Chapter

Pediatric Skull Base Tumors

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Abstract

Management of pediatric skull base tumors requires a multi-disciplinary team that integrates advances in neuro-imaging, radiation, medical and surgical treatments, and allied therapies. Tumors of the skull base harbor complex genetic and molecular signatures that have major implications on prognosis and quality of life. Individualized management requires a strong inter-disciplinary alliance amongst practitioners, as well as a strong therapeutic alliance with the patient and family to navigate the complex decision-making process of treatments. In this chapter, we present our experience managing surgical lesions of the pediatric skull base. General considerations to tumor pathology genetics and radiobiology, diagnostic imaging, rehabilitation of cranial neuropathies and cognitive function, surgical anatomy and reconstructive options, and quality of life should be applied to each case. We also present location- and tumor-specific considerations in the anterior, middle, and posterior fossa skull base with a focus on surgical approaches and complication avoidance. Special consideration is given to syndromic tumors, particularly those from neurofibromatosis type 2 (NF-2). Tumors can exist in multiple cranial compartments and as such some redundancy in concepts is unavoidable. Nevertheless, each patient presents with a unique clinical picture and tumor behavior. Knowledge and proficiency in skull base approaches is a necessary tool in every pediatric neurosurgeon's armamentarium.

Keywords: pediatric brain tumors, skull base tumors, pediatric neuro-oncology, pediatric neurosurgery

1. Introduction

Contemporary management options for skull base tumors include observation, stereotactic radiosurgery or radiotherapy, primary or adjuvant chemotherapy, and microsurgical resection. Factors influencing treatment decisions include patient age and medical condition, cranial neuropathies, tumor size, tumor genetics, and provider bias. Advances in imaging and treatment technologies have led to improved detection of small skull base tumors, a better understanding of the natural history of tumor growth, and reductions in post-operative morbidity and mortality.

We strongly advocate for a team-based approach to treat skull base tumors. Our program is led by a neuro-oncology and neurosurgery team, and composed of neurophysiologists, head and neck surgeons, radiation oncologists, ophthalmologists, plastic and reconstructive surgeons, as well as occupational- physical- and speech- therapists. Microsurgical resection is carried out in cases not amenable to observation or radiation therapy. Where applicable, and when neurologic function

is not deteriorating, biopsy and individualized medical treatment is pursued in favor of radical resection. For example, advances in epigenetics and tumor expression profiles sensitive to *BRAF-V600E* confer favorable treatment response to kinase inhibitors in papillary craniopharyngioma [1]. In such cases, resection as index treatment is carried out in cases of neurologic deterioration, failed medical therapy, or favorable tumor handling at the time of biopsy.

Cranial nerve function takes priority when deciding to proceed with surgery. This is true both for extra-medullary lesions and intra-medullary lesions with exophytic components threatening cranial nerve function. The goals of resection should be considered when tailoring the surgical approach. For lower grade tumors, which comprise the majority of lesions, gross total resection with preservation of cranial nerve function is the standard of care. When cranial nerve function is threatened by poor tumor handling or adherence to adjacent neural or vascular structures, subtotal resection should be considered. This is especially relevant to lower cranial nerve function, which protects the airway and is associated with mortality when injured. Vision, oculomotor function, facial, and vestibulocochlear nerve function should also be considered.

Tumors that affect multiple cranial nerves together deserve special attention. This includes tumors that could affect all three oculomotor nerves, the fifth and seventh nerve together leading to insensate corneal abrasions and vision loss, and the lower cranial nerves together resulting in airway failure and death. Patients with contralateral cranial nerve dysfunction, such as in neurofibromatosis type 2 (NF-2), should also be given special consideration. In the case of bilateral acoustic neuromas, when contralateral hearing is absent, every attempt should be made to preserve ipsilateral hearing before attempting surgical resection. Bevacizumab has shown variable effect on tumor size and hearing function in such cases.

2. Anterior skull base

2.1 Introduction

The sellar and parasellar skull base contain several critical neurovascular structures. These include cranial nerves II through VI, the internal carotid arteries, the cavernous sinus, and the pituitary gland. Tumors in this area are likely to involve the olfactory nerves and the visual system in its orbital and cisternal course [2, 3]. Good pre-operative cranial nerve function predicts favorable neurologic outcome and pre-operative evaluation of cranial nerve function is essential. Anosmia in particular can herald the presence of a tumor [4]. Similarly, loss of olfactory function can significantly affect a patient's quality of life and should be taken into consideration when planning surgery. Ophthalmologic evaluation of visual function, including acuity, fundoscopy, and visual field testing may be useful in surgical planning. Evaluation by a multi-disciplinary team of neurosurgeons, ophthalmologists, and otolaryngologists is recommended for all anterior skull base tumors. We routinely obtain hi-resolution magnetic resonance imaging (MRI) and computed tomography (CT) during pre-operative evaluation. Constructive interference steady state (CISS) is especially useful in determining the course of cranial nerves involved in the tumor and surgical corridor. Gadolinium enhanced T1 weighted, and T2 weighted images help evaluate the extent of tumor invasion along the cranial nerves (peri-neural spread) as well as the bony skull base. MR or CT angiography is obtained in cases of suspected vascular encasement to determine the safety of surgical access and if bypass should be planned before resection. Formal angiography is performed in cases

where bypass is planned. A detailed endocrinologic history and serologic workup should be completed for tumors involving the sellar and parasellar structures.

2.2 Regional anatomy

The anatomy of the anterior and parasellar skull base is complex and develops throughout childhood [5, 6]. Pathology that affects the skull base directly is relatively rare in children. Pathology and surgical intervention can significantly affect development of the pediatric skull base and potentially confer substantial morbidity. For this reason, surgical intervention is reserved for cases where neurologic or endocrinologic function are threatened or compromised, and where no other options for tumor control are possible. This should be determined by a multidisciplinary team.

We favor the endoscopic endonasal approach (EEA) for most pathology involving the anterior and parasellar skull base. Transcranial and transfacial approaches, or a combination of approaches are used for pathologies that span beyond the access of a single approach. Variability in the development of the pediatric skull base has relevance to all stages of the endonasal approach, including the (a) nasal phase (b) sphenoid phase (c) sellar and intradural phase and (d) closure and reconstruction. The anterior skull base and midfacies develop later than the posterior skull base and continue growing until 14 years of age.

The nasal aperture grows throughout childhood and can restrict access of endonasal instrumentation. We prefer to operate through a nasal aperture larger than 5 mm, which can be performed as early as 2 years [5]. The piriform aperture, limited by the nasal bones and maxilla, can limit the rostral-caudal extent of dissection. As a general rule, the working angle and distance to the sella from the piriform aperture increases with age. Endonasal approaches, particularly expanded approaches, may be more feasible in younger patients for this reason. The choanal aperture, limited by the middle and inferior turbinates, also has relevance to expanded approaches. We do not perform expanded approaches to the clivus in cases where choanal atresia is present, or where the choanal aperture is smaller than 10 mm [7].

The sphenoid sinus has conchal anatomy until 2 years of age [8, 9]. Pneumatization of the sphenoid sinus begins in the inferior-medial sphenoid bone and moves superiorly and laterally, ultimately determining the location of the carotid arteries. The inter-carotid distance is mature at 9 years, though pneumatization may continue beyond this age and affect the degree of protrusion of the carotid arteries into the sphenoid sinus [9]. Sellar lesions are best approached in sphenoid sinuses with greater than 10 mm between the cavernous carotid arteries. Pneumatization of the ethmoid sinuses begins anteriorly and moves posteriorly, with the posteromedial ethmoids pneumatizing last [9]. The degree of ethmoid sinus pneumatization has relevance to its communication with the maxillary sinus and the working trajectories available to the anterior skull base.

Growth of the nasal septum, and the potential use of a nasoseptal flap for reconstruction, lags behind the development of other anterior skull base structures [10]. Large defects in the anterior skull base may not be adequately covered by a nasoseptal flap before 10 years of age, and may limit the utility of the endonasal approach. Traditional sellar and tuberculum/planum approaches can be covered as early as 6 years, when needed. We do not routinely reconstruct with nasoseptal flaps, reserving their use only for cases where a high flow cerebrospinal fluid (CSF) leak is expected. Traditional reconstruction with fat, fibrin, collagen, and expandable polyvinyl acetate is performed routinely.

2.3 Regional pathology

The most common tumors involving the anterior skull base and parasellar space in children include meningiomas, fibrous dysplasia, craniopharyngiomas, pituitary adenomas, juvenile nasopharyngeal angiofibromas (JNA), dermoid and epidermoid tumors, and gliomas.

Meningiomas can arise from the dura of the olfactory groove, planum/tuberculum sphenoidale or anterior clinoid process [11, 12]. Pediatric meningiomas are rarer in children than adults and typically associated with NF-2 or prior radiation treatment. Some studies suggest that meningiomas in children are more aggressive than meningiomas in adults, but these findings have yet to be validated in large studies.

Adamantinomatous craniopharyngiomas are the most common craniopharyngiomas found in children [13]. The diversity of their clinical presentation reflects their relationship to the surrounding pituitary, infundibulum, hypothalamus, and optic apparatus (**Figure 1**). A majority of craniopharyngiomas have a suprasellar component, and approximately one third extend into the anterior or middle cranial fossa [13]. Extension into the third ventricle can contribute to hydrocephalus, which can produce nonspecific symptoms such as headaches, nausea, and vomiting. Visual field or acuity defects are commonly present, as are symptoms of endocrine dysfunction, of which growth hormone (GH) appears to be the most commonly affected. Some may have large cystic components (**Figure 2**). Adenomas can present similarly, but typically have a more benign clinical course than craniopharyngiomas with respect to cranial neuropathy and hydrocephalus. The specific clinical presentation depends on the secreting subtype of tumor, with prolactinomas occurring most commonly.

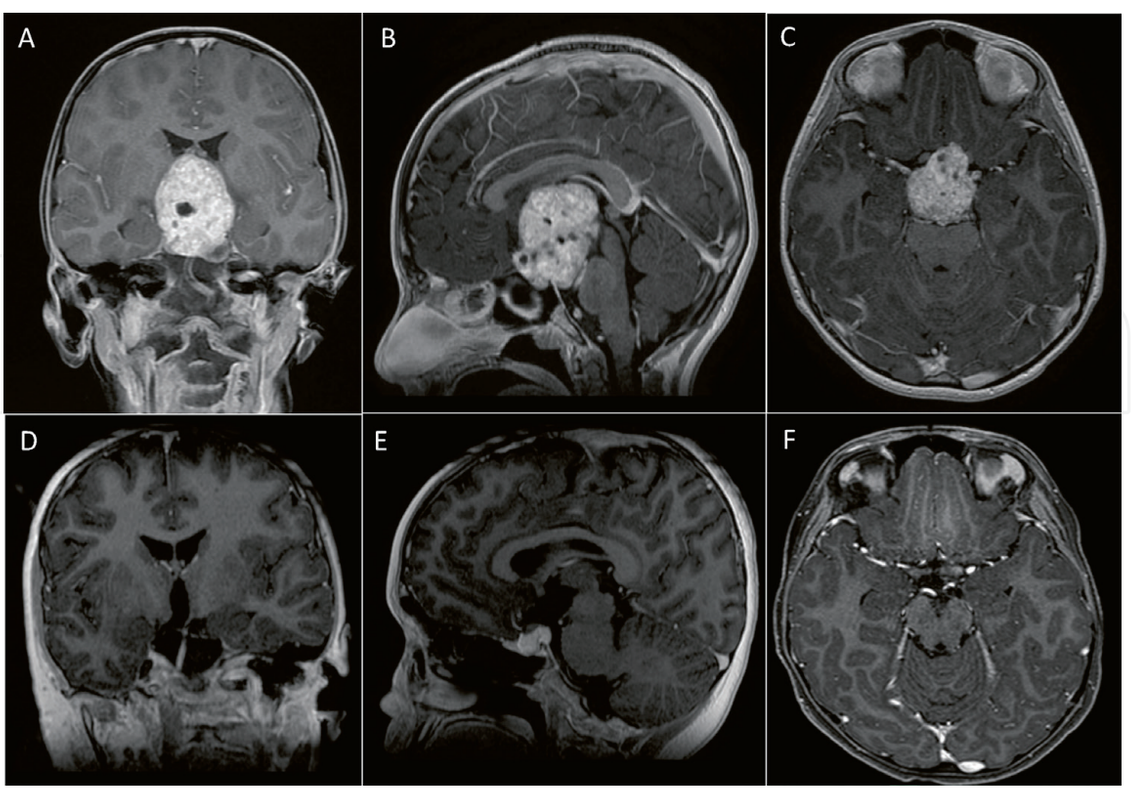

Figure 1.
A 13-year-old male presented with short stature and worsening peripheral vision, with a large papillary craniopharyngioma. MRI with contrast (A) coronal, (B) axial, (C) sagittal. Post operative MRI after resection through an endonasal transsphenoidal approach is shown in the bottom row (D-F). A small amount of fat graft can be seen in filling the cranial defect (E).

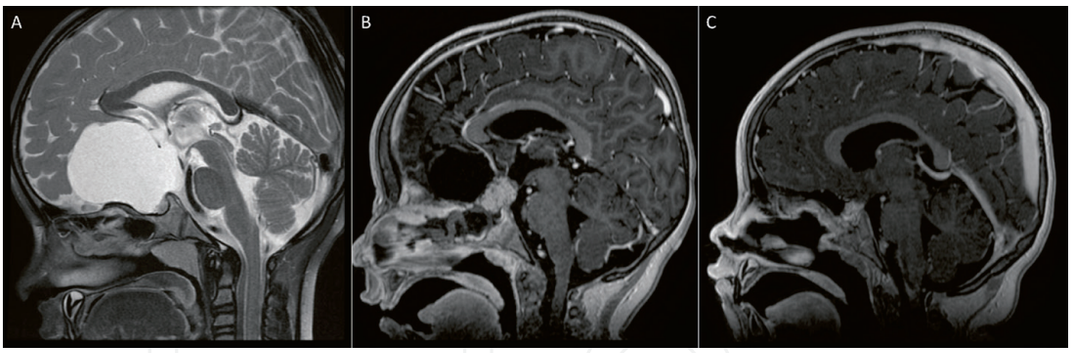

Figure 2.
This is a 4-year-old male who presented with vomiting and progressive vision loss with a suprasellar cystic papillary craniopharyngioma (A). An endoscopic trans-nasal, trans-cribriform approach was taken for resection. Fat graft is seen filling the craniotomy in the immediate post operative (B) and is partially resorbed with return of normal anatomic structure three months post-operatively (C).

JNAs classically occurs in adolescent boys and present with painless nasal obstruction and intermittent epistaxis [14]. They can originate in any part of the nasal cavity, but have a predilection for the posterolateral wall of the nasal cavity, adjacent to the sphenopalatine foramen. From here they can spread to the nasal cavity, nasopharynx, orbit, paranasal sinuses and intracranial compartment. The tumor often has a rich blood supply from the internal maxillary artery, which can serve as a target for pre-operative liquid particle embolization.

Dermoid and epidermoid cysts are indolent lesions that present with vague symptomatology related to intracranial hypertension and aseptic meningitis. Occasionally, they produce cranial nerve deficits, seizures, and behavioral changes. Dermoid cysts occur in the midline and epidermoid cysts occur in the parasellar spaces. Dermoid cysts are typically associated with a sinus tract, which are most commonly found at the glabella. Epidermoid cysts are classically associated with high intensity on diffusion-weighted images (DWI) [15].

Optic pathway gliomas (OPG) are prevalent in neurofibromatosis type 1 (NF1) and virtually all cases occur before 10 years of age. Sporadic OPGs have a more aggressive clinical course than NF1-associated OPGs, especially hypothalamic OPGs, which are less frequent in NF-1. Considered indolent, OPGs rarely progress after adolescence and optimal treatment remains controversial. When possible, visual function should be spared as long as possible before attempting resection [16].

2.4 Surgical approaches

The endonasal corridor can be used to access lesions in the anterior skull base via the classic trans-sellar/parasellar approach, the trans-tuberculum and trans-planum approach, and at its rostral extent the trans-cribriform approach. Each of these anatomic modules are delimited by critical neurovascular structures in the coronal plane.

All the endonasal approaches are performed with bi-nostril access and with a bimanual four-hand neurosurgery-otolaryngology team. Pre-operative evaluation of the paranasal sinuses with high resolution CT is essential, and care is taken to note deviated septum or bony spurs that may limit visualization or movement in the endonasal corridor. We do not routinely give peri-operative steroids, unless hypocortisolism is seen on preoperative workup. A microscope is always kept in the room and balanced with the observer scope on the left side of the primary surgeon.

A septal flap is raised before the sellar phase of the surgery only in cases where a high-flow CSF leak is expected. The posterior septum is resected before entering the sphenoid phase to facilitate visualization of the entire sella. The sella is expanded laterally to the lamina papyracea and anteriorly to the planum. Pneumatization of

the sphenoid sinus aids in this phase of the exposure and identification of critical neurovascular structures surrounding the sella [17, 18]. Doppler ultrasonography can help identify the carotid artery where tumors may distort or encase vascular anatomy. The dura of the sella is then exposed between the cavernous sinuses. The medial optico-carotid recesses and tuberculum sphenoidale may also be resected for more lateral and rostral exposure, respectively, than is typically afforded by a trans-sellar approach.

Extension of this exposure rostrally can provide access to the posterior wall of the frontal sinus, between the medial orbital walls limited by the laminae papyracea. In this case, the nasal corridor described above is expanded with uncinectectomy, maxillary antrostomy, and ethmoidectomy. Care should be taken to avoid avulsing the ethmoidal arteries during ethmoidectomy, or coagulating the stumps of the ethmoidal arteries into the orbital wall, resulting in retrobulbar hematomas and orbital compartment syndrome. The lamina papyracea can be removed itself to provide access to the medial orbital wall [19].

2.5 Complication avoidance

Carotid artery injury is the most formidable complication of the EEA. Avoidance of carotid artery injury comes from meticulous planning, the use of stereotaxy, and adjunct tools including ultrasonography and fluorescence. Control of carotid artery injury can be achieved by an experienced two-surgeon team, and with coordination with anesthesiology and case support staff. We utilize a carotid artery injury "time out" to rehearse such a scenario in cases where the carotid artery may be encountered. This includes the possibility of endovascular sacrifice of the blood vessel, which is the safest immediate option in brisk bleeds. Endovascular sacrifice should only be attempted after hemorrhage is controlled.

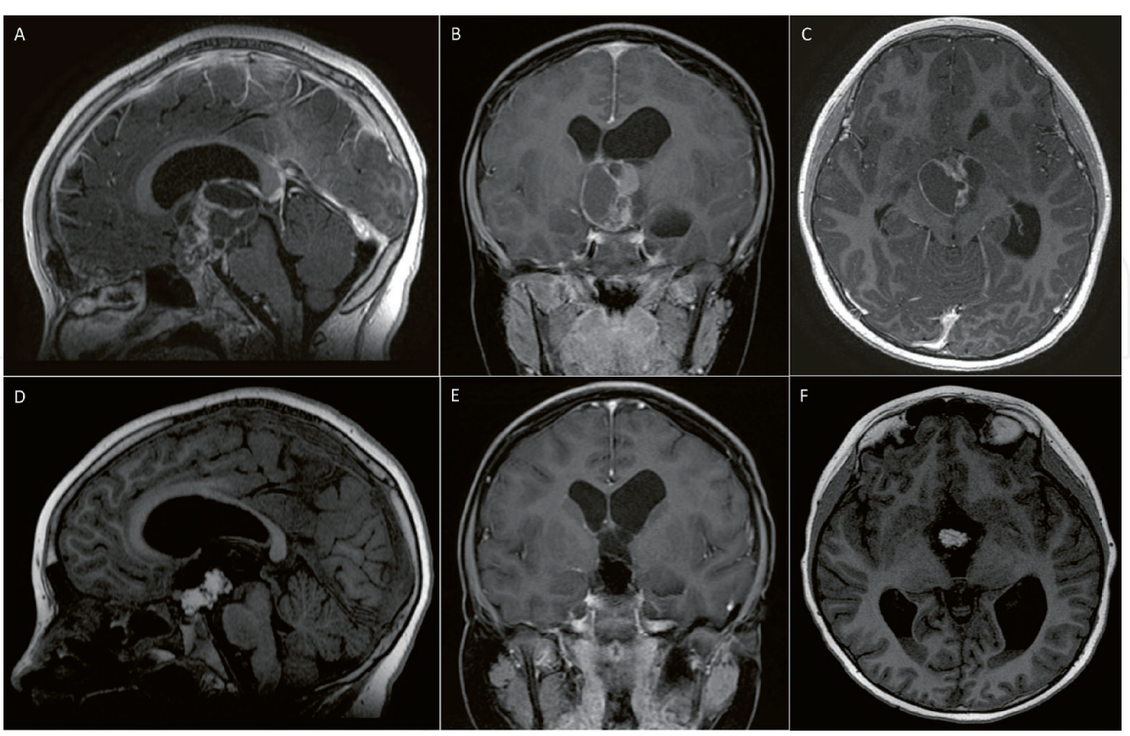

Figure 3.
A 7 year old male presented with vision changes and was diagnosed with craniopharyngioma on MRI with contrast (A) sagittal (B) coronal, (C) axial. This was resected by endonasal transsphenoidal approach. Post operative MRI (D-F) after gross total resection. A high flow CSF leak was identified intraoperatively, which was closed with a nasal septal flap and abdominal fat graft.

High flow venous bleeding should also be avoided, especially during exposure of the anterior intercavernous sinus. Bleeding from a robust intercavernous sinus can be brisk and is best avoided by isolating and dividing the sinus with cuts in the sellar and planum dura before moving forward in the exposure. Hemostatic agents and warm irrigation can aid in hemostasis from venous bleeding. Finally, while rare, carotid-cavernous fistula should be suspected in patients with mid-face or skull base trauma, and if present, treated before tumor resection is attempted.

CSF leaks are best avoided by respecting the arachnoid planes of dissection surrounding the tumor and sella. Entry into a subarachnoid cistern or ventricle can predict a CSF leak with confidence. We do not routinely use lumbar drainage for peri-operative care, unless such a leak is expected or encountered by misadventure. High flow CSF leaks can be addressed by raising a nasoseptal or turbinate flap for closure, though as described above, development of the septum and turbinates may lag behind development of the skull base and limit coverage of the flap (**Figure 3**).

Persistent leak can predispose a patient to developing tension pneumocephalus. Multi-layered closure can help prevent this rare complication, which is thought to arise from a ball-valve effect of air entry into the resection bed and intracranial compartment. CSF leaks can also confer a risk for meningitis and ventriculitis, and positive pressure ventilation (CPAP) is strictly avoided peri-operatively.

3. Middle fossa, infratemporal fossa, and petrous apex

3.1 Introduction

The middle fossa and petrous apex are at the center of the skull base and are surrounded by several critical structures. Tumors in this area grow from or envelope multiple cranial nerves, as well as deep venous and arterial structures with little collateral flow. The risks posed in the pre-pontine cistern are formidable, and surgical resection in this anatomically complex region should be performed by an experienced, multi-disciplinary skull base team. Most pathologies occurring in this area are benign, and gross total resection confers a benefit to the prognosis and quality of life of a child. Regardless of histology, maximum safe resection should be carried out. Outcomes are best in centers with experienced pediatric skull base, neuro-anesthesiology, critical care, and rehabilitation teams.

3.2 Regional anatomy

In our practice, resection of such tumors in the middle and infratemporal fossae, as well as the petrous apex is carried out by a combined neuro-otology and neurosurgery skull base team in all cases. A thorough understanding of the anatomy of the petrous temporal bone, anterior and posterior clinoid processes, and sphenoid bone is essential to safe removal of tumors in this area. Landmarks are neither constant nor readily apparent, and laboratory dissection is essential to familiarizing the surgeon with anatomy in this region.

The floor of the middle fossa is delimited by several key structures. Anteriorly, the middle meningeal artery can be identified as it enters foramen spinosum. An accessory meningeal artery is inconsistently seen in foramen ovale, anterior and medial to the middle meningeal artery [20]. A ridge of bone frequently obscures visualization of the foramen spinosum and can be drilled away for better exposure. The greater superficial petrosal nerve (GSPN) runs in a groove medial to the middle meningeal artery and enters the vidian canal under the mandibular

nerve (V3). The GSPN is frequently dehiscent through the middle fossa floor in its course. The maxillary nerve (V2) enters the foramen rotundum superior and medial to foramen ovale. The area between V2 and V3 forms the lateral loop [21]. The sphenoid sinus and its invested vidian canal can be accessed through the lateral loop. The vidian canal is encountered laterally in patients with an over-developed sphenoid sinus, and medially when the sinus has conchal anatomy. The infratemporal fossa is accessed lateral to V3 at the floor of the middle fossa.

The arcuate eminence demarcates the location of the superior semicircular canal as well as the geniculate ganglion, which typically lies anterior to its lateral border [22]. The relationship of the arcuate eminence to both these landmarks is inconsistent, and drilling of the arcuate eminence is often necessary to clarify the anatomy of the middle fossa floor. Drilling to better visualize the anatomy of the middle fossa floor should be balanced against "blue-lining" the membranous labyrinth of the superior semi-circular canal, which may lead to inadvertent injury and hearing loss. Injury of the membranous labyrinth should be controlled with bone wax packing instead suction. The face of the superior semicircular canal invariably lies perpendicular to the two ridges of the petrous apex. These ridges cradle the superior petrosal sinus. Two important working windows are defined in this area. Kawase's rhomboid is bounded by the middle meningeal artery, mandibular nerve, GSPN, and petrous ridge. Glasscock's triangle (the posterolateral triangle of the cavernous sinus) is bounded V3, GSPN, and a line between the arcuate eminence and foramen spinosum. Drilling the bone in either of these spaces reveals the carotid artery, running deep to GSPN and medial to the eustachian tube. The cochlea has no external landmarks in this region, and its constant location medial to the genu of the carotid artery and the geniculate ganglion must be kept in mind during exposure of the internal auditory canal (IAC).

3.3 Regional pathology

Tumors affecting the skull base of the middle fossa include chordomas, meningiomas, and schwannoma.

Chordomas arise from the clivus and extend into the middle crania fossa in approximately one third of cases. They tend to grow locally but aggressively. Radical resection can be curative, but recurrence rates are high when subtotal resection is achieved, even with adjuvant proton beam therapy.

Meningiomas of the middle fossa are typically slow growing and most commonly present with headaches and visual disturbances. Tumors that invade the adjacent cavernous sinus may cause additional cranial neuropathies that affect extra-ocular movement. Meningiomas of the middle fossa typically arise from the medial sphenoid wing or the petrous ridge, and grow to span multiple cranial compartments (**Figure 4**).

Schwannomas in children are rare. Bilateral vestibular schwannomas are a hallmark of NF-2. Intracanalicular vestibular schwannomas can be resected via the middle cranial fossa approach, whereas larger lesions are typically resected via trans or retro-mastoid approaches. Observation is recommended for small or incidentally discovered trigeminal schwannomas. Small tumors show excellent control with radiosurgery in adults, but data is limited in children, and even stereotactic radiation in children may be linked to meningioma development later in life. For this reason, surgery is favored in our practice for schwannomas that show growth on surveillance imaging alongside cranial neuropathy or brainstem compression. Trigeminal schwannomas typically present with facial numbness. Trigeminal neuralgia tends to occur in lesions at and beyond the Gasserian ganglion, and involves all three divisions of the trigeminal nerve.

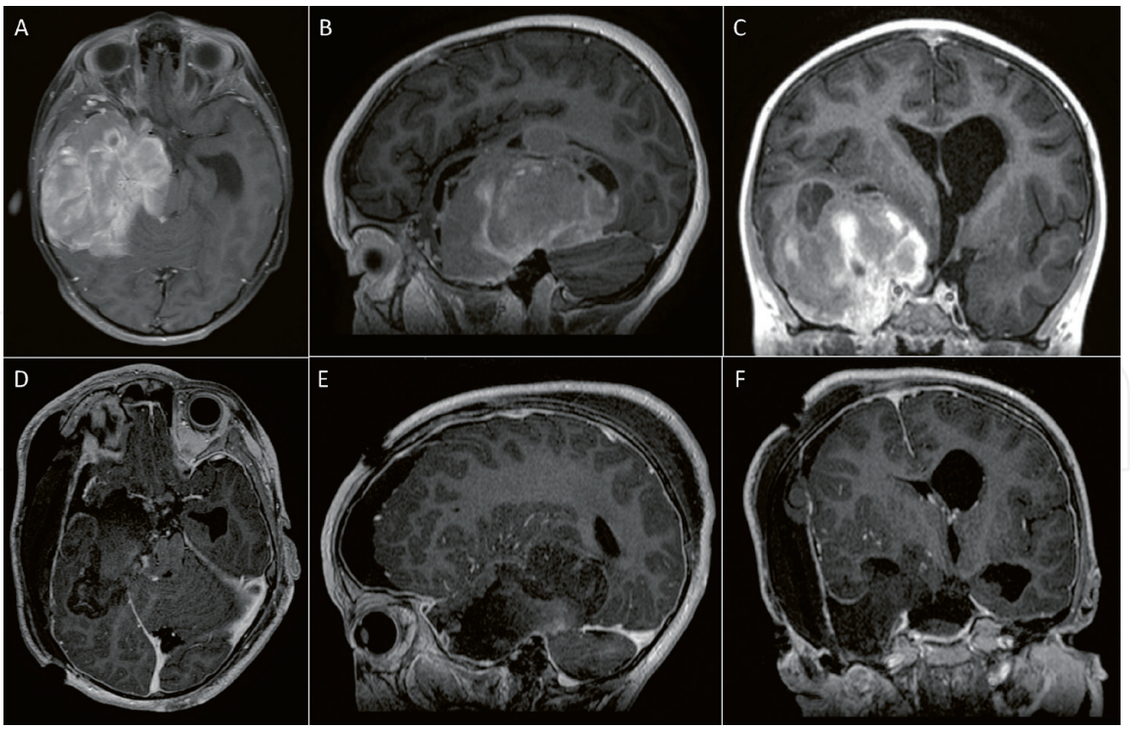

Figure 4.
A 4-year-old male presented with one month of nausea and headaches with a large cystic meningioma filling the temporal fossa and extending across the tentorium (A-C). Tumor was resected through a modified orbitozygomaticapproach. Immediate post-operative MRI (DF) with gross total resection and normal swelling.

3.4 Surgical approaches

We perform all middle cranial fossa, petrous ridge, and infratemporal fossa cases with a neurosurgery-neuro-otology skull base team. The middle fossa approach incision is a reverse question mark based at the root of the zygoma and extending to the superior temporal line. The muscle is elevated separately from the skin anteriorly and inferiorly. We use cutting and diamond burrs to drill a 5x5cm square craniotomy based 2/3rd anterior to the root of the zygoma, and 1/3rd posterior. Two points should be stressed in this exposure. First, the craniotomy should extend low, to the floor of the middle fossa, which is approximated by the root of the zygoma. Second, every attempt should be made to adequately expose the anterior petrous ridge to aid in deeper parts of the dissection. Failure to adequately expose the anterior floor of the middle fossa and petrous ridge places the neural structures (GSPN, IAC) in the exposure at risk.

The dura is elevated anteriorly until the middle meningeal artery (MMA) is identified. It is coagulated closer to the dural base than to the skull base, to prevent retraction and hemorrhage into the infratemporal fossa. Once the MMA is identified, elevation of the middle fossa dura proceeds in a posterior to anterior course, to avoid avulsion and injury to GSPN, which carries parasympathetic innervation to the lacrimal gland. Every attempt is made to avoid dividing the GSPN, as concomitant GSPN and V1 injury can lead to devastating insensate corneal abrasions and blindness. Elevation of the dura allows for identification of the arcuate eminence. This is followed medially to the petrous ridge, where the groove of the superior petrosal sinus is identified and divided. A shallow depression in the petrous ridge just above the porus acusticus can be used as a landmark for drilling.

The bone overlying the superior semicircular canal is drilled down and a House-Urban retractor is placed against the true petrous ridge. Care should be taken to avoid lacerating the dura during elevation and retraction, as seizure may occur.

Injury to the dominant temporal lobe can also result in aphasia, and is more likely when the vein of Labbe drains from an anterior position. Drilling begins at the pre-meatal petrous ridge, just anterior and medial to the IAC. Once saucerized, drilling of the post-meatal petrous ridge is done to expose a 270-degree arc of the IAC tunnel. All drilling is done with suction-irrigation to avoid thermal injury to the facial and cochlear nerves. Drilling laterally exposes the labyrinthine segment of the facial nerve, Bills bar, and the superior vestibular nerve. There is very low tolerance for a drilling misadventure in this area, as the labyrinthine segment of the facial nerve lies within 1 mm of the basal turn of the cochlea. The dura is opened along the length of the IAC, and on its posterior edge, to avoid injury to the expected location of the facial nerve anteriorly. Resection of inferior vestibular nerve tumors, the most common intracranial schwannoma, requires division of the superior vestibular nerve [23].

Access to the pre-pontine cistern, as well as the premeatal posterior cranial fossa can be accomplished through an extended middle fossa approach (eMFC). Drilling of the premeatal triangle in eMFC is generous, extending anteriorly to just under the Gasserian ganglion and V3, and laterally to the horizontal segment of the petrous internal carotid artery (C2) (**Figure 5**) [24].

Meckel's Cave, the lateral petrous apex, as well as the pterygopalatine and infratemporal fossae can be accessed through the endonasal corridor via a trans-maxillary, trans-pterygoid approach [25]. Bi-nostril access is required, with working access achieved through the contralateral nostril. This should be accounted for by the operative team and referral to experienced skull base teams is recommended for this approach. The posterior maxillary wall provides access to the pterygopalatine fossa. The pterygopalatine fossa is exposed in its entire anterior–posterior extent, taking care to protect the sphenopalatine ganglion, vidian nerve, palatine and orbital

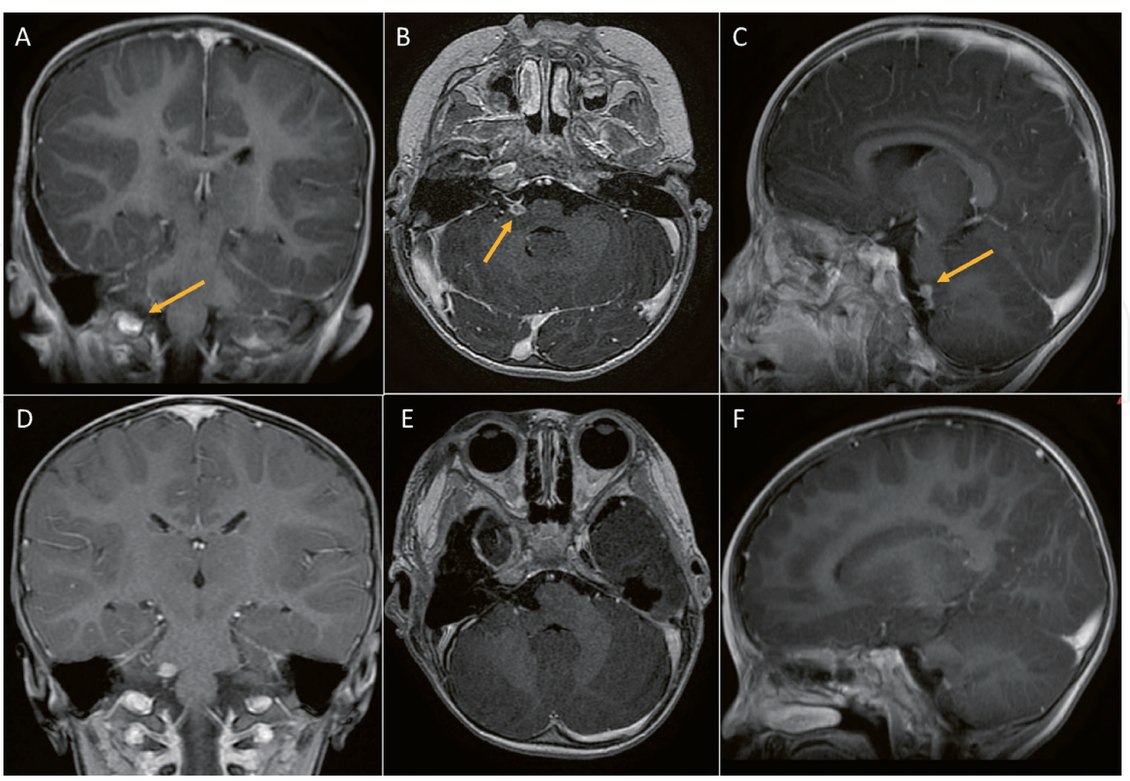

Figure 5.
A 21 month old female presented with right facial weakness since 5 months of age. A small meningioma in the right cerebellopontine angle was found(upper row A-C). This tumor was observed at first, but her weakness progressed and the lesion had grown. A middle fossa anterior petrosectomy was performed. Post-operative images are seen on the bottom row (D-F). Pathology demonstrated meningioma.

nerves. The inferior orbital nerve serves as a landmark for the perpendicular plate of the palatine bone [26]. Resection of the orbital process of the palatine bone exposes V2, near the sphenopalatine foramen. Dissection of the sphenoid process of the palatine bone exposes the vidian nerve at the pterygoid canal and the maxillary nerve at the foramen rotundum. It also exposes the base of the pterygoid process, which when resected allows for access to Meckel's cave through the quadrangular space bounded by V2, V3, cranial nerve VI, the and the transition of the petrous internal carotid artery to its laceral segment, in close proximity to the petrolingual ligament [27].

3.5 Complication avoidance

Cerebrospinal fluid leak is one of the most common complications of surgery to the middle fossa and petrous apex. CSF leak typically manifests two ways, as rhinorrhea or leakage from the surgical wound. Otorrhea is not commonly encountered through the middle fossa or trans-pterygoid approaches. We routinely obliterate communication between pneumatized air cells in the temporal bone with fat, to prevent leakage of CSF through the skin incision or the eustachian tube. Before doing so, the exposed air cells or dehiscence in the middle fossa floor are covered with wax or fascia. Incisional leaks are managed with wound oversewing and lumbar drainage. Rhinorrhea is managed with lumbar drainage. If either method fails to control the leak, wound exploration is performed.

Stroke can be a result of arterial or venous injury. We perform pre-operative CT or MR angiography on all patients with tumors adjacent to the arteries or veins of the skull base. If there is evidence of invasion or stenosis of the blood vessels of the skull base, formal cerebral angiography is performed. This helps evaluate the degree of collateral inflow and outflow from the resection site. A balloon occlusion test may help establish the feasibility of vessel sacrifice at the time of surgery. Whenever possible, sacrifice is avoided for benign lesions should be avoided.

4. Tumors of the cerebellopontine angle, jugular foramen, and craniovertebral junction

4.1 Introduction

The majority of pediatric brain tumors are located in the posterior fossa, with the most common pathologies being juvenile pilocytic astrocytomas, medulloblastomas, and ependymomas, all of which may require complex approaches when expansive. In this chapter, however, we will discuss primarily extra-axial tumors that specifically involve the skull base. Far lateral or ELITE (extreme lateral infrajugular transcondylar-transtubercular) for ventrolateral pathology, transpetrous approaches for access to the cerebellopontine angle, and anterior approaches can all be used in appropriate situations to maximize exposure to facilitate safe resection and preservation of critical neural structures. As above, we work closely with our otolaryngology partners to assist with transpetrous approaches when indicated and for endoscopic anterior approaches to the clivus and ventral brainstem.

4.2 Regional anatomy

A comprehensive knowledge of the relevant bony and vascular anatomy is required prior to performing approaches to the posterior fossa. The vertebral artery takes a lateral to medial course after exiting from the transverse foramen of C1 and travels in a groove along the superior edge of the posterior arch of C1 prior to

entering the dura. The artery at this level is sheathed in an organized venous plexus which can bleed briskly but is easily stopped with hemostatic agents. If necessary, the vertebral artery can be mobilized by removing the posterior wall of the transverse foramen which further exposes the occipital condyle. Intradurally, the transverse and sigmoid venous sinuses frame the borders of the posterior fossa. Children less than two years old are more likely to have a persistent occipital sinus, and children with an occipital sinus are more likely to have an absent transverse sinus [28].

The occipital condyles form the connection of C1 to the foramen magnum laterally. The hypoglossal canal runs anterolaterally through the condyle and marks the border of the posterior and middle third of the condyle. Radiographic review of 50 pediatric CT scans demonstrated relative stability in the size and depth of the occipital condyle and hypoglossal canal throughout pediatric development. The jugular tubercle is located superiorly and anteriorly to the hypoglossal canal. Conversely, the jugular tubercle demonstrates significant growth during childhood and only measures 65% of adult size prior to puberty, therefore its removal may not confer as much benefit for lateral skull base approaches in younger children [29].

Laterally, the skull base is defined by the petrous pyramid located between the sphenoid and occipital bones, and houses the facial canal, the petrous carotid artery, and the osseous structures of the inner ear. The superior surface of the petrous bone forms the floor of the middle fossa, and the posterior wall of bone forms the anterior wall of the posterior cranial fossa. The internal auditory meatus houses the meatal segment of the facial nerve and the vestibulocochlear nerve as they exit the cerebellopontine angle and enter the middle of the petrous bone. The cochlea is located just anterior to the fundus and the otic capsule housing the bony labyrinth is located posterior to the internal auditory canal and above the jugular foramen, and can be easily delineated from the surrounding mastoid bone by its yellowish, hard cortical surface.

4.3 Regional pathology

The most common tumors of the cerebellopontine angle in pediatric patients are schwannomas (65%), meningiomas (5%), and epidermoid cysts (5%). Up to 10% of tumors of the cerebellopontine angle in pediatric patients may be malignant, which is significantly greater than in adults (**Figure 6**) [30]. Schwannomas are

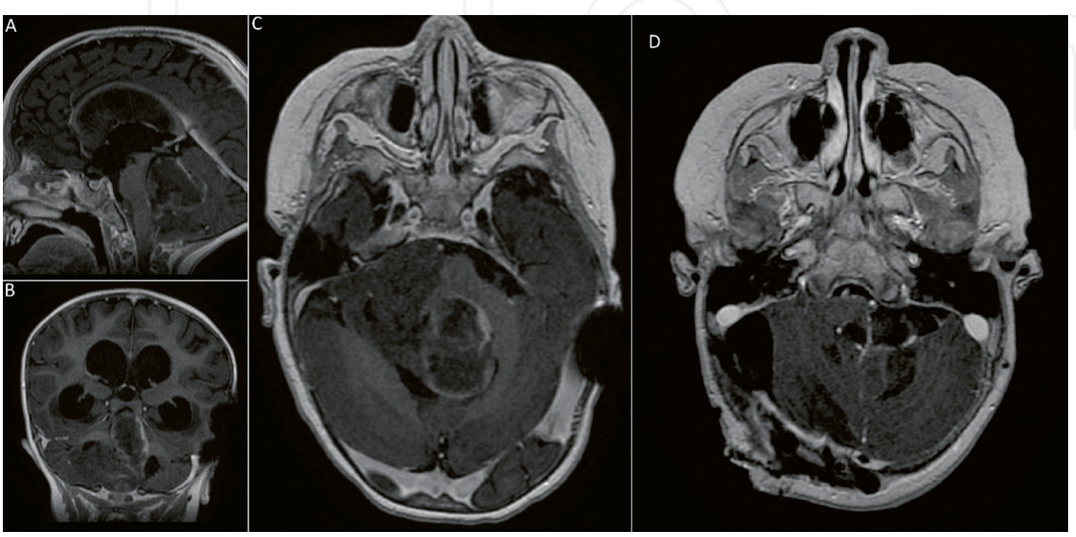

Figure 6.
A 21 month old male developed upgazepalsy and gross motor regression. MRI brain with contrast demonstrated large fourth ventricular ependymoma extending into the cerebellopontine angle (A-C). Gross total resection was achieved with a far lateral craniotomy (D).

rare tumors and rarer still in pediatric patients, with about 10% of cases diagnosed in patients younger than 21. These are considered benign masses that arise from Schwann cells of the nerve sheath and may be found anywhere in the body, with 16–45% reported to be in the head and neck [31]. The vestibular nerve is thought to be the most common location for intracranial schwannomas, though they can also occur on the trigeminal nerve, facial nerve, and lower cranial nerves in decreasing frequency.

Vestibular schwannomas present with unilateral hearing loss, tinnitus, headache, and disequilibrium, and they can cause cerebellar ataxia and brainstem compression with significant extension into the cerebellopontine angle [32]. Pediatric vestibular schwannomas tend to be diagnosed in adolescence and the tumors tend to be larger at presentation than in adults [32, 33]. Surgical resection, stereotactic radiosurgery, and observation are all valid treatment options for schwannomas, however the long life-span of pediatric patients argues for more aggressive definitive management. In one series of 148 pediatric vestibular schwannomas 82 (55.4%) patients were treated with surgery only, 45 (30.4%) with observation, 6 (4.1%) with radiation only, and 12 (8.1%) with surgery and radiation [33]. Residual tumors after surgery may grow at a faster rate than in adults, therefore the surgeon should safely attempt gross total resection or should consider radiosurgery in cases with significant residual tumor [32].

Sporadic schwannomas are rare in children, but they are the hallmark of genetic conditions, neurofibromatosis 2 (NF2) and schwannomatosis, with bilateral vestibular schwannomas affecting 95% of individuals with NF2 [34]. Overall treatment goals change in these patients due to the high lifetime number of tumors. Efforts should be made to avoid surgery unless necessary to preserve vital cranial nerve function and radiation should be avoided. Recent clinical trials have demonstrated hearing and quality of life improvement in both adult and pediatric NF2 patients with bevacizumab therapy. Pediatric patients did not demonstrate tumor regression unlike their adult counterparts in this trial [35].

Epidermoid cysts are rare dysontogenic lesions with a predilection for the cerebellopontine angle in 40–60% of cases and are the third most common lesion in the cerebellopontine angle. They tend to grow along arachnoid planes and frequently extend into neighboring compartments. These tumors tend to encase neurovascular structures and are quite adhesive. There is a characteristic appearance on MRI of a lesion filling and expanding the subarachnoid space that is dark on T1, bright on T2 and is avidly diffusion restricting. Patients present with cranial nerve impairments, most commonly of the trigeminal and the vestibulocochlear nerve.

Trigeminal neuralgia may be more common than sensory impairment when the trigeminal nerve is involved. Depending on the size of the tumor, almost all cranial nerve impairments have been described. Complete surgical excision can be curative; however, the surgeon must take great care to reduce morbidity and injury to cranial nerves. Complex or combined approaches may be necessary for tumors that span multiple compartments. Aseptic meningitis may occur post operatively and can be treated with a course of dexamethasone [36, 37].

At the craniocervical junction, chordomas are rare bony tumors that arise from notochordal remnants. These tumors are slow growing but locally aggressive. Only 5% of chordomas present in children, and they tend to be more aggressive in younger children. The most common location overall is the sacrum, with a minority of tumors occurring at the skull base. However, the more frequent location in pediatric patients is midline at the spheno-occipital synchondrosis of the clivus. Tumors present with headaches, other signs of increased intracranial pressure, diplopia, or mixed cranial neuropathies. Optimal treatment includes maximal safe resection followed by high dose radiotherapy, though there is still controversy regarding the

type and dose of radiation. Proton beam may have benefits in pediatric patients over conventional radiotherapy due to a reduced radiation dose to neighboring structures. There is little role for chemotherapy due to the slow-growing nature of the disease [38, 39]. The future of chordoma treatment will likely be in molecular and targeted therapies and there are active clinical trials investigating a drug targeting programmed cell death ligand 1 (PD-L1), an immune checkpoint inhibitor expressed in over 90% of chordomas [40].

Chondrosarcomas are often grouped together with chordomas as they are both locally destructive, slow growing bony lesions, but they are a distinct histopathologic entity and have a better prognosis than chordomas. Chondrosarcomas are typically found in paramedian locations, arise from chondrocytes, and comprise 5–12% of cases found at the skull base. The most common location is the clivus followed by the temporal-occipital junction. There are four histologic subtypes: conventional, mesenchymal, clear cell, and dedifferentiated, and tumors are graded I-III based on the level of differentiation. The mesenchymal subtype tends to be the most aggressive. Radical surgical resection is again the mainstay of treatment with adjuvant radiation therapy, specifically proton beam, for most patients due to high rates of residual tumors and locoregional recurrence. Radiation has been shown to significantly decrease recurrence rates [41–43].

4.4 Surgical approaches

Pediatric tumors have a predilection for the posterior cranial fossa, specifically the cerebellar hemispheres and the fourth ventricle. A majority of these common intrinsic brain tumors such as medulloblastomas, juvenile pilocytic astrocytomas, and ependymomas do not require complex skull base approaches and can be accessed by a suboccipital craniotomy with or without a C1 laminectomy. However, many extrinsic tumors or large exophytic intrinsic tumors that extend to the cerebellopontine angle, the craniocervical junction, and the jugular foramen require knowledge of skull base approaches to maximize exposure.

The workhorse of posterior fossa approaches is the suboccipital craniotomy for dorsal midline lesions. The suboccipital craniotomy is performed by creating a dorsal midline window from the foramen magnum to the confluence of sinuses. There are many methods to perform this craniotomy including drilling bur holes, using a craniotome, a cutting and diamond bur, and Kerrison rongeurs. In children, we find it is safe and efficient to perform using a craniotome by stripping the dura from the foramen magnum and inserting the footplate under the lip of foramen magnum. This can be augmented by a C1 laminectomy for a more inferior to superior view. In rare cases, we have extended our craniotomy superior to the transverse sinus to perform a concurrent interhemispheric transtentorial approach to posterior fossa tumors.

For more inferior and lateral exposure than a standard suboccipital approach, the far-lateral, or extreme lateral transcondylar (ELITE), craniotomy may be required. This provides additional access to lower clival lesions, the craniocervical junction, and lesions of the upper cervical spine (**Figure 7**). In addition to a lateral suboccipital craniotomy, the ipsilateral occipital condyle is drilled extradurally until the hypoglossal canal is skeletonized. The hypoglossal canal generally is a marker that the posterior third of the condyle has been removed, which should not result in craniocervical instability. The lateral mass of C1 is also removed and the vertebral artery is sometimes mobilized. Though rarely necessary, the jugular tubercle can be drilled at this point to provide greater access to the lower cranial nerves and clivus.

The cerebellopontine angle (CP angle) is almost exclusively accessed by lateral skull base approaches, namely retrosigmoid and transpetrosal craniotomies. The

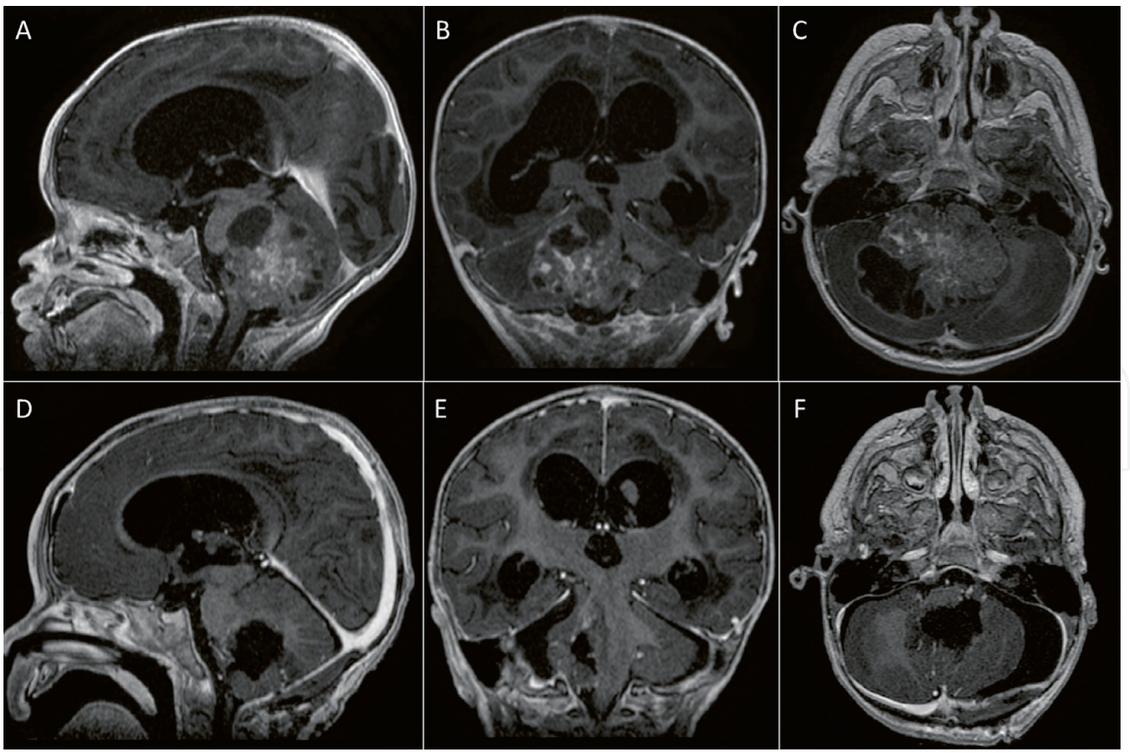

Figure 7.
A 13-month-old male presented to the emergency department with failure to thrive and eye movement abnormalities. A large atypical teratoid rhabdoid tumor (ATRT) was diagnosed with MRI brain (A-C). Tumor was resected using a suboccipital craniotomy with a modified far lateral approach to reach the tumor extending to the anteromedial brainstem.

retrosigmoid craniotomy is a standard neurosurgical approach. It is performed by creating a bony window just inferior and posterior to the transverse sigmoid junction. This can be performed with craniotome, bur holes and Kerrison rongeurs, or a cutting and diamond bur. Additional intradural drilling to open the internal auditory canal can be performed for vestibular schwannomas that extend from the auditory canal into the CP angle. The retrosigmoid craniotomy has immense flexibility, however it does rely on cerebellar retraction and therefore puts neural elements at some risk.

Transpetrosal approaches involve varying degrees of removal of the petrous temporal bone in order to expose the anterolateral brainstem from the tegmen to the jugular tubercle. With greater bony removal, there is increasing exposure of lesions of the anterior brainstem. However, the more extensive the petrosectomy, the greater the risk to cranial nerves, so the preoperative cranial nerve function and the goals of surgery are critically important when choosing an approach. Presigmoid retrolabyrinthine craniotomy preserves hearing and facial function. Translabyrinthine craniectomy sacrifices hearing but preserves the facial nerve well.

Transcochlear approaches sacrifice hearing by removing the labyrinth and closing the ear canal and puts the facial nerve at risk by mobilizing it from its canal. It is recommended that all these approaches are performed with a neurotology partner, as the mastoid is not well pneumatized in children and it can be difficult to identify the labyrinthine and facial recess. Any of these approaches can be combined with middle fossa approaches for combined exposure of lesions that span multiple compartments.

Transnasal, transmaxillary and transoral approaches provide access from the sella to odontoid process and upper cervical spine. These are generally reserved for midline extradural lesions such as chordomas and chondrosarcomas. The morbidity of these approaches is significantly decreased since the advent of endoscopic surgery.

4.5 Complication avoidance

As with other approaches to the skull base, cerebrospinal fluid leak is a common complication of posterior fossa surgery, especially because patients frequently have concomitant hydrocephalus. This is best avoided by multilayer water-tight closure and aggressive treatment of hydrocephalus either with an endoscopic third ventriculostomy, or temporary/permanent CSF diversion. Otorrhea or rhinorrhea after transpetrosal craniotomy can be treated again with CSF diversion, careful attention intraoperatively to packing of the middle ear, and external ear canal closure in persistent cases.

Sinus injury and sinus thrombosis are additional risks given their exposure in majority of posterior fossa approaches. It is advisable to use neuronavigation whenever possible to identify the location of the sinuses prior to performing the craniotomy and to study preoperative imaging to identify any aberrant anatomy such as persistent occipital sinuses or low-lying torcula, both of which may be present in children.

5. Conclusion

Brain tumors are the most common cancer in the pediatric population and often present late as presenting symptoms can be vague and children may not be able to communicate well. As targeted medical therapies develop the role for radical resections may decline, however when performed safely with appropriate execution of skull base approaches, surgical resection can provide excellent outcomes.

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