Tumors of the skull base in children: review of tumor types and management strategies

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Although many treatment strategies for skull base tumors in adults have been reported, relatively little has been reported regarding such therapies in the pediatric population. Skull base tumors in children present a therapeutic challenge because of their unique pathological composition, the constraints of the maturing skull and brain, and the small size of the patients. In this review, the authors examine the pediatric skull base lesions that occur in the anterior, middle, and posterior cranial base, focusing on unique pediatric tumors such as encephalocele, fibrous dysplasia, esthesioneuroblastoma, craniopharyngioma, juvenile nasopharyngeal angiofibroma, cholesteatoma, chordoma, chondrosarcoma, and Ewing sarcoma. They review management strategies that include radio- and chemotherapy, as well as surgical approaches with emphasis on the modifications and complications associated with the procedures as they apply in children. Evidence for the advantages and limitations of radiotherapy, chemotherapy, and surgery as it pertains to the pediatric population will be examined. With a working knowledge of skull base anatomy and special considerations of the developing craniofacial skeleton, neurosurgeons can treat skull base lesions in children with acceptable morbidity and mortality rates. Outcomes in this population may be better than those in adults, in part because of the benign histopathology that frequently affects the pediatric skull base, as well as the plasticity of the maturing nervous system.

KEY WORDS • skull base tumor • pediatric neurosurgery • angiofibroma • encephalocele • esthesioneuroblastoma • Ewing sarcoma • fibrous dysplasia

Skull base tumors have been difficult to treat because of the complexity involved in approaching them. With recent technical advances and the development of specialized centers, however, removal and cure are now possible. Although many of the surgical routes developed to approach skull base tumors have been reported for adults, few such reports exist for managing these lesions in children. In general, the unique anatomy in children poses challenges for the skull base surgeon because of the constraints of the developing skull and the small size of the patients.

A few reports on skull base tumors in the pediatric population have been published.^{3,13,22,68,129,141} In our review of skull base tumors, fewer than 5% of all frameless stereotactic surgeries were performed for skull base lesions.³ In this article, we will review the presentation and treatment of some of the relevant tumors of the anterior, middle, and posterior skull base that occur in the pediatric population (Fig. 1). Additionally, we will examine the common surgical approaches, with particular emphasis on their modifications and complications as they apply to children.

DISTINGUISHING FEATURES OF PEDIATRIC SKULL BASE TUMORS

Pediatric skull base tumors differ from adult tumors in

many aspects. Epidemiologically in the pediatric population, there are proportionately fewer skull base lesions than in adults, and more males (69%) than females are affected.¹²⁹ This sex difference may be related to the different tumor types that occur in children, as there are considerably fewer meningiomas and more benign nerve sheath tumors.^{101,129} In terms of operative approach, the surgeon must be careful, because of differing anatomy and involvement of growth centers in children. For example, anterior approaches in children are hindered by the shallow anterior fossa floor and the immaturity of the sinuses. Those involving maxillotomy may require reconsideration because tooth buds can be compromised. Because tissue planes are reportedly better defined in children, a higher percentage of complete resection in the initial attempt has been noted.¹²⁹ The higher rate of complete resection, together with the high incidence of benign tumors, helps to explain why a better prognosis in children with skull base lesions is often reported.¹²⁹

TUMORS OF THE ANTERIOR CRANIAL BASE IN CHILDREN

Clinical findings in pediatric patients with anterior cranial base lesions are related to the tumor location and do not differ significantly from those observed in the adult population. Whereas the most common anterior cranial base tumors in adults are nasal or paranasal malignancies and meningiomas, these tumors are relatively rare in chil-

Abbreviations used in this paper: CSF = cerebrospinal fluid; CT = computerized tomography; MR = magnetic resonance.

Fig. 1. Interactive figure in which the tumor and surgical approaches correspond to each skull base region. Click on a skull base region to view tumors and surgical approaches associated with this region.

dren,¹⁰² in whom the most common lesions of the anterior cranial base are encephaloceles, fibrous dysplasia, and esthesioneuroblastomas.

Encephaloceles of the Anterior Cranial Fossa

Encephaloceles are extensions of intracranial structures outside the normal confines of the skull, and their incidence is approximately 0.2 per 1000 live births and fetal deaths.¹²¹ Whereas convexity encephaloceles especially in the occipital region predominate in North America, encephaloceles of the anterior cranial fossa most frequently occur in Southeast Asia. These lesions can be classified into sincipital and basal encephaloceles. Sincipital encephaloceles can be further subdivided into frontonasal, -ethmoidal, and -orbital subtypes. Basal encephaloceles may be sphenoorbital, -maxillary, -ethmoidal, or transethmoidal.⁷⁸ The University of Toronto experience with 17 sincipital and five basal encephaloceles has previously been reported.⁷⁸

Surgery-related strategies for repair of anterior cranial fossa encephaloceles usually require a bicoronal scalp incision, frontal craniotomy, and bilateral orbitotomy (Fig. 2). The dural defect is defined at the anterior skull base, and the dura is then opened. Normal-appearing herniated brain tissue can sometimes be restored to the intracranial compartment; however, frequently this tissue is dysplastic and irretrievable. The dura is closed in a watertight fashion, and the craniofacial skeleton is reconstructed in conjunction with the craniofacial surgeons charged with cosmetic repair of the facial skin defect. In cases in which marked hypertelorism has resulted, an orbital translocation procedure may be required.⁷⁸ In contrast to occipital encephaloceles, which are frequently associated with hy-

Fig. 2. *Upper Left:* Photograph showing a girl with large sincipital, frontoorbital encephalocele, prepared for surgery. *Upper Right:* Three-dimensional CT scan obtained in the same girl, demonstrating osseous erosion of medial orbit by encephalocele. *Lower Left:* Sagittal MR image obtained in a patient with a large predominantly cystic frontonasal mass protruding through the osseous defect. *Lower Right:* Intraoperative photograph demonstrating repair of nasofrontal encephalocele. A bifrontal craniotomy and bilateral orbitotomies have been performed. The encephalocele sac has been dissected free from the facial skin and is continuous with the intracranial dura.

drocephalus, marked herniation of brain tissue, and microcephaly, management of encephaloceles of the anterior cranial base usually does not require CSF diversionary procedures for hydrocephalus.

Fibrous Dysplasia

Fibrous dysplasia is a developmental anomaly of bone-forming mesenchyme in which the transformation of woven bone to lamellar bone does not occur and there is an overgrowth of a well-vascularized fibrous stroma surrounding the haphazardly arranged osseous trabeculae.⁴⁹ It can occur in a monostotic form, in a polyostotic form involving multiple osseous sites, and as part of the McCune-Albright syndrome.⁴⁹ Consideration of aggressive surgical approaches to control disease-related complications must be weighed against the known difficulties associated with reconstructing large bone defects and patients' unpredictable clinical courses.²⁷ Advocates for early surgery believe that conservative treatment during the "active" phase in children is unacceptable¹⁶ because there is no indication that surgical procedures inhibit the growth rate of residual normal tissues⁴⁹ and progression of disease can continue into adulthood (Fig. 3).⁵⁹ Therefore, surgery is indicated for the prevention of neurological deficit or substantial deformity in patients of all ages. One of the most frequent and feared complications of fibrous dysplasia of the sphenoid wing is encroachment of the optic

Fig. 3. *Upper Left:* Axial CT scan with bone windows revealing right sphenoid wing fibrous dysplasia. *Upper Right:* Three-dimensional CT reconstruction obtained in the same patient, revealing the involved region of the anterior cranial base. *Lower Left:* Intraoperative photograph of anterior cranial base fibrous dysplasia following decompression of bilateral optic nerves and orbits. *Lower Right:* Intraoperative photograph showing the thickness of the affected skull secondary to the fibrous dysplasia.

nerve and progressive visual loss. In such cases, decompression of the optic nerve with or without craniorbital reconstruction may be indicated. We have reported our experience in two such cases in which we used frameless stereotactic systems and intraoperative image guidance to assist in unroofing the optic canal in the presence of distorted anterior cranial base anatomy.³

Although an incidence (25%) of recurrence associated with partial removal of the lesion has been reported,⁵⁹ radiotherapy has not been recommended because of the risk of malignant transformation.⁸⁹ Even without radiotherapy, however, there have been reports of spontaneous malignant transformation.¹²⁶

Esthesioneuroblastoma of the Anterior Cranial Fossa

Esthesioneuroblastomas or olfactory neuroblastomas are tumors of neuroectodermal origin believed to arise from the mitotically active basal layer of the olfactory epithelium normally located within the superior one third of the nasal septum, cribriform plate, and superior turbinates.⁷ Resection alone or in combination with radio- and/or chemotherapy has been performed in their management.^{56,61,86} Their staging has been performed using the Kadish system⁶¹ depending on the extent of disease. In Kadish Stage A, the tumor is limited to the nasal cavity; in Stage B, it is localized to the nasal cavity and paranasal sinuses; and in Stage C, it extends beyond the nasal cavity and paranasal sinuses. Five-year survival rates in patients with Stage A, B, and C disease have been reported to be 75, 60, and 41%, respectively.²⁹

In a series of 49 patients with esthesioneuroblastoma treated at the Mayo Clinic between 1951 and 1990, pathological grade of the lesion was identified as the most important prognostic factor.⁸⁶ Their clinical manifestations and treatment results were reviewed to identify possible prognostic factors. Whereas the overall 5-year survival rate in all patients was 69%, that in patients with low- and high-grade tumors was 80 and 40%, respectively. Surgery alone was advocated in cases of low-grade tumors if tumor-free margins could be obtained. Radiotherapy was recommended in cases of low-grade tumors when margins are close, in those of residual or recurrent disease, and in those of all high-grade cancers. The addition of chemotherapy was suggested in the management of patients with high-grade tumors.

Chemotherapeutic agents have been mostly used to treat patients with recurrent, metastatic, or inoperable disease. Single chemotherapeutic agents include thiotepa, doxorubicin, cyclophosphamide, vincristine, decarbazine, and nitrogen mustard.⁵⁶ Consistent responses have been demonstrated using combinations including cyclophosphamide with or without vincristine usually when administered every 21 days, toxicity permitting.⁵⁶ Neoadjuvant combination therapies include cyclophosphamide/doxorubicin/vincristine,²¹ cisplatin/VP-1621, and cisplatin and 5-fluorouracil by continuous infusions daily for 6 days, repeated every 21 days for four cycles, and followed by resection.⁹⁴ An alternating regimen of cyclophosphamide and vincristine with cisplatin and VP-16 every 3 weeks has been used and a good palliative response achieved.

High-dose chemotherapy combined with autologous bone marrow transplantation has also been used in patients with recurrent disease.^{93,122}

NEUROSURGICAL APPROACHES TO THE ANTERIOR CRANIAL BASE

Surgical approaches to the anterior cranial base include transfacial, anterior craniofacial, craniotomy with orbital and/or zygomatic osteotomy, and transsphenoidal.^{88,129} The transfacial approaches can be categorized into transoral, transpalatal, lateral rhinotomy, Le Fort I osteotomy, and midfacial degloving.⁷² Although these approaches are undertaken in adults, their use in children frequently requires modification. The transoral, and specifically the labial-mandibulotomy approach provides adequate exposure but destroys the pediatric patient's central incisors, and it may jeopardize other tooth buds in patients younger than 6⁷² or 10 years of age.⁶⁸ The bulk of soft tissue that must be retracted when performing the transpalatal approach restricts exposure of the upper clival and sphenoidal regions.⁷² The major transpalatal approach-related concerns are the development of a palatal fistula or wound dehiscence.¹⁰⁹

Lewark, et al.,⁷² performed Le Fort I osteotomies in 11 children and reported related complications including loss of unerupted tooth buds and epiphora in one case each. Disruption of facial growth was assumed to be unlikely because the osteotomy did not pass through growth centers.¹¹ Although disruption of facial growth has been a source of concern, several groups have reported no such disruption when performing anterior (transzygomatic, orbital, transoral, and transmandibular) and lateral (petrous, transcondylar, translabyrinthine, and transbasal) approaches.^{68,95,129} Although they did not conduct formal morphometric studies on facial bones obtained in children with craniofacial procedures, Teo, et al.,¹²⁹ found normal facial skeletal growth in patients as young as 4 years of age in whom 20 months of follow-up data were available.

Midfacial degloving provides good anterior exposure and, when combined with complete ethmoidectomy or medial maxillectomy, can create central skull base exposure⁷² without leaving external facial deformity. With endoscopic assistance, this approach has been performed in infants.¹³⁴ Drawbacks include sensory disturbances involving the teeth and infraorbital nerve distribution,⁷² oroantral fistula, and epiphora.⁵⁵ In the anterior craniofacial approach a conventional bifrontal craniotomy is combined with a transfacial approach, thereby allowing excellent access to tumors of the anterior cranial base and sinuses and nasal cavities.^{72,129}

Craniotomy, when combined with the orbital and/or zygomatic osteotomy, provides a lower trajectory approach and allows access to suprasellar and cavernous sinus lesions.^{117,129} In children younger than 6 years of age, the anterior cranial fossa is generally relatively shallow and the frontal sinuses have not developed fully. This makes anterior cranial approaches less difficult in children than in adults.⁶⁸

The transsphenoidal approach has many variations including a sublabial transnasal dissection, perinasal, transethmoid, pure transnasal, and endoscopic.^{75,129,135} Trans-

sphenoidal surgery in children may be limited by virtue of the small sella and the absence of a fully aerated sphenoid sinus. In such cases, image guidance may be invaluable for keeping the neurosurgeon directly on the midline when approaching the sella.³

TUMORS OF THE MIDDLE CRANIAL BASE IN CHILDREN

Middle cranial base lesions in children can cause symptoms relating to the central (sphenoid sinus/sella turcica), paracentral (cavernous sinus), or lateral (sphenoid wing/infratemporal fossa) middle fossa.⁸⁸ Central middle fossa lesions result in pituitary and hypothalamic abnormalities such as panhypopituitarism, precocious puberty, secondary amenorrhea,³ and diabetes insipidus,⁸⁸ or they cause deficits secondary to mass effect on the optic nerve and chiasm.⁸⁸ In cases of lesions of the paracentral middle fossa, patients can develop intractable facial pain and dysesthesia, and tumors can affect the optic nerve in the apex, third through sixth cranial nerves, temporal and frontal lobes, and the cavernous carotid artery.⁸⁸ Lateral middle fossa lesions affect the divisions of the trigeminal nerve, lateral orbit, and infratemporal fossa and can cause facial deformity and oropharyngeal obstruction.⁸⁸

In adults, meningiomas and schwannomas of the gasserian ganglion are the most common middle cranial base tumors.⁷⁶ In children astrocytomas, pituitary adenomas, craniopharyngiomas,³ hemangiomas, giant cell tumors, malignant fibrous histiocytomas, optic nerve gliomas, osteoblastomas,⁷⁷ and juvenile nasopharyngeal angiofibromas⁷² have been reported. We discuss the craniopharyngiomas and juvenile nasopharyngeal angiofibromas with respect to presentation, surgery, radio-, and chemotherapy.

Craniopharyngioma of the Middle Cranial Base

Craniopharyngiomas are slow-growing, benign epithelial neoplasms of the sellar region believed to originate from remnants of embryonic squamous cell rests of an incompletely involuted hypophyseal-pharyngeal duct.⁸⁵ Although not strictly a tumor of skull base origin, the frequent use of skull base approaches and the minimal brain retraction required when resecting this tumor justify its inclusion.

Authors of recent series have shown that craniopharyngiomas account for 1.8 to 4.4% of pediatric brain tumors^{60,101} and occur equally between sexes.⁸⁵ Craniopharyngiomas occur sporadically and generally have no direct pattern of familial inheritance.⁸⁵ No consistent and specific chromosomal abnormalities have been associated with craniopharyngiomas. Children harboring these lesions can present with headaches, visual disturbance, endocrine disorders, and mental disturbance. Compared with adults, children present more often with headache and vomiting due to mass effect or obstructive hydrocephalus than with visual difficulties.^{87,114} In 20 to 30% of cases children present with visual changes,¹¹⁴ which can include decrease in visual acuity, diplopia, blurred vision, bitemporal hemianopia, homonymous hemianopia, various quadrantanopias, central scotomas, see-saw nystagmus, and uni- or even bilateral blindness.^{85,125} A significant relationship between tumor location and clinical presentation has been found;

Skull base tumors in children

authors reported that patients with prechiasmatic tumors presented with more significant losses of visual acuity and field than did those with retrochiasmatic tumors.⁵²

Although an endocrine abnormality is found in 80 to 90% of patients, it is not a frequent cause of medical consultations.⁸⁵ In children medical attention is sought because of short stature and retarded linear growth, whereas in adolescents delayed or arrested puberty is observed. Growth hormone is the most common hormonal deficiency, followed by luteinizing hormone or follicle-stimulating hormone, adrenocorticotrophic hormone, and thyroid-stimulating hormone. Hyperprolactinemia may be caused by compression of the pituitary stalk or hypothalamus, regions that normally inhibit prolactin release. Diabetes insipidus and the syndrome of inappropriate antidiuretic hormone secretion^{44,45} are also seen in the pediatric population. Although mental disturbance secondary to tumor expansion into the frontal and temporal lobes can occur frequently in adults, it is unusual in children.⁸⁵

Management of these lesions requires multidisciplinary strategies involving neuroophthalmology, endocrinology, neuropsychology, and radiation oncology, as well as neurosurgery. Because visual disturbances frequently occur in patients with craniopharyngiomas, full visual acuity and field examination should be performed prior to any surgical management. Endocrinologists should be involved to correct hormonal deficiencies including diabetes insipidus, hypoadrenalism, and hypothyroidism, which have been shown to increase intra- and postoperative morbidity rates.¹³¹

There is controversy regarding the optimum surgical management, particularly between subtotal resection combined with postoperative radiotherapy compared with gross-total resection. The location of the tumor dictates the surgical approach. Some of the common surgical approaches include subfrontal, pterional, transsphenoidal, transcallosal, transtemporal, and subtemporal. Proponents of subtotal resection combined with radiotherapy assert that this therapeutic combination decreases tumor recurrence and results in fewer neurological, endocrinological, and psychological deficits compared with aggressive resection.^{8,33,100} Various radiotherapy modalities include external fractionated irradiation, fractionated stereotactic radiotherapy, stereotactic radiosurgery, and stereotactic intracavitary implantation of radionuclides.⁸⁵ Neurological, vascular, and endocrinological morbidities have been correlated to radiation dosage,^{100,125} with the neurological and vascular deficits reported only in patients who had received a greater than 6100-cGy radiation dose. Because radiotherapy treatment in preschoolers can be hazardous to the developing brain, Kennedy and Haines⁶⁴ have advocated a policy of total or subtotal resection in conjunction with follow-up serial MR imaging and periodic physical examination. Radiation therapy was only initiated in cases of recurrence or symptomatic tumor regrowth at a later date.

Advocates of total resection believe that the long-term effects of radiotherapy may expose patients to significant risks of secondary endocrinopathy, vasculopathy, and malignant neoplasms.^{92,131} Neurosurgical adjunctive procedures that we have found that aid in the removal of craniopharyngioma via the extended subfrontal approach

include a unilateral orbitotomy up to the midline, en bloc removal of the orbital roof, ligation and transection of the anterior superior sagittal sinus, and generous aspiration of CSF from the cisterns and/or release of CSF from an external ventricular drain in cases in which hydrocephalus is present (Fig. 4).

[Click here to view Video Clip: Removal of prechiasmatic portion of solid craniopharyngioma.](#)

Radiotherapy is thought to make resection more difficult, resulting in increased rates of morbidity and mortality in cases of tumor recurrences.^{137,143} At our institution, we found no incidence of recurrence in 17 children who underwent total resection between 1950 and 1989,⁵³ and a tumor recurrence rate of 29% in patients who underwent surgery between 1975 and 1989.⁵² Endocrinopathies are common after gross-total resection,^{52,67,100,125,132,138,143} however, they may be associated with the surgical approach, and the incidence of endocrinopathy is decreased after transsphenoidal or subtotal tumor resection combined with radiotherapy.^{69,70,100} Other surgery-related complications include postoperative drowsiness and a persistent confusional state associated with the transtemporal approach,¹²⁵ fusiform dilation of the internal carotid artery,¹²⁴ fatal intraoperative internal carotid artery rupture associated with transsphenoidal resection,⁶⁷ rhinorrhea or meningitis after drilling of the tuberculum sellae, or transsphenoidal surgery.^{52,54} Ectopic craniopharyngioma has been

Fig. 4. *Upper Left:* Sagittal MR image obtained in a 10-year-old girl harboring a giant craniopharyngioma. *Upper Right:* Coronal MR image obtained in the same patient, demonstrating the vertical extent of the lesion. *Lower Left:* Photograph showing the excised orbit. An orbitotomy assists with the exposure of the anterior cranial fossa via the subfrontal approach. *Lower Right:* Intraoperative photograph obtained after the tumor resection, demonstrating the extent of exposure obtained via the subfrontal approach.

found in cases in which the transcallosal approach has been undertaken.⁷⁴

In cases of cystic craniopharyngiomas, drainage and injection of radioactive isotopes or chemotherapeutic agents, specifically bleomycin,¹²⁸ have been reported. Complications of intralesional chemotherapeutic treatment have been reported to be associated with the toxic effects of bleomycin on the hypothalamus,⁴⁸ as in a case in which, after intracystic injection of bleomycin, a patient developed hypersomnia, personality changes, memory impairment, and thermal dysfunction. Bremer, et al.,¹⁴ have reported finding neurological improvement and decreased cyst size following systemic combination treatment with vincristine, carmustine (BCNU), and procarbazine.

Juvenile Nasopharyngeal Angiofibromas of the Middle Cranial Base

Juvenile nasopharyngeal angiofibromas are rare, histologically benign, locally invasive tumors⁵⁷ or vascular malformations⁹ of the nasopharynx that are found primarily in the pubescent male. We have recently reported on a 12-year-old boy who harbored paranasal tumor that extended into the cavernous sinus; we performed preoperative embolization and then resected the lesion via a subfrontal transbasal approach, orbitozygomatic osteotomy, lateral rhinotomy, and medial maxillotomy. The boy had presented with facial asymmetry, proptosis, progressive visual failure, and partial progressive oculomotor palsy. He is currently undergoing radiotherapy targeting a small infratemporal residual mass (Fig. 5).

Although usually localized to the nasopharyngeal regions, intracranial invasion can occur in as many as 36% of cases.⁵⁷ Surgery and radiotherapy are the mainstays of treatment. Because of the increased intra- or postoperative hemorrhage associated with these lesions, preoperative embolization^{91,118} has been used to minimize blood loss. Common postoperative complications include eustachian tube dysfunction,^{30,47} palatal dehiscence, and rhinolalia aperta.²⁸

Radiotherapy has been advocated as a primary treatment^{24,140} and as an adjunct to surgery^{28,46} in patients with

advanced disease. In one study the authors reported long-term results demonstrated in 15 patients who underwent radiotherapy alone, and they found that two developed recurrent disease requiring salvage surgery.⁹⁹ Whereas chemotherapy trials are difficult because of the rarity of the disease, chemotherapeutic agents have been used as adjuncts to surgery. A testosterone receptor blocker, flutamide, has been found to shrink tumors an average of 44%, while allowing patients to retain normal testosterone levels 2 or more years posttherapy.⁴⁰ Other agents associated with varying success include doxorubicin and decarbazine,¹¹⁰ doxorubicin, vincristine, dactinomycin, and cyclophosphamide.⁴²

NEUROSURGICAL APPROACHES TO THE MIDDLE CRANIAL BASE

Middle cranial base approaches^{64,88} undertaken in the pediatric population include: 1) frontotemporal with orbital and/or zygomatic osteotomy;^{71,81} 2) temporal with zygomatic osteotomy and/or anterior petrosectomy;^{19,35,83,119} 3) preauricular infratemporal with or without mandibular dislocation or resection;^{1,123} and 4) transsphenoidal.^{45,129} Complications reported in association with the first anterolateral approach include death, pneumonia with septicemia, wound infection, meningitis, CSF leakage, cranial nerve palsy,⁷¹ minimal transient complications (mild trismus, frontal branch paresis, serous effusion, and cheek hypesthesia),¹⁵ and poor cosmetic result.⁸¹ The temporal approach in conjunction with petrosectomy was associated with new deterioration of facial nerve function,¹⁹ subdural temporal lobe hemorrhage, and CSF rhinorrhea.¹¹⁹ Complications associated with the infratemporal alone or in conjunction with mandibular manipulations include wound infections, CSF leakage,¹²³ temporary restriction of mandibular opening,¹ conductive hearing loss, numbness of the lower lip, temporal depression caused by the use of the temporalis muscle flap, and facial paresis secondary to translocation of the facial nerve.^{32,72} Because the effect of mandibular resection in the child is not well known, some authors have recommended avoiding mandibular resection whenever possible.⁶⁴ The classic transsphenoidal approach involves a sublabial transnasal dissection; however, several modifications have been described involving a perinasal, transthemoid, pure transnasal, microsurgical, or endoscopic technique.^{26,75,129,135} Complications associated with the transsphenoidal technique have already been described.

TUMORS OF THE POSTERIOR CRANIAL BASE IN CHILDREN

Patients harboring posterior cranial base lesions present with symptoms secondary to the anatomical location within the posterior fossa.⁸⁸ Symptoms of dysphagia or nasal obstruction can occur in cases involving local tumor extension into the retropharynx or nasal cavity, and headaches or neck pain can occur in cases involving the occipital condyle and/or atlantooccipital instability.¹¹³ Patients most commonly present with headaches or diplopia and are found to have an abducent paresis or palsy.⁷⁶

Although most posterior cranial base tumors such as

Fig. 5. *Left:* Axial MR image obtained in a 12-year-old boy with juvenile angiofibroma affecting the middle and anterior cranial skull base compartments. *Right:* Coronal MR image demonstrating proximity of the lesion to the cavernous sinuses bilaterally.

Skull base tumors in children

meningioma,^{4,79} schwannoma,^{43,50,84} epidermoid,^{108,111} cholesteatoma,^{39,97} chordoma,¹³ and chondrosarcoma³⁸ are more common in adults, other rare tumors such as Ewing sarcoma are more common in children.⁴⁹ We will review the current management strategies associated with cholesteatomas, chordomas and chondrosarcomas, and Ewing sarcoma.

Cholesteatomas of the Posterior Cranial Base

Cholesteatomas are tumors with a stratified squamous epithelium and keratinous debris derived from the sloughing epithelium⁸² and are categorized as congenital or acquired. Congenital cholesteatomas are believed to be secondary to a congenital rest of epithelial tissue trapped in the temporal bone, and acquired cholesteatomas are thought to result from a retraction pocket, otitis media, or abnormal epithelial migration secondary to tympanic membrane perforation.¹² Because cholesteatomas have been reported to be more invasive in children than adults, some authors have advocated a more aggressive approach in children.¹²

The mainstay for treatment of cholesteatoma is surgery. In both congenital and acquired cholesteatomas, the goal of surgery is complete removal of the squamous epithelium, preservation or restoration of hearing, and maintenance of normal anatomy.³⁶ There are two main surgery-related strategies in the management of these lesions. One strategy is to perform aggressive exteriorization of the diseased ear and create a common cavity that exists as a “bowl” after the procedure. This procedure, termed the canal-wall-down mastoidectomy, provides better exposure and allows for postoperative surveillance of the disease.³⁴ The canal-wall-down directive refers to the removal of the posterior ear canal wall. A second strategy involves removing the cholesteatoma while attempting to preserve middle ear hearing and function.³⁴ Because these canal-wall-up procedures have been reported to increase the incidence of recurrent cholesteatomas,¹³³ surgeons perform second-look procedures to search for tumor recurrence.¹³⁶ A minimal endoscopic second-look procedure has been reported to be better accepted by patients.¹³⁰ Because the incidence of residual or recurrent disease has been reported to be as high as 57% after 5 years,¹⁰⁵ long-term follow-up examination is essential.

Microbial therapy should be topical, but systemic therapy may occasionally be helpful.¹⁰³ There is no accepted medical treatment of cholesteatoma.³⁴ Antimetabolites, such as 5-fluorouracil, have been used to inhibit the keratin formation and reduce mucous hypersecretion, and results have been shown to persist even 12 months after suspending treatment.^{107,142} Intratympanic prednisolone has also been found to decrease experimental cholesteatoma production.¹¹⁶ Other investigated agents include hyaluronic acid and cyclophosphamide, but no success has been observed.^{96,139}

Chordomas and Chondrosarcomas

The location and surgical treatment of chordomas and chondrosarcomas are similar.¹¹³ They are typically slow-growing, locally invasive tumors that occur at the cranial base.⁶⁴ In our experience, chordomas in the young (particularly in females) behave more aggressively with a rela-

tively shorter history of symptoms, shorter interval to progression, and a tendency for early development of metastatic disease.

Chordomas are dysontogenetic neoplasms that originate from the embryonic notochord and have the fairly consistent features of an overall lobular arrangement of cells, cells that grow in cords, irregular bands or pseudo-acinar form, mucinous matrix, and large physaliphorous and vacuolated cells.¹⁰⁶ Tending to occur in a paramedian location, chondrosarcomas have been classified as classic, mesenchymal, and dedifferentiated;⁶⁶ the mesenchymal and dedifferentiated types are more aggressive than the classic type.¹¹³ Children tend to present with atypical chordomas.¹³

Treatment generally consists of an attempt at complete resection (Fig. 6) and postoperative radiotherapy.^{20,23,127,141} These tumors are generally soft and cartilaginous or gelatinous; however, they may also be calcified.¹¹³ The core of the tumor is resected piecemeal or by using a drill, and the margins are then removed until normal bone or venous channels within the bone are encountered.¹¹³ The otic capsule, compared with the clivus, remains relatively resistant to tumor invasion.¹¹³ Ensuring complete removal of the tumor margins is difficult because quick sections of bone are not available.¹¹³ Complete excision of any intradural extension of tumor is also attempted, taking care to avoid encased vessels, nerves, and the brainstem.¹¹³ Dural defects are repaired by placing grafts as required.¹¹³

Radiotherapy has been performed as an adjunct to surgery.^{20,23,127,141} The radiation treatments have included pre-²³ or postoperative conventional radiotherapy,^{2,20} as well as postoperative stereotactic proton-photon beam therapy.^{2,20} Compared with chordomas,¹⁰⁴ chondrosarcomas have been found to respond better to radiotherapy; however, the neurotoxicity associated with the use of radiotherapy in young children must be considered and avoided if possible.

The results of chemotherapy have generally been dis-

Fig. 6. *Left:* Axial CT scan obtained in a 14-year-old boy with clival chordoma. *Upper Right:* Three-dimensional reconstruction of the skull base, demonstrating a massive lesion that has replaced the clivus. *Lower Right:* Intraoperative photograph obtained during transoral resection of clival chordoma.

appointing, and this intervention is performed when other therapies have failed.⁵⁶ Symptomatic improvement in some patients has been shown after administration of vincristine,^{51,98} but this agent has failed in combination therapy with others.^{31,112} Single-agent chemotherapy (carboplatin,³⁷ cisplatin,³⁷ or methotrexate²⁵) has been found to be ineffective in terms of tumor response and pain relief. Combination therapies that are associated with varying degrees of success include hydroxyurea with 5-fluorouracil;⁵ cisplatin, vinblastine, and bleomycin with concurrent radiotherapy;⁶ preoperative cyclophosphamide, vincristine, doxorubicin, and decarbazine together with radiotherapy;⁶² vincristine and methotrexate with leucovorin rescue;³⁷ and ifosfamide and doxorubicin with intrathecal or intraventricular therapy with hydrocortisone, ara-C, and methotrexate.¹¹² No benefit has been reported with the combination of actinomycin-D, cyclophosphamide, and vincristine, nor with cisplatin and 5-fluorouracil or high-dose methotrexate.¹¹²

Ewing Sarcoma

Ewing sarcoma is a primitive neuroectodermal tumor that can involve the pediatric skull base. It can be massive, and children can present in extremis secondary to mass effect. Currently, the diagnosis of Ewing sarcoma has been facilitated through the use of molecular diagnostic modalities such as spectral karyotyping that have shown a characteristic 11;22 chromosomal translocation. Other molecular studies have shown a frequent EWS/FLI1 fusion transcript.¹⁷ Whereas surgery plays a role in decompressing important neural structures at the skull base (Fig. 7), Ewing sarcoma is known to be responsive to aggressive chemotherapeutic agents such as carboplatin, etoposide, and ifosfamide. Radiotherapy is reserved for patients in whom no response to chemotherapy is demonstrated.

NEUROSURGICAL APPROACHES TO THE POSTERIOR CRANIAL BASE

Posterolateral surgical approaches in the pediatric population can be categorized as transpetrosal, retrosigmoid,^{73,80} translabyrinthine,⁶⁸ retrolabyrinthine,⁶⁵ and partial labyrinthectomy,¹¹⁵ transcochlear,^{41,90,120} far-lateral/extreme-lateral transcondylar,^{10,64} and extreme-lateral, transjugular.^{63,18,88}

Like the anterior sinuses, the mastoid air cells are also immature and less fully developed. The solid bone makes both identification of the labyrinth and drilling more difficult and requires the expertise of a neurootologist. The available exposure to the lateral posterior fossa, however, requires less retraction of the neural structures in children than adults.⁶⁸ Frequent approach-related complications include cranial nerve deficits and CSF leaks.¹¹⁵ The retrosigmoid and translabyrinthine techniques can preserve facial nerve function in children, although CSF leakage has also been reported in pediatric series.⁶⁸ The transcochlear approach allows access to lesions anteromedial to the internal auditory meatus that are equally distributed within both the middle and posterior cranial fossae.¹²⁹ It offers only limited exposure to the lateral aspect of the clivus.⁷² Facial nerve deficits may occur⁹⁰ because this approach requires facial nerve transposition. The ap-

proach also involves drilling of the temporal bone, including the entire labyrinth, and thus, if hearing requires preservation, the transcochlear approach is inappropriate.¹²⁹

At our institution an infralabyrinthine, infracochlear hearing-sparing approach was recently performed for the drainage and permanent aeration of a cholesterol granuloma of the petrous apex. The lesion occurred in a 16-year-old young woman with normal hearing who presented with headaches, progressive diplopia secondary to an abducent palsy, and facial asymmetry (Fig. 8). Postoperatively her cranial nerve deficits and headaches resolved, and hearing remains intact.

The transcondylar approach allows access to lower clival lesions, foramen magnum, and the upper cervical spine. In such cases the sigmoid sinus and jugular bulb will be exposed, and a C-1 laminectomy is continued to expose the vertebral artery. Once the vertebral artery is mobilized, the ipsilateral occipital condyle is resected, as is the lateral process of C-1 or C-2 if necessary. The transjugular approach involves lateral suboccipital craniotomy and resection of the posterior one-third of the occipital condyle. The jugular foramen is opened by removing the posterior wall, without performing a mastoidectomy, to preserve hearing and facial nerve function.⁶³

COMPLICATIONS AND OUTCOMES

Because few series of skull base procedures performed purely in pediatric populations have been reported, it is necessary to extrapolate the complications reported in the adult or mixed populations to the pediatric population. The complications associated with adult or mixed populations will not be reviewed in this paper; rather, we note some of the complications that have been described in pediatric skull base series.^{3,68,129}

In a study published by Alshail, et al.,³ 13 children with skull base lesions underwent various neurosurgical procedures including the following: transsphenoidal, pterional, frontal, transoral, subtemporal bifrontal, bifrontal midfacial, and transnasal approaches.³ They reported several transient but no permanent neurological deficits. Lewark, et al.,⁷² reported on 11 patients (mean age 14.3 years) who underwent a Le Fort I osteotomy in the treatment of the following angiofibromas (eight cases), hemangioma, giant cell tumor, and malignant fibrous histiocytoma (one case each). Complications that occurred in a mean follow-up period of 2.5 years (range 6 months–2.5 years), included loss of tooth buds, mild enophthalmos, and epiphora. They observed that disruption of facial growth is unlikely, because the osteotomy does not pass through growth centers.

In the large pediatric series reported by Lang, et al.,⁶⁸ the authors discuss the results in 20 children (age range 3 months–14 years) harboring the following lesions: arteriovenous malformation, juvenile nasopharyngeal angiofibroma, capillary hemangioma, craniopharyngioma, exophytic brainstem glioma, acoustic schwannoma, hypoglossal and posterior inferior cerebellar artery aneurysm, cranial fasciitis, optic nerve glioma, clivus chordoma, intraorbital cavernoma, craniocervical instability caused by peg migration, epithelioid hemangioendothelioma, optic sheath meningioma, and meningioma. Surgical procedures included transzygomatic, translabyrinthine, cranio-

Fig. 7. *Lower:* Coronal CT scan obtained in an infant with massive skull base Ewing sarcoma. The lesion arises from the petrous bone. Coronal (*center*) and axial (*right*) MR images obtained in the same infant, revealing a tumor occupying the middle and posterior cranial fossae. Following tumor decompression, the lesion was treated with aggressive adjuvant chemotherapy, and the child is tumor free and well now 10 years after diagnosis.

facial, transbasal, superior orbitotomy, transcondylar/suboccipital, Le Fort I maxillotomy, orbitozygomatic, transoral, transpetrous, and transmandibular and transzygomatic approaches. Postoperative complications included hypertrophic preauricular scar, temporal hollowing, nasal obstruction, ptosis, visual field defect, visual failure, facial nerve palsy, subarachnoid hemorrhage, diabetes insipidus, CSF leakage, meningitis, and hydrocephalus. No disruption in facial growth was noted in patients orbital or transmandibular access was created; no temporomandibular

joint dysfunction was observed in those who underwent surgery via a transzygomatic approach. Based on the indices of the Glasgow Outcome Scale,⁵⁸ good recovery was demonstrated in 18 cases, moderate disability occurred in one, and severe disability was documented in one case. In terms of overall neurological condition, 14 improved, five were unchanged, and one was worse.

In another large series, Teo, et al.,¹²⁹ retrospectively reviewed 26 patients (mean age 10.5 years, range 4–20 years) who underwent skull base surgery for various tu-

Fig. 8. *Upper:* Intraoperative photographs of the infralabyrinthine and infratrochlear windows obtained during drainage of the cholesterol granuloma cyst and following insertion of silastic drainage tube for permanent aeration. *Lower:* Postoperative axial CT scan, and axial and coronal T₁-weighted MR images demonstrating drainage and aeration of the cholesterol granuloma cyst.

mor types including schwannoma, chordoma, fibrous dysplasia, plexiform neurofibroma, ependymoma, and esthesioneuroblastoma. Surgery was performed using anterior craniofacial, cranioorbitozygomatic, transsphenoidal, transpetrosal, retrosigmoid, transcochlear, and transcondylar approaches. There were five deaths, three of which were caused by the primary disease, one of aspiration pneumonia secondary to surgery-induced cranial nerve deficits, and one of fulminant diabetes insipidus. The rate of immediate postoperative complications was 57%, not including "expected deficits" such as deafness in patients with large acoustic tumors and in whom there was no functional hearing preoperatively. These complications included: facial nerve palsy or paresis, ninth, 10, and 11th cranial nerve palsies, aspiration pneumonia, dysphagia, dysphonia, facial anesthesia, panhypopituitarism, CSF leakage, meningitis, and memory disturbance. Permanent complications were only slightly lower at 30.7%, and these included facial palsy or paresis, dysphagia, hydrocephalus, quadriparesis, dysphonia, panhypopituitarism and corneal ulceration, and blindness. In 27% of the patients there were no expected deficits or postoperative complications; in an additional 15% there were expected deficits but no complications. The authors also noted no disruption in facial growth.

Teo, et al.,¹²⁹ allocated their patients into outcome categories of good (complete tumor resection with acceptable postoperative deficits), fair (complete tumor resection with significant postoperative deficits that did not affect the patient's function), and poor (unacceptable postoperative deficits that affected the patient's function). Overall, they attributed one death to be a direct result of surgery. Overall good, fair, and poor outcomes were reported in 62, 15, and 4%, respectively. The 2-year tumor-free survival rate was 81%.

CONCLUSIONS

Tumors of the skull base in pediatric patients pose unique challenges to the neurosurgeon. The differential diagnosis of a skull base tumor in this population differs from that in the adult population. With a working knowledge of skull base anatomy, as well as special considerations given to the developing craniofacial skeleton, skull base lesions can be treated in children and the related morbidity and mortality rates can be acceptable. Outcomes in children with skull base tumors may be better than those in adults, in part because of the benign histopathology that frequently affects the pediatric skull base as well as the plasticity of the developing nervous system.

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Skull base tumors in children

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