Pediatric Skull Base Tumors: A Management Challenge

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Context: Skull base tumors are varied in children and are particularly challenging to pediatric neurosurgeons, with few papers in the literature describing the evolution, complications, and outcome. The authors evaluated long-term outcomes in children submitted to skull base tumor surgery and performed a literature review. Aims: The aim of this study was to analyze surgical results, complications, and outcomes, on comparison with previous publications. Materials and Methods: A retrospective analysis of children undergoing surgery at a single institution between 2000 and 2018 for lesions of the cranial base was carried out. In addition, a literature review was carried out describing a total of 115 children operated on for skull base tumors. Statistical Analysis: Chi-squared and Fisher’s exact tests were performed to compare the distribution of categorical variables and a nonparametric Mann–Whitney U test was used to perform intergroup comparisons of continuous variables. Results: Seventeen children ranging in age from 8 months to 17 years (mean, 10.9 years) underwent skull base approaches. Tumor types included schwannoma, meningioma, chondroid chordoma, mature teratoma, epidermoid cyst, hemangiopericytoma, rhabdomyosarcoma, myofibroblastic inflammatory tumor, fibromyxoid sarcoma, Crooke’s cell adenoma, ossifying fibroma, osteoblastoma, nasopharyngeal angiofibroma and Ewing’s sarcoma. Gross total resection was achieved in 6 patients (35.3%), 12 patients (70.6%) had benign histology, and 5 patients (29.4%) had a malignant tumor. Transient postoperative cerebrospinal fluid leak affected only one patient. Thirteen children (76.4%) had a residual neurological deficit at last follow-up evaluation. Three (17.6%) surviving patients received adjuvant therapy. The rate of recurrence or lesion progression was 17.6%. Conclusions: Skull base tumors in children present a therapeutic challenge because of their unique pathological composition and can lead to considerable morbidity and mortality in pediatric age.

Keywords: Children, skull base, surgery, tumor

INTRODUCTION

Tumors of the skull base are complex and rare in the pediatric population. Skull base tumors are not a particular type of brain neoplasm, but are rather lesions that expand to the bones of the cranial base, compromising vital structures such as the venous sinuses, cranial nerves, brain stem, and orbit.[¹] Skull base surgery is particularly challenging to the pediatric neurosurgeon because of the small size, variable location of key anatomical landmarks, potential long-term commitment to the developing craniofacial skeleton, and possible spinal instability.[²] Radiotherapy and/or chemotherapy may have adverse effects specific to children.[³]

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Primary tumors can be histologically varied in children.40 A few reports on skull base tumors in the pediatric population have been published [Table 1]. As a result, there is very little consensus regarding the ideal multidisciplinary approach to these lesions.

In this paper, we retrospectively reviewed a pediatric series operated on for a skull base tumor in a single center, specialized in skull base surgery, with the aim of analyzing surgical results, complications, and outcomes, on comparison with previous publications.

Subjects and Methods

A retrospective study was performed on 17 children operated for a skull base lesion at our institution, a tertiary care hospital, in the last 25 years. We included patients under the age of 18 years diagnosed and operated on for a tumor with a skull base localization.

This study was approved by the local Ethics Committee (CAAE: 14021919.6.0000.5440) and carried out in accordance with the Declaration of Helsinki.

Data were collected from medical records, and information was obtained on age, imaging, tumor location, surgery performed, histopathological diagnosis, degree of resection, surgical complications, adjuvant therapies, and recurrence/progression. All patients were followed clinically and radiologically (computed tomography [CT] and/or magnetic resonance [MR] imaging).

In order to reduce the well-known heterogeneity of a pediatric series of skull base tumors, optic glioma, craniopharyngioma, typical pituitary adenoma, congenital lesions (e.g., basal encephaloceles), and bone fibrous dysplasia were excluded from this series.

Furthermore, a literature review was carried out in PubMed/MEDLINE until December 2019, with the search term “skull base tumors”, limited to papers written in English and Spanish with a focus on the pediatric age-group. The following inclusion criteria were used: reports of a total of 10 or more patients in the pediatric age group (<18 years) undergoing a surgical procedure, excluding papers without enough information or focusing a particular neoplasm or localization. Because not every paper could provide all information, data were calculated only from valid patients.

Descriptive and statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) (version 22.0, IBM, Armonk, NY, USA) and Microsoft Excel (version 2016) software. Chi-squared and Fisher’s exact tests were performed to compare the distribution of categorical variables, and a nonparametric Mann–Whitney U test was used to perform intergroup comparisons of continuous variables; \( P < 0.05 \) was considered as statistically significant.

Results

Of a total of 17 children, there were 11 males (64.7%) and 6 females (35.3%). Mean age at first intervention was 10.9 years (range from 8 months to 17 years). Histopathological examination was very heterogeneous revealing 5 malignant (29.4%) and 11 benign tumors (70.6%). The characteristics of the patients are described in Table 1. Figure 1 shows different MR scans of our cohort.

The main tumor localization in skull base was the posterior fossa in 9 (52.9%), the anterior fossa in 4 (23.5%), and the middle fossa in another 4 (23.5%). There was no statistical relationship between localization and tumor recurrence (\( P = 0.991 \)) or long-term impairment (\( P = 0.357 \)).

The most common surgical approach was retrosigmoid in five patients (29.4%), subtemporal in five (29.4%), subfrontal in two (11.7%), pterional in two (11.7%), and others including anterior petrosal, fronto-orbitozygomatic, and transfacial approach. No statistical significance was found between the surgical approach and recurrence (\( P = 0.47 \)), long-term impairment (\( P = 0.5 \)), or resection degree (\( P = 0.21 \)).

Gross total resection was achieved in 6 (35.3%) and subtotal resection in 11 (64.7%) patients; no relationship was found between resection degree and long-term impairment (\( P = 0.1 \)). The average length of stay in hospital was 10.23 days (range from 3–26 days; median of 9 days); this variable was related to tumor recurrence (\( P = 0.006 \)).

Cerebrospinal fluid (CSF) leak was present in only one child (5.3%). No fistula was detected in 9 (52.9%), but in 4 (23.5%) subjects a continuous lumbar CSF drain was placed during surgery and in another 3 (17.6%), a ventriculoperitoneal shunt was performed. Radiotherapy was performed in two children (11.8%) and chemotherapy in three (17.6%).

Regarding the long-term surgical complications, 13 (76.4%) evolved with long-term neurological impairment. Five (29.4%) patients evolved with facial paresis, five (29.4%) with hypoacusia, four (23.5%) with ocular motricity deficit, three with hydrocephalus (17.6%), two with dysphonia (11.7%), two with visual impairment (11.7%), one with epilepsy (5.9%), and one with dysphagia (5.9%). In four children (23.5%), there was no long-term impairment.
### Table 1: Data from 17 children operated for a skull base lesion at our institution

| Case no. | Age (yrs) | Gender | Histology                                      | Skull base location       | Surgical Approach | Extend of Resection | GOS | Long-term deficit                                      | RT/CT | Recurrence | Follow up (mos) |
|----------|-----------|--------|------------------------------------------------|---------------------------|-------------------|---------------------|-----|-------------------------------------------------------|-------|-------------|-----------------|
| 1        | 11        | F      | Chondroid chordoma                              | Sphenoid bone             | Anterior petrosal | GTR                 | 3   | Dysphonia, visual impairment, dysphagia               | No    | Residual and prograding                              | 15, 2 |
| 2        | 13        | F      | Schwannoma                                      | CPA                       | Retrosigmoid      | STR                 | 4   | Facial paresis, hypoacusia                            | No    | Residual                              | 109, 5 |
| 3        | 3 mos     | M      | Mature teratoma                                  | CPA                       | Retrosigmoid      | STR                 | 5   | Facial paresis, hypoacusia, HCP                       | No    | Residual and prograding                              | 108, 0 |
| 4        | 17        | M      | Epidermoid cyst                                 | CPA                       | Subtemporal       | STR                 | 5   | None                                                   | No    | Residual                              | 94, 4 |
| 5        | 16        | F      | Schwannoma                                      | CPA                       | Retrosigmoid      | STR                 | 5   | Facial paresis, HCP                                  | No    | Residual                              | 32, 8 |
| 6        | 10        | F      | Undifferentiated neuroendocrine carcinoma        | Petrosclival              | Subtemporal       | STR                 | 5   | Ocular motricity deficit, HCP                         | No    | Residual                              | 21, 9 |
| 7        | 12        | M      | Meningioma                                       | Jugular foramen           | Retrosigmoid      | STR                 | 4   | Ocular motricity deficit, dysphonia, facial paresis  | No    | Residual                              | 180, 3 |
| 8        | 3         | F      | RMS                                             | Petrous temporal subtemporal bone | Subtemporal       | STR                 | 5   | Hypoacusia, visual impairment, facial paresis         | RT/CT | Residual                              | 166, 8 |
| 9        | 15        | M      | Hemangioepicytoma                                | Petrous temporal subtemporal bone | GTR               | 5                  | Hypoacusia                            | No    | No                                    | 85, 2 |
| 10       | 6         | M      | Myofibroblastic inflammatory tumor Schwannoma   | Sphenoid bone             | Pterional         | GTR                 | 4   | HCP                                                   | No    | Recidivate                              | 38, 1 |
| 11       | 13        | M      | Schwannoma                                       | Geniculate ganglion       | Subtemporal       | STR                 | 5   | Hypoacusia                            | No    | Residual                              | 45, 9 |
| 12       | 5         | M      | Fibromyxoid sarcoma                              | Sphenoid bone             | Pterional         | STR                 | 5   | Epilepsy                                               | No    | Residual                              | 73, 9 |
| 13       | 15        | F      | Crooke’s cell adenoma                            | Cavernous sinus           | Fronto-orbitozygomatic | STR | 5 | Ocular motricity deficit                          | RT/CT | Residual                              | 58, 2 |
| 14       | 9         | M      | Ossifying fibroma                                | Ethmoid sinus             | Subfrontal        | GTR                 | 5   | None                                                   | No    | No                                    | 56, 3 |
| 15       | 9         | M      | Osteoblastoma                                    | Petrous temporal          | Retrosigmoid      | GTR                 | 5   | None                                                   | No    | No                                    | 84, 7 |
| 16       | 10        | M      | JNA                                             | Sphenoid bone             | Transfacial       | STR                 | 1   | Ocular motricity deficit                             | CT    | Residual and prograding                              | 52, 8 |
| 17       | 15        | M      | Ewing’s sarcoma                                  | Olfactory groove          | Subfrontal        | STR                 | 5   | None                                                   | No    | Residual and prograding                              | 4, 8 |

Yrs = years, mos = months, F = female, M = male, CP = cranioopharyngioma, CPA = cerebelloptine angle, F = female, GOS = Glasgow Outcome Scale, GTR = gross total resection, HCP = hydrocephalus, JNA = juvenile nasopharyngeal angiofibroma, LOS = length of stay, CT = chemotherapy, RT = radiotherapy, RMS = rhabdomyosarcoma, STR = subtotal resection
The residual lesion was stable in 11 (64.7%) children and progressed in 3 (17.6%). One patient had a recurrence of the lesion after gross total resection (GTR) (case 10) and one patient died (5.9%) because of tumor progression (case 17). Follow-up ranged from 4.8 to 180 months, with a mean period of 72 months.

**Systematic review**

The literature search identified 1745 articles, and after excluding papers without pediatric cases, papers with insufficient data, or papers including more than 5% of patients with optic glioma, craniopharyngioma, pituitary adenoma, congenital lesions (e.g. basal

**Figure 1**: Skull base tumors in pediatric cases. Axial T1-weighted images after gadolinium showing a heterogeneous localization of the lesion as well as histology, tumors is highlighted with a white arrow. (A) Petroclival undifferentiated neuroendocrine carcinoma. (B) Cerebellopontine angle epidermoid cyst. (C) Jugular foramen meningioma. (D) Cavernous sinus Crooke's cell adenoma. (E) Petrous temporal bone osteoblastoma. (F) Ethmoid bone ossifying fibroma. (G) Sphenoid bone fibromyxoid sarcoma. (H) Olfactory groove Ewing's sarcoma. (I) Geniculate ganglion Schwannoma (VII nerve). (J) Bilateral cerebellopontine angle Schwannoma (VIII nerve)
encephaloceles) and bone fibrous dysplasia, only four publications were selected and included with a total of 115 patients.

Mean age was 11.6 years with 56.5% males and 43.59% females. Regarding histopathology, 16 were malignant (36.5%) and 26 (63.5%) were benign. The review found 13% schwannomas, 9.6% rhabdomyosarcomas (RMSs), 9.6% other sarcomas, 8.7% juvenile nasopharyngeal angiofibromas, 6.1% chordomas, 4.4% meningiomas, and 48.7% other histopathology.

GTR was achieved in 74.6% and subtotal resection in 19.3% of children. Radiotherapy was performed in 37.1% and chemotherapy in 11.2%. Recurrence occurred in 39.0% of children. The overall rate of CSF leak was 10.4% with surgery-related infection in 8.7% of children.

No long-term impairment was found in 78.2% of children, and sequelae included facial weakness in 6.1%, hearing loss in 3.5%, visual impairment in 3.5% and lower cranial nerve impairment in 2.6%. This review found that 20.9% of subjects were deceased due to neoplasm or surgery morbidities [Table 2].

**Case study**

A 15-year-old girl presented with a moon face (Cushingoid facies) and lumbar fracture after minor trauma. Examination showed facial plethora and purple striae. The neurological examination was unremarkable. Cortisol tests were all increased, and an MR scan of head showed a 2.5-cm pituitary lesion extending to the right cavernous sinus. The patient evolved with headache, right ptosis, and ophthalmoplegia. New MR scans demonstrated pituitary apoplexy, and the patient underwent urgent endoscopic transphenoidal surgery removing the entire sellar component [Figure 2]. Anatomopathological examination found a Crooke’s cell adenoma of the pituitary, that is, an aggressive variant of corticotroph adenoma (5% Ki-67+). The patient was referred to radiotherapy with an improvement in ophthalmological symptoms.

After 2 years of follow-up, the intraorbital lesion progressed with worsening of V1 and V2 right

| Study                        | N   | Mean age (yrs) | Gender (M/F) | Histology                                      | Resection degree | Long-term impairment                                      |
|------------------------------|-----|----------------|--------------|-----------------------------------------------|------------------|----------------------------------------------------------|
| Teo et al. 1999[5]           | 26  | 10.5           | 18/8         | 26.9% Schwannoma/7.7% (each) chordoma, fibrous dysplasia, ependymoma, plexiform neurofibroma, ENB/3.9% (each) CP and sarcoma/26.8% Others | 92.3% GTR/7.7% STR | 69.2% None/19.2% deaths/15.4% facial weakness/11.5% deafness/7.7% dysphagia/7.7% blindness/15.4% others |
| Hanbali et al. 2004[3]       | 24  | 13.9           | 13/11        | 16.7% JNA/12.5% (each) RMS, schwannoma and sarcoma/8.3% desmoid tumor/4.2% chordoma/45.8% others | 75.0% GTR/5.0% STR/4.2% biopsy | 79.2% None/12.5% death/4.2% (each) hearing loss, hypoglossal neuropathy, facial and maxillary neuropathies, inadequate zygomatic growth |
| Mandonnet et al. 2008[6]     | 42  | 13.5           | 21/21        | 14.3% Sarcoma/11.9% JNA/9.5% RMS/7.1% lymphangioma/7.1% chordoma/4.8% meningioma/45.4% others | 78.5% GTR / 21.5% STR | 85.7% None / 31.0% Dead / 4.8% (each) Visual impairment, Third nerve palsy and trigeminal neuropathy |
| Hayhurst et al. 2013[2]      | 23  | 6.8            | 13/10        | 17.7% RMS/13.0% MGM/13.0% NB/8.7% angiofibroma/8.7% dermoid/4.3% (each) JNA, chordoma and sarcoma/26.0% others | 52.2% GTR/43.5% STR/4.3% NTR | 73.9% None/13.0% deaths/8.7% facial weakness |
| Overall (ponderated)         | 115 | 11.6           | 56.5%/43.5%  | 13.0% schwannoma/9.6% RMS/9.6% sarcoma/8.7% JNA/6.1% chordoma/4.4% MGM/48.7% others | 74.6% GTR/19.3 STR |                                                          |

M = male, F = female, CP = craniopharyngioma, EHE = epithelioid hemangioendothelioma, ENB = esthesioneuroblastoma, GTR = gross total resection, JVA = juvenile nasopharyngeal angiofibroma, MGM = meningioma, NB = neuroblastoma, N = number of patients, NI = no information, RMS = rhabdomyosarcoma, STR = subtotal resection
hypesthesia. MR imaging showed advancement of the intracavernous lesion with orbit invasion. The patient was submitted to new surgery through a right fronto-orbito-zygomatic approach, achieving effective decompression and subtotal resection [Figure 3]. After 1.5 years of follow-up, the patient remains oligosymptomatic with minor visual deficits, but the neoplasm is stable.

This case was included in the casuistic because of the rare and unusual histology. Furthermore, the tumor posteriorly invaded the skull base, requiring a second surgery by craniotomy.

**Discussion**

Skull base tumors are very complex pathologies, especially in pediatric patients. This study found a prevalence of male patients (64.7%) compatible with Hayhurst et al. [2] (56.5% males) and Teo et al. [5] (66.7% males); only Mandonnet et al. [6] found an incidence of 50% males and females. Santos et al. [7] studying pediatric meningiomas, found a male prevalence, different from adults in whom meningiomas are twice more common in women than in men. This review found an incidence of 56.5% males and 43.5% females. No reasonable explanation has been found for this gender difference.

In our cohort, schwannomas predominated (17.6%); however, anatomopathological results were very heterogeneous. Hanbali et al. [3] reviewing 24 patients (mean age of 13.9 years), found 16.7% juvenile nasopharyngeal angiofibroma (JNA), 12.5% nerve sheath tumor, and 12.5% RMS. Teo et al. [5] described 26 skull base tumors in children (mean age 10.5 years) and found 26.9% schwannomas, 7.7% chordoma, fibrous dysplasia, plexiform neurofibroma, ependymoma, and esthesioneuroblastoma. No meningioma was described. This review corroborates with these heterogeneity data [Table 2], and therefore no incidence or prevalence conclusion can be established.

Regarding localization, in our cohort, the cerebellopontine angle was the primary tumor site in 23.5%, the sphenoid bone in 23.5%, and the petrous temporal bone in 17.6%. Hayhurst et al. [3] found 17.4% of tumors extending to the paranasal, 17.4% to the frontal, 13% to the orbit, 13% to the infratemporal, only 8.7% to the cerebellopontine angle, and another 8.7% to the sphenoid bone. Due to the heterogeneity of the data, the present review could not compare localization in the studies analyzed by the review. The difficulty comes from the lack of standardization in lesion localization.

The surgical approach of choice was retrosigmoid in 5 (29.4%) and subtemporal in another 5 (29.4%), compatible with the series of Teo et al. [8] who performed 23.1% cranio-orbito-zygomatic approaches and 19.2% retromastoid approaches. On the other hand, Brockmeyer et al. [8] performed 46.4% orbit zygomatic osteotomies and did not describe any retromastoid approach. Again, due to the heterogeneity of the data, this review could not compare surgical approaches in the analyzed studies. Complex skull base tumors may need complex approaches, combining surgical approaches such as the pre- and subtemporal transtentorial approach to access the cerebellopontine angle. [9] Figure 4 illustrates some possible surgical approaches to access skull base tumors.

None of our cases was operated with full endoscopic approach. Endoscopic approach can be challenging in pediatric population, especially in young patients who have certain limitations because of small noses, developing air sinuses, and possible interference with craniofacial growth. Also the repair of the defects at the skull base at this age can be difficult because of the size of endoscopes and surgical equipment. Therefore, it is essential to develop new techniques for closing and to avoid possible CSF leaks. [10]

Although endoscopic skull base surgery in the subpopulation of adult patients has become a

![Figure 2](https://example.com/figure2.png)

**Figure 2:** Case no. 13. First surgery preoperative MR scan showing pituitary lesion extending to right cavernous sinus (white arrow). (A) Coronal T2-weighted. (B) Sagittal T1-weighted after contrast injection

![Figure 3](https://example.com/figure3.png)

**Figure 3:** Case no. 13. Second surgery preoperative MR scan showing lesion extending to right cavernous sinus and posterior fossa (white arrow). (A) Axial T1-weighted after contrast injection. (B) Coronal T1-weighted after contrast injection
well-established field, the same is not true for the pediatric population.[12,13]

In our cohort, total resection was complete in 35.3% of patients and subtotal in 63.7%; the present review found that gross total resection was achieved in 74.6%. However, in our patients, the residual lesion was stable in 64.7% of children, progressing in only 17.6%, showing that a less aggressive approach can lead to stable lesions. Moreover, the literature review found 20.9% mortality, while only one death (5.9%) occurred in our cohort.

A great concern related to skull base surgery is CSF leak. In our cohort, fistula was detected as a surgical complication in only one patient (5.9%) and in 10.4% of the reviewed cases. Open approaches are related to less incidence of CSF fistula.[14] In our review, Mandonnet et al.[6] used endoscopic assistance to complement resection in one case (no information about leak) and Teo et al.[5] used a full endoscopic approach in two cases (no CSF leak) and assistance in one case (CSF leak). Stapleton et al.[15] operating on skull base tumors in children with full endoscopic endonasal surgery, had encountered postoperative CSF leaks in 23% (11 of 47); these required secondary operative repair, but this study only considered patients with intraoperatively detected CSF leak. Nation et al.[16] had no postoperative leaks after treating 39 children with endonasal endoscopy using a rigid protocol based on low- or high-flow CSF fistulas during surgery. The authors used nasoseptal flap repair, nasal sponges, and even DuraSeal or a lumbar drain. However, in that study, 46.6% had no intraoperative fistula (and Stapleton et al.[15] included only patient with intraoperative leak), which could explain the differences found in fistula incidence.

Kim et al.[12] recently published their casuistic of 82 children operated by endoscopic endonasal approach (mean age, 11.4 years) with only five patients with bony skull base lesions who fit the description chosen by our article of skull base tumors, none of them evolved with CSF leak.

Endoscopic repair of CSF has many advantages over open approach, such as minor damage to the tissues, no new scar or no reapproach to original surgical site, and fast postoperative recovery. Therefore, it has become the primary approach to the treatment of CSF leak.[17]

Radiotherapy was performed in 5.9% and chemotherapy 17.6% of our children. According to our review, radiotherapy was performed in 29.0% and chemotherapy in 16.1% of patients. These differences can be explained by the heterogeneity of diagnosis, approach, and resection degree.

Regarding long-term surgical complications, 76.4% of our patients evolved with long-term neurological impairment, predominantly facial paresis (29.4%) and hypoacusia (29.4%). The literature review showed no long-term impairment in 78.3% of children, with variable neurological deficits. These differences can be explained by the level of detail presented in our review, which assessed every detail in the patient medical data.

Although many of the surgical routes developed to approach skull base tumors have been reported for adults,
in general, the same approaches are possible, however, the unique anatomy in children creates challenges for the pediatric neurosurgeon because of the small size and the developing skull of the children.[18] Skul base surgery did not undoubtedly show an adverse effect on the development of the craniofacial skeleton. However, radiotherapy is associated with negative consequences, such as delayed growth of facial bones and tissues, visual or auditory dysfunction, short stature, dental abnormalities, and various endocrinopathies.[13,19]

Skull base surgery in children presents a unique challenge, since the potential benefits of therapy must be balanced against the cumulative impact of multimodality treatment on craniofacial growth, donor site morbidity, and possible psychosocial problems.

There are several differences between adults and children regarding the morphology of the skull base, for example, the size of the cranial base and the maxillofacial complex in children is smaller, the cranial bone is thinner, and the floor of the frontal and middle cranial fossa may be flatter.[8]

Common skull base surgical approaches, with appropriate adjustments, can be safely and effectively implemented in pediatric patients. Many surgical considerations are important when performing skull base surgery in the pediatric population: the smaller, thinner skull lends to varying decisions in pinning, drills, handling, and plating of the bone.[20]

Surgeons and anesthetists have to monitor the blood loss during surgery, considering that patients have considerably smaller circulating blood volumes than in the adult, thus seemingly small amounts of intraoperative blood loss can require intraoperative transfusion.[20] Another important concern is about body temperature, the higher ratio of body surface area to volume in children can result in precipitous falls in body temperature.[21]

**Conclusion**

Skull base tumors are relatively rare in pediatric age, predominating in boys, with very heterogeneous histopathology, leading to different surgical strategies and complementary treatments. Because of the considerable morbidity and mortality in pediatric age, these tumors should be managed by multidisciplinary teams with expertise in skull base surgical techniques. Pediatric skull base management requires a complex scenery to be executed, counting on experienced neurosurgeons, neuropediatricians, neuroanesthesiologists, neurophysiologists, dedicated intensive care units, specialized nursing care, as well as a competent rehabilitation team.

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**Conflicts of interest**

There are no conflicts of interest.

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