arm, tongue, and cheek hypoesthesia, and foot dysesthesia were presented as permanent complications, and transient hemiparesis, transient aphasia, and transient brachyfacial paresis were presented as temporary complications. They have also reported that 11 cases (61.2%) presented postoperative subcortical ischemic infarcts related to injuries to perforating branches (mainly of M2).[25] The remaining three other studies classify results according to the Engel classification. In a small study, Park et al.[26] reported excellent results showing that 5 cases (83.4%) became Engel I and 1 patient (16.6%) became Engel II after surgery. They did not describe any complications.[26] In their study, Malak et al.[27] also showed excellent outcomes, with 9 patients (100%) becoming Engel I after insulectomy. They reported hemiparesis and dysphasia as complications.[27] Bouthilier et al.[3] also reported excellent outcomes in their work, showing that 20 (80%) patients achieved Engel class I, 3 (12%) Engel class II, and 1 (4%) Engel class III. As complications, the study reported permanent decrease in oromotor speed and transient hemiparesis, transient dysphasia, hyperosmia, facial asymmetry, alteration of taste, altered pain and thermal sensation, hyperacusis, and postural tremor as temporary complications.[3]

Lesions located in the nondominant hemisphere are usually resected under general anesthesia with IONM, whereas lesions located in the dominant side may require an awake procedure to map language areas and minimize deficits. The inferior frontal and superior temporal gyri and the inferior occipitofrontal (IFOF) and arcuate fascicles (AFs), which project along the subcortical region of the insula, are important white matter tracts on the left hemisphere and should be preserved if possible to avoid language deficits. In addition, stimulation of the dorsal stream, typically performed by the AF, leads to speech apraxias, phonological paraphasias, and repetition disorders, while stimulation of the ventral stream, performed by the IFOF, leads to semantic paraphasia.[12,28,29]

Prybylowski et al.[4] compared the surgical morbidity of 52 patients submitted to the transsylvian approach with 48 patients operated on by the transcortical approach for glioma resection. The results suggest that both techniques are associated with equivalent and reasonable morbidity profiles, even though gliomas located within the superior-posterior quadrant of the insula are usually considered for a transcortical approach. To date, however, there are no objective and clear criteria that guide the conduct of neurosurgeons to adopt one technique over the other. In fact, most studies reflect a preference for one technique rather than the other based on subjective criteria, such as the historical preference of the institutions themselves and/or personal tendencies of professionals.[4]

Characteristically, the transopercular approach (►**Fig. 6**) involves the creation of "cortical windows" above or below the sylvian fissure, through nonfunctional cortical areas of the operculum (by subpial dissection) to avoid blood vessel coagulation and ensure better exposure of the insular cortex. The transsylvian technique (►**Fig. 7**), developed by Yaşargil, on the other hand, guarantees an alternative strategy, using a natural corridor provided by the sylvian fissure. One of the major advantages of this technique is the ability to identify and control vascular structures during surgical resection, such as the MCA (and its branches) and the lenticulostriate arteries. However, this approach is frequently associated with surgical manipulation of superficial plus perisylvian vessels and, along with opercular retraction, potentially increases the risks of postoperative deficits and of vascular injury or spasm.[3,4,28,30–32]

The main postoperative complications were hemiparesis and worsening of previous neurological motor and visual deficits (hemianopsias) (►**Table 1**). Different hypotheses may explain the occurrence of these complications; however, it is important to remember that the insula plays an associative/nonessential role in gustation, olfaction, memory, drive, sympathetic control of cardiovascular tone, somatosensory input and pain processing, motor planning, and language.[12,13,15,27,30,33] Hence, transient postoperative deficits may reside in the interruption of motor and/or linguistic functions of the insula during surgery or in the shrinkage of the operculum, being subsequently compensated and even fully recovered due to a secondary nature of the insular cortex in performing these functions, while permanent postoperative deficits would be much more associated with the manipulation of the lenticulostriate arteries or with injury causing deep strokes, for example. (►**Figs. 3** and **4**).[19,27,34]

The lateral lenticulostriate arteries (LLAs) have particular importance because the vertical plane formed by their course corresponds to the medial limit of resection in insulectomies. The LLAs supply blood flow to the lentiform nucleus and the internal capsule. Furthermore, early dissection of the proximal M1 segment allows the neurosurgeon to follow and identify the LLAs, which originate precisely from the M1 segment as it runs inferiorly through the anterior perforated

Table 2 Review of Insulectomy case series reported in the literature since 2009[3,24–27]

Authors and Year	Patients (*n*)	Mean age (years old)	Preoperative symptoms	Surgical approach	Postoperative complications	Mean follow-up	Outcome/ seizure outcome	Pathology
von Lehe et al., 2009[24]	24	27 (1–62)	Viscerosensory, emotional and nonspecific sx (including the experience of fear)	*n* = 7: partial insulectomy with or without lobectomies *n* = 17: total insulectomy with or without lobectomies **Obs:** Transsylvian app for strictly insular lesions and temporoinsular lesions; transcortical app for temporoinsular and frontoinsular lesions; transsylvian and transcortical app in some patients with strictly insular lesions and frontotemporoinsular lesions.	**Permanent morbidity:** *n* = 1: increased hemiparesis *n* = 1: hemi hypoesthesia *n* = 2: hemianopia **Temporary morbidity:** *n* = 1: hemiparesis and dysphasia *n* = 1: hemiparesis **Other complications:** *n* = 1: aseptic inflammatory meningeal response	37.5 months (12–168 months)	Seizure outcomes according to ILAE classification: *n* = 15: Class 1 *n* = 2: Class 2 *n* = 2: Class 3 *n* = 5: Class 4	*n* = 2: cavernoma *n* = 2: DNT (WHO grade I) *n* = 3: gliosis *n* = 5: other gliomas (WHO grades II–III) *n* = 6: ganglioglioma (WHO grade I) *n* = 6: cortical dysplasia
Park et al., 2009[26]	6	4.2 (4–7 years)	unspecified	**Pt.1**: total insulectomy **Pt.2**: frontal and temporal lobectomy and total insulectomy **Pt.3**: hemispherectomy and total Insulectomy **Pt.4**: frontal lobectomy and partial insulectomy **Pt.5**: frontal lobectomy and partial insulectomy **Pt.6**: temporal lobectomy and partial insulectomy	none	17.8 months (6–33 months)	Seizure outcomes according to the Engel classification: **Pt.1,2,3,4,6**: Class I **Pt.5**: Class II	**Pt.1**: cortical dysplasia **Pt.2**: could not be diagnosed **Pt.3**: could not be diagnosed **Pt.4**: cortical dysplasia **Pt.5**: hypertrophic astrocyte **Pt.6**: microdysgenesis
Malak et al., 2009[27]	9	29.4 (16–36)	Somatosensory, viscerosensory, and somatomotor sx; paresthesia; throat constriction; tonic posturing; nausea; dysphasia	**Pt.1**: temporal lobectomy and partial (ant) insulectomy **Pt.2**: partial (post) insulectomy **Pt.3**: frontal lobectomy and total insulectomy **Pt.4**: frontal, parietal, and temporal operculoinsulectomy **Pt.5**: frontal operculoinsulectomy **Pt.6**: temporal lobectomy and total insulectomy **Pt.7**: frontal and parietal operculoinsulectomy **Pt.8**: total insulectomy **Pt.9**: partial insulectomy	**Trans increase of dysphasia:** *n* = 1 **Trans hemiparesis (or increase):** *n* = 4	54 months (14–122 months)	Engel Class I was achieved in all patients **Obs:** one patient had an Engel Class III outcome after partial insulectomy but later became seizure-free (Engel Class I) following insular gamma knife surgery	*n* = 2: tumor associated with seizures *n* = 7: refractory epilepsy with no tumor
Boucher et al., 2015[25]	18	35 (22–52)	Cognitive impairments; hemiparesis	*n* = 1: insulectomy and lobectomies *n* = 2: operculoinsulectomy and lobectomies *n* = 5: insulectomy *n* = 10: operculoinsulectomy **Obs:** *n* = 2: partial (inferior) insulectomy *n* = 3: total insulectomy *n* = 4: partial (post) insulectomy *n* = 9: partial (ant) insulectomy	**Permanent morbidity:** *n* = 1: arm, tongue, and cheek hypoesthesia and foot dysesthesia **Temporary morbidity:** *n* = 3: trans hemiparesis (or increase) *n* = 3: trans aphasia *n* = 1: trans brachyfacial paresis and/or: trans depression, hyperosmia, facial asymmetry, altered pain and thermal sensation, etc. **Obs**: 11/18 postop subcortical ischemic infarcts related to injury of perforating branches (mainly of M2)	21.8 months (5–142 months)	General improvement of seizures in all patients, as well as equivalent pre- and postoperative neurophysiological results	*n* = 1: tuberous sclerosis *n* = 1: congenital encephalomalacia *n* = 2: hippocampal sclerosis *n* = 4: cortical dysplasia

(*Continued*)

Table 2 (*Continued*)

Authors and Year	Patients (*n*)	Mean age (years old)	Preoperative symptoms	Surgical approach	Postoperative complications	Mean follow-up	Outcome/ seizure outcome	Pathology
Bouthilier et al., 2017[3]	25	35 (9–51 y)	Somatosensory and viscerosensory sx; auditory, gustatory, and olfactory sx; throat constriction	*n* = 1: operculoinsulectomy and frontal lobectomy *n* = 2: operculoinsulectomy and orbitofrontal resection *n* = 2: insulectomy *n* = 4: operculoinsulectomy and temporal lobectomy *n* = 16: operculoinsulectomy	**Permanent morbidity:** *n* = 1: decrease in oromotor speed **Temporary morbidity:** *n* = 5: trans hemiparesis (or increase) *n* = 5: trans dysphasia and/or: trans depression, hyperosmia, facial asymmetry, alteration of taste, postural tremor, altered pain and thermal sensation, hyperacusis etc.	56.4 months (12–192 months)	Seizure outcomes according to Engel classification: *n* = 20: Class I *n* = 3: Class II *n* = 1: Class III *n* = 1: sudden unexpected death 3 months after insulectomy	**Inside operculoinsular area:** *n* = 1: tuberous sclerosis *n* = 1: encephalomalacia *n* = 5: cortical dysplasia **Outside operculoinsular area:** *n* = 1: tuberous sclerosis *n* = 3: atrophy/ encephalomalacia *n* = 5: hippocampal sclerosis

Abbreviations: ant, anterior; app, approach; ILAE, International League against Epilepsy; mo, months; Obs, observation; post, posterior; postop, postoperative; preop, preoperative; pt, patient; sx, symptom; trans, transient; WHO, World Health Organization; yrs., years.

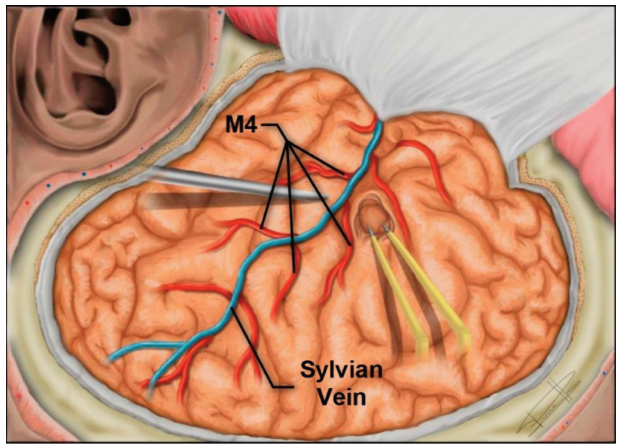

Fig. 6 Illustration of the transcortical approach for resection of the insular cortex – by subpial dissection of the operculum between the M4 branches of the middle cerebral artery. M4 = M_4 segment of the MCA.

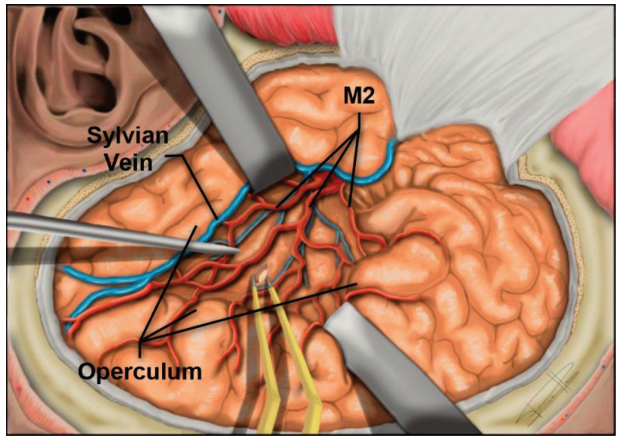

Fig. 7 Illustration of the transsylvian approach for resection of the insular cortex, allowing to observe the divisions of the M2 trunks. M2 = M_2 segment of MCA.

substance and up to the region of the limen insulae. From this point, the M1 bifurcates into M2 segments (►**Fig. 1B**), whose branches originate the short and long perforating arteries that supply the insular cortex and the corona radiata, respectively. For this reason, is important to preserve the long perforating branches to avoid ischemic lesions and motor deficits.[12,13,35,36]

Conclusions

Surgical resection of insular lesions can be a challenge regarding the extent of resection and maintaining quality of life with minimal neurological deficits. The present case series presented results comparable with the most recent ones in the literature in terms of seizure control, life expectancy, and quality of life. Despite complications associated with these procedures, in general, the benefits outweigh the risks since, for many patients, the natural history of the baseline condition could be more devastating, thus reinforcing surgical indication. Finally, it is paramount to better understand the insular surgical anatomy when performing

a procedure in this complex region. The utilization of modern microsurgical techniques, ultrasound, neuronavigation, and specially IONM, are important to prevent neurological deficits. Insulectomies can be performed in the context of achieving not only oncological resection but also to accomplish seizure reduction by adding to the lesion resection an extension to include the epileptogenic surrounding cortex.

Conflict of Interests

The authors have no conflict of interests to declare.

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Endoscopic Third Ventriculostomy in the Pediatric Population: Case Series Report*

Terceiro ventriculostomia endoscópica na população pediátrica: Relato de série de casos

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Abstract

Objective Hydrocephalus is characterized by multi- or uniloculated ventricular dilatation, and there are differences between the etiology and therapeutic response of each type. Endoscopic third ventriculostomy (ETV) is indicated for the treatment of obstructive hydrocephalus, with a reported efficacy between 50% and 76%. Reduced efficacy of the procedure has been demonstrated in communicating hydrocephalus due to multifactorial pathogenesis, and, in patients with myelomeningocele, its efficacy ranges from 15% to 20% at birth. The present study aims to compare the efficacy of ETV in the treatment of congenital obstructive hydrocephalus (COH) and acquired obstructive hydrocephalus (AOH) in the pediatric population.

Methods A retrospective study of 169 endoscopic surgeries performed by the senior author in two institutions, one public (Hospital João XXIII, Belo Horizonte, Minas Gerais) and another private (Hospital Felício Rocho, Belo Horizonte, Minas Gerais), in the period from 2003 a 2020. From the selection of 169 patients, only 77 cases fit the age profile $\leq$12 years of the present study. Of these, 46 were male, and the age range ranged from 10 days to 12 years. The study included multiple etiologies, which were divided into 2 groups, 34 related to COH, and 43 to AOH.

Results Regarding the cases of COH, 22 were submitted to ETV as the main treatment, with 14 (63.63%) effective and 8 (36.36%) ineffective procedures. As for

Keywords
- hydrocephalus
- therapy
- ventriculostomy
- pediatric
- management

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the cases of AOH, 13 patients underwent ETV, and 8 (61.53%) procedures were effective, and 5 (38.46%), ineffective.
Conclusions Through the calculation of the *p*-value of 0.49, we concluded that it cannot stated that the efficacy of ETV is greater in COH than in AOH.

Resumo

Objetivo A hidrocefalia é caracterizada por dilatação ventricular multi ou uniloculada, e há diferenças entre a etiologia e a resposta terapêutica de cada tipo. A terceiro ventriculostomia endoscópica (TVE) está indicada no tratamento da hidrocefalia obstrutiva, com uma eficácia relatada entre 50% e 76%. O procedimento demonstrou eficácia reduzida em hidrocefalia comunicante devido à patogênese multifatorial, sendo que, em pacientes com mielomeningocele, sua eficácia é de 15% a 20% no nascimento. Este estudo visa comparar a eficácia da TVE no tratamento da hidrocefalia obstrutiva congênita (HOC) e hidrocefalia obstrutiva adquirida (HOA) na população pediátrica.
Métodos Realizou-se um estudo retrospectivo de 169 cirurgias endoscópicas realizadas pelo autor sênior em duas instituições, uma pública (Hospital João XXIII, Belo Horizonte, Minas Gerais) e outra privada (Hospital Felício Rocho, Belo Horizonte, Minas Gerais), no período de 2003 a 2020. Da seleção de 169 pacientes, apenas 77 casos se enquadraram no perfil de idade $\leq$12 anos do presente estudo. Destes, 46 eram do sexo masculino, e a faixa etária variou de 10 dias a 12 anos. O estudo contemplou múltiplas etiologias, que foram divididas em 2 grupos, sendo 34 relacionadas à HOC, e 43, à HOA.
Resultados Entre os casos de HOC, 22 foram submetidos a TVE como tratamento principal, sendo que 14 (63,63%) procedimentos foram eficazes, e 8 (36,36%), ineficazes. Já entre os casos de HOA,13 pacientes foram submetidos a TVE, sendo 8 (61,53%) procedimentos eficazes, e 5 (38,46%), ineficazes.
Conclusões Por meio do cálculo do valor de *p* de 0,49, concluiu-se que não se pode afirmar que a eficácia da TVE é maior nas HOCs do que nas HOAs

Palavras-chave
- hidrocefalia
- terapia
- ventriculostomia
- pediátrico
- manejo

Introduction

Hydrocephalus is a disease that can be characterized by multi- or uniloculated ventricular dilatation, and there are significant differences between the etiology and therapeutic response of each type.[1] Endoscopic third ventriculostomy (ETV) is indicated for the treatment of hydrocephalus related to obstructive mechanisms, with a reported efficacy rangong from 50% to 76%. Reduced efficacy has been shown in communicating hydrocephalus due to multifactorial pathogenesis, and, in patients with myelomeningocele, its efficacy ranges from 15 to 20% at birth.[2] The present study aims to compare the efficacy of ETV in the treatment of congenital obstructive hydrocephalus (COH) and acquired obstructive hydrocephalus (AOH) in the pediatric population.

Methodology

We conducted a retrospective study of 169 endoscopic surgeries performed by the senior author in two institutions, one public (Hospital João XXIII, Belo Horizonte, Minas Gerais, Brazil) and one private (Hospital Felício Rocho, Belo Horizonte, Minas Gerais, Brazil), from 2003 to 2020. Patients aged $\leq$ 12 years were selected. We excluded cases of communicating hydrocephalus, or those in which, besides the ETV, additional procedures were performed, such as septostomies or tumor biopsies. Thus, only 77 cases were selected for research analysis.

Results

Out of the 77 cases found, 34 were of COH, and 43 were of HOA. Regarding the cases of COH, 22 underwent ETV as the main treatment, with 14 (63.63%) effective and 8 (36.36%) ineffective procedures. As for the cases of AOH, 13 patients were submitted to ETV, and 8 (61.53%) procedures were effective and 5 (38.46%), ineffective. Through the calculation of the *p*-value of 0.49, we concluded that it cannot be stated that the efficacy of ETV is greater in COH than in AOH.

Case Flowchart

►Fig. 1.

Discussion

An analysis of 158 children under the age of 2 was performed by The International Infant Hydrocephalus Study,[4] and the authors found that the shunt was more successful than ETV.

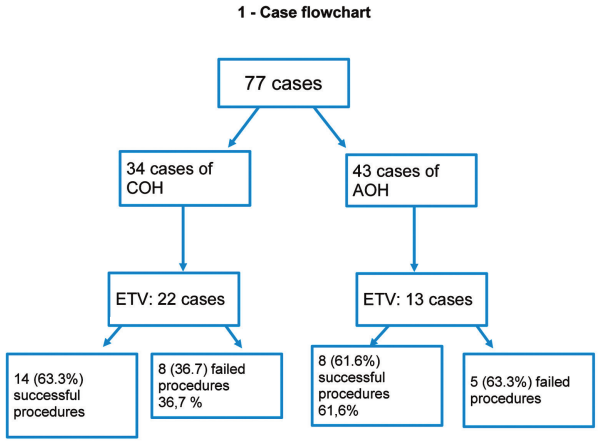

Fig. 1 Case flowchart: Of the 77 patients with hydrocephalus, 34 had congenital obstructive hydrocephalus (COH) and 43 had acquired obstructive hydrocephalus (AOH). Of the 34 cases of COH, 22 patients underwent endoscopic third ventriculostomy (ETV), with a success rate of 63.3% (14 patients). As for the cases of AOH, 13 patients underwent ETV, with 61.6% of effectiveness (8 cases). We excluded cases in which other procedures associated with the ETV had been performed, such as intraventricular drain (IVD) placement, septostomies, tumor biopsies, or choroid plexus coagulation.

Actual comparisons of the outcomes of pediatric patients submitted to long-term peritoneal ventricle shunt and ETV have not been made yet, because the studies are often limited by a retrospective design and relatively heterogeneous patients. If we evaluate the results of ETV throughout time and the effects of the shunt in the treatment of infant hydrocephalus, it is clear that aqueductal stenosis has a high efficacy and results in good quality of life for the patients, with no differences in the comparison of patients initially treated through ETV or shunt.[3,4]

The study by Kulkarni et al. indicates that the ETV Success Score (ETVSS) increases with age. If we compare the ETVSS with the success rate of the peritoneal shunt, the former has less failure with the progression of postoperative days.[3]

Furthermore, in the same literature by Kulkarni et al. it was possible to analyze that, in infants, the ETV failure rate is higher when compared to that of children. However, our study could not conclude information about comparisons of the failure rate of the third ventriculostomy in infants and children, since there was no age division, and the pediatric population was grouped in a filter of less than 12 years. Moreover, this point was not addressed in the study because the objective is to compare the efficacy of TVE in the treatment of congenital obstructive hydrocephalus (COH) and acquired obstructive hydrocephalus (AOH) in the pediatric population. According to Baldauf et al.,[5] the ETVSS in children younger than 2 years of age depends on etiology and age. These authors evaluated 21 patients, and found a ETVSS of 43% in the treatment of COH. In children younger than 2 years of age, the ETVSS was of 37.5%. In contrast, Sufianov et al.[6] evaluated 41 infants and children younger than 2 years of age, and concluded found a ETVSS of 71.4% among children, and of 75% among infants.

To assess the efficacy of the surgery, an evaluation of the need to place a valve a posteriori is required. Therefore, for the evaluation of the patient, we suggest requesting a magnetic resonance imaging (MRI) scan of the brain after three months of longitudinal follow-up. The MRI enables the analysis of the dimensions of the third ventricle, and this is an important test for the definition of the concept of effectiveness. It should be emphasized that the follow-up is individual, using the particularities of the patient's condition to adjust the frequency of consultations. Furthermore, in case of ineffective surgery, the patient must be submitted to placement of the shunt drainage valve.[3,4]

To better elucidate the concepts of efficacy or inefficacy according to the proposed therapy, we provide a brief description of two cases managed by the supervisor of the present work. The first case involved a 5-year-old child with symptoms of intracranial hypertension (headache, vomiting, and papilledema). A computed tomography (CT) scan revealed a triventricular hydrocephalus (3rd and 4th ventricles and the lateral ventricles) due to a possible congenital obstruction of the aqueduct. A third ventriculostomy was performed, which was effective, and implantation of a drain valve was not required.

The other case involved a 10-month-old infant with COH and an arachnoid cyst, resulting in a significant increase in cranial perimeter and bulging fontanel. On endoscopy, an arachnoid cyst was observed obstructing the interventricular foramen, and a septostomy and third ventriculostomy were performed. The cyst was opened, with the possibility of accessing the third ventricle, and the third ventriculostomy procedure could be performed. The procedure was efficient, uneventful, and there was no need for readmission for valve placement. The procedure was efficient, uneventful, and there was no need for read-mission for valve placement.

Conclusion

The study aimed to select 77 individuals from the pediatric range $\leq$ 12 years, evaluating success rate of third ventriculostomy as an innovative procedure for the treatment of hydrocephalus obstructive congenital and acquired obstructive hydrocephalus. With this, the p-value calculation was performed and resulted in 0.49, concluding that it is not possible to state that the effectiveness of TVE is higher in COHs than in AOHs.

Conflict of Interests

The authors have no conflict of interests to declare.

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Traumatic Atlanto-occipital Dislocation in Children Followed by Hydrocephalus – A Case Report and Literature Review

Deslocamento atlanto-occipital em crianças seguido por hidrocefalia – Relato de caso e revisão da literatura

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Abstract

Traumatic atlanto-occipital dislocation (TAOD) are uncommon injuries associated with high immediate mortality rate and occurs more than twice in children than adults, due to biomechanical properties and immaturity of children's cervical spine. We report a pediatric patient with TAOD, who underwent occipitocervical stabilization and also developed a late hydrocephalus requiring a shunt procedure. A six-year-old boy was admitted to the emergency department after a car accident with refractory cervical pain. A cervical computed tomography (CT) scan showed an anterior C1–C2 level hematoma, and a dynamic CT scan demonstrated an increasing basion-dens interval on extension. Cervical magnetic resonance imaging (MRI) showed discontinuity of the tectorial membrane and diffused hyperintense signal on the left alar ligament. These findings were attributed to TAOD, and an occipitocervical fusion was performed. The pain and neurological status improved after surgery, but after 3 months he returned with persistent vomiting, headache, and a CT scan showing hydrocephalus. Then, a ventriculoperitoneal shunt was performed, improving the symptoms. One year after the injury, the patient remained asymptomatic, and a later radiography demonstrated satisfactory bone fusion. In conclusion, the decision-making process regarding treatment should consider several clinical and radiographic findings. Occipitocervical fusion is the treatment of choice, while hydrocephalus is not an unusual complication in children.

Keywords

- atlanto-occipital dislocation
- pediatric spine
- trauma
- hydrocephalus

Resumo

O deslocamento atlanto-occipital (DAO) é uma lesão incomum associada a uma alta taxa de mortalidade imediata que ocorre duas vezes mais em crianças do que em adultos, fato relacionado às propriedades biomecânicas e à imaturidade da coluna cervical pediátrica. Relatamos o caso de um paciente pediátrico com DAO traumático

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submetido à fixação occipitocervical, evoluindo com hidrocefalia e necessidade de um procedimento de derivação liquórica. Paciente do sexo masculino de 6 anos de idade admitido no pronto-socorro após um acidente automobilístico, apresentando dor cervical refratária. A tomografia computadorizada (TC) de coluna cervical demostrou um hematoma epidural ao nível de C1–C2, e a TC dinâmica evidenciou um intervalo basion-odontoide aumentado em extensão. A ressonância magnética (RM) da coluna cervical demonstrou descontinuidade da membrana tectorial e hiperintensidade difusa no ligamento alar esquerdo. Esses achados permitiram o diagnóstico de um DAO, sendo realizada uma fusão occipitocervical. A dor e o status neurológico melhoraram após a cirurgia, mas 3 meses após, o paciente evoluiu com vômitos persistentes, cefaleia e TC de crânio evidenciando hidrocefalia. Em seguida, foi realizada uma derivação ventriculoperitoneal, com melhora dos sintomas. Um ano após, o paciente permaneceu assintomático, e a radiografia demonstrou fusão óssea satisfatória. Em conclusão, o processo de tomada de decisão quanto ao tratamento deve levar em consideração diversos achados clínicos e radiográficos. A fixação occipitocervical é o tratamento de escolha, enquanto a hidrocefalia não é uma complicação incomum em crianças.

Palavras-chave
- deslocamento atlanto-occipital
- coluna vertebral
- trauma
- hidrocefalia

Introduction

Traumatic atlanto-occipital dislocation (TAOD) is a rare injury that is associated with a high mortality rate, since it is frequently related to cardiorespiratory arrest at the trauma scene and severe neurological impairment due to injury of the cervicomedullary junction.[1–3] Traumatic atlanto-occipital dislocation occurs more than twice in children than in adults. This is due to biomechanical properties and the immaturity of the pediatric cervical spine, such as smaller occipital condyles, and a horizontal atlanto-occipital joint, which is less resistant to shear forces.[4,5] Some case series reported that a certain number of children who survive the initial trauma have a positive outcome despite presenting neurological deficits.[6,7]

Because of a wide range of clinical presentations, from a neurologically intact patient to one with cardiac arrest at the emergency department, as well as the association with other traumatic brain injuries, the diagnosis of pediatric TAOD can be delayed or even missed entirely, risking irreversible damage to the upper cervical spinal cord and the brainstem.[8] Determining the stability of the pediatric occipitocervical junction is not always straightforward, given that some patients may present subtle dislocation despite tremendous ligamentous injuries. As a consequence, treatment for less severe cases is not well established, especially in the setting of a normal computed tomography (CT) and only magnetic resonance imaging (MRI) findings.[8]

Additionally, occipitocervical stabilization in children remains a surgical challenge due to small bone dimensions, as well as the regional anatomical complexity, poor occipital bone purchase, significant thinness of the occipital bone, and the lack of instrumentation designed and sized for children.[9] Furthermore, surgical fixation permanently limits upper cervical spine mobility and predisposes to long-term morbidity; thus, it should be reserved for truly unstable injuries.

In the present study, we report a pediatric patient with TAOD who underwent occipitocervical stabilization and also developed a late hydrocephalus requiring a shunt procedure. The diagnosis of TAOD is discussed in detail.

Case Report

A six-year-old boy was admitted to the pediatric emergency department following a car accident, where he was on the backseat wearing a conventional seat belt, and the driver ran off the road and crashed. On admission, he was reporting abdominal pain and had undergone two episodes of emesis. He was otherwise stable, wearing a cervical collar, notifying neck pain. Neurological examination showed evident pyramidal signs, with mild left side weakness. An initial cranial CT scan revealed traumatic subarachnoid hemorrhage, and a cervical CT scan showed an anterior C1–C2 level hematoma (►**Fig. 1**). We performed all the following radiological measurements to diagnose TAOD using a CT scan: Wholey dens-basion interval (DBI),[10] Powers' ratio,[11] Harris' basion-axis interval (BAI),[12] and Sun's interspinous ratio,[13] but all results had normal values (►**Fig. 1**). Additionally, the abdominal CT scan showed a mesenteric rupture, treated non-operatively. He was then admitted to the intensive care unit with cervical immobilization. Despite the analgesic management, the cervical pain was refractory, leading us to perform a dynamic (flexion and extension) cervical CT and a MRI.

On the dynamic CT scan, the vertebral bodies and facet joints remained aligned, except for the increasing distance between the basion and the odontoid process on extension (►**Fig. 2A-B**). The cervical MRI demonstrated a transfixing rupture between the posterior arches of C1 and C2, an anterior arch subluxation with discontinuity of the anterior longitudinal ligament on the medium third of the dens and on the tectorial membrane. The diffuse hyperintense signal on the nuchal ligaments and on the left alar ligament was attributed to a distension/partial

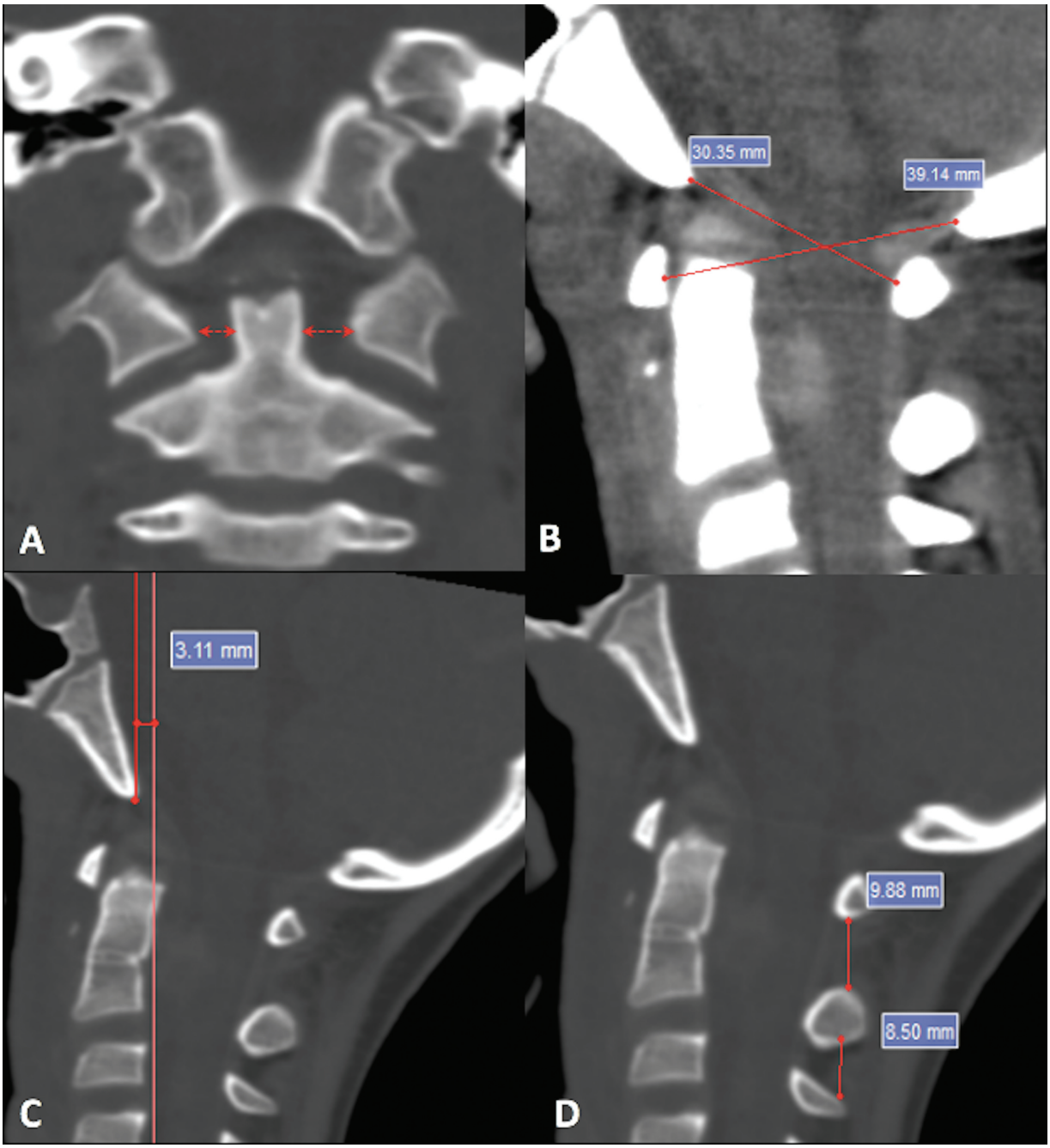

Fig. 1 Admission cervical computed tomography (CT) scan. (**A**) Slightly Left–right asymmetry between the atlas and vertebrae axis in the coronal plane. (**B**) Sagittal CT scans showing a normal Powers ratio measurement (0.79; normal $\leq$ 1), but an epidural collection in the upper cervical canal. (**C**) Normal Harris' basion-axis interval (3.11). The normal distance is between 12 and 0 mm in children. (**D**) Normal Sun'si ratio (1.16). The interspinous ratio is indicative of atlanto-occipital dislocation (AOD) by a C1–C2/C2–C3 ratio of more than 2.5.

lesion (►**Fig. 3A-B**). The transverse ligament was unimpaired as on method (►**Fig. 3C**). Additionally, an epidural hematoma of 1.9 mL was attached to the left anterolateral spine canal. The entirety of the findings allowed us to diagnose the TAOD, despite the near normal CT findings. Based on the exams and clinical presentation, a multidisciplinary case discussion was held, and a decision was made to perform an occipitocervical fusion (OCF).

While under general anesthesia, the patient was prone positioned, the neck was kept neutral using a Mayfield head holder, and the shoulders were retracted caudally. We performed a posterior median incision from the inion to C3. A subperiosteal dissection exposed the squamous part of the occipital bone, the posterior tubercle of C1, and the spinous process of C2, and then the lamina, and the inferior articular process of C2 and the C2–C3 joint. The posterior arch of the C1 was exposed further with some bleeding from the vertebral plexus, controlled by hemostatic agents and bipolar cauterization. We found and drained the epidural hematoma, secondary to the traumatic avulsion of the right C1 nerve root, with a dural injury and a high debit cerebrospinal fluid (CSF) leakage, fixed with a fat graft and fibrin

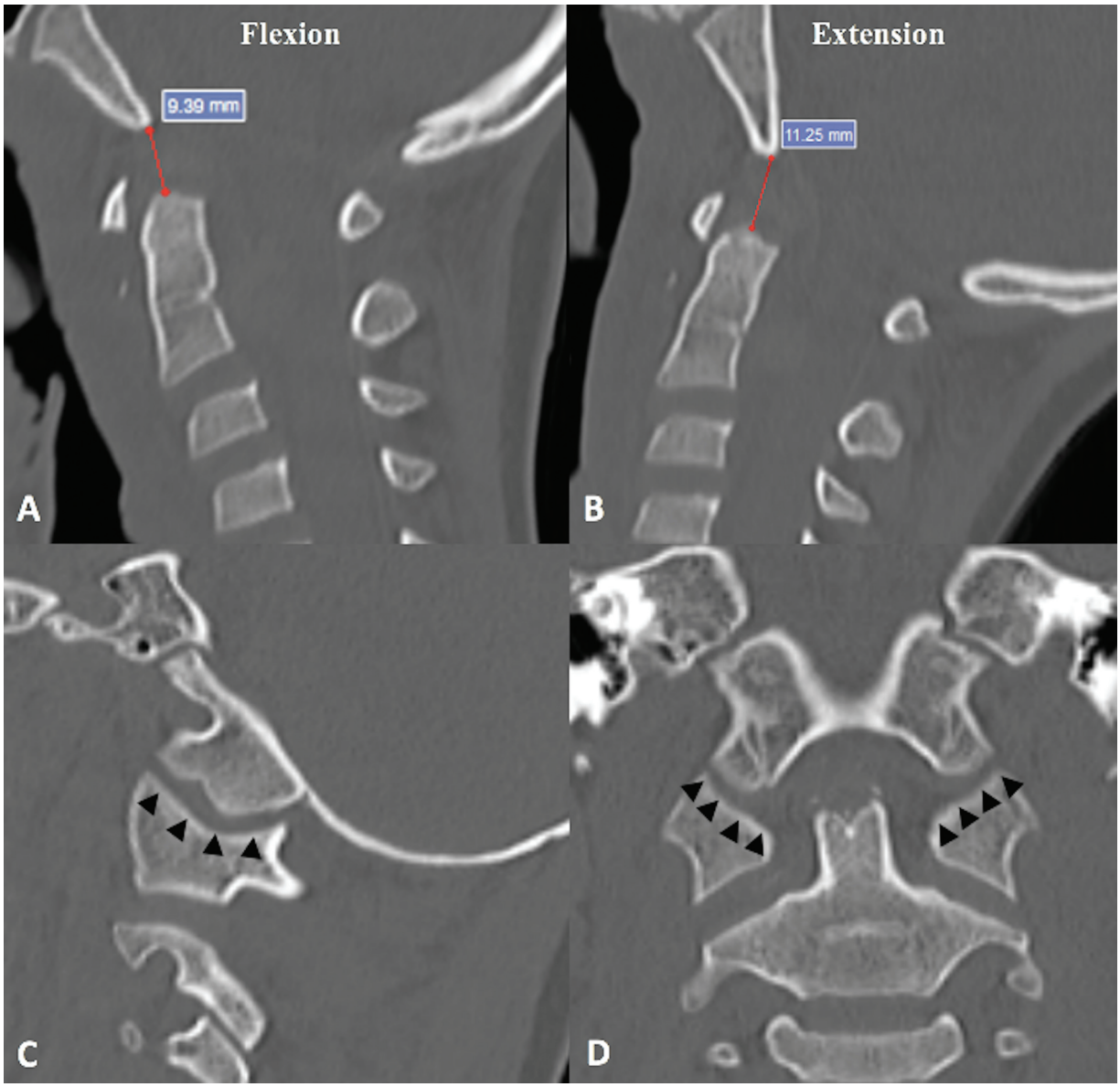

Fig. 2 (A and B) Dynamic computed tomography (CT) scan showing the Wholey's dens-basion interval. Note an increasing dens-basion interval on extension, in this case. (C and D) Conventional CT scan with placement of the measurement points (arrowheads) on the coronal (A) and sagittal (B) planes for calculation of the occipital condyle–C1 interval (CCI) in this case. A value of 4.05 mm was obtained (normal is < 4 mm).

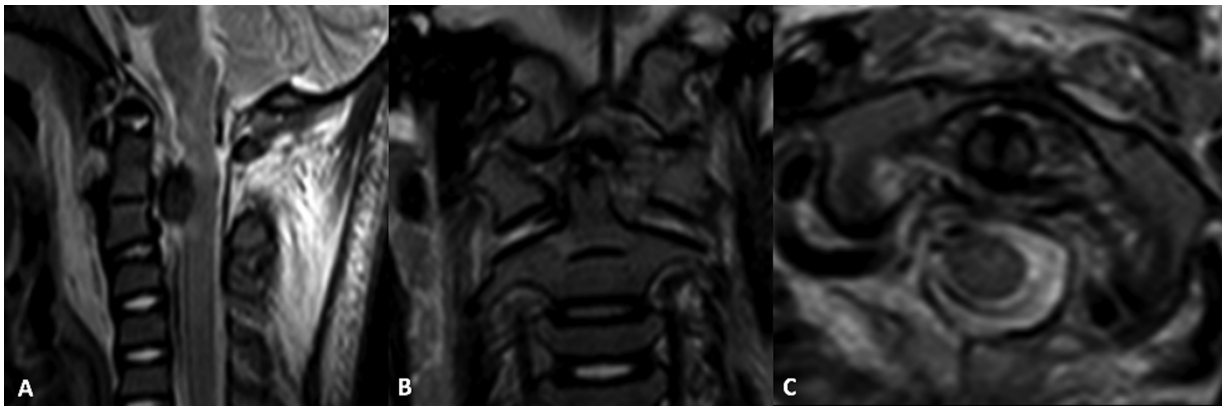

Fig. 3 Cervical magnetic resonance imaging (MRI). (A) Evident hypointense collection on anterior spine canal, causing spinal cord edema, compatible with subacute hemorrhage. There is diffuse hyperintensity on nuchal ligaments. (B) On coronal plane, a left-right asymmetry and also a left alar hyperintensity are evident. (C) The transverse ligament was preserved as on method.

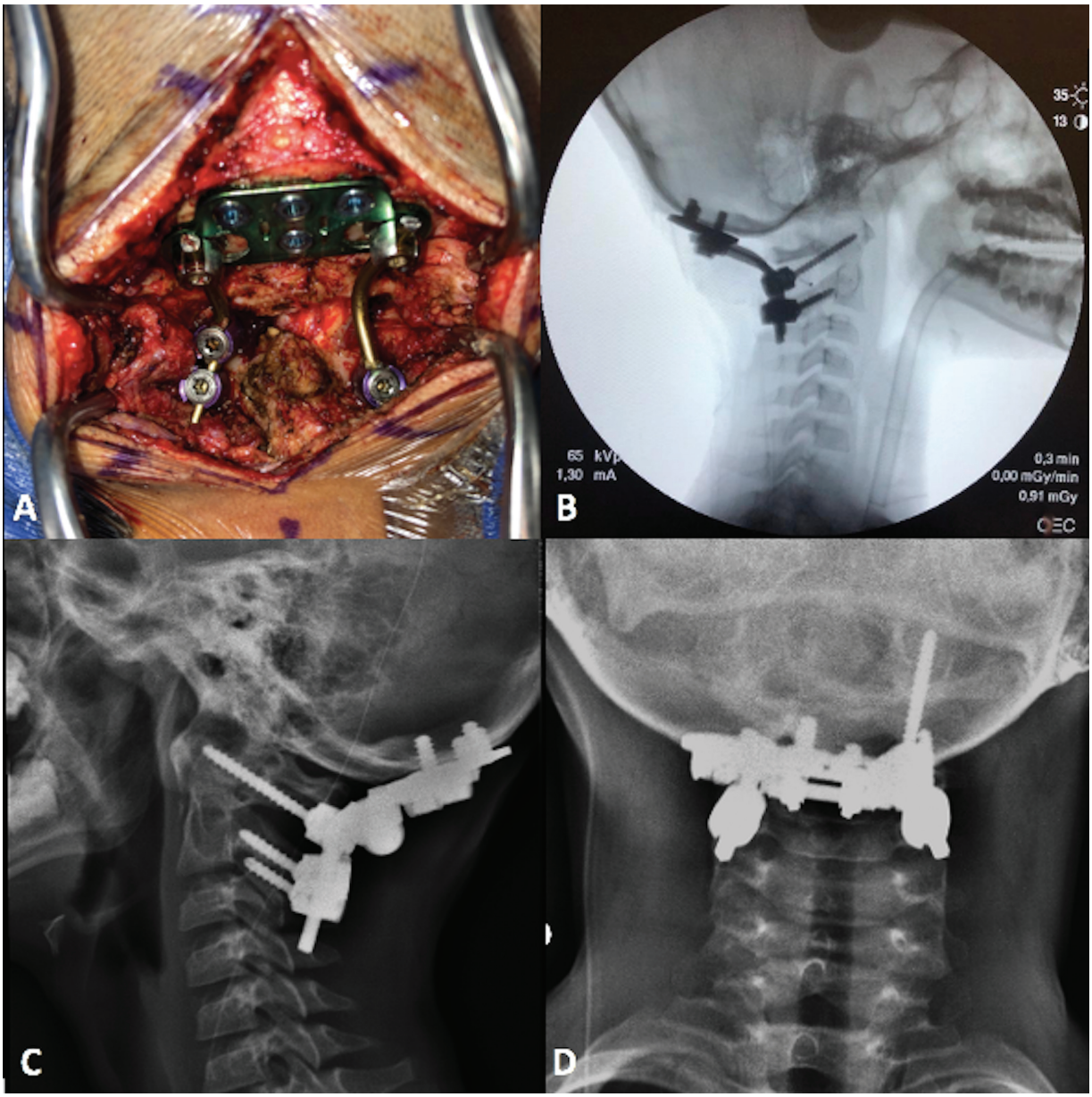

Fig. 4 (A) Intraoperative picture of the occipital plate and bilateral polyaxial pars screws at C2, and a unilateral left C1 lateral mass screw. (B) Lateral radioscopy confirms adequate positioning of the construction. (C and D) Follow-up X-rays with adequate screws positioning and fusion.

glue. An occipital plate was fixed with four screws of 4.5×6 mm (2) and 4.5×8 mm (2), centered over the thickest portion of the occipital bone. Guided by fluoroscopy, bilateral polyaxial screws were positioned on the C2 pars (3.5×14 and 3.5×12 mm) and unilateral ones on the left C1 lateral mass (3.5×26 mm). The system was fixed with 2 adjusted bars, and positioned with an additional cross-link (►**Fig. 4A-B**). Bone graft was extracted from the iliac crest and placed between the occipital bone and C2. There was no significant intercurrence during surgery. A follow-up CT further confirmed the adequate screw positioning.

Thereafter, the patient was transferred to an intensive care unit with significant improvement of the pain, being able to sit on day 1, and having no further symptoms. After hospital discharge, he underwent the follow-up process at the outpatient unit, remaining pain-free. Three months after surgery, however, he presented repetitive nighttime vomiting and headache with no signs of fever. Following a CT scan, a communicating hydrocephalus was diagnosed (►**Fig. 5**). We collected a CSF sample and ruled out meningitis. Then, a frontal medium pressure ventriculoperitoneal shunt was performed, with radiological resolution of hydrocephalus and clinical improvement. One year after the injury, the patient remains asymptomatic, and later radiography showed satisfactory bone fusion (►**Fig. 4C-D**).

Discussion

Traumatic atlanto-occipital dislocations are uncommon injuries associated with high immediate mortality rates. However, the likelihood of a pediatric patient surviving this almost invariably lethal injury clearly improved with time, due to

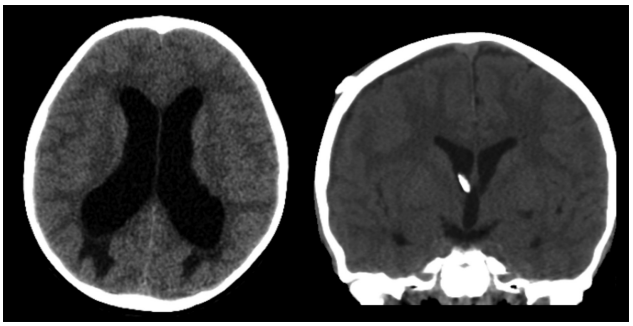

Fig. 5 **Left:** Head computed tomography (CT) scan showing moderate communicating hydrocephalus. **Right:** Postoperative CT scan with resolution of hydrocephalus.

advances in emergency resuscitation and prehospital care, as well as in the quality of radiological imaging.[14,15] Children who survive initial injury may have a favorable outcome with early diagnosis and treatment, before irreversible damage occurs in the cervicomedullary junction.[16]

High-energy trauma is usually required to cause TAOD, typically in the form of sudden acceleration-deceleration forces on the head.[17] The mechanism of injury most often reported is an automobile accident,[18] although accident in which a pedestrian is struck by a motor vehicle is also a common cause in children. The high-energy mechanism of injury with TAOD frequently results in further additional injuries, especially traumatic brain injury, which may hamper the diagnosis of TAOD.[19] Our patient had traumatic subarachnoid hemorrhage and blunt abdominal trauma in addition to TAOD.

Anatomical Background

The craniocervical junction is the most mobile part of the spine, and stability is provided mainly by the ligaments.[3] The transverse ligament secures anteriorly the odontoid process against the anterior arch of the C1, while the alar ligament attaches the dens to the anterolateral part of the foramen magnum.[20] The tectorial membrane is the continuation of the posterior longitudinal ligament and connects the axis with the clivus.[3,20]

Children younger than 10 years of age are particularly predisposed to TAOD because of the larger head-to-body ratio, smaller and flatter atlantooccipital joints and more flexible and weaker ligaments.[21] Previous studies showed that rupture of the alar ligaments and the tectorial membrane are sufficient to result in TAOD, since the remaining ligaments that attach the upper cervical spine to the occiput are insufficient to maintain adequate stability, and these abnormalities were also noted in this case.[22–24] There are usually no fractures associated with this injury, although in older children or adolescents, stronger ligaments can result in avulsion fractures at the ligamentous attachment of the skull base.

Imaging/Diagnosis

Although several radiographic methods to detect TAOD have been described, such as those proposed by Power, Harris, Wholey, and Sun,[10–13,25] none have been proven adequate as a single diagnostic criterion.[18] Also, there have been reports of significant variances from the previously accepted normal values on plain radiographs compared with the CT scans for most of these methods.[26] High-quality MRI is valuable for detecting ligamentous injury and careful surgeon-supervised flexion-extension CT scan (or even a CT scan performed under cranial traction) can also be informative.

In 1979, Powers et al.[11] described the Powers-ratio as a tool for the evaluation of TAOD, diagnosed by a ratio of more than 1. However, this method is only sensitive for the diagnosis of anterior TAOD. A vertical dissociation injury could result in a normal value, like in this case, and consequently go undiagnosed.

Harris et al.[12] established a reliable and accepted method to diagnose TAOD on lateral cervical radiographs, the BAI. In all 50 children (100%) with no occipitocervical abnormalities, the BAI was less than 12 mm, which is considered as the upper limit of normal.[12] However, this test alone has been found to have a sensitivity of 50%.[16–27]

The DBI was originally described by Wholey et al.,[10] and the commonly accepted cutoff on plain radiograph is 12 mm. However, normal values on CT scans were significantly different from the accepted ranges of normal on plain radiographs.[26,28] Considering the pediatric population, Bertozzi et al.[28] showed that the DBI was shorter than 10.5 mm in 97.5% of patients.

Pang et al. describe both the normal anatomy and radiographic findings suggestive of TAOD,[15,16] but it has been discussed that these parameters cannot be applied to all age groups.[8] They showed that the normal occiput–C1 joint in children has an extremely narrow joint gap (condyle–C1 interval or CCI).[15] With a cutoff value of 4 mm, the CCI criterion had the highest diagnostic sensitivity and specificity for TAOD among all other radiographic criteria in their study.[16] In this case, the combined CCI value (average of both the sagittal and coronal CCIs) was 4.05 and represents the only abnormal radiographic standard test, proving this test as an important tool for TAOD diagnosis in children with less evident dislocations (►**Fig. 2C-D**).

Treatment and Complications

Occipitocervical fusion in the pediatric population has been a challenging surgery even for experienced spine surgeons. Posterior spinal fusion is the pillar treatment for TAOD, and the use of screws has now become more common in young children, in whom other techniques, such as rib grafting with wiring followed by a halo vest, are used.[29–34] In a systematic review in which 285 patients underwent OCF, Hwang et al.[35] found that both screw and wiring groups had very high fusion rates (99% and 95%, respectively, $p = 0.08$); however, wiring was associated with a higher complication rate.

Pediatric OCF carries serious risks, and the complication rates reported in the literature range from 7.5 to 26%.[36] Short-term complications include vertebral artery injury, blood loss, neurologic deterioration, dural tear, and CSF leak.[36] There are also long-term risks, including hardware-related complications, infection, pseudoarthrosis, and deformity.[36]

In our case, the patient developed hydrocephalus, which is a complication has also been described in previous case reports of TAOD.[18,37,38] In a series of 14 patients, the most common postoperative complication was hydrocephalus, and the authors hypothesize that it occurs as a result of posthemorrhagic scarring within the basal cisterns or outlets of the 4th ventricle.[18] In our case, the CSF leak associated with the epidural hematoma may have played a role in the development of a CSF disturb, as well as the root injury.

Conclusion

In conclusion, TAOD is an uncommon and challenging subject in the pediatric population. Surgical stabilization is life-saving in cases of TAOD, while missing an unstable injury could have catastrophic consequences. The diagnosis criterion is not unique, generally requiring multimodal image, especially in less evident dislocations. Fixation of the occipitocervical junction with screws have a higher fusion rate and should be considered as the treatment of choice when feasible. Finally, hydrocephalus is not an unusual complication in children, and attention is necessary, with close clinical and radiological follow-up.

Conflict of Interests

The authors have no conflict of interests to declare.

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Isolated Intradural Prepontine Chordoma Presenting with Imaging Features of Epidermoid Cyst

Cordoma pré-pontino intradural isolado apresentando características de imagem de cisto epidermóide

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Abstract

Chordoma is an erratic aggressive tumor of the brain that typically involves the clivus. The majority of the clivus chordomas reside in the extradural space. Here, we report a unique case of chordoma arising from the prepontine intradural space without bony involvement and presenting with radiological features typical of an epidermoid cyst on magnetic resonance imaging.

Keywords

- cyst
- epidermoid
- chordoma
- clivus
- differential diagnosis
- MRI
- prepontine

Introduction

Chordoma, which is as an erratic, aggressive tumor with slow growth, is thought to be derived from the embryonic notochord remnants, as a cartilage-like structure shaped like a rod serving a scaffold for forming the spinal column.[1] They usually occur in adults with a peak occurrence within the age 50 to 60 years.[2] Approximately 35 to 40% of these tumors have an intracranial localization, where they typically involve the clivus. The majority of the clivus chordomas reside in the extradural space.[3] Here, we report a unique case of chordoma arising from the prepontine intradural space without bony involvement and presenting with radiological features typical of an epidermoid cyst (EC) on magnetic resonance imaging (MRI).

Case Report

History

A 24-year-old patient presented to our clinic with headache complaints. The patient's headache had begun 6 months before admission, increased progressively, aggravated by coughing and laughing and was sometimes accompanied by dizziness. The patient reported no other associated symptoms, and no specific neurological deficits were found in this case.

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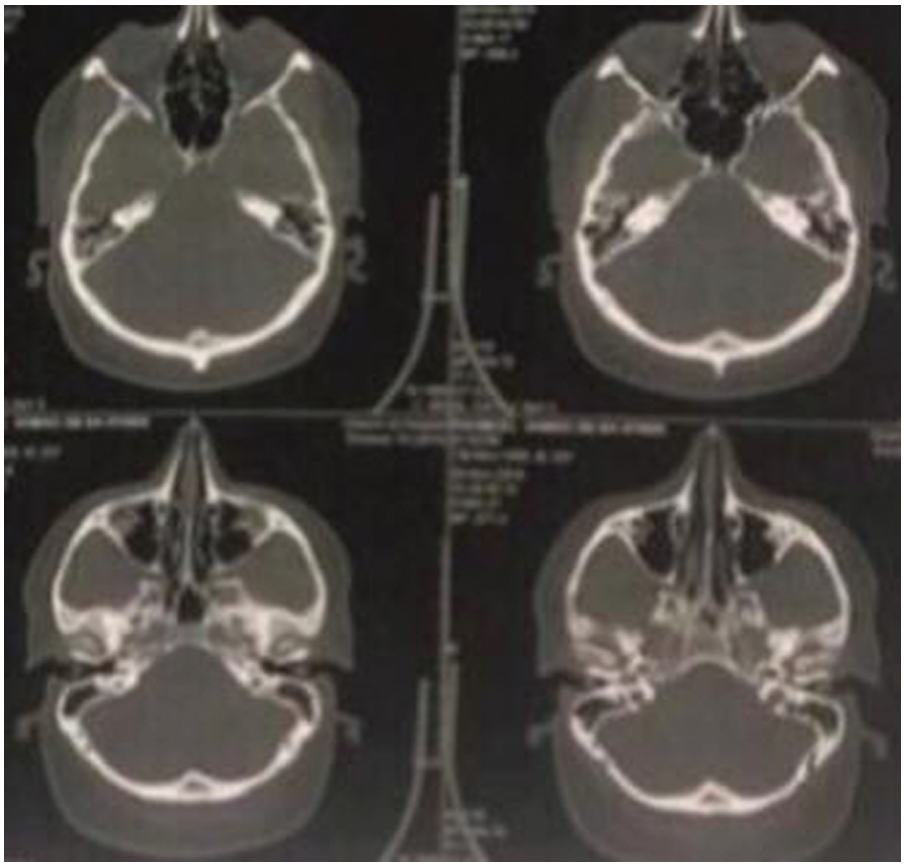

Fig. 1 Brain magnetic resonance imaging.

Radiological Imaging

Brain MRI with and without contrast showed a well-defined hypodense mass about 34 × 25 × 36 mm in prepontine cistern with mass effect on the pons. The tumor had heterogenous high T2 and flair signal intensity. Areas of high T1 intensity were seen. No significant enhancement is seen in areas with fluid restriction is noted in diffusion-weighted imaging (DWI). The finding is suggestive of an epidermoid cyst (►**Fig. 1**).

A brain computed tomography (CT) scan showed a well-defined hypodense mass about 34 × 25 × 36 mm in the prepontine cistern with mass effect on the pons; no calcification and no bone erosion were seen and the clivus was normal (►**Fig. 2**).

Operation, Histological Examination, and Postoperative Course

The patient underwent prepontine mass resection with a retrosigmoid mass resection surgery in a sitting position. After mass removal, tissue samples were sent to the laboratory for pathological examination, which revealed that the tumoral tissue was composed of lobules of cell beating round nuclei and abundant clear or lightly eosinophilic cytoplasm. Areas of chondroid differentiation cells showed cytokeratin, epithelial membrane antigen (EMA), s100 positive, and glial fibrillary acidic protein (GFAP) negative, which are compatible with chordoma (►**Fig. 3**).

Discussion

Chordomas are erratic tumors of the axial skeleton, and they happen mostly in the sacrum and at the base of the skull. It is thought that chordomas arise from fetal notochord remnants remaining in the axial skeleton during life and probably undergoing malignant transformation into chordoma at any point in life.[4,5] Macroscopically, chordomas seem to be a white-gray lobulated, gelatinous, soft tumor with dens fibrous trabeculae.[6] Mucoid material, necrotic areas, current, old hemorrhages, and sequestration and calcification of bone fragments are observed in the tumor.[7] An unfinished pseudocapsule with pressured nearby tissue imitating a true capsule surround the soft tissue frequently.[8] A heterogeneous cytology is displayed by all chordoma subtypes. The large cells containing prominent solitary or multiple vacuoles are the main cell types, also known as physaliphorous cells. These vacuoles are rich in mucopolysaccharides.[9–11] On non-contrast CT, chordomas are characteristically found as well-constrained, heterogeneous, hypoattenuating lesions with widespread lytic bone destruction.[6] The tumor bulk is typically hyperattenuating based on the nearby neuronal axis.[12] Distinguishing between intratumoral calcifications is difficult that are representative of the chordoma's chondroid variant,[13] and appropriated fragments of the damaged clival bone.[6] In the late 1980s and early 1990s, the MRI features of chordoma with the normal MRI sequences were described well.[6] Chordoma is able to impose inconstant signal intensity on T1, typically mostly low-to-

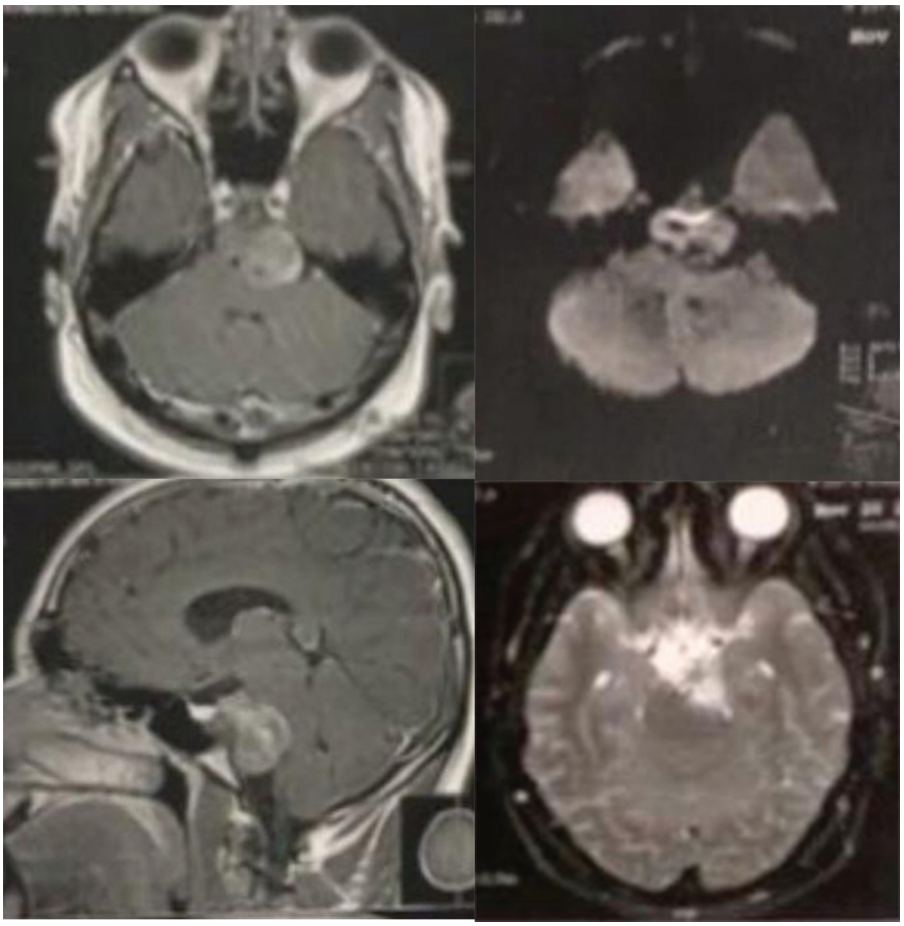

Fig. 2 Brain computed tomography scan.

intermediate signal strength, occasionally with minor hyperintensity foci, related to hemorrhage or mucus.[14] High T2 signal strength with heterogeneous hypointensity is observed in classic chordoma, probably related to hemorrhage, mucous, and calcification as well. The existence of calcification or hemorrhagic foci can be observed in susceptibility-weighted imaging (SWI), which are gradient echo images indicating vulnerability artifacts.[14] It is also possible to find low signal intensity septations probably correlated with areas of cartilage or necrosis observed in histology. Various imaging features may be shown by weakly distinguished chordoma.[15] Yeom et al. indicated hypo intensity on T2-weighted images in 3 weakly distinguished chordoma. Nevertheless, there are no studies in the literature that investigating greater weakly distinguished chordoma cohorts. Chordoma characteristically indicate fair-to-high gadolinium contrast improvement with honeycomb appearance, with linear non-improvement areas.[16] This is probably clarified with the areas of necrosis, connective tissue, or cartilage in the tumor at histology. In delineating the clival chordoma, fat suppression imaging with suppression of the clivus fatty bone marrow may be effective.[12] Epidermoid cysts are among the most prevalent benign intracranial cystic lesions commonly found. Through current imaging technology, their recognition and the radiologic diagnosis are nearly always easily possible.[17] As a result of protein, calcium, lipid, and hemosiderin content[18] together with occasional calcification (more in dermoids), the tumor seems to be isodense or hypodense or occasionally spontaneous hyperdense on CT scan. Magnetic resonance imaging scan is the modality of choice for diagnosing. The lesion is hyperintense on T2-weighted, hypointense on T1-weighted and FLAIR, with hyperintense constraint on diffusion-weighted imaging (DWI) [19]and without any contrast enhancement.[18] When contrast improvement occurs, it is typically at the tumor's margins.[18] In intrinsic lesions, the absence of the tumor edema distinguishes from the gliomas. In extrinsic locations, DWI is useful to differentiate from the arachnoid cyst and abscess.[20,21] Diffusion-weighted imaging is useful to know the remnant by its restriction, differentiation from abscess, and arachnoid cyst.[22] There are very few reports in the English literature on cases that were clinically followed as EC, yet found to be as chordoma in the pathological examination. Such a case was described in 2004, but, in this case, the lesion demonstrated partial bony erosion.[23] The lesion showed hyperintensity on T2-weighted MRI, hypointensity on T1-weighted MRI and hyperintensity on DWI with no contrast enhancement. The tumor was surgically removed and despite a suspicion of EC, the pathological examination revealed a chordoma. In 2018, a similar case of a prepontine mass was reported. A 35-year-old Caucasian woman was admitted to an outpatient clinic with complaints of progressive dizziness, ataxia, and diplopia. The patient's lesion was previously diagnosed as a prepontine EC. The lesion

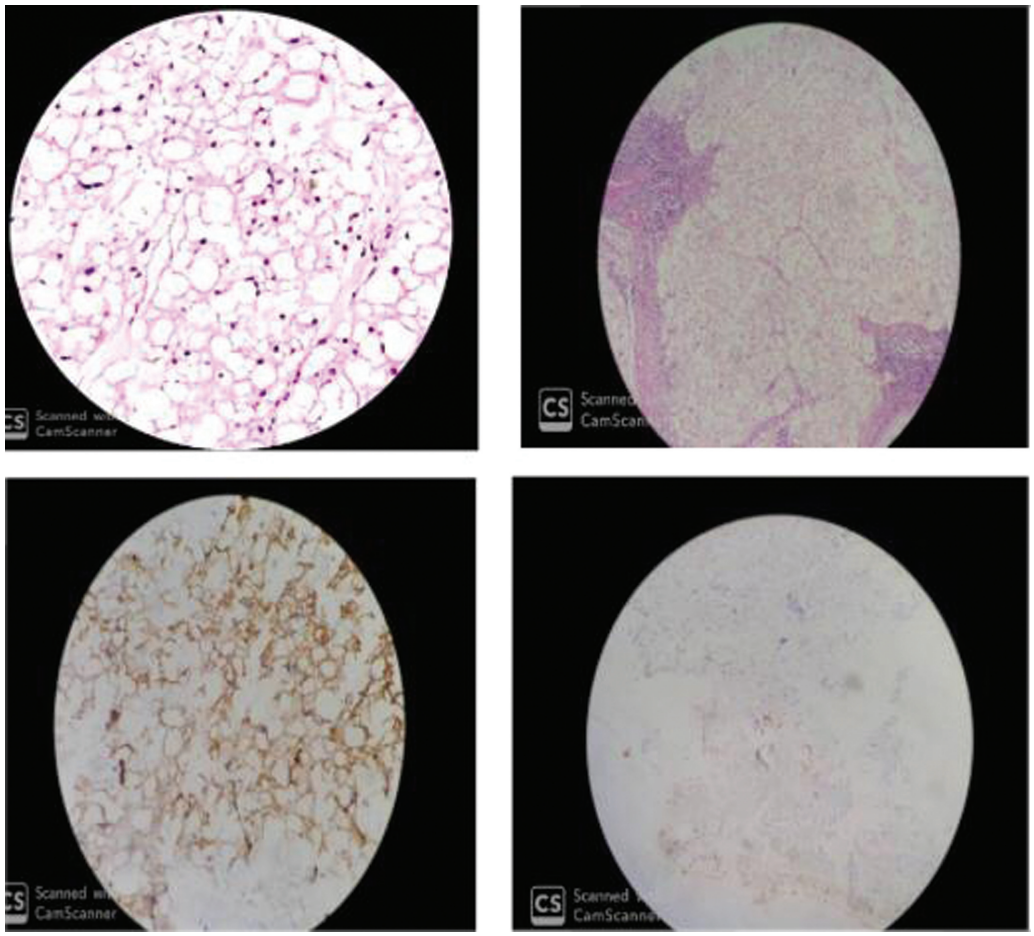

Fig. 3 Microscopical pathology of the tumor.

seemed as hypointense in T1 and hyperintense on T2-weighted images. The lesion also indicated hyperintensity on DWI and hypointensity on apparent diffusion coefficient (ADC) images. The lesion did not demonstrate any contrast enhancement. No obvious destruction of the clivus or bony erosion with conserved normal fatty marrow on MRI. The patient was operated, and a gray-purple soft tumor tissue was noted perioperatively, having neither macroscopical features of a typical EC nor a vascular pattern typical of chordomas. Unexpectedly, the frozen section analysis reported a chordoma. Similar to the frozen section, the pathological analysis also revealed a chordoma. The patient was discharged on the 5th postoperative day, following radiotherapy referral for the residual tumor. The pathological analyses revealed the following features.[3] In 2017, A 44-year-old female visited a clinic with progressively worsening right facial dysesthesia, which had persisted for 10 years. The MRI indicated a $32 \times 30 \times 16$ mm tumor in the prepontine-to-interpeduncular cistern, which was hypointense on T1-weighted images (T1WIs), isointense on fluid-attenuated inversion recovery (FLAIR) sequences, hyperintense on T2WIs, iso-to-hyperintense on DWI, and hyperintense on ADC map ($1.2–1.6 \times 10–3$ mm^2/s). No deceptive contrast improvement exists on postcontrast T1WIs. In consideration of these imaging properties, we supposed that the tumor was an EC according the DW results. The tumor was light-yellowish, transparent, jelled, and cystic after removing the mass, unlike an EC. The pathology was compatible with ecchordosis physaliphora. Follwing the surgery, the symptoms of the patient were enhanced, and she was discharged on the postoperative day.[24] In 2014, a similar case of prepontine mass was reported. The MRI examination of a 15-year old girl with complaints of headache revealed a well-defined, lobulated prepontine mass that was profoundly hypointense on T1- and FLAIR sequences and hyperintense on T2W, suggesting a lesion with fluid content. Small scattered areas of hyperintensity were evident on T1 and FLAIR sequences, presumed as likely signs of a hemorrhage. The clivus was intact with no bone erosion. Peroperatively, the tumor was greyish and semi-solid in texture, and the cranial nerves were stretched and encased by the tumor. Pathological analysis revealed a chordoma. The patient required a second excision 13 months later as the residual tumor expanded in size; the patient also received 3 months of radiotherapy. The most recent MRI performed two years postsurgery showed no tumor progression.[25] In 2012, another prepontine chordoma was reported, which was initially suspected as a benign EC. The CT examination of a 32-year-old male with complaints of dysarthria showed a hypodense pontine mass with no contrast improvement or clival bony erosion. The MRI revealed a multi lobulated contour bulging lesion in the prepontine cistern and invagination into

the pontine parenchyma, which somewhat covered the mid basilar artery. The mass was hyperintense on T2-weighted MRI and hypointense on T1. Most of the mass indicated no post-contrast improvement, excluding some minor dominant multiple reticulonodular heterogenous improvements. On DWI, a heterogenous and mildly incremented signal intensity was indicated by this mass. The postoperative pathological analysis revealed a chordoma, and centrally enhanced foci were defined as profound vascularity.[26]

Conclusion

The chordoma case reported here had radiologic features similar to those of ECs. In cases in which there is a tumor near the clivus, chordoma should always be considered as a differential diagnosis, even without the presence of bone erosion.

Conflict of Interests

The authors have no conflict of interests to declare.

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Probable Hydrocephalus Decompensation after Immunization with Pentavalent Vaccine: Case Report and Literature Review

Descompensação provável de hidrocefalia após imunização com vacina pentavalente: Relato de caso e revisão da literatura

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Abstract

There are several complications associated with immunization with the pentavalent vaccine. Most of them are mild reactions, of spontaneous resolution; however, though rare, serious and potentially-fatal adverse effects can occur. We report a case of acute intracranial hypertension syndrome in an infant with a previously-unknown suprasellar arachnoid cyst who developed acute obstructive hydrocephalus after immunization with the pentavalent vaccine. He underwent neuroendoscopic treatment, showing complete resolution of the condition. The present article aims to compare the activation of the immune system by the pertussis component of the vaccine and the mechanisms that hypothetically potentiated the pathological decompensation.

Keywords

- pentavalent vaccine
- hydrocephalus
- arachnoid cyst
- inflammation
- blood-cerebrospinal fluid barrier
- neuroendoscopy

Resumo

Várias são as complicações associadas à imunização com a vacina pentavalente (VP). Em geral, são reações leves, de resolução espontânea; entretanto, raramente podem ocorrer efeitos adversos graves, potencialmente fatais. Relatamos um caso de síndrome de hipertensão intracraniana aguda (HIA) em lactente portador de cisto aracnoide suprasselar até então desconhecido, que desenvolveu hidrocefalia obstrutiva aguda pós imunização com VP. Ele foi submetido a tratamento neuroendoscópico, e apresentou resolução completa do quadro. Este artigo pretende comparar a ativação do sistema imune pelo componente pertússis da vacina e os mecanismos que hipoteticamente potencializaram a descompensação patológica.

Palavras-chave

- vacina pentavalente
- hidrocefalia
- cisto aracnoide
- inflamação
- barreira hematoliquórica
- neuroendoscopia

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Introduction

The pentavalent vaccine (PV), which prevents against diphtheria, tetanus, whooping cough, haemophilus influenzae type B infection and hepatitis B, was introduced in the Brazilian childhood vaccination schedule in 2012, and is generally administered to infants aged 2, 4 and 6 months.[1]

According to the "Handbook for the Epidemiological Surveillance of Adverse Events after Vaccination" (*Manual de vigilância epidemiológica de eventos adversos pós-vacinação*),[1] published in 2014 by the Brazilian Ministry of Health, mild local and systemic adverse effects are common, usually between 48 and 72 hours after immunization. Symptoms such as low or moderate fever (in 4.1% to 58.8% of the cases), drowsiness (in 28% to 48.8% of the cases), loss of appetite (in 2% to 26.5% of the cases), vomiting (in 1.1% to 7.8% of the cases), irritability (in 2.6% to 85.8% of the cases), and persistent crying (in 0 to 11.8% of the cases) are some examples.[1,2]

They mainly occur in children under three months of age and are usually treated according to guidelines, with medication administration. It may also be necessary to change the vaccine formulation in future immunizations to prevent new events.[2]

Despite the fact that its safety has been extensively tested, severe adverse effects may occur on rare occasions, which, if not treated properly, can cause lasting damage, such as severe postvaccination neurological complications: encephalitis, meningitis, myelitis, optic neuritis, Guillain-Barré syndrome (GBS), narcolepsy, and parkinsonism.[3]

Such adverse effects are also observed after the administration of several other vaccine preparations, such as Bacille Calmette-Guérin (BCG), influenza hemagglutinin 1 and neuraminidase 1 (H1N1), *H. influenzae*, the human papillomavirus (HPV), and diphtheria, tetanus and pertussis (DTP).[3]

There are no specific studies on the complications after the administration of the PV; however, there are studies[1,4] which mention the occurrence of complications after the administration of the in the DTP and tetravalent vaccines (DTP + *H. influenzae* type B conjugate).

Severe postvaccination complications include hypotonic hyporesponsive episodes (1/1,750 cases), convulsive crises (1/5,266 cases), apnea, anaphylactic reactions, and postvaccinal encephalopathy (0 to 10.5 cases per million doses administered).[1,4]

Among the serious post-vaccination complications, those involving central nervous system (CNS) manifestations will be highlighted, as well as a discussion about the immunological mechanisms possibly involved in its genesis.[5–8]

Since the most frequent adverse effects after vaccination are mild and sometimes nonspecific, they could be confused with the symptoms observed in the early stages of acute intracranial hypertension (AIH, such as irritability, crying, drowsiness etc.), especially in infants with compensated hydrocephalus of which the parents and pediatricians are unaware, causing undesirable diagnostic delays.[9–11]

Although there are privileges regarding the protection of the CNS from unwanted immune processes, in the case herein reported, we noted that there was decompensation of a preexisting and previously unknown neurosurgical condition, potentially harmful if not treated, emphasizing the need for a better understanding of the inflammatory postvaccine response over the blood-cerebrospinal fluid barrier (BCSFB).[12–14]

The present article aims to report a case of acute obstructive hydrocephalus in an infant after immunization with the PV, and to discuss the possible mechanisms related to the immune response and BCSFB dysfunction.

Case Report

A male infant aged 6 months and 22 days was brought by his parents to the emergency room 3 days after the immunization presenting irritability, crying, profuse vomiting, and apparent visual loss.

His mother reported that the symptoms had already occurred on the first day after the application of the PV. He started with irritability and a high fever (38.5° C), which was controlled with the use of antipyretics.

The infant was previously healthy. He had no comorbidities, no history of allergic or vaccine reactions, presented neuropsychomotor development that was adequate for his age group, had been exclusively breastfed until the sixth month of life, and his vaccination booklet was up to date.

A physical examination revealed macrocrania (head circumference of 46 cm/greater than the 97th percentile) not previously reported in childcare consultations, and sensorineural impairment characterized by drowsiness and frequent vomiting. Signs of meningeal irritation were present, denoted by a tense anterior fontanelle +/4+, Kernig sign, and mild opisthotonus. The discreet presence of the sign of Parinaud drew attention.

At the pediatrician's request, a brain magnetic resonance imaging (MRI) scan was performed in the emergency room, under sedation and with anesthesiological follow-up. An evaluation by the neurosurgeon was requested because acute obstructive hydrocephalus with a lesion suggestive of suprasselar arachnoid cyst was evidenced (►**Figure 1**).

The lesion had an important extension to the cavity of the third ventricle, obstructing both the outflow tracts of the lateral ventricles and the opening of the cerebral aqueduct. The fourth ventricle had usual dimensions.

On magnetic resonance imaging of the brain, no signal alterations were observed in the brain parenchyma, or uptake by paramagnetic contrast in any of the sequences performed, and encephalitis could be excluded at first.[15]

With the parents' agreement, an emergency neuroendoscopy was chosen, without previous collection of cerebrospinal fluid (CSF). Although rare, the risks of further deterioration of the sensorium due to descending herniation (after the lumbar puncture) or the occurrence of intraventricular hemorrhage (after the transfontanellar puncture) were considered.[16,17]

The CSF collection was performed at the time of ventricular puncture, through the endoscopic system, in a satisfactory manner. The possibility of placing an external ventricular shunt (EVS) at the same operative time or later, in case of

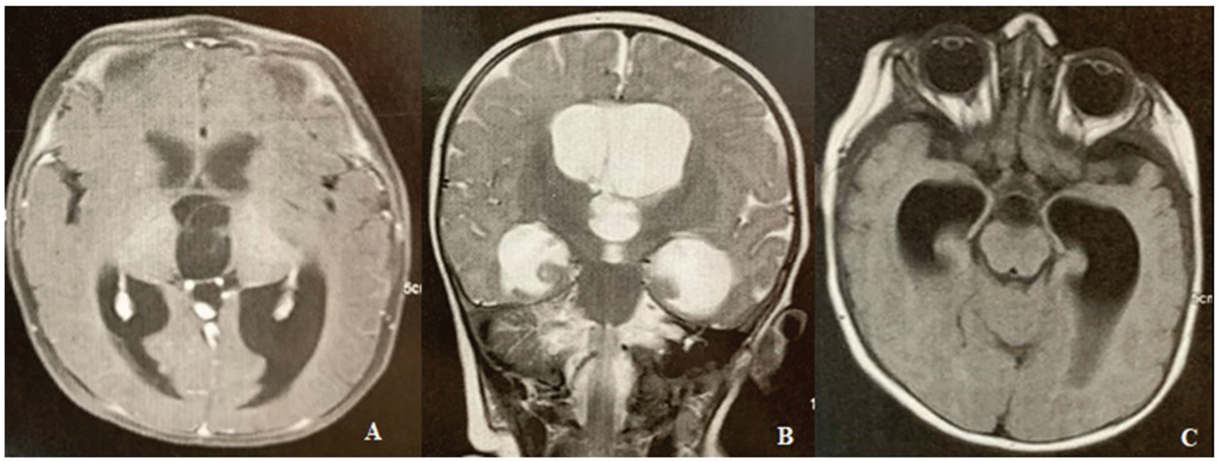

Fig. 1 Preoperative cranial magnetic resonance imaging (MRI) scan showing a cystic lesion in the suprasellar region, obstructing the flow of cerebrospinal fluid (CSF) and causing obstructive hydrocephalus upstream. (**A**,**C**) Axial T1-weighted MRI of the skull. (**B**) Coronal T2-weighted MRI of the skull.

suspicion or proof of infectious etiology, was also explained.[18]

The infant underwent general anesthesia, with the head in a slightly flexed neutral position, eye protection, and a thermal blanket. Cefazolin was administered as a prophylactic antibiotic.

We opted for the classic access to the right lateral ventricle, opening at the Kocher point, with trepanation using a number 15 scalpel blade, collecting the powder and bone micelles to occlude the orifice created. Linear durotomy was performed without coagulation of the dural edges, using a Karl Storz (Tuttlingen, Germany) Deqc 0° endoscope for the ventricular puncture.[19–22]

Upon entering the right ventricular cavity, a large cystic lesion occluding the foramen of Monro was evidenced. The cyst had several cotton-wool spots on its surface (►**Figure 2**). Protein materials could also be observed floating inside the ventricular cavity, which led us to assume a probable inflammatory reaction as an origin for the decompensation of the condition.[11,23,24]

The cyst was fenestrated using microscissors and, when entering it, the floor of the third ventricle was visualized in detail. This was open and displaced by the lesion, as well as the various arterial and venous structures and pituitary stalk.

The lower portion of the Arachnoid Cyst was opened towards the Carotid Cistern with Fogart Balloon number 2. After its communication, the lesion collapsed onto the floor of the third ventricle, also providing the permeability of the cerebral aqueduct.

A meticulous closing of the planes was carried out, occluding the burr hole with the powder and bone fragments collected.[21,25]

An additional contralateral approach was chosen with caution. When entering the left lateral ventricle, it is possible

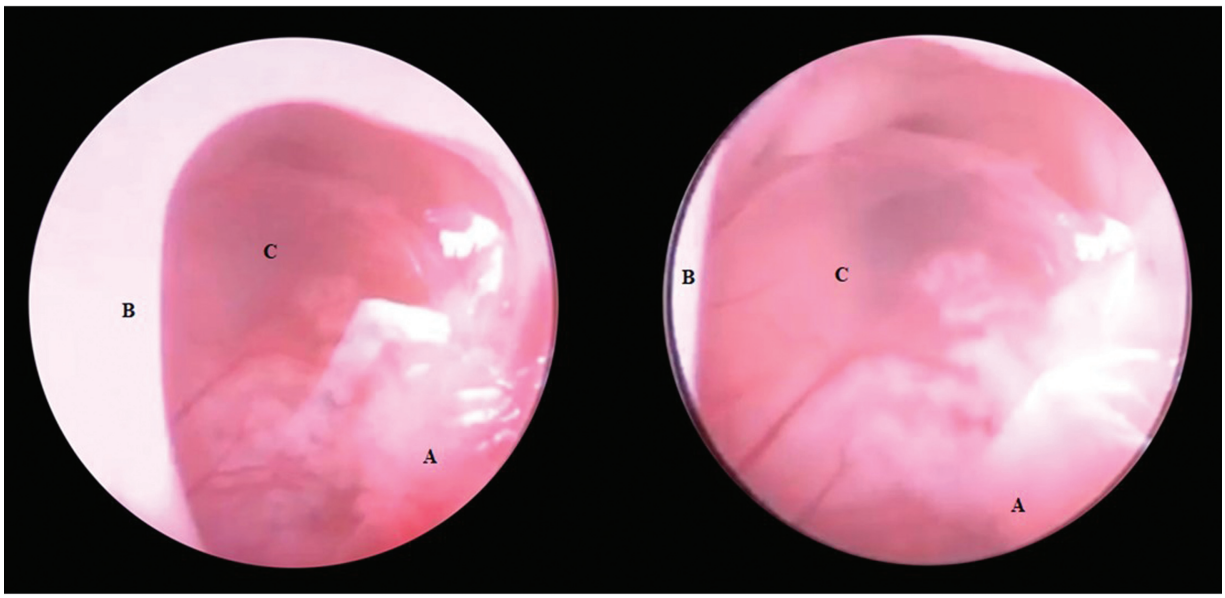

Fig. 2 Intraoperative view of the arachnoid cyst (**C**) occupying the ventricular cavity and covered by cotton-wool spots (**A**). Foramina of Monro (**B**).

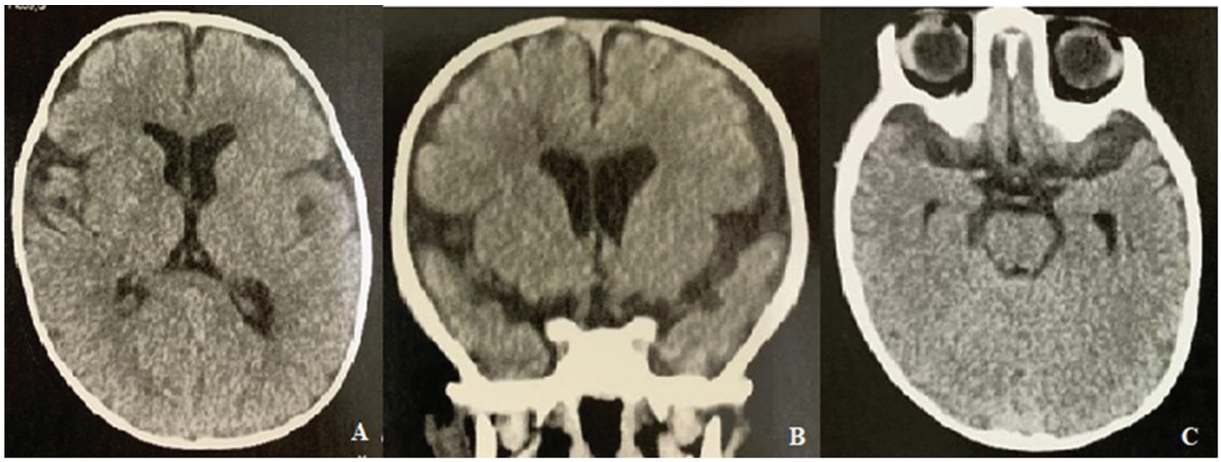

Fig. 3 Postoperative cranial computed tomography (CT) scan showing a reduction in ventricular cavities. (**A, C**) Axial section of skull CT. (**B**) Coronal section of skull CT.

to observe the total opening of the ipsilateral foramen of Monro. The cyst was completely collapsed, and was not submitted to resection, for we chose to interrupt the surgical procedure at this time. The same synthesis procedure was performed on the right side.

The patient was sent awake and responsive along with the mother to the Pediatric Intensive Care Unit, where, one day later, he was discharged to the ward without symptoms.[26]

The analysis of the cerebrospinal fluid collected during the operation was performed. No alterations were observed in cellularity (8 cells / 100% lymphocytes) or in glucose (48 mg/dl), identifying only hyperproteinorraquia (80 mg/dl). Cultures did not demonstrate bacterial growth. Postoperative cranial tomography and brain MRI showed a significant reduction in supratentorial ventricular cavities (►**Figure 3**, ►**Figure 4**).

The large amount of particulate matter observed in the CSF and on the cystic surface led to the assumption of a inflammatory reaction, which may or may not be associated with vaccination. Classic works such as those by Spina-França and Saraiva[27] (1961) and Rocha et al.[28] (1971) have already reported the occurrence of leptomeningeal reactions in infectious and inflammatory processes and in aseptic causes.

Discussion

The neurosurgical pathologies that affect the sellar and suprasellar regions of children are varied. They comprise solid, cystic or mixed tumors, are most often histopathologically benign, but have a recognized potential for invasion of adjacent structures.[29]

Examples of sellar and suprasellar lesions are craniopharyngeomas, pituitary adenomas, and optic-chiasmatic gliomas. Granulomatous lesions such as histiocytosis X, tumoral lesions derived from germ cells (germinomas), and cystic lesions secondary to defects of normal embryogenesis (Rathke cleft cysts) and arachnoid cysts may also be found more rarely.[29]

Arachnoid cysts are benign lesions usually arising from a duplication of the arachnoid, but they can also have a rare posttraumatic etiology. They are filled with CSF, and comprise about 1% of all intracranial lesions. Sellar and suprasellar arachnoid cysts comprise 9% to 21% of these lesions. They usually predominate in men (with a ratio of 2:1), and their most frequent location is the middle fossa, representing about 50% of the cases.[20,29,30]

Carriers of arachnoid cysts are mostly asymptomatic, however, in some patients they can become clinically manifest. These manifestations can range from simple paroxysmal headaches to severe cases of symptomatic intracranial hypertension.[31]

Focusing on the specific type of cyst in this report, of suprasellar location and extension to the cavity of the third ventricle, it is commonly manifested by obstructive hydrocephalus, visual alterations, endocrine alterations (short stature and delayed pubertal development), delayed neuropsychomotor development. Less frequently, seizures, head movement disorders (Bobbing Head Doll) and appendicular (tremors) may occur.[20]

Several pathophysiological theories have been proposed to explain the symptomatology of these lesions. Some of them are the development of a valve mechanism, in which there is an imbalance between intracystic CSF inflow and outflow, intracystic CSF production, and an increase in the intralesional osmotic gradient due to an increase in the protein content.[29]

There are different types of therapeutic approaches, from fenestrations (open, under microscopy or endoscopy with or without navigation) to derivations (cyst-peritoneum, cyst-subdural shunts), and they must be chosen on a case-by-case basis and depending on the structure of the service.[20,31–33]

In the case in question, endoscopic fenestration of the cyst was chosen with satisfactory results. Furthermore, we believe that the increase in CSF protein content, both in the intraventricular and intracystic components, may have been the underlying cause of the decompensation and would be related to the recent immunization of the infant with cellular

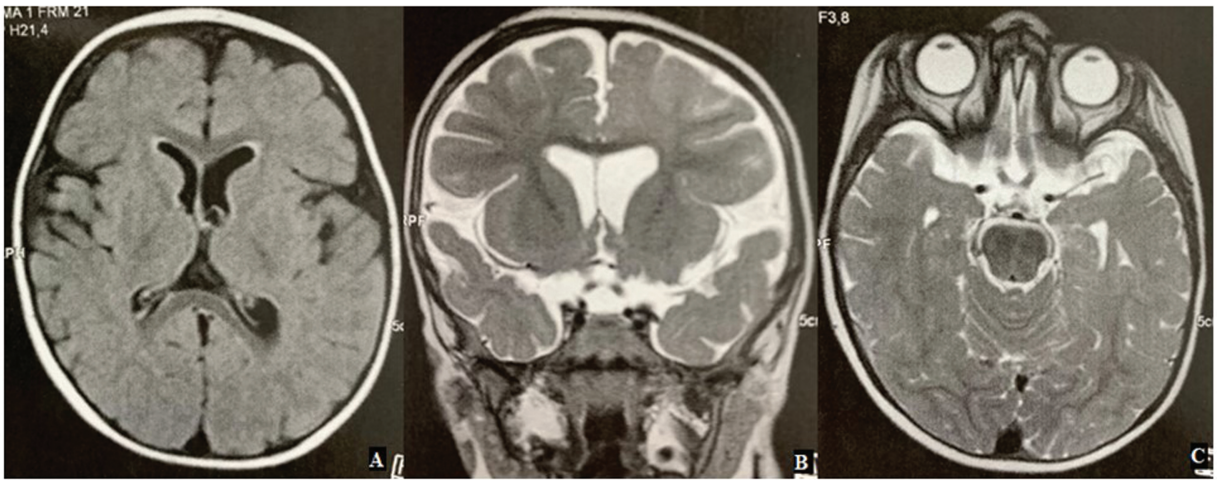

Fig. 4 Control skull MRI one year after the procedure, showing complete resolution of the pathology. (**A**) Fluid attenuated inversion recovery-weighted skull MRI in axial section. (**B**) Coronal T2-weighted MRI of the skull. (**C**) Axial T2-weighted MRI of the skull.

DTP, of recognized immunogenic potential, which will be detailed below.

Bordetella pertussis is a gram-negative bacterium that exclusively infects susceptible humans, causing pertussis, a respiratory disease that, in some cases, presents severe neurological complications. These are related to the antigenic components of the pathogen, mainly the pertussis toxin (TP), hemagglutinins, agglutinogens, adenylate cyclase, pertactin and tracheal cytotoxin.[5,34–36]

In particular, PT causes ciliary paralysis of the airways due to exacerbated local inflammation. This leads to the accumulation of secretions and/or their inadequate removal, favoring secondary pneumonic processes (which can be severe, especially in the first six months of life).[34,37]

Such inflammation leads to massive migration of lymphocytes, which are the first line of defense. Although the pathogenicity model is toxin-mediated, some bacteria can also be found in local macrophages, denoting tissue penetration.[34]

Pertussis has an incubation period of 7 to 10 days, starting with a nonspecific cough and fever, similar to other infectious diseases of the airways. However, after about a week, the period of paroxysmal attacks of a characteristic (whooping) cough begins, which can last up to six weeks, causing great suffering to the patients and their families.[1,37]

In uncomplicated cases, full recovery occurs within two to three months. Although pneumonic conditions are the most common complications, in 5.2% of all cases and in 11.8% of infants younger than 6 months, neurological complications such as encephalopathies can occur. These are severe conditions, worsened by hypoxia caused by airway obstruction, and a neuroimmune-mediated mechanism must be considered.[2,35,37]

There are no animal reservoirs or vectors related to the transmission of pertussis, with humans playing an essential role in its life cycle. It is a highly contagious disease that can affect 80% of susceptible household contacts.[37]

The mass immunization of communities played a crucial role in the reduction of the cases of pertussis. The first "whole-cell" (cellular) pertussis vaccine was administered in the United States in 1914. Later, in 1948, it became associated with diphtheria and tetanus components, receiving the name DTP.[38]

The DTP vaccine provides protective levels in 70% to 90% of the population immunized with four doses, but, due to the drop in levels of protective antibodies, it would need to be repeated every 10 years.[4,35]

Due to the local reactions and adverse effects, an acellular DTP vaccine was developed, which purports to cause a lower incidence of adverse effects. However, the traditional DTP vaccine is still being used in several countries, including Brazil, where it is conjugated with two more components (constituting the PV), immunizing against *H. influenzae* and hepatitis B.[1]

After immunization, the antigens present in VP, in particular those of the cell formulation, activate CD4 + 1 (Th1) T Helper lymphocytes that secrete cytokines such as Interleukin 2 (Il-2), Interferon γ and Tumor Necrosis Factor α (TNF-α).

These cytokines in turn promote the activation of CD4+ T Helper Lymphocytes 17 (Th-17) producing Interleukin 17 (Il-17), which seems to play a crucial role in the long-term post-immunization immune response and which is also related to the production experimental encephalomyelitis.[34]

There are several proposed mechanisms for postimmunization CNS inflammation, with the granulocyte-macrophage colony-stimulating factor (GM-CSF) and the activation of T lymphocytes playing a crucial role in this process.[6,39]

In experimental animal models, decreased GM-CSF activity was associated with reduced development of encephalomyelitis. The use of exogenous administration demonstrated an increase in the severity/onset of the condition. The GM-CSF is secreted by T Helper lymphocytes and induces microglial proliferation and activation.[6,39]

Microglial activation increases the local production of oxygen free radicals, nitrogenous species, glutamate, TNF-α, neurotoxic phenotypic differentiation of microglia and an increase in pro-inflammatory mediators such as Interleukin-1B (Il-1B) and Interleukin-16 (Il-16).[39]

The GM-CSF also contributes to the "break" of the BCSFB and to the recruitment of inflammatory cells from the peripheral blood. It also induces the proliferation of macrophages involved in the positive feedback of Th-1 and Th-17 cells.[6,7,34]

The systemic inflammatory process postimmunization with the PV could decompensate hydrocephalus through a multifactorial mechanism related to the BCSFB.

The "break" of the BCSFB, which causes a higher concentration of proteins in the CSF, could increase the intracystic oncotic pressure. This would cause a slight increase in volume and secondary mechanical obstruction of the CSF drainage pathways.

The greater inflow of water through the BCSFB by diffusion would cause an unbalance in the cystic water inflow/outflow (valvular mechanism) which could also explain the deterioration of the patient's clinical condition.[14]

The BCSFB differs from the blood-brain barrier (BBB) in several respects, but it is no less important. It has distinct regulatory and secretion mechanisms that give it great importance in the physiology and mechanical protection of the brain parenchyma. It is formed by the arachnoid and choroid plexuses and their interface with the cerebral cortex (convexity) and ependymal surfaces of the ventricular cavities.[40,41]

The choroid plexuses are structures composed of highly-permeable capillaries and lined with a specialized epithelium that do not ultrafilter plasma CSF, but rather secrete it. They have microvilli that increase their surface and still receive differentiated irrigation, about ten times that received by the cerebral cortex.[42]

In adults, the choroid plexuses produce about 600 mL of CSF daily, which shows the high "turnover" of the CSF. They not only help from a biomechanical point of view, protecting CNS structures by reducing their weight (floating effect), but they also have an essential metabolic role, as they carry micronutrients, peptides and hormones.[43]

Their simple cubic epithelium has a basement membrane rich in type-IV collagen (α 3, α 4, and α 5 monoclonal chains), and are similar to renal glomeruli in terms of selective permeability. They are rich in utrophin A, a transmembrane protein that provides structural stability and plays important roles related to cell signaling and homeostasis.[44]

Choroid plexus cells capture HCO3−, Cl− and Na+ ions by active transport, and are rich in the number of mitochondria, endoplasmic reticulum and Golgi complex, mainly related to the secretion of products by transcellular transport.[42,45,46]

The cells of the choroid plexuses have a modified apical surface, which is responsible for ion secretion via active transport (via apical Na+, K+, 2Cl− cotransporters). This structure enables the passage of water through an osmotic gradient, regulated by mediated cellular transport channels such as aquaporin-1 (AQP1).[42,45,46]

The passage of small proteins and other solutes by pinocytosis and/or exocytosis (transcellular transport) occurs on this surface.[42,45,46]

Claudins 1, 2 and 11 proteins, especially Claudin 2 (CLDN-2), promote firm cell junction of this epithelium in the so-called occluding zone of the choroidal apical surface. Its genomic expression provides resistance to the cell surface, modulating inappropriate ionic exchanges and preventing larger molecules such as peptides, ferritin, and immunoglobulins from crossing the BCSFB.[42,47]

The inflammatory response through TNF-α and interferon could negatively modulate CLDN2, enabling the disruption of the BCSFB, favoring paracellular transport, decreasing the selective permeability of the cell surface and increasing the protein content of the CSF.

The occurrence of an inflammatory reaction in the apical region and consequent dysfunction would promote inadequate modulation of ionic transport, enabling a greater ionic inflow into the CSF and the consequent increase in the passage of water through AQP1, resulting in an increase in CSF volume.[42]

Thus, the immune and inflammatory effects caused by postPV immunization may have been the determining factors for the alteration of homeostasis, causing decompensation of the infant's hydrocephalus.

Conclusion

Vaccination is crucial for the prevention of numerous infectious diseases. Despite its clear benefit, some patients may experience severe adverse reactions, especially when using preparations with greater immunogenic potential, such as the whole-cell pertusis component in the VP (cellular) vaccine.[5,48]

In theory, the vaccine with the acellular pertussis component (DTPa) has a lower immunogenic potential. The DTPa immunizing agent is now used in all individuals in countries such as the United States, precisely because it provides similar protection and may lead to a reduction in serious adverse events.[7,36,48]

Patients such as the one herein described, with a condition previously unknown to family members, could not have developed such a complication with the acellular vaccine formulation, and would have avoided emergency surgery due to harmful intracranial hypertension.[4,5,35]

Further studies are suggested in patients with ventricular shunts (ventriculoatrial and ventriculoperitoneal) to understand if there is an impact of vaccination with the whole-cell pertussis component, a vaccine currently used in a large scale in Brazil, in the origin of malfunctioning valves.

Conflict of Interests

The authors have no conflict of interests to declare.

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Radiofrequency Thermocoagulation of the Gasserian Ganglion for Trigeminal Neuralgia using a Stereotactic Approach due to a Pterygoalar Bar

Termocoagulação por radiofrequência do gânglio de Gasser na nevralgia do trigêmeo, guiada por estereotaxia devido à presença de barra pterigoalar

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Abstract

The treatment of trigeminal neuralgia (TN) consists of pharmacotherapy and neurosurgical procedure, such as percutaneous radiofrequency rhizotomy. Here, we present the case of a patient with TN refractory to clinical treatment who presented an anatomical variation in the oval foramen, which required stereotactic-guided surgery to access the Gasser ganglion.

This is a 63-year-old male patient who presented with TN refractory to drug treatment. He used carbamazepine and nortriptyline, with no satisfactory response. The percutaneous approach to radiofrequency thermocoagulation was indicated, in view of the comorbidities presented and the patient's age. Due to the presence of a rare anatomical variation, stereotactic-guided surgery was used to cannulate the foramen ovale and, thus, successfully perform the neurosurgical procedure with an excellent clinical response. The use of stereotaxy to guide cannulation of the foramen ovale due to anatomical variation was essential for the success of the procedure. The knowledge of the existence of this anatomical variation, and the mastery of the stereotactic technique enabled the adequate management in the face of the unusual situation.

Keywords

- Gasserian ganglion
- trigeminal neuralgia
- stereotactic
- pterygoalar bar

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Resumo

O tratamento da neuralgia do trigêmeo (NT) consta de farmacoterapia e procedimento neurocirúrgicos, como a rizotomia percutânea por radiofrequência. Aqui apresentamos o caso de um paciente com NT refratária ao tratamento clínico que apresentava uma variação anatômica no forame oval, o que exigiu a realização de cirurgia guiada por estereotaxia para acesso ao gânglio de Gasser.

Trata-se de um paciente do sexo masculino, com 63 anos de idade, que apresentava quadro de NT refratária ao tratamento medicamentoso. Fez uso de carbamazepina e nortriptilina, sem resposta satisfatória. Foi indicada a abordagem percutânea para termocoagulacão por radiofrequência, tendo em vista comorbidades apresentadas e a idade do paciente. Devido à presença de uma rara variação anatômica, utilizou-se a cirurgia guiada por estereotaxia para canular o forame oval, e, dessa forma, realizar o procedimento neurocirúrgico com sucesso e uma excelente resposta clínica. A utilização de estereotaxia para guiar a canulação do forame oval devido à variação anatômica foi essencial para o sucesso do procedimento. O conhecimento da existência dessa variação anatômica, e o domínio da técnica estereotáxica possibilitaram o adequado manejo frente a uma situação incomum.

Palavras-chave

- gânglio gasseriano
- neuralgia trigeminal
- estereotáxico
- ligamento pterigoalar

Introduction

Trigeminal neuralgia (TN) is one of the most common diseases that affect the cranial nerves, with an annual incidence of 12.6 per 100 thousand inhabitants.[1,2] French doctors described it as *ticdoulourex*, due to the presence of facial spasms that could occur[3]. The main clinical features were described by the English physician John Fothergill in 1773.[2] Currently, TN is defined by the International Headache Society as a pain in the hemiface, in shock, brief, limited in one of the most dermatomes of the trigeminal nerve.[4]

The latest Guideline of the European Academy of Neurology 2019[5] indicates the surgical treatment of TN in cases of clinical refractoriness and consists of neurovascular decompression procedures or percutaneous therapies. These interventions include radiofrequency thermocoagulation, the alcoholization of nerves, and even balloon compression.

The surgical modality chosen for each patient will depend on the surgeon's experience as well as on criteria related to the patient, such as the presence of neurovascular conflict evident in imaging tests, and age (there is a tendency to perform decompression surgeries in younger patients).[5]

Among the options for percutaneous access, radiofrequency rhizotomy has the potential to offer definitive treatment for the disease's typical symptom of pain.[1]

Recently, the use of 3D tomography, associated with stereotaxis, has been used to optimize the proposed treatment, considering that 2 to 4% of patients present anatomical variation, making it impossible to access the foramen ovale. The use of this technique enables surgeons to analyze the patient's anatomical characteristics and the relative position of the access.[1]

Here we present the case of a 63-year-old patient with TN who presented an anatomical variation that prevented access to the foramen ovale, culminating in the need for a complementary surgical approach.

Case Report

A 63-year-old male patient presented with severe left hemifacial neuropathic pain, shock-like, in paroxysm, triggered by touch and mood changes. The onset of the pain happened about 1 year prior to the appointment, and it got progressively worse. Initially, the patient was treated with 200 mg carbamazepine, 3 times daily, associated with nortriptyline 25 mg for anxiety, with progressive increase in doses, but there was no satisfactory clinical response. Given the intense pain, percutaneous radiofrequency rhizotomy was proposed, considering the patient's age and the comorbidities presented, such as difficult-to-control arterial hypertension associated with anxiety disorder. In this specific case, we had to use general anesthesia because of the anxiety of the patient, in order to do the procedure. The electrode was guided by stereotomography until it reached the Gasser ganglion.

However, percutaneous puncture of the ipsilateral foramen ovale was not successful, with an apparent bone barrier. The patient was subsequently submitted to a computed tomography scan with 3D reconstruction that identified the presence of a pterygoalar bar (complete ossification) in front of the foramen ovale (►**Figure 1**). Therefore, we proposed to use stereotaxy to plan the trajectory for a new puncture attempt.

We proceeded to the positioning of the radiofrequency electrode, guided by stereotomography, with a stereotaxic ring installed 2 cm above the upper orbital rim, with fiducials facing caudally. The path and angle of entry into the foramen ovale was defined using the MNPS software (Mevis Informatica Médica Ltda., São Paulo, SP, Brazil), so that there was no collision with the pterygoalar bar (►**Figure 2**). During the procedure, the mandible was kept open to allow proper positioning (►**Figure 3**). The thermocoagulation electrode was successfully installed in the Meckel cavum, its position was confirmed with

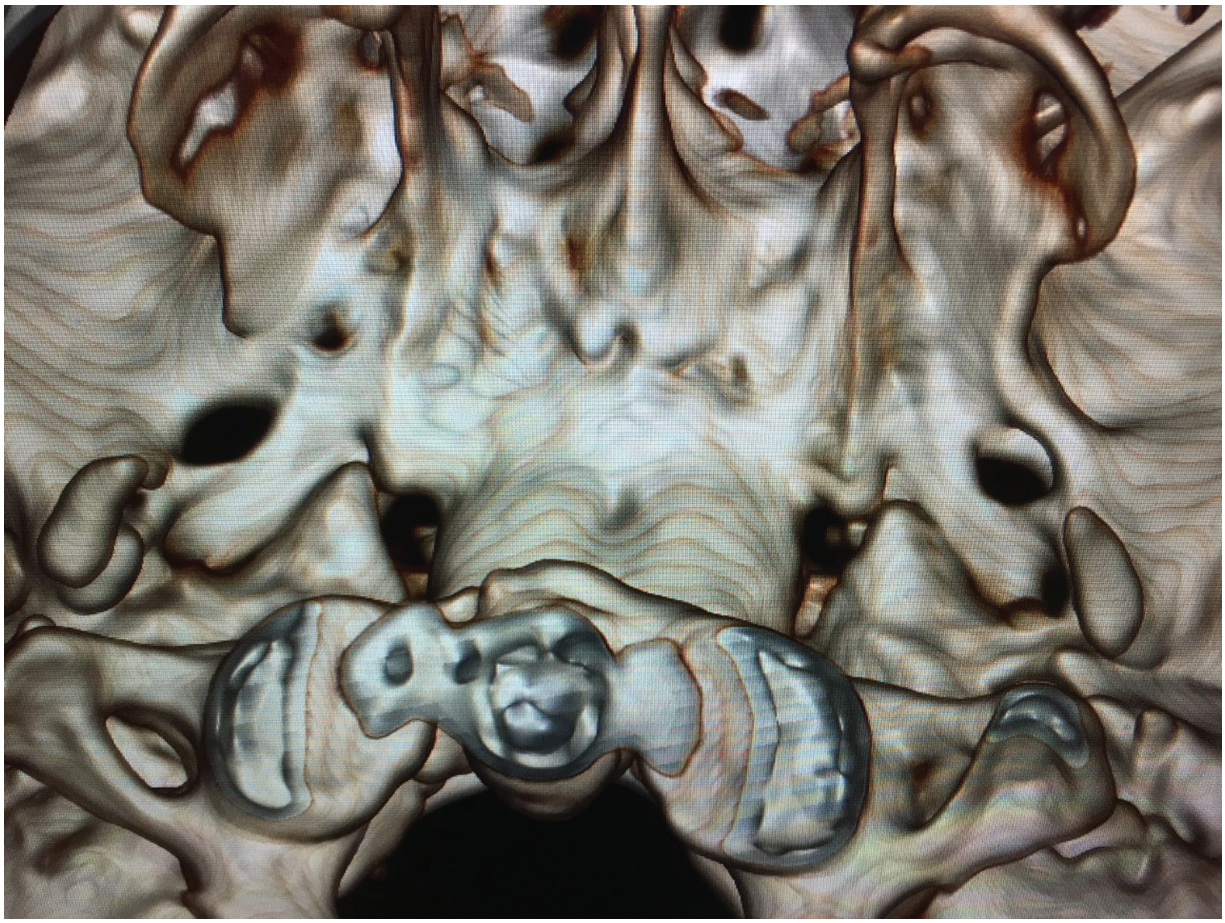

Fig. 1 3D tomographic image, inferior view of the skull revealing the presence of the pterygoalar bar.

radioscopy, and the thermocoagulation of the left Gasser ganglion was performed at a temperature of 60 to 65 degrees for about 60 seconds[3] (►**Figure 3**). The patient showed clinical improvement of TN. During the last outpatient review with a 24-month follow-up, he had a Barrow Neurological Institute pain score of III,[6] and visual analogue scale score of 03/10.

Discussion

Trigeminal neuralgia is a pathology described early in the medical literature, with its first reports going back to the time of Aretaeus of Capaddocia. It is defined as paroxysmal pain in one or more branches of the trigeminal nerve, frequently causing pain of great magnitude.[7]

The diagnosis is eminently clinical, and this criterion has been defined by the International Headache Society. Pain attacks are paroxysmal, lasting for fractions of seconds up to 2 minutes in one or more territories of innervation of the trigeminal nerve. The frequency of which can vary from hundreds of attacks per day to years of remission between one crisis and another.[7,8]

The treatment consists basically of two modalities, clinical and surgical. Anti-seizure drugs are among the most widely used medications, and carbamazepine has control rates of up to 70%.

When there is refractoriness to clinical treatment, or in cases of identified vascular compressions, surgical intervention can be indicated. The most used techniques consist of neurovascular microdecompression and ablative techniques: alcoholization of the peripheral branches of the trigeminal nerve, balloon rhizotomies in addition to electrocoagulation, or radiofrequency thermocoagulation.[4]

Radiofrequency rhizotomy selectively destroys sensory nerve fibers by crushing or applying heat. Pain relief occurs in up to 97% of initial cases and 58% within 5 years, while balloon compression also produces satisfactory results, but they are not long-lasting.

The percutaneous procedure for the treatment of TN was first described by Hartel in 1914.[9] The surgical technique employed consists of puncture via an ascending anterolateral extra-buccal transoval, guided by fluoroscopy in a lateral sub-vertical position.

Three points of reference are used: 3 cm anterior to the external auditory meatus; the mid-pupillary aspect; and 2.5 to 3 cm lateral to the labial commissure. It is important to emphasize the need to follow a plan parallel to the clivus.[7]

The foramen ovale has a diameter between 4 and 7 mm[3] and is located about 2 mm posterior to the pterygoid process.

The rates of failure in puncturing the foramen ovale using fluoroscopy by image intensifier are 0.5 to 4.0%, with an average of 2.7%.[10]

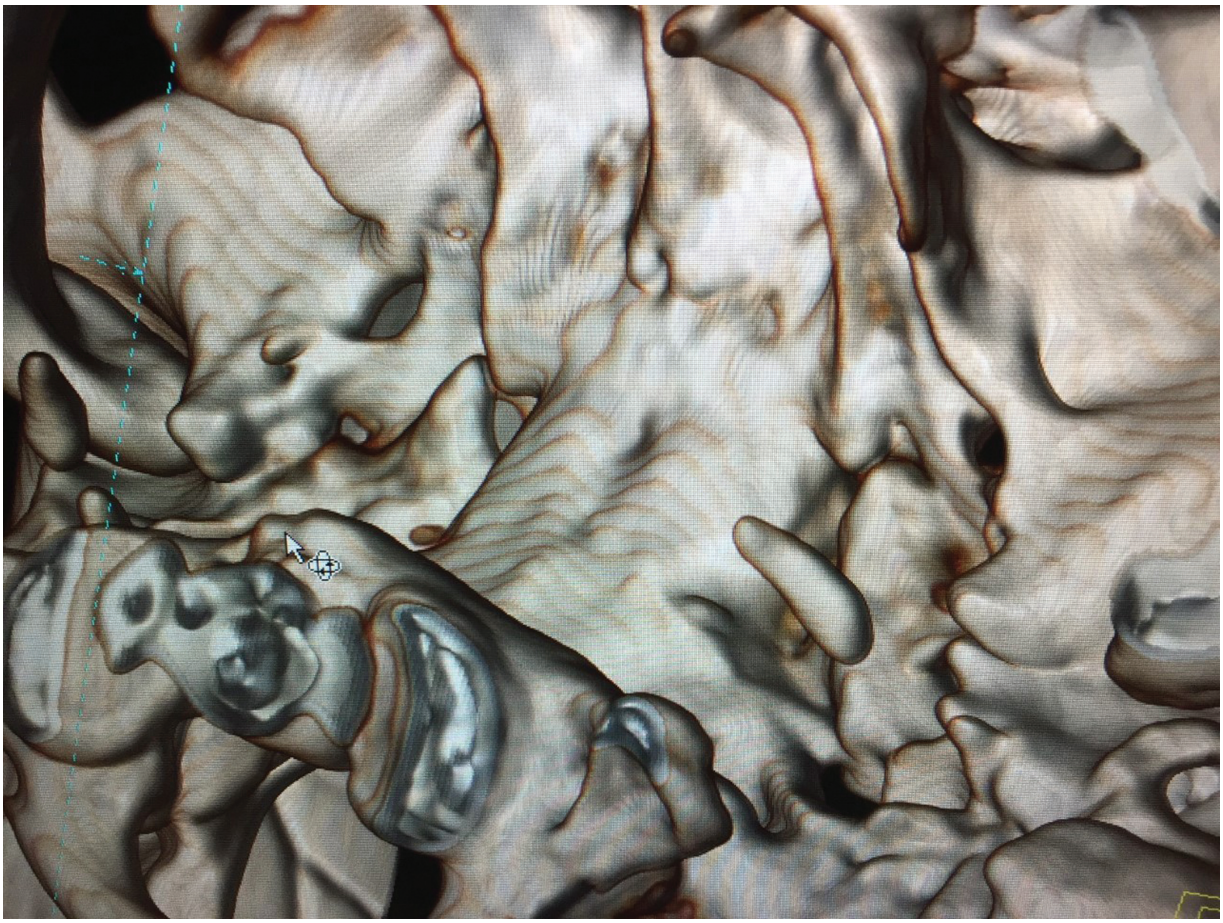

Fig. 2 3D tomographic image, inferior view of the skull, revealing the interposition of the pterygoalar bar in the trajectory to access the foramen ovale.

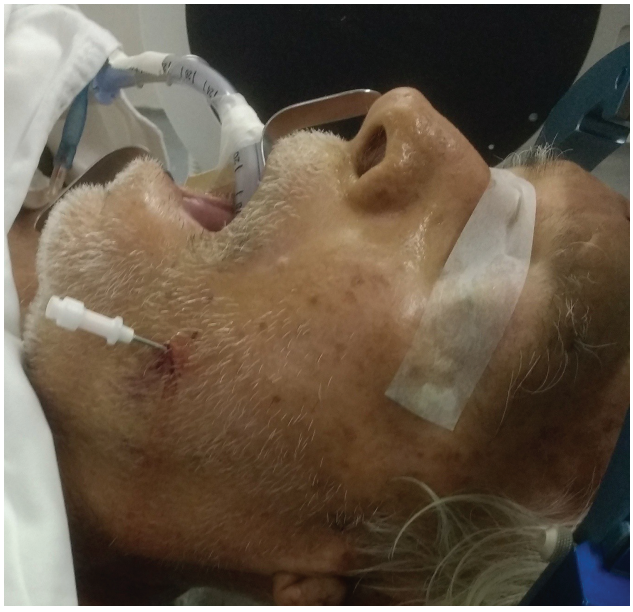

Fig. 3 Demonstrates a more caudal and lateral entry point in relation to the conventional technique.

Such failures may be implicated in technical difficulties, increased surgical time and even inability to perform the procedures.

The complete or incomplete ossification of the pterygoalar ligament (Hyrtl ligament) forms the pterygoalar bar that blocks the passage of the needle towards the foramen ovale.[11] It originates at the root of the lateral pterygoid process, extending to the lower surface of the larger sphenoid wing, close to the anterolateral edge of the spinous foramen.[12]

This rare anatomical variation (about 2–4% of the general population) is a barrier, with only a small passage (Hyrtl foramen) of access to the Meckel cavum.

The use of stereotomography or intraoperative tomography for cases of percutaneous rhizotomies appears to be a safe and low-cost methodology involved in the procedure.

Gusmão, in 2004,[13] had already reported the use of fluoroscopy by computed tomography to perform the puncture of the foramen ovale, in view of the failures to access the foramen. There was a decrease in the attempts to puncture the foramen ovale and in the surgical time.

This case illustrates the importance of adequate anatomical assessment of patients for neurosurgical procedures. Likewise, it demonstrates the importance of mastering the stereotaxic technique in the neurosurgeon's daily practice.

In a literature review through PubMed, 6 articles[14–19] were found regarding the relationship between the pterygoalar bar and TN, 5 of which are anatomical studies on cadavers, and another study[19] in which a retrospective

analysis of operated cases was performed. We did not find any report of a patient with pterygoal bar and TN who needed to change the proposed approach.

Conclusion

The use of stereotaxy as a planning tool in unusual situations, generated by the presence of anatomical variations such as the presence of the pterygoalar bar, is an excellent alternative. This minimizes the need for additional procedures.

The procedure brings good cost/benefit ratio and satisfactory results as seen in the case described above, being an important neurosurgical apparatus.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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Malignant Ocular Melanoma with Intradural Cervical Metastasis: Case Report and Literature Review*

Melanoma ocular maligno com metástase cervical intradural: Relato de caso e revisão de literatura

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Abstract

Introduction The occurrence of malignant ocular melanomas is uncommon, and the association of these tumors with intradural extramedullary metastases in the cervical spine is exceptionally rare.

Case Report A 62-year-old woman undergoing adjuvant chemotherapy after surgical treatment for malignant ocular melanoma begins to experience vertigo and headache. The condition evolved with walking difficulty and neck pain that was exacerbated by swallowing and mobilizing the neck. During her ocular melanoma follow-up, lesions suggestive of metastasis in the central nervous system were not evidenced until this moment. The physical examination did not show significant findings, and a cranial computed tomography scan was performed. The image showed a hyperdense lesion with postcontrast enhancement inside the vertebral canal, at the level of C1-C2. Spinal decompression and subtotal resection were performed. The anatomopathological report revealed intradural metastasis of a malignant ocular melanoma. The postoperative period was uneventful, with significant pain improvement and no recurrences.

Keywords
- intradural extramedullary metastasis
- malignant ocular melanoma
- surgery

* *Study conducted at Hospital Erasto Gaertner, Curitiba - PR, Brazil.*

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Conclusion Intradural extramedullary metastases are rare presentations of malignant ocular melanoma. In addition, less than ten similar cases have been reported in the literature. When caring for a patient with melanoma and neurological deficits, always consider evaluating central nervous system metastases. To evaluate this patient, a sensible and detailed neurological exam is extremely important to recognize the location of the deficits and guide the best approach, such as an indication for surgery.

Resumo

Introdução É infrequente a ocorrência dos melanomas oculares malignos, e menos frequente ainda é a sua associação às metástases intradurais extramedulares na região cervical.
Relato de Caso Uma mulher de 62 anos, submetida a quimioterapia adjuvante após tratamento cirúrgico para melanoma ocular maligno, abre um quadro de vertigem e cefaleia. O quadro evoluiu com dificuldade para deambular e dor cervical que se exacerbava ao se alimentar e mobilizar o pescoço. Durante o seguimento do melanoma ocular, não foram evidenciadas lesões sugestivas de metástase no sistema nervoso central até este momento. O exame físico não denotou alterações significativas, sendo então realizada tomografia computadorizada de crânio, cuja imagem evidenciou lesão hiperdensa com realce após contraste no interior do canal vertebral, no nível de C1-C2. Foram realizadas descompressão medular e ressecção subtotal, cujo laudo anatomopatológico revelou metástase intradural do melanoma ocular maligno. O pós-operatório seguiu sem intercorrências, com melhora significativa da dor e ausência de recidivas.
Conclusão As metástases intradurais extramedulares são apresentações raras de melanoma ocular maligno. Além disso, há menos de dez casos similares relatados na literatura mundial. Ao tratar de um paciente com melanoma e déficits neurológicos, sempre considere avaliar metástases no sistema nervoso central. Para avaliar este paciente, um exame neurológico criterioso e detalhado é essencial para reconhecer a localização dos déficits e guiar o manejo adequado, como a indicação cirúrgica.

Palavras-chave
- metástase intradural extramedular
- melanoma ocular maligno
- cirurgia

Introduction

Melanoma is a potentially-fatal malignant disease, and its frequency is higher in fair-skinned individuals.[1] Epidemiological studies[1,2] indicate melanoma as the fifth and sixth most common cancer among men and women in the United States respectively. In addition, an increase in the incidence of cases is observed between 25 and 50 years of age, with 57 years as the median age at diagnosis.[1] Ocular malignant melanoma occurs in less than 5% of all melanomas, and the liver is the most frequent metastatic site.[2]

Studies indicate that early identification of these lesions is the most important factor in terms of prognosis.[1] Such lesions can cause distant metastases, mainly in the lungs, brain, liver, bones, and intestines, most of them with low rates of success regarding treatment.[3] However, intradural extramedullary (IDEM) metastases are exceptionally rare, especially when there is no other metastasis in the central nervous system (CNS).[1–3]

We herein describe a rare presentation of IDEM metastasis, with an ocular malignant melanoma as the primary site of the lesion. So far, less than ten similar cases have been reported in the literature, and the present report aims to contribute to this context.

Case Report

A 62-year-old female patient was referred to the oncology surgery service due to a diagnosis of ocular malignant melanoma, initially investigated due to progressive decrease in left visual acuity and local pain. There was a history of prolonged exposure to sunlight since the age of 10 years. She denied smoking and drinking, and reported a family history of leukemia. A cranial computed tomography (CT) scan (►**Fig. 1**) identified intraocular hyperdense heterogeneous material. The patient initially refused to get surgical treatment, and sought the service three years later, due to a progressive increase in the lesion over the past six months. At the time, surgical treatment was suggested for the purpose of providing her comfort. A brain magnetic resonance imaging (MRI) scan (►**Fig. 2**) revealed an expansive ocular and extraocular lesion in the left eye, with a large mass extending to the preseptal region and retrobulbar fat, measuring ~ 46 mm in the anteroposterior direction, compatible with primary neoplasia (melanoma), and the presence of left optic nerve atrophy, without unequivocal evidence of intracranial extension. The procedure performed included orbital exenteration and maxillectomy of the orbital floor. There was an absence of lymph node metastases at the time of the

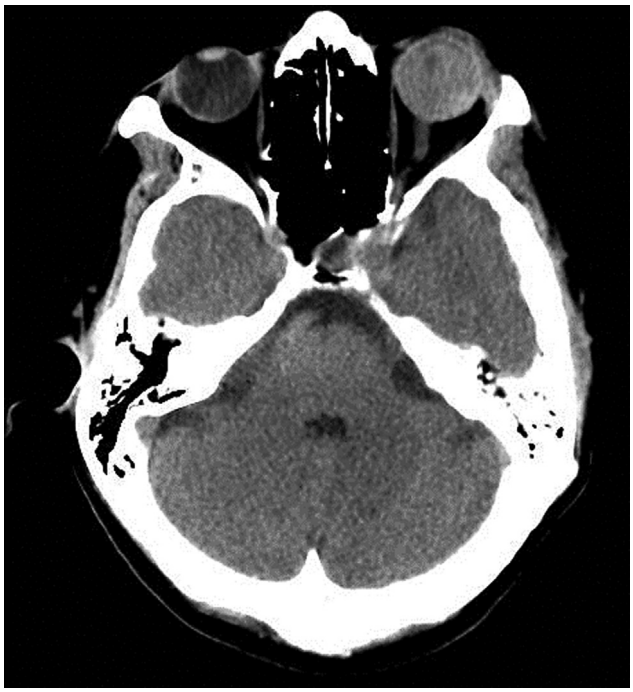

Fig. 1 Brain computed tomography scan showing heterogeneous material inside the left eyeball.

surgery. The histopathological analysis of the specimen revealed mixed-cell melanoma (spindle cell and epithelioid – grade II). The immunohistochemical analysis showed a type III receptor tyrosine kinase, which is localized in various neoplasms, CD117 (cKIT), with diffuse weak positivity.

The postoperative control brain CT revealed no expansive lesions. After the procedure, the patient was referred to start

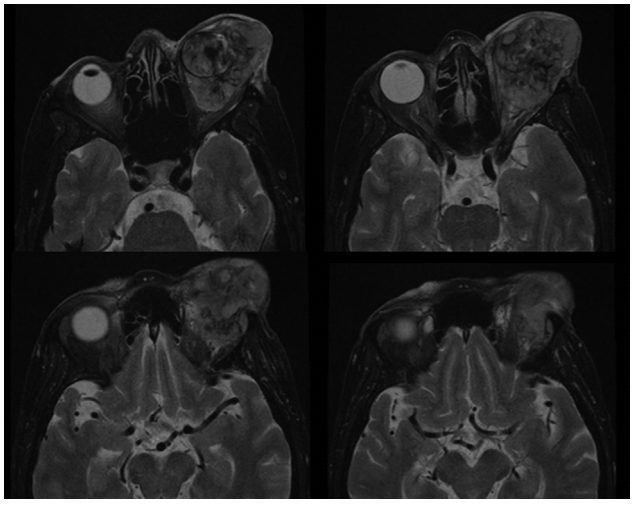

Fig. 2 Brain magnetic resonance imaging scan showing an expansive lesion in the left eye, measuring $\sim$ 46 mm in length in the antero-posterior direction, presenting heterogeneous signs with hypo- and hyperintense foci on T1- and T2-weighted images and postgadolinium heterogeneous enhancement. Impression of discrete postgadolinium enhancement in the canalicular portion of the left optic nerve, with atrophy of its prechiasmatic segment, is also observed.

adjuvant therapy. Chemotherapy with interferon-α 2A and radiotherapy (34 Gy) were indicated for locoregional control of the orbit. She remained in bimonthly outpatient follow-up but did not complete the recommended time for adjuvant therapy, having undergone 1 year and 8 months of chemotherapy. She was lost to follow-up for 8 months due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, reporting isolation. Upon return, in agreement with the patient and family, we identified that there was no benefit from the continuation of the treatment with interferon, but the bimonthly follow-up was maintained. Despite this, she did not perform the imaging exams requested. Three months after resuming follow-up, the patient started to present vertigo and headache. A CT scan of the brain revealed a spontaneously hyperdense, contrast-enhanced nodule within the vertebral canal, at the level of C1-C2. The nodule had approximate dimensions of 14×10 mm in the axial plane and 19 mm in the sagittal plane. The lesion was not present in previous exams. In addition, a hypoattenuating area was identified in the left frontal lobe, adjacent to the anterior horn of the lateral ventricle, mainly affecting the white matter, and not promoting effacement or retraction of the cerebral sulci. We identified the presence of a tenuous nodular enhancement focus measuring 2 mm in the cortical-subcortical transition. We recommended that the investigation should proceed with a cervical spine MRI.

One month after identifying the changes in imaging exams, the patient sought the emergency room of the service due to difficulty in walking, dizziness, and neck pain, which had evolved for weeks, in addition to an episode of emesis the day before. The pain was exacerbated with neck mobilization and swallowing, leading to reduced food intake. Upon physical examination, muscle strength was normal in all four limbs, and sensitivity was preserved. She was admitted for a specialized evaluation, which determined the need for surgical management for spinal-cord decompression. Dexamethasone 4 mg was started every 6 hours until the procedure, which was performed two days later. The cervical spine MRI (►**Fig. 3**) showed a solid intradural extramedullary nodule located posteriorly to the vertebral canal at the level of C1 and C2, measuring $28 \times 17 \times 15$ mm.

Intraoperatively, after laminectomy of C1 and opening of the dura mater, a black lesion measuring $\sim$2.5 cm in the longitudinal direction (►**Fig. 4**) was observed, which partially infiltrated nerve roots and vascular structures and compressed the left lateral region of the spinal cord. Most of the tumor was resected, except for the infiltrated regions, considering the risks to mobility and sensitivity. The patient had no neurological deficits on the first postoperative day, reporting only pain in the left ear canal.

Discussion

Intradural extramedullary metastases (IDEM) from malignant melanomas are exceptionally rare. Also, IDEM metastases correspond to approximately 5% of spinal metastases.[4]

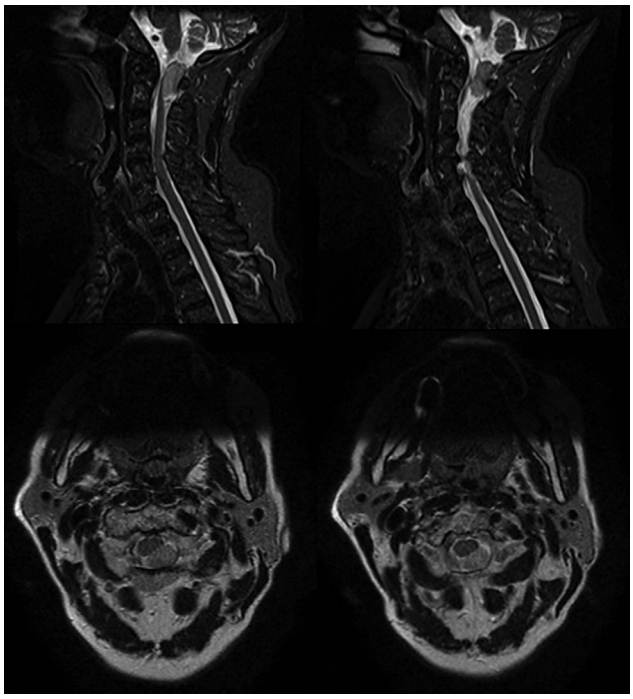

Fig. 3 Magnetic resonance imaging scan of the cervical spine showing a solid intradural extramedullary nodule located posteriorly to the vertebral canal at the level of C1 and C2 measuring 28 × 17 × 15 mm, compressing the posterior surface of the medullary cord. It presents isosignal on T1 and hypersignal on T2 with the musculature and moderate/slightly heterogeneous post-gadolinium uptake.

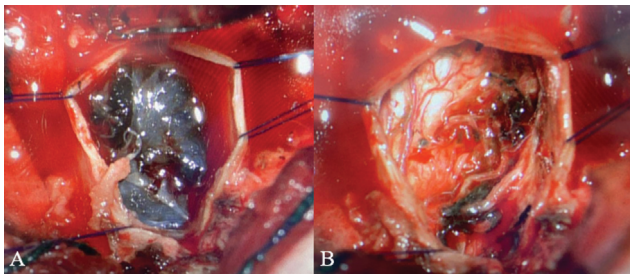

Fig. 4 (A) Intraoperative appearance of the lesion. (B) Intraoperative appearance after subtotal resection.

The overall prevalence of spinal melanoma metastases estimated by clinical studies[5] is only 2.4%, and the ocular site corresponds to 10% of the primary melanoma sites. Metastases to the brain are more prevalent than those to the spinal, and CNS metastases occurs in 10% to 40% of melanoma patients, and in up to 90% of the cases in autopsy studies.[6]

The first report of IEMs occurred in 1982, when Perrin et al.[7] analyzed 200 patients with non-neurogenic spinal metastases, and found that 10 cases occurred in the intradural space. By 2020, 14 cases of IEM metastasis of malignant melanoma had been published,[2] and only 3 were located between cervical vertebrae. The comparison of those 3 studies[3,5,8] and the present case are shown in ►**Table 1**.

Multiple theories have been proposed to explain the spread to the intradural space. Among them, the most accepted and which corroborates the fact that most IEMs are associated with other metastases in the CNS is the theory of dissemination through the cerebrospinal fluid (CSF), also called "drop metastases."[2,4] In a review,[8] a rate of positivity of 50% for malignant cells was observed in the CSF analysis. Even though a CSF examination was not performed in the present study during the reported period, the authors agree with its importance, notably when leptomeningeal commitment is a plausible differential diagnosis.

In those patients without coexisting CNS metastasis, other theories of hematogenous spread seem more plausible. When analyzing tributary veins of the vertebral venous plexus, it is possible to establish drainage routes communicating the eyes and the maxilla (primary surgical sites) to the craniovertebral junction. A possible drainage route is after the ophthalmic veins reach the cavernous sinus, the hematogenous metastasis would be drained to the basilar venous plexus, and via the marginal sinus disseminate to vertebral venous plexus. However, due to the drainage anatomy, the most plausible route is the hematogenous metastasis draining to the inferior petrosal sinus and reaching the superior bulb of the internal jugular vein, which does not corroborate to explain the dissemination of the present case.

Among the 14 similar cases reported in the literature,[2] the thoracic and lumbar regions were the most affected, and the predominant symptoms in these cases were weakness in the lower limbs and paresthesia. Lumbar, radicular or cervical pain, urinary dysfunction or incontinence, and loss of thermal sensitivity were other symptoms reported according to the location of the metastasis.[2] The time from the diagnosis of malignant melanoma to the diagnosis of cervical IDEM metastasis was also variable, as reported by Knafo et al.,[8]

Table 1 Literature review of intradural extramedullary metastasis of malignant melanoma in the cervical region

Reference	Age and gender	Vertebrae	Symptoms
Shakur et al.,[5] 2012	66, female	C1–2	Weakness and sensory loss
Knafo et al.,[8] 2013	74, male	Cervical (not specified)	Cervical pain
Stein et al.,[3] 2018	63, male	C1–2, C7-T1, conus medullaris, L4-S1	Cervical pain, weakness, and sensory loss
Present case, 2021	62, female	C1–2	Cervical pain, headache, dizziness, walking difficulty, and emesis

occurring in less than 1 year, and by Shakur et al., after 14 years.[5] In the present case, the time from the diagnosis of melanoma until the patient manifested symptoms of IDEM metastasis was of 6 years.

Regarding treatment, the information available in the literature is scarce. Only a few authors[2,4,9] report good recovery after surgery with or without adjuvant radiotherapy, yet resection is still indicated with a strictly palliative purpose to try to preserve neurological function.[5,9] Among patients with spinal metastasis deficits from malignant melanoma, Donaldson et al.[10] reported a median survival of 5.3 months with surgery, and of 1.2 months without surgery. However, although the prognosis remains unfavorable, there has been a trend toward better results since 2012 compared with the results observed between 1982 and 1999, which may be related to advances in imaging diagnosis, chemotherapy, and early diagnosis.[2]

Conclusion

In the present article, we report a rare form of intradural extramedullary metastatic tumor in an elderly patient. In our review, only a few studies have reported such a presentation. When caring for a patient with melanoma and neurological deficits, always consider evaluating CNS metastases. Brain metastases are more probable, and can spread as "drop metastases" through the CSF, predisposing spinal metastases. To evaluate this patient, a sensible and detailed neurological exam is extremely important to recognize the location of the deficits and guide the best approach, such as an indication for surgery.

Ethics Statement

The present study was approved by the Ethics in Research Committee of Centro de Projetos de Ensino e Pesquisa (CEPEP) from Hospital Erasto Gaertner, in the city of Curitiba, Southern Brazil, and approved under CAAE number 87548518.2.0000.0098. Written consent was obtained from the patient.

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Conflict of Interests

The authors have no conflict of interests to declare.

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Extrinsic Compression of the Gastric Wall by a Ventriculoperitoneal Shunt Catheter: Case Report and Literature Review*

Compressão extrínseca de parede gástrica por cateter de derivação ventriculoperitoneal: Relato de caso e revisão de literatura

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Abstract

Introduction Ventriculoperitoneal (VP) shunt is commonly used in the treatment of hydrocephalus and may present complications in up to 30% of patients. The present report addresses an uncommon complication in the abdominal cavity, in which the catheter caused extrinsic compression of the gastric wall.

Case report A 30-year-old man presented a decreased level of consciousness, associated with severe headache and vomiting. He had a history of congenital neurotoxoplasmosis and VP shunt insertion at 7 years of age. Imaging exams demonstrated the formation of an encapsulated retrogastric pseudocyst and extrinsic compression of the gastric wall by a VP shunt catheter. Through videolaparoscopy, decompression of the gastric wall and removal of the pseudocyst were performed, with the reestablishment of the drainage of cerebrospinal fluid. An analysis of the distal fragment of the removed catheter revealed obstruction by fibrotic material. The patient was discharged with a reestablished baseline after four days of hospitalization.

Comments The literature shows that ~ 47% of the complications presented by patients are related to the distal end of the catheter, and 8.2% of these come from

Keywords
- hydrocephalus
- ventriculoperitoneal shunt
- complications
- extrinsic compression
- gastric wall

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migration to the abdominal cavity. However, there is an extreme paucity of studies that demonstrate extrinsic compression of the gastric wall by a VP shunt catheter. Therefore, we suggest that further studies on complications involving the VP shunt be performed to improve diagnostic and therapeutic results, in addition to complementing the literature on this complication.

Resumo

Introdução A derivação ventriculoperitoneal (DVP) é comumente empregada no tratamento da hidrocefalia, e pode apresentar complicações em até 30% dos pacientes. Este relato aborda uma complicação incomum na cavidade abdominal, em que o cateter promoveu compressão extrínseca da parede gástrica.

Relato de caso Um homem de 30 anos apresentou rebaixamento do nível de consciência associado a cefaleia de forte intensidade e vômitos. O paciente tinha histórico de neurotoxoplasmose congênita e inserção de DVP aos 7 anos. Os exames de imagem demonstraram formação de pseudocisto encapsulado retrogástrico e compressão extrínseca de parede gástrica por cateter de DVP. Por meio de videolaparoscopia, foram realizadas a descompressão da parede gástrica e a remoção do pseudocisto, com o restabelecimento da drenagem de líquido cefalorraquidiano. Uma análise do fragmento distal do cateter removido revelou obstrução por material fibrótico. O paciente recebeu alta com quadro basal reestabelecido após quatro dias de internação.

Comentários A literatura mostra que ∼ 47% das complicações apresentadas pelos pacientes relacionam-se com a extremidade distal do cateter, sendo que 8,2% destas são oriundas de migração para a cavidade abdominal. Entretanto, há extrema escassez de estudos que demonstrem a compressão extrínseca da parede gástrica por cateter de DVP. Portanto, sugerimos que novos estudos envolvendo complicações de DVP sejam realizados, a fim de melhorar os resultados diagnósticos e terapêuticos, além de complementar a literatura acerca dessa complicação.

Palavras-chave
- hidrocefalia
- derivação ventriculoperitoneal
- complicações
- compressão extrínseca
- parede gástrica

Introduction

Hydrocephalus is a condition in which there is an accumulation of cerebrospinal fluid (CSF) in the cranial cavity, whose pathophysiology is disorders related to its production, circulation or reabsorption, which enables its classification into obstructive and non-obstructive.[1,2] The understanding of the mechanisms that lead to this condition has been sought since the time of great scholars, such as Hippocrates, Galen and medieval Arab doctors.[3] Thus, the understanding of these processes enabled the development of procedures that would reduce the excess of CSF in the cranial box, such as the insertion of catheters inside the cerebral ventricular system.[2–4] This technique is called ventricular bypass, and its principle is the drainage of excess CSF from the skull to places such as the peritoneal cavity, the pleural space, or the atrium.[2,4,5] The peritoneal cavity, however, is the most common drainage site, and the procedure is called ventriculoperitoneal (VP) shunt.[1–5] Nevertheless, complications are observed in the long term in some of these surgeries, and the most frequent are obstructions of the VP shunt catheter, formation of pseudocysts in the abdominal cavity, intestinal perforations, migration of the distal extremity, torsions, catheter breakage, infections, or even subdural hematoma.[2–5]

The literature estimates that approximately 30% of patients undergoing this treatment will experience procedural failure, with patients free from other complications being restricted to 15% over 10 years. In addition, it is estimated that around 8,17% of patients will experience migration of the catheter to the abdominal wall, with extrinsic compression by the catheter into an abdominal organ being less frequent.[5,6] In this scenario, the present report addresses an unusual form of complication of the VP shunt in the abdominal cavity, in which the distal catheter remained tied around the stomach due to migration, with the respective extrinsic compression of this organ.

Case Report

A 30-year-old man weighing ∼ 70 kg was admitted to the emergency department with a lowered level of consciousness, associated with severe headache and vomiting. He had a history of cognitive sequelae caused by congenital neurotoxoplasmosis, and prior hospitalization at the age of 7 years for acute hydrocephalus, which was then treated with a VP shunt. The neurological examination yielded a score of 10 on the Glasgow Coma Scale (eye opening: 3; verbal response: 2; motor response: 5), in addition to showing severe

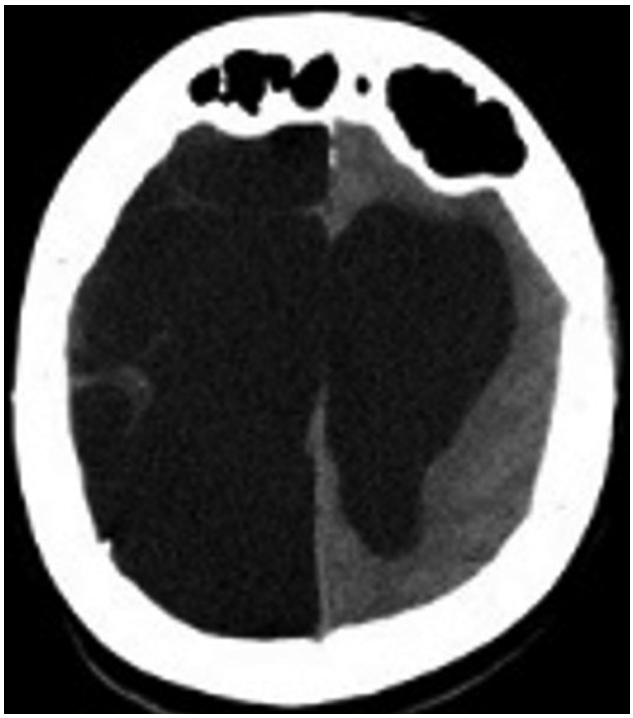

Fig. 1 Cranial computed tomography (CT) showing supratentorial ventriculomegaly

neurotoxoplasmosis sequelae, with atrophy of the lower limbs. The examination maneuver of the VP shunt device revealed normal functionality proximal to the valve. A computed tomography (CT) scan of the skull was then performed, which revealed an important cerebral malformation, with areas of encephalomalacia in the right hemisphere, in addition to supratentorial ventriculomegaly (►**Fig. 1**).

The patient underwent lumbar puncture, and the analysis of the CSF showed normal biochemistry and negative culture for bacteria. During hospitalization, an ultrasound (US) of the abdomen showed the formation of a peritoneal pseudocyst encapsulated in the left flank, which might be associated with the distal end of the VP shunt catheter. The follow-up of the case was performed with investigation by means of radiography (XR), which suggested invasion of a distal catheter into the stomach (►**Fig. 2**). An abdominal CT scan showed proximity of the catheter to the gastric walls (►**Fig. 3**), while the complementary report of the upper digestive endoscopy concluded that the catheter had caused bulging of the gastric wall, as it surrounded part of this organ with the respective extrinsic compression.

After the diagnosis of extrinsic compression, the patient was submitted to videolaparoscopy for drainage of the retrogastric cyst and distal section of the obstruction point of the VP shunt catheter. During the surgical procedure, in addition to multiple adhesions, with the mesocolon adhered to the abdominal wall, we found that the obstructed VP shunt catheter was compressing the gastric wall. With the section $\sim$ 2 cm proximal to the point of obstruction, spontaneous drainage of the CSF was evidenced. The fragment of the VP shunt catheter (►**Fig. 4**) was submitted to an anatomopathological examination, and the analysis of the specimen that

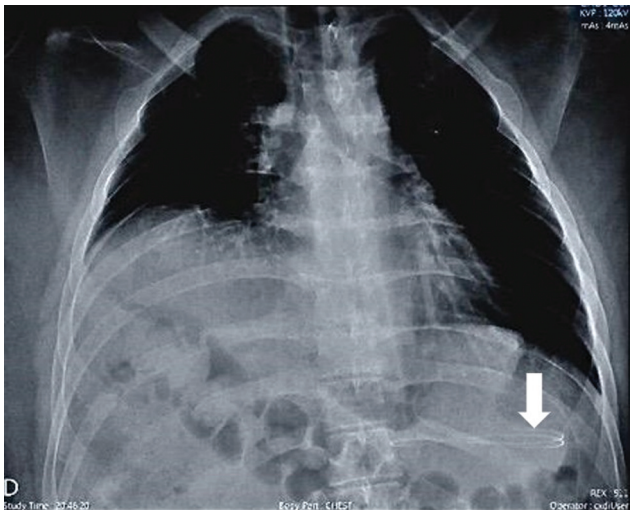

Fig. 2 Chest X-ray showing a ventriculoperitoneal (VP) shunt catheter in the gastric region

obstructed it revealed that it was composed of fibroadipose tissue, with a moderate chronic inflammatory process.

Postoperative control examinations confirmed a reduction in ventricular volume and correct positioning of the VP shunt catheter, which enabled us to discharge the patient from the hospital with a reestablished baseline after four days of hospitalization.

Discussion

The first description of the VP shunt was made by Kaush in 1908.[2] Since then, this has been the procedure most commonly performed by neurosurgeons for the treatment of hydrocephalus.[1,2] The technique basically consists in connecting the catheter proximal to a VP shunt valve, while the distal catheter is connected to the distal end of the same valve, and is then tunneled through the subcutaneous tissue until it is inserted into the peritoneal cavity.[2,3] With the dissemination of this technique, catheters made from silicone emerged in the 1990, a material that proved to be a predisposing factor to allergic reactions, which would

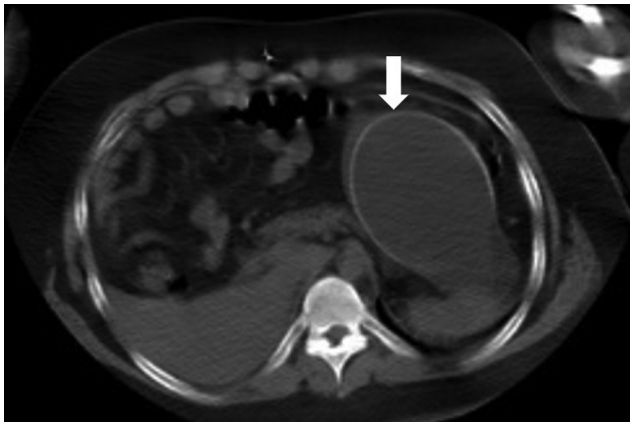

Fig. 3 Abdominal CT showing the distal end of the VP shunt catheter in contact with the stomach walls

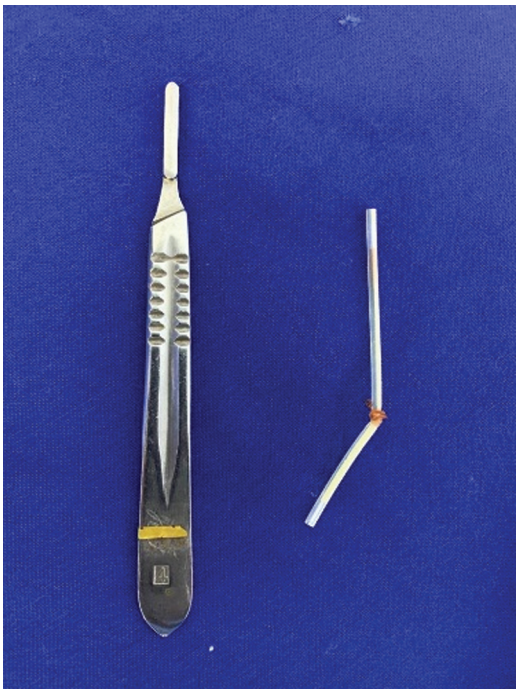

Fig. 4 Fragment of a VP shunt catheter with the fibrotic material that obstructed it

culminate in chronic inflammatory processes around it, with the formation of fibrosis.[1,5,6] Thus, based on the scenario in which distal-end malfunction corresponds to 47% of VP shunt complications, it would be possible to obtain a plausible explanation for the development of obstruction of the distal catheter, which represents up to 15.3% of the total of complications.[6] In addition, other postoperative complications, such as infection, cerebrospinal pseudocyst, perforations of abdominal organs and migration of distal catheter to the abdominal cavity, mediastinum or heart are also described.[1,3,4,6]

The present is a report of a complication not often described in the literature, considering that studies[5,6] indicate that, in the event of migration, the catheter is restricted in up to 8.2% to the abdominal wall, with an association with the stomach being infrequent. However, when in contact with this organ, there is a higher incidence of gastric perforation, with protrusion of the catheter into the lumen of the organ, which often does not generate significant clinical changes.[3–6] Cohen-Addad et al.[3] suggest what would be the pathophysiological mechanism related to this finding, which is based on the interaction of the catheter with the organ wall, either at the time of insertion or later, which leads to local inflammation, tissue changes, and fibrosis, which may generate organ adhesion or even delayed perforation.[3,5,6] However, perforation was not observed in the case herein reported, but extrinsic compression of the stomach by a VP shunt catheter was observed.

In their retrospective review, Abode-Iyamah et al.[2] evaluated the risks of developing VP-shunt complications regarding different age groups and catheter insertion techniques, and they also made a subsequent postinsertion analysis of the VP shunt. As a technique, the conventional insertion in the peritoneal cavity was established.[3,5] Imaging exams were used to verify the correct positioning of the catheter in the peritoneum throughout the years, which made it possible to establish that the incidence of complications increased with advancing age.[2–4] In the present study, we inferred that age and, consequently, the patient's growth was shown to be a predisposing factor for catheter migration. Alonso-Vanegas et al.[4] reported that the patient's position, postprandial gastric distension, and diaphragm movements are other risk factors for chronic irritation in the region of contact with the stomach, which could lead to perforation.[4,5] In the case herein reported, intraoperatively, it was possible to visualize areas of chronic inflammation and the respective fibrosis around the catheter, as was found in most studies[2–8] in which there was perforation of abdominal organs; however, no perforation of the gastric wall was evidenced through the VP shunt catheter. Moreover, in other studies,[5–7] CSF culture revealed infection by *Staphylococcus capitis* and *Enterobacter cloacae*, which was linked to distal catheter migration in the stomach. In the present report, however, no positive cultures for any microorganisms were found in the respective analysis.

The diagnosis of these complications can be made through US, XR, CT, or even with the study of radioisotope elements by fluoroscopy; however, the CT and XR are the most requested exams by the services.[5–7,9] Another study[3] suggests that upper digestive endoscopy can also help in the diagnosis and treatment, which is useful in cases of gastric perforation without peritoneal irritation. Therefore, to study the cause of obstruction in the case herein reported, we used US, XR and CT. The CT allowed us to assess the relationship of the catheter with the gastric walls, for correct surgical management, while the US helped us detect the pseudocyst in the gastric wall. The RX, however, was not sufficiently accurate to differentiate the possible perforation from the involvement of the catheter in the abdominal wall.

As for the treatment, the literature[9,10] shows a different kinds of management for each type of complication. The procedures of choice include infection control with antibiotics, section of the point of obstruction, external proximal drainage, repositioning of the catheter, and a new procedure to remove the current catheter and insert another VP shunt on the contralateral side.[3,8–11] Therefore, the treatment chosen for our patient was the removal of the obstructed part of the catheter, without the need to insert a new VP shunt. However, the access route for catheter removal was not through exploratory laparotomy, as usual, but through videolaparoscopy, given that no signs of peritoneal irritation were found.[1–11] Furthermore, the advent of the minimally-invasive technique enabled the treatment of this complication without significantly increasing the patient's morbidity and mortality rates, in addition to ensuring a shorter hospital stay. The anatomopathological analysis in the postoperative period was suggestive of fibrosis around the catheter, which led to obstruction of the CSF drainage, while promoting extrinsic compression of the gastric wall. Thus, as in other studies,[1,3,6,10,11] fibrosis around the VP shunt catheter

proved to be a plausible explanation for the finding of drainage obstruction in our patient.

Therefore, when analyzing the conditions related to complications, diagnosis and treatment found in the literature, we inferred that some of these characteristics had some degree of similarity in relation to those of our patient. Millward et al.[1] described the case of a foreign body granuloma around the valve and the VP shunt catheter in a patient who underwent multiple VP shunt replacements, with the CSF presenting eosinophilia. Furthermore, the correlation between perforation of the gastric wall and the formation of fibrosis around the VP shunt catheter has also been observed and reported by Alonso-Vanegas et al.,[4] Masuoka et al.[5] and Cheng et al.[7] Moreover, there are reports of the incidental finding of a VP shunt catheter in the gastric fundus in an asymptomatic patient, migration of the VP shunt catheter to the mediastinum, and spontaneous knot formation at the distal end of the VP shunt catheter, which were published by Cohen-Addad et al.,[3] Fukamachi et al.[8] and Borcek et al.[6] respectively. In addition, Fukamachi et al.[8] also described two other cases of complications associated with the VP shunt catheter: extrusion of a VP shunt catheter through a healed abdominal incision, and migration of a subdural catheter to the brain parenchyma. ►**Table 1** summarizes the main characteristics of the aforementioned cases of VP shunt complications.

We included in ►**Table 1** other studies, which are not specifically case reports, but which contribute to the understanding of the risk factors and diagnosis of the complications. Thus, Abode-Iyamah et al.[2] observed that obesity and the number of previous procedures are closely associated with complications involving the distal end of the VP shunt catheter. In addition, Ezzat et al.[11] identified other risk factors for the development of these complications, such as peristaltic activity, shunt characteristics, and insertion technique, while Grosfeld et al.[10] and Goeser et al.[9] pointed out that the high rate of suspicion, followed by the early treatment of these complications, reduces the risks to the patient. In our case, fibrosis around the catheter, the diagnostic and therapeutic methods were similar to the data found in the literature, with extrinsic compression of the gastric wall without its perforation by the VP shunt catheter, the unique characteristic of the case herein reported.

Thus, we suggest that further studies on the prognosis and recurrence of migration of the VP shunt catheter are needed to improve the therapeutic results and complement the literature on this subject.

Table 1 Summary with the main findings of the literature review

Author (year)	Patients	Findings	Treatment	Results
Millward et al.[1] (2013)	Male/14 years old	Foreign body granuloma around the valve and VP shunt catheter in a patient with multiple changes of VP shunt and CSF with eosinophilia.	Removal of the VP shunt catheter and insertion of a hypoallergenic catheter.	The patient was asymptomatic after the intervention.
Abode-Iyamah et al.[2] (2016)	137 patients, with a mean age of 57.7 years	Retrospective study evaluating the risk factors involved in VP shunt complications.	Identification of the occurrence of migration of the distal end of the VP shunt catheter in 16 patients.	It was observed that obesity and the number of previous VP shunt procedures were associated with the occurrence of complications with the distal end of the catheter.
Cohen-Addad et al.[3] (2018)	Male/72 years old	Incidental finding of a VP shunt catheter in the gastric fundus during percutaneous endoscopic gastrostomy.	No surgical treatment was performed to change the VP shunt.	The baseline was restored after the intervention.
Alonso-Vanegas et al.[4] (1994)	Female/4 months old	Gastric perforation and fibrosis around the VP shunt catheter, associated with signs and symptoms of intracranial hypertension.	Removal of the fibrosis, suture of the stomach, removal of the VP shunt, and replacement by the left ventricle-atrial system.	The patient was asymptomatic after the intervention.
Masuoka et al.[5] (2005)	Male/47 years old	Gastric perforation and fibrosis around the VP shunt catheter.	Extraction of the VP shunt catheter through a scalp incision.	The patient was asymptomatic after the intervention.

(*Continued*)

Table 1 (*Continued*)

Author (year)	Patients	Findings	Treatment	Results
Borcek et al.[6] (2012)	Male/5 years old	Spontaneous knot formation at the distal end of the VP shunt catheter in a patient with signs and symptoms of intracranial hypertension.	Node clearance and revision of the derivation system.	The baseline was restored after the intervention.
Cheng et al.[7] (2007)	Male/87 years old	Gastric perforation and fibrosis around the VP shunt catheter in a patient with upper gastrointestinal bleeding due to associated gastric ulceration.	Removal of the fibrosis stitch and suturing of the gastric wall through laparotomy.	The patient was asymptomatic after the intervention.
Fukamachi et al.[8] (1982)	Female/7 months old	Migration of the VP shunt catheter to the mediastinum on two occasions.	Removal of the VP shunt catheter from the chest and fixation of the distal end to the peritoneum and abdominal fascia through laparotomy.	The patient was asymptomatic after the intervention.
	Male/49 years old	Extrusion of the VP shunt catheter through the healed abdominal incision.	Fixation of the VP shunt catheter to the peritoneum and reinforcement of the sutures in the muscle layers.	The baseline was restored after the intervention.
	Male/1 year old	Migration of the subdural catheter to the brain parenchyma after a subdural-peritoneal shunt procedure to treat hygroma after traumatic subdural hematoma.	Complete shunt removal.	Progressive improvement was observed during the follow-up.
Goeser et al.[9] (1998)	Pediatric patients with VP shunt catheter.	Correlation between imaging exams with signs and symptoms of acute hydrocephalus.	Use of imaging exams for the early diagnosis of the complications associated with the VP shunt and to guide the treatment.	The early identification, through imaging exams, of VP shunt complications is essential to guide the treatment and minimize the risks to the patient.
Grosfeld et al.[10] (1974)	185 pediatric patients with VP shunt catheter.	Retrospective study with 45 cases presenting intra-abdominal complications associated with the distal end of the VP shunt.	Treatment of the intra-abdominal complications, followed by serial follow-up of the patients.	The high level of suspicion for complications and postoperative follow-up is essential for these conditions to be identified and treated early.
Ezzat et al.[11] (2018)	1,092 patients, under the age of 12 years	Retrospective study with complications involving the distal end of the VP shunt catheter in 15 patients with a mean age of 1,5 years.	Early treatment of the complications and postoperative follow-up and identification of the risk factors for these conditions.	Peristaltic activity, shunt characteristics and the technique for the insertion of the catheter were the main risk factors for these complications.
Present case report	Male/30 years old	Extrinsic compression of the gastric wall.	Decompression of the gastric wall, removal of the pseudocyst, and sectioning of the distal end through videolaparoscopy.	Restoration of the basal state.

Abbreviations: CSF, cerebrospinal fluid; VP, ventriculoperitoneal.

Conclusion

Extrinsic compression of the gastric wall by a VP shunt is rare and requires a high index of suspicion to establish the diagnosis. The treatment includes changing the VP shunt, or sectioning in cases of associated obstruction, preferably in specialized centers and with an experienced multidisciplinary team.

Ethics Statement

The present study complied with all institutional guidelines for research in human beings. Informed consent was obtained from the person responsible for the patient.

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Conflict of Interests

The authors have no conflict of interests to declare.

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Treatment of Cluster Headache by Occipital Nerve Stimulation: Case Report

Tratamento de cefaleia em salvas por estimulação do nervo occipital: Relato de caso

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Abstract

Cluster headache (CH) is a primary headache characterized by severe pain that is strictly unilateral, with orbital, supraorbital, or temporal location, accompanied by ipsilateral autonomic manifestations. It has a considerable socioeconomic impact and impairs patients' quality of life. The present study aimed to report the case of a patient presenting with CH who underwent occipital nerve stimulation and to verify the improvement in her quality of life after this procedure.

Keywords
- cluster headache
- treatment
- neuromodulation
- quality of life
- nerve
- anesthetic block

Resumo

A cefaleia em salvas (CS) é uma cefaleia primária caracterizada por dor intensa estritamente unilateral, com localização orbital, supraorbital ou temporal, acompanhada por manifestações autonômicas ipsilaterais. A CS tem considerável impacto socioeconômico e prejudica a qualidade de vida dos pacientes. Este estudo teve como objetivo relatar o caso de uma paciente com CS submetida a neuroestimulação occipital e verificar a melhora de sua qualidade de vida após este procedimento.

Palavras-chave
- cefaleia em salvas
- tratamento
- neuromodulação
- qualidade de vida
- nervo
- bloqueio anestésico

Introduction

Cluster headache (CH) is a primary type of headache that is classified in to the group of trigeminal autonomic cephalalgias.[1] The main characteristics of CH are severe and strictly-unilateral pain, with orbital, supraorbital, or temporal location, associated with ipsilateral autonomic manifestations. Crises can last from 15 to 180 minutes, occurring one or several times a day for a few weeks, generally followed by a period of remission.[2,3]

Since CH is characterized by intense, excruciating, and highly-incapacitating pain, accompanied by prominent cranial autonomic manifestations or a feeling of restlessness or agitation, it is common for CH patients to experience

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problems regarding their family relationships and professional life due to their inability to participate in activities or perform normal work during crises. Consequently, CH has a considerable socioeconomic impact and compromises the quality of life of the patients. Its pharmacological treatment includes a wide range of drugs such as triptan, lithium carbonate, verapamil, and corticosteroids. In addition, oxygen inhalation can be used to treat CH.[4–6]

In cases refractory to the pharmacological treatment, neuromodulation procedures such as deep brain stimulation, spinal cord stimulation, and occipital nerve stimulation can be employed. Not only has occipital nerve stimulation been shown to be less invasive compared to the other procedures, but it also significantly reduces the frequency and the number of crises of CH, thus improving patients' quality of life.[7,8] Patients can control the implanted system with a handheld remote control, which enables them to turn the device on or off and to adjust the stimulator parameters, contributing to a reduction in painful events.[9] Therefore, the present study aimed to report the case of a patient with CH who underwent occipital nerve stimulation and to verify the improvement in her quality of life after this procedure.

Case Report

The present study was approved by the Ethics Committee of Pontifícia Universidade Católica de Goiás (under CAAE: 30101019.6.0000.0037). It was conducted following the principles of the Declaration of Helsinki, and the patient signed the informed consent form.

A 29-year-old female patient sought medical attention due to severe periorbital left frontal headache that came in crises (score of 10–10 in the numeric pain rating scale-10, NRS-10), associated with eyelid ptosis, miosis, ocular hyperemia, and rhinorrhea. She reported having had 3 to 4 daily episodes of severe headache for the past 7 years, lasting around 50 minutes, followed by remission periods of approximately 7 days. The patient was unresponsive to the pharmacological treatment with lithium carbonate, fluoxetine, topiramate, verapamil, prednisone, olanzapine, duloxetine, quetiapine fumarate, codeine, and codeine phosphate associated with paracetamol. She underwent blockages of the stellate ganglion, sphenopalatine ganglion, and occipital nerve without effective pain control. She frequently needed assistance in the emergency department for the use of nasal oxygen (8–10 L/min) for pain relief. Hence, the patient fulfilled the international criteria for the diagnosis of CH.[1]

Due to the refractory nature of her case to the clinical approach, test electrode implantation in the left occipital nerve region coupled to an external pacemaker was indicated (►**Fig. 1A and –1B**). The test was carried out for 3 weeks, and the patient reported improvement in CH from a score of 10–10 to 3–10 on the NRS-10, as well as reduction in the frequency of crises from 3 times a week to ~1 crisis every 3 weeks. Subsequently, a permanent octopolar electrode (amplitude: 2 V; frequency: 40Hz; pulse width: 400 µs) was implanted using a left-sided retromastoid approach,[10] with an expected battery life of approximately 4–5 years. After the implant, the patient complained of pain at the generator site for 3 months and of cutaneous electric shock at the implant site. The pain at the battery site disappeared spontaneously, whereas the electric shock in the skin was solved through adjustments in the stimulation parameters (telemetry).

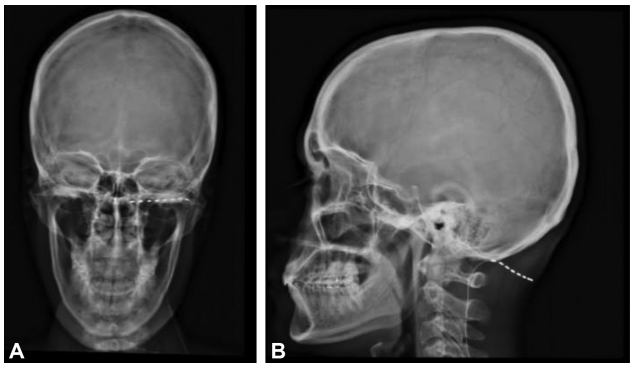

Fig. 1 (A) Radiograph on coronal section. Radiograph on sagittal section.

She remains in outpatient clinic follow-up and has reported an improvement in the intensity and frequency of painful events. She has also experienced a reduction in the need for assistance in the emergency department and greater job stability due to a decrease in health-related absenteeism.

Discussion

Compared to migraine, CH is a rare condition, since its prevalence is lower than 1%. It mostly affects the male population in a ratio of 3:1, mainly between 20 and 40 years of age. The crises are serial and can last for weeks or months, associated with periods of remission that generally last for months or years.[1,2,11]

The clinical manifestations that accompany CH include autonomic symptoms ipsilateral to the pain, such as conjunctival hyperemia, tearing, nasal congestion, rhinorrhea, sweating on the forehead and face, miosis, ptosis, and eyelid edema. During the crises, most patients exhibit uneasy behavior and marked agitation.[1,3,12]

Many studies on CH have been conducted so far, and this condition has been recognized for many years. Typical CH attacks are characterized by severe strictly-unilateral pain, and the most severe pain is localized deep behind one eye or the temple, in association with ipsilateral facial autonomic symptoms.[13,14]

Currently, the diagnosis of CH can be made based on the well-characterized clinical history of headache.[15] Given that two major temporal patterns of CH have been identified, episodic and chronic, the differential diagnostic criteria should be considered when deciding on the proper treatment. The patterns are based on the presence as well as on the duration of the periods of remission. On the one hand, episodic CH is the most common subtype (affecting 80% of the patients), and it is characterized by discrete but repetitive daily attacks, which can last from 1 week to 1 year, usually followed by a period of 3 to 12 months without pain

before another attack. On the other hand, chronic CH is characterized by daily attacks, which can last longer than 1 year, with no remission or with pain-free periods lasting less than 3 months each.[1,2,16,17]

The prevalence of CH has historically been higher among men, and the male-to-female ratio tends to be the highest when its onset is in the age ranges from 20 to 49 years, and the lowest, when its onset is after the age of 50.[4,18] In Brazil, an observational cross-sectional study[19] demonstrated the highest prevalence of CH among men (86.67%) and in the age group between 35 and 45 years (53.34%).[19]

In general, the treatment of CH relies on the pharmacological therapy to control acute attacks, because they reach the peak of maximum intensity in a few minutes after the beginning, and on the prophylactic treatment, consisting in the administration of daily doses of medication, to reduce the attacks during the cluster bout.[20,21] For the treatment of acute attacks, triptans are the most effective drugs of choice for the majority of patients. A 6-mg single dose of sumatriptan can be administered subcutaneously and is effective approximately 15 minutes after administration. Single 5- and 10-mg doses of zolmitriptan nasal spray and a single 20-mg dose of sumatriptan nasal spray are effective 30 minutes after administration.[17,22]

For more than 60% of the patients with CH, oxygen therapy is often very useful. Oxygen is administered using a high-flow mask at a flow rate of 12 L/min to 15 L/min, and the effect is usually felt 15 to 20 minutes after the treatment begins. The main advantages of oxygen inhalation are the nonexistence of side effects and the prospect of employing the same therapy as many times as necessary.[17,23]

In addition, lidocaine is also effective in treating acute attacks in more than 30% of the patients with CH. This medication can be taken into consideration if the patient does not respond to oxygen therapy and triptans. Lidocaine dripped or sprayed into the ipsilateral nostril, at concentrations ranging from 4% to 10%, usually provides relief within 10 minutes after administration.[24]

The preventive treatment of patients with a history of episodic or chronic CH includes several drugs that have already been proven to be effective in reducing the frequency of these attacks. Verapamil has been considered the first choice and the most prescribed drug at doses ranging from 360 mg/day to 560 mg/day. Severe cases may require, doses of up to 960 mg/day. However, due to the adverse effects of verapamil on cardiac function, it is advisable to perform electrocardiograms before and after the dose needs to be increased.[17,25]

Lithium has also been broadly used worldwide in the first-line preventive treatment of CH, and it effectively reduces the frequency of attacks. The dose, ranging between 600 mg/day and 1200 mg/day, needs to be adjusted. Patients should start the treatment at a lower dose, which should gradually increase until the disappearance of the pain indicates that the optimal therapeutic response has been achieved.[23,25,26]

Another option of pharmacological therapy for the prophylactic treatment of CH is anticonvulsant drugs such as topiramate. The most used dose for these patients varies between 100 mg/day and 200 mg/day, and it can be administered in isolation or added to an ongoing treatment with verapamil.[17,25–27]

Although corticosteroids have been successfully used to treat CH, their adverse events should be taken into consideration, mainly in long-term treatments. The common dose of oral prednisone or prednisolone is of 60 mg/day (in a single daily dose) for a period of 5 to 10 days or until the attacks stop. After that, the dose should be gradually reduced by 5 mg to 10 mg at intervals of 4 to 10 days. Dexamethasone can be administered as an intramuscular injection or orally at a dose of 8 mg/day for 5 to 10 days.[25,26]

Surgery is indicated in CH patients who are clinically intractable and refractory to the pharmacological treatment. Neurostimulation techniques such as hypothalamic deep brain stimulation, spinal cord stimulation, stimulation of the sphenopalatine ganglion, vagus nerve stimulation, and occipital nerve stimulation have yielded favorable outcomes.[26,28]

In deep brain stimulation, electrodes are placed on the posterior hypothalamus. This procedure has been proven to be effective in the control of CH crises in most patients. These outcomes provide evidence of the considerable role the hypothalamus plays in the pathophysiology of this disease. Hypothalamic stimulation is believed to increase the blood flow in the ipsilateral trigeminal system as well as in the brain areas involved in the pain center.[28,29]

Another important target for the treatment of CH is spinal cord stimulation; however, few reports[12,28] on this procedure are available. Using this neuromodulation technique, cervical epidural electrodes, with power supplied by a battery, can be implanted in patients with CH, making it possible to reduce the average frequency of attacks and the intensity of crises.[12,28]

The sphenopalatine ganglion, an extracranial structure located in the pterygopalatine fossa, has sympathetic and parasympathetic components. Due to the direct and indirect connections of this structure with somatic and visceral nervous components of the face, trigeminovascular system, upper salivatory nucleus, and hypothalamus, it plays a distinctive role in the pathophysiology of CH. Therefore, it has been used as a therapeutic target to treat CH, showing some successful outcomes. The physiological stimulation of the sphenopalatine ganglion blocks the parasympathetic flow, resulting in improvement in pain and autonomic symptoms.[21,28]

Another procedure introduced in the treatment of CH is vagus nerve stimulation. The existence of several connections between the solitary tract nucleus and the spinal nucleus of the trigeminal nerve suggests that the inhibition of pain by stimulating the vagus nerve occurs due to the inhibition of the vagal afferents of the caudal nucleus of the trigeminal nerve.[21,28]

Stimulation of the occipital nerve, the neuromodulation therapy chosen for the treatment of the patient in the present case report, exerts its effectiveness through several mechanisms. Spinal cord modulation at C2–C3, the point of convergence of the trigeminal nerve and upper cervical

afferents, may account for the beneficial effects of occipital nerve stimulation. To perform the technique, the major occipital nerve is stimulated by means of a subcutaneous electrode that crosses the nerve path in order to provoke paresthesia in this region. Patients presenting with clinically-intractable CH who underwent stimulation of the occipital nerve showed favorable results with reduced attacks.[3,28]

In cases of chronic refractory CH, neuromodulation of the occipital nerve should be considered, because this pain management technique can be safer than other more invasive procedures. In general, neurostimulation of the distal branches of C2–C3 (the greater and the lesser occipital nerves) is used. The patient undergoes minimal sedation and should be in the prone or lateral positions. Either a lateral or a retromastoid approach can be used, and the incision at the level of C1 can be performed posteriorly or inferiorly to the mastoid process. A Tuohy needle is then inserted subcutaneously and transversely, carefully bent and adjusted to the specific curvature of that patient's occipital nerve. After that, an electrode should be inserted through the Tuohy needle, which, in turn, is removed, leaving the electrode at the correct site.[10]

The electrodes should be inserted subcutaneously and superficially to the cervical muscle fascia, usually under fluoroscopic guidance.[9] Painful stimulation requires electrode repositioning. This system is maintained by an external power source, the pulse generator, which can be implanted in the infraclavicular region. After the surgical procedure, radiographs of the skull can be taken to document the final position of the electrode, preventing cases of electrode migration or fracture. If the patient finds neurostimulation uncomfortable, the stimulation parameters (amplitude, frequency, and pulse width), can be adjusted by telemetry.[10]

The system for the neuromodulation of peripheral nerves requires that batteries work at higher intensities than those needed in other kinds of stimulation.[10] In the case herein reported, the battery lasted only 2 years, although this device has a useful life of around 4 to 5 years according to the manufacturer. Battery depletion is a disadvantage in this type of implant, but replacements can be avoided by using rechargeable systems.[10]

Conclusion

The professional, social, functional, economic, and psychological well-being of those affected by refractory CH can be significantly hampered, consequently reducing their quality of life. In the case herein reported, it became evident that, after the implantation of the neuromodulator in the left occipital nerve, the patient experienced an improvement in the intensity and frequency of the painful episodes. Therefore, stimulation of the occipital nerve should be considered as a therapeutic approach for CH patients refractory to the pharmacological therapy.

Conflict of Interests

The authors have no conflict of interests to declare.

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Giant Temporal Bone Angiosarcoma: Case Report and Literature Review

Angiossarcoma do osso temporal: Relato de caso e revisão da literatura

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Abstract

The authors describe a very rare case of an angiosarcoma originating from the petrous portion of the temporal bone that evolved as an indolent lesion until it became a giant retroauricular mass. A biopsy demonstrated that it was an angiosarcoma. A presurgical embolization from the left occipital and left parietal branches of the left middle meningeal artery was performed, followed by a total resection of the tumor. The patient developed a transient dysphasia during early follow-up, from which, subsequently, she fully recovered. There were no signs of recurrence in the current 3 years of follow-up. Free margins can be achieved even in some giant tumors and remain the most important prognostic factor for soft tissue malignant tumors with intracranial infiltration.

Keywords
- sarcoma
- skull base
- temporal bone
- case report

Resumo

Os autores descrevem um raro caso de angiossarcoma proveniente da porção petrosa do osso temporal, que evoluiu como uma tumoração indolente até tornar-se uma volumosa lesão retroauricular. Foi realizada uma biópsia incisional, cujo diagnóstico foi de angiossarcoma. Foi realizada embolização pré-operatória da lesão pela artéria occipital esquerda e pelo ramo parietal da artéria cerebral média esquerda, seguida de ressecção do tumor. No pós-operatório imediato, a paciente evoluiu com disfasia transitória, recuperando-se completamente durante o seguimento. Não houve sinais de recidiva nos três anos de seguimento pós-operatório. A ressecção com margens livres de tumores de grande volume segue sendo o fator prognóstico mais importante para tumores malignos de partes moles com infiltração intracraniana.

Palavras-chave
- sarcoma
- base de crânio
- osso temporal
- relato de caso

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Introduction

The temporal bone is an unusual site of tumor pathologies. When they occur, they are more likely to be secondary to advanced periauricular skin cancer or to parotid gland tumors.[1] Primary tumors that affect the temporal bone are rare.[2] The most typical histology varies with age, since younger patients are likely to have sarcomas while older patients are likely to have carcinomas. Angiosarcoma is a malignant soft tissue neoplasm (accounting for $< 2\%$ of sarcomas[3]) that arises most often from the skin ($\sim 60\%$ of the cases), particularly in the head and the neck, but that can also originate from the soft tissue, viscera, and bones.

Angiosarcoma of the skull is a rare entity with < 20 cases reported in the literature by the year of 2013,[4,5] most commonly involving the frontal and parietal bones. Only seven cases involving the temporal bone have been reported.[6] The authors report the case of a patient who presented with an indolent swelling in the left posterior temporal region that became a giant mass whose pathological diagnosis was angiosarcoma. The tumor was completely resected, and the patient evolved with an excellent outcome with no signs of tumor recurrence during 3 years of follow-up. The patient authorized the authors to publish the present case report by signing an informed consent form.

Case Report

A 56-year-old, previously healthy woman, was referred to the department of oncological neurosurgery from a general hospital presenting with a huge tumor in the left temporo-occipital region of the skull. She had no personal or family history of cancer. The patient had noticed the lesion 10 months before the medical evaluation, and during that period it grew progressively. The neurological exam of the patient was normal, and she reported no pain in the tumor area. The patient was admitted to the hospital and submitted to imaging investigation. A computed tomography (CT) exam showed an exophytic lesion in the temporal bone, posterior to the external acoustic meatus, displacing the pinna, eroding the petrous portion of the left temporal bone, and presenting an intense but heterogenous enhancement after contrast infusion (►**Fig. 1**). Magnetic resonance imaging (MRI) demonstrated an isointense pattern of the tumor (compared to brain parenchyma) on T1 images, with a heterogenous but predominantly hypointense signal on T2 images with small areas of enhancement after gadolinium infusion (►**Fig. 2**). Furthermore, the MRI confirmed that most of the tumor was exophytic; however, there was an intracranial component with dural and parenchymal invasion of the tumor with no signs of edema. The patient was submitted to an incisional biopsy whose pathological diagnosis was angiosarcoma. Surgical resection of the tumor was planned and accepted by the patient and her relatives. Preoperative angiography and embolization were programmed for the patient. An angiography study demonstrated that the tumor had no vascularization from the left internal carotid or from the left vertebral arteries, and its vascularization was exclusively from branches of the left external carotid artery. The main arterial feeders (left occipital artery and parietal branch of the left meningeal artery) were embolized with microparticles (►**Fig. 3**).

The first surgical step was to remove the soft tissue components infiltrated by the tumor (*en bloc* resection of the muscle and the skin on the tumor topography). Craniectomy was performed by drilling the bone with normal aspect, respecting a margin of 2 cm from the infiltrated bone. Mastoidectomy with skeletonization of the sigmoid and transverse sinuses were performed. The intracranial portion of the tumor was removed as well as the infiltrated dura mater adjacent to the tumor and the intracranial component. The left transverse and sigmoid sinuses infiltrated by the tumor were resected. The left Labbé vein was also infiltrated and had to be sacrificed to remove the tumor with free margins. Watertight duroplasty was performed using fascia latta graft. The skin and subcutaneous soft tissue reconstruction was performed with a trapezious myocutaneous flap (►**Fig. 4**). The postoperative CT scan showed a gross total tumor resection, but the patient developed a left temporal edema and intraparenchymal hematoma in the territory of Labbé drainage secondary to vein infarction (►**Fig. 5**). During the early postoperative period, the patient had a sensitive dysphasia, from which she recovered gradually in four weeks with full recovery. In the 7th day of postoperative follow-up,

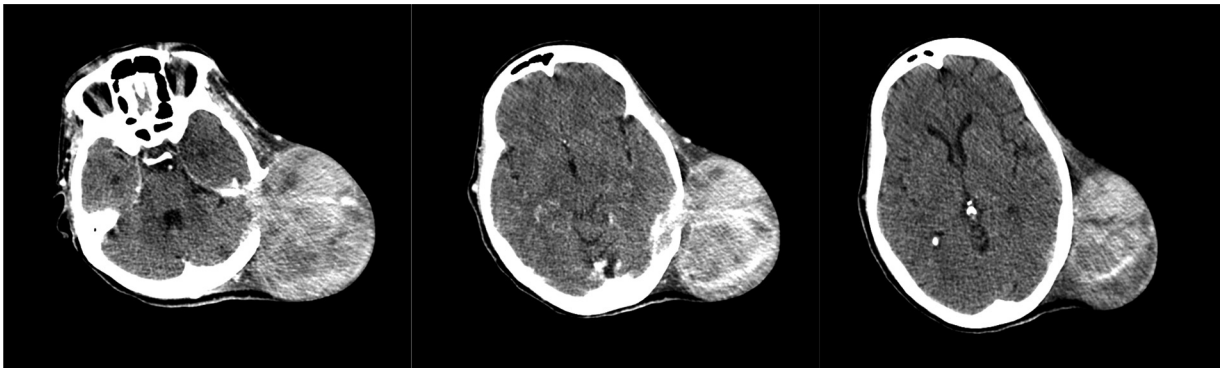

Fig. 1 Computed tomography showing an exophytic lesion eroding the petrous portion of the left temporal bone and presenting an intense but heterogenous enhancement after contrast infusion.

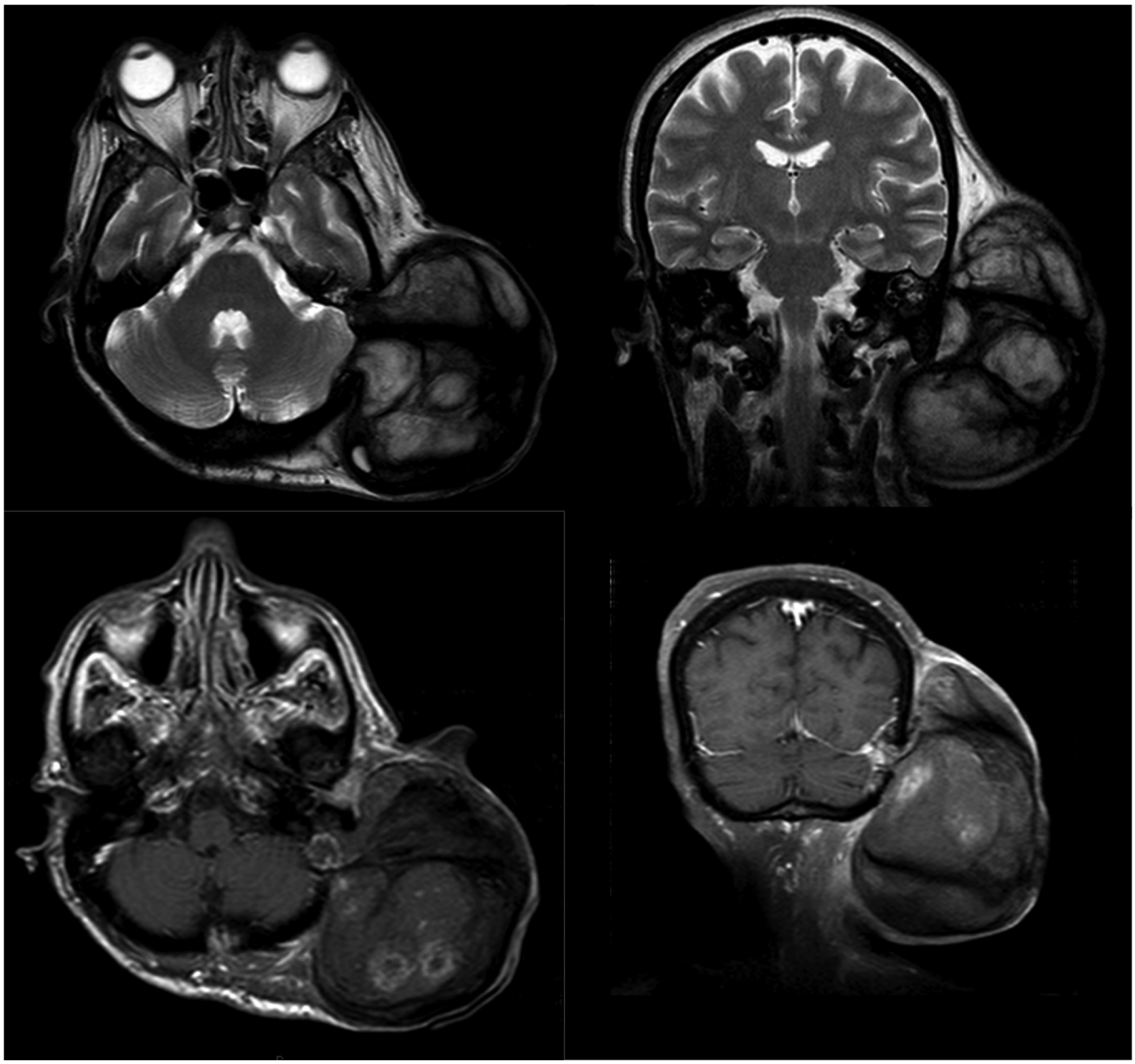

Fig. 2 Magnetic resonance imaging demonstrating a heterogenous but predominantly hypointense signal on T2 images with small areas of enhancement after gadolinium infusion.

the patient was discharged from the hospital, sustaining excellent wound healing and complete neurological recovery. The patient was referred to adjuvant radiotherapy. However, she did not attend to the medical neurosurgery and radiotherapy appointments during the follow-up. In 2020, the authors performed an active search of the patient. She remained asymptomatic and with no signs of tumor recurrence in 3 years of current follow-up.

Discussion

Angiosarcoma is a rare and highly aggressive malignant tumor, originating from lymphatic or vascular endothelial cells.[7] A recent study analyzed 1,250 cases of angiosarcoma exclusively from the head and neck regions; among those patients, there was no case of angiosarcoma involving the temporal bone.[8] Endothelial-derived neoplasms of the temporal bone may range from self-limited benign hemangiomas to tumors of intermediate malignancy, such as hemangioendotheliomas, or highly malignant and aggressive angiosarcomas.[3]

Primary skull angiosarcoma is twice more common in men, with a median age of 32 years old.[9]

Previous radiation therapy, arsenic exposure, chronic lymphoedema, and history of trauma are known risk factors for extracranial angiosarcomas.[10] However, primary skull angiosarcoma has no known risk factors.[9,11]

Temporal bone tumors present nonspecific symptoms that are often attributed to inflammatory ear diseases. Therefore, the diagnosis is often delayed, despite the superficial location of the tumor.[12]

The most common presentation of skull base angiosarcoma is a swelling in the affected region.[9,13] Otorrhea, otalgia, and hearing loss make up a classic triad for temporal bone cancer, but this classic triad is seen only in 10% of the patients who have temporal bone cancer, and it is related to the topography of the tumor, not to its specific histopathology.[2]

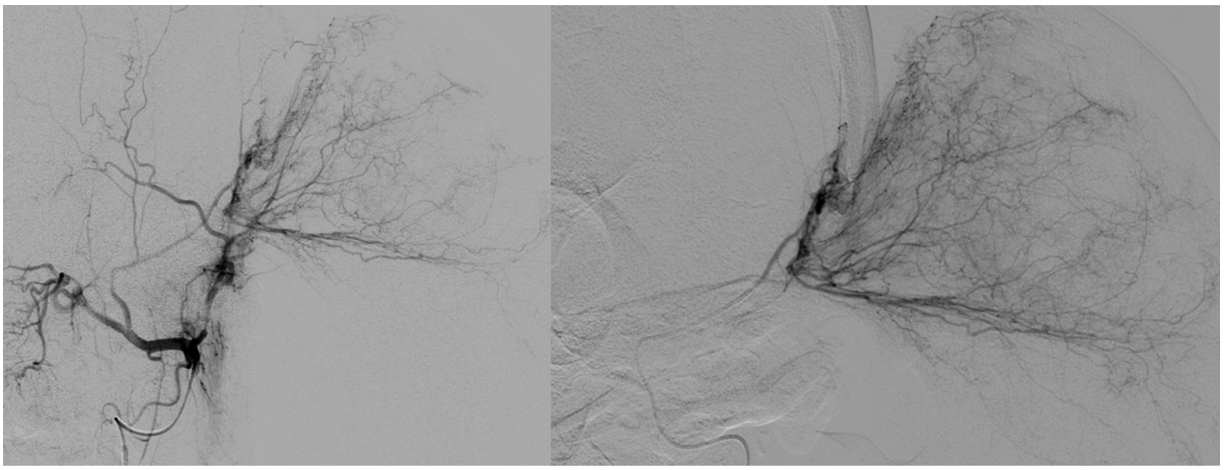

Fig. 3 Main arterial feeders of the tumor: the left occipital artery and the parietal branch of the left meningeal artery.

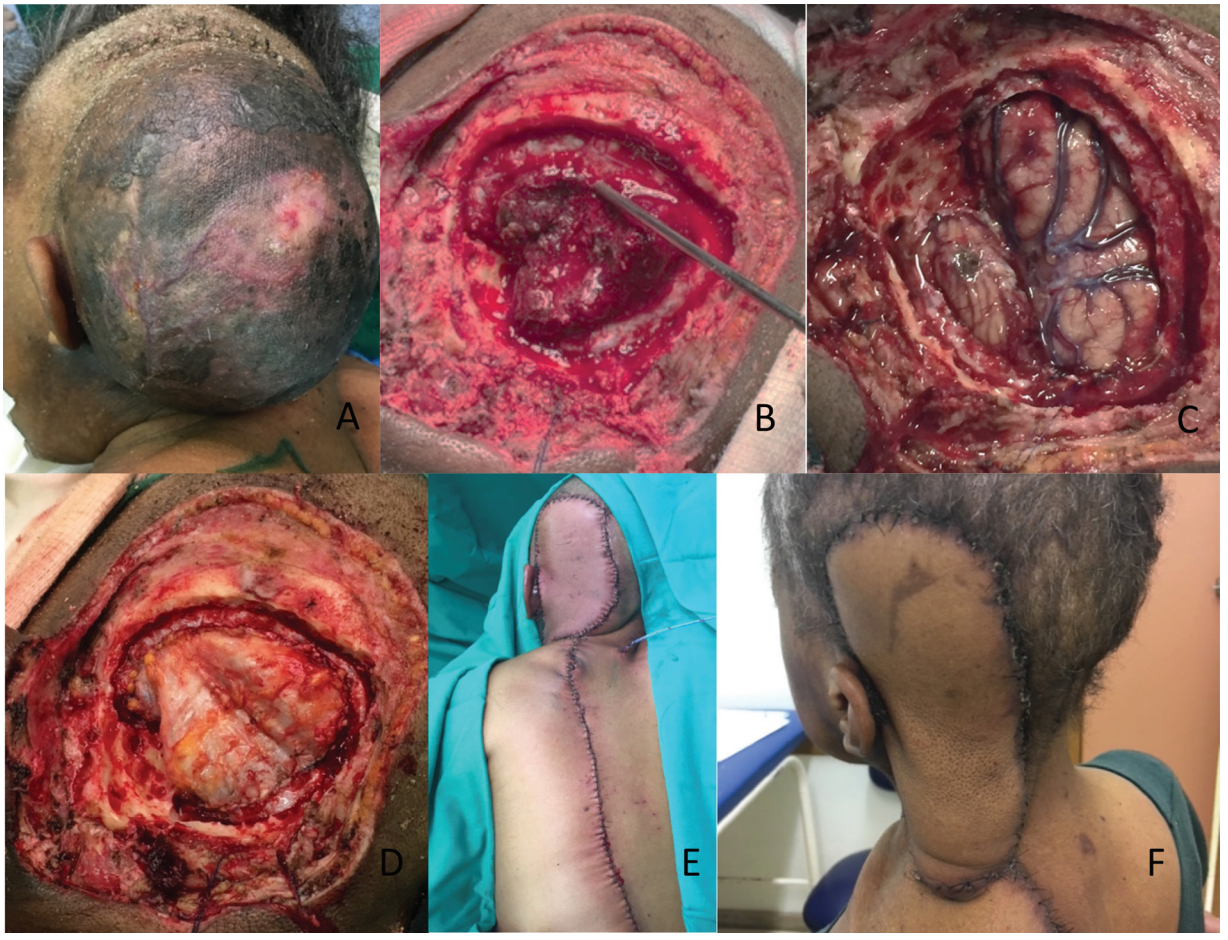

Fig. 4 Preoperative, surgical technique, and postoperative aspect.

Radiographically, skull angiosarcomas usually demonstrate a well-demarcated lytic, hypervascularized, and hemorrhagic mass.[14] However, these neuroradiological features are not pathognomonic, being also seen in other sarcomas or metastasis to the skull.[15] On MRI, angiosarcoma of the temporal bone usually shows an isointense mass compared to cerebral parenchyma on T1-weighted images, and hyperintense on T2-weighted images.

The histologic features of skull angiosarcomas range from well-differentiated to poorly-differentiated tumors. Well-differentiated tumors are seen as abnormal endothelial cells retaining some degree of well-differentiated vascular

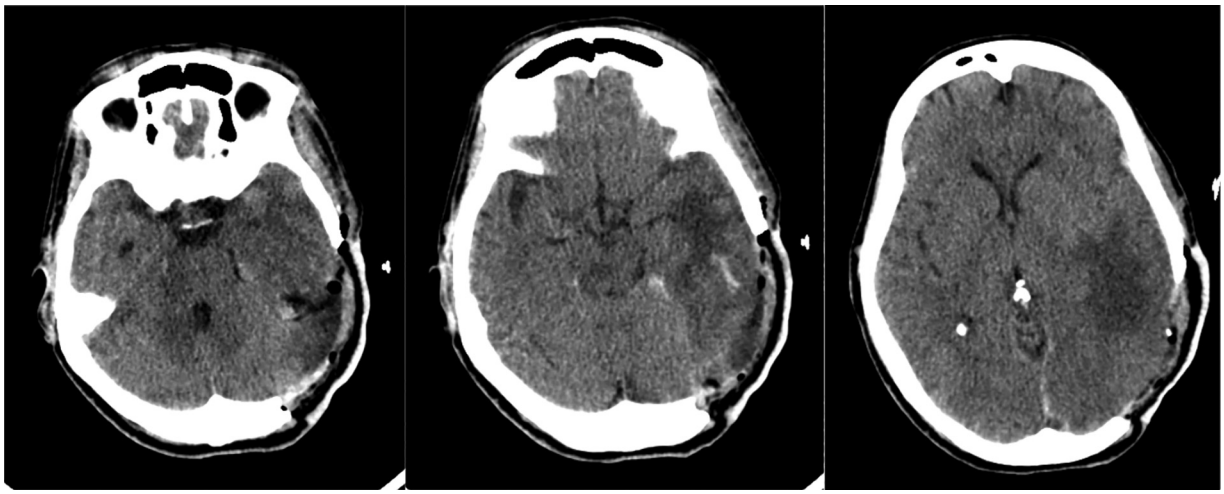

Fig. 5 Postoperative computed tomography showing an excellent tumor resection, but the patient presented with a left temporal edema and intraparenquimatous hematoma in the territory of the Labbé drainage secondary to vein infarction.

architecture. On the other hand, poorly-differentiated tumors present sheets of abnormal cells with significant hemorrhage and necrosis.[3]

Immunohistochemistry is crucial for the diagnosis of poorly-differentiated tumors. Positive staining for the erythroblast transformation specific related gene (ERG) endothelial marker, factor VIII-related antigen, CD31, FLI-1, CD99, S-100 protein, signal transducer and activator of transcription 6 (STAT6) and smooth muscle actin (SMA) are characteristic of angiosarcomas. Among these markers, some are related to vascular and endothelial origin and proliferation (such as CD31, CD34, FLI-1, and ERG), with CD31 being the most specific marker of angiosarcoma.[3,11]

Because of the rarity of skull angiosarcomas, a gold standard management has not been defined. Therefore, at present, the treatment of angiosarcomas is often individualized. The medical literature suggests that complete surgical excision followed by adjuvant radiotherapy is the most effective treatment.[2] This association has demonstrated local control benefit particularly in cases with close surgical margins[16] and, based on some retrospective studies, can prolong survival.[3]

As with any traditional oncologic resection, a free margin excision is the main aim of temporal bone oncological surgery,[17] especially an *en bloc* resection when feasible.

Surgical resection of the tumor can be achieved by a wide local excision (WLE), *en bloc* lateral temporal bone resection (LTBR), *en bloc* subtotal temporal bone resection (STBR), total temporal bone resection (TTBR), or near total temporal bone resection (NTTBR).[12,17,18]

Besides the tumor, adjacent involved tissue should also be included within the resection specimen. In the medical literature, the discussion about the proper technique that should be used is based on cases of epithelial derived tumors, not angiosarcomas. In standard practice, a key point to decide the surgical technique is the relationship of the tumor with the tympanic membrane (TM). Tumors located lateral to the tympanic membrane can be resected by LTBR, including removal of the cartilaginous and bony external auditory meati (with the eardrum), of periauricular soft tissues, of the parotid (with or without the facial nerve), and of neck lymph nodes. An alternative to LTBR is the STBR, which includes the removal of the petrous bone, of the mastoid, of the bony and cartilaginous canals, of the parotid gland with the facial nerve, of part of the mandible, and neck dissection.[17] However, if the malignant lesion invades medially to the TM, NTTBR is the best option for total resection.[18]

The cavity of temporal bone resection is best reconstructed with free-tissue transfer. The defect can also be repaired with local or regional myocutaneous flaps. The reconstruction should provide proper soft tissue covering for the underlying vasculature, dura, bone, and obliterated dead spaces.[18]

Even though there is a consensus regarding the importance of systemic chemotherapy in advanced and metastatic cases,[19] there is no robust data in the medical literature supporting outcome improvement in terms of recurrence-free period or of overall survival with adjuvant chemotherapy. Besides, in the case of skull angiosarcomas, the effectiveness of chemotherapy has not been substantiated.[5]

Even with optimal treatment, skull angiosarcoma has been associated with transient responses and a poor prognosis. The outcome is poor regardless of the stage of the disease (localized or metastatic). In patients harboring a localized tumor at diagnosis who were submitted to a large *en bloc* resection, 40% present with tumor relapse during close follow-up.[20] The involvement of the meninges and of the brain and the difficulty to perform a complete surgical resection are factors associated with incomplete resection of the tumor, and, therefore, with higher rates of recurrence and a worse prognosis.[5] For giant tumors, *en bloc* resection can be technically very difficult, but free margins are imperative in order to achieve local control.

The present article has some limitations that must be stated. First, it is a case report, which, in a scientific point of view, does not have the same power of evidence as other

most sophisticated study designs. Second, the patient was not submitted to adjuvant radiotherapy as most expert opinions in the literature suggest. Actually, the patient was referred to the treatment; however, she did not accept it. Therefore, optimal treatment was not performed, which may increase the risk of late recurrence of the tumor.

However, the present article has some strengths that deserve to be highlighted. The case report highlights significative information about the case, with illustrations of imaging exams demonstrating the relation of the tumor with intracranial and cervical structures, as well as its vascularization. Key steps of the surgical procedure are demonstrated in ►**Figure 4**. The literature review presented embraces important information about skull base angiosarcoma, describing the rare involvement of the temporal bone by this type of cancer. Also, the discussion brings information about suggested investigations and treatments for skull base angiosarcoma, based on specialized opinion (since there is no standard protocol due to the rarity of this lesion in the temporal bone). Finally, the present case report and review have one main note: temporal bone angiosarcoma must be treated aggressively, with resection of all involved structures (when feasible). The accomplishment of this goal is the most important factor for the prognosis of the patient.

Conclusion

The authors describe a giant angiosarcoma of the temporal bone with intracranial extension that was completely resected with the sacrifice of the Labbe vein, which was infiltrated to achieve free margins. The patient presented a transient dysphasia with full recovery and no signs of recurrence in the last 3 years. Free margins can be achieved even in some giant tumors and remain the most important prognostic factor for soft tissue malignant tumors with intracranial infiltration.

Conflict of Interests

The authors have no conflict of interests to declare.

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