



Review Article

Pediatric sinonasal and skull base lesions

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Abstract Pediatric skull base lesions are complex and challenging disorders. Safe and comprehensive management of this diverse group of disorders requires the expertise of an experienced multidisciplinary skull base team. Adult endoscopic skull base surgery has evolved due to technologic and surgical advancements, multidisciplinary team approaches, and continued innovation. Similar principles continue to advance the care delivered to the pediatric population. The approach and management of these lesions varies considerably based on tumor anatomy, pathology, and surgical goals. An understanding of the nuances of skull base reconstruction unique to the pediatric population is critical for successful outcomes.

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Introduction

Pediatric skull base lesions are complex disorders with a highly variable presentation (Table 1). Some patients may be asymptomatic, while others may present with nasal obstruction, epistaxis, rhinorrhea, endocrinopathies, headaches, vision changes, cranial neuropathies, or other neurologic changes. The approach to the patient with a skull base lesion requires a comprehensive history and physical examination, with particular attention to neurologic, ophthalmologic, and rhinologic evaluations, including nasal endoscopy when possible. Imaging of the sinuses, orbits, and skull base with CT and MRI is recommended to establish lesion boundaries, where angiography, CT angiography (CTA), and MR angiography (MRA) are radiographic adjuncts that may be helpful to establish vascular anatomy.

A multidisciplinary team approach to the management of these patients is invaluable. The comprehensive skull base team often includes Otolaryngology, Neurosurgery, Anesthesiology, Ophthalmology, Neurology, Hematology-Oncology, Radiation Oncology, Endocrinology, Intensivists, and others. To facilitate multidisciplinary discussion, institutions with skull base centers routinely have skull base-specific tumor boards to facilitate optimal treatment planning. The collaborative partnership between

Otolaryngology and Neurosurgery has significantly improved surgical success and outcomes.¹ Surgeon experience and meticulous surgical technique result in optimal tumor extirpation and reconstruction while preserving sinonasal and neurologic structure and function.²⁻⁴

Post-operative management often includes a brief admission in an intensive care setting to allow for appropriate recovery following surgery, prompt recognition of post-operative complications, and management of neurologic, metabolic, cardiopulmonary, or endocrinological sequelae. Long-term post-operative management is as much of a collaborative effort as the actual procedure, where coordinated surveillance is critical to providing timely interventions.

Congenital skull base lesions

Skull base lesions may result from embryologic developmental abnormalities. The fonticulus frontalis and prenasal space are two spaces transiently present during development that may allow the dural diverticulum to extend from the anterior cranial fossa to the nasal dorsal skin. The fonticulus frontalis temporarily separates the frontal and nasal bones, while the prenasal space is between the nasal bones and developing nasal cartilage. As the frontal and

Table 1 Differential diagnosis of congenital tumors, neoplasms, and fibro-osseous lesions.

Tumor	Characteristics
Congenital	
Dermoid Cyst	Incomplete separation and involution of the dural diverticulum through foramen cecum from overlying skin
CSF leak/encephalocele	Accidental trauma Iatrogenic trauma (surgical) Spontaneous Congenital Tumor-related
Glioma	Similar to encephaloceles, but lack communication to subarachnoid space
Neoplasms	
Juvenile Nasopharyngeal Angiofibroma	Vascular, in adolescent males Benign, arise from pterygoid canal Locally aggressive
Rhabdomyosarcoma	Rare malignancy with poor outcomes Multimodality treatment is associated with best survival outcomes
Pituitary adenoma	Rare in children Microadenoma (<10 mm) Macroadenoma (>10 mm) Secreting adenoma Non-secreting adenoma
Rathke's Cleft Cyst	Benign cystic lesion close in proximity to pituitary gland Ectopic remnant of Rathke's pouch
Craniopharyngioma	Benign Typical presentation includes endocrine and visual deficits
Chordoma	Locally destructive Malignant Embryologic remnant of the notochord
Fibro-Osseous Lesions	
Fibrous dysplasia	Benign, ground-glass appearance on CT
Osteoma	Slow-growing, often asymptomatic
Juvenile ossifying fibroma	Aggressive, locally destructive

nasal bones grow, the dural diverticulum and prenasal spaces involute and regress. At the same time, the cribriform plate develops due to the fusion of the fonticulus frontalis and foramen cecum. A congenital encephaloceles or glial heterotopia may arise due to a defect of the anterior neuropore closing during embryogenesis, which results in herniation or sequestration of tissue through the fonticulus frontalis or foramen cecum, while incomplete separation of dura from the overlying skin may result in nasal dermoid.^{5,6}

Dermoid cysts

Nasal dermoids develop when the path of the dural diverticulum fails to completely involute through the foramen cecum and remains connected to the overlying skin.⁷ This results in a persistent attachment of the dura to the dermis, resulting in trapped epithelium along the diverticulum path. As time passes, the trapped epithelium produces a dermoid with hair and glandular structures.⁸ On exam, a midline pit in the nasal skin at the rhinion is frequently seen. CT and MRI provide complementary information and often assist with the diagnosis. In addition, imaging helps to determine if intracranial extension is present,⁹ which would place the patient at an increased

risk for meningitis and intracranial abscess.¹⁰ The surgical approach is dependent on the location, size, and extension of the dermoid, as well as the degree of overlying skin involvement.¹¹ The external approach excises the pit in combination with an open rhinoplasty.¹² Larger tumors with intracranial extension require neurosurgical intervention, either through traditional coronal incision with craniotomy or through a recently described endoscopic endonasal or endoscopic-assisted technique.¹¹

Encephaloceles

Congenital defects of the skull base can lead to the development of meningoencephaloceles into the sinonasal cavity (Fig. 1A). Occasionally, these may be identified incidentally on imaging. Alternatively, patients may present with nasal obstruction, respiratory distress, meningitis, or a cerebrospinal fluid (CSF) leak. Ma et al.¹³ reviewed 23 children with a mean age of 7 years undergoing endoscopic endonasal surgery for repair of CSF leak with or without meningocele or meningo-encephalocele. The defect sites were the ethmoid roof in ten patients, cribriform plate in five patients, and lateral to the foramen cecum in three patients. Favorable outcomes without recurrence was achieved in all patients with an average

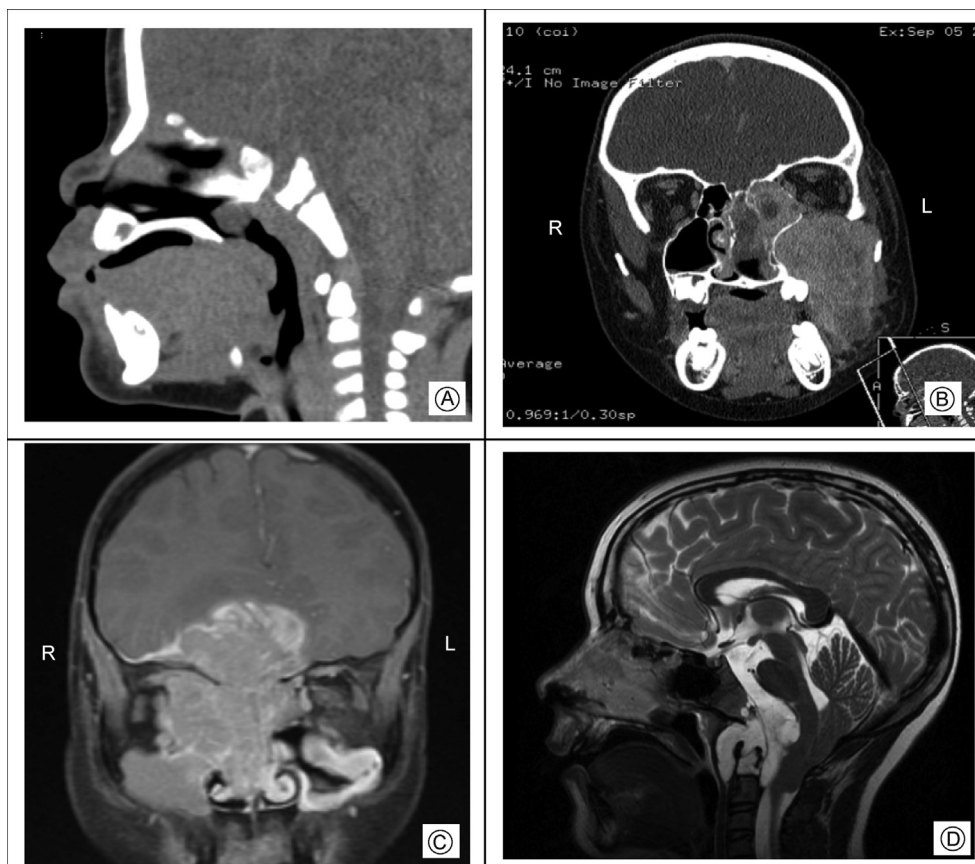


Fig. 1 A: Computed tomography of a 6-month old male with a patent craniopharyngeal canal and meningocele. This was successfully resected, and the skull base reconstructed with a nasoseptal flap. B: CT of an 11-year old male with a juvenile nasopharyngeal angiofibroma. C: MRI of a 10-year-old male with rhabdomyosarcoma. D: MRI of an 11-year-old female with chordoma. (Images are property of Columbia University Division of Rhinology).

follow up of 61.1 months. Endonasal endoscopic surgery for congenital encephaloceles can decrease hospital stay, cost of treatment, and achieve more desirable cosmetic outcomes.^{14–16}

Nasal glial heterotopia

Nasal glial heterotopias are a collection of congenital malformations consisting of ectopic mature neuroglial tissue. As opposed to encephaloceles, nasal glial heterotopia lesions do not communicate with the subarachnoid space. Typically, cases of glial heterotopia present as a pale mass in the nasal cavity. These masses are non-compressible, smooth, and do not exhibit pulsation or expansion with straining or crying. Surgery is recommended to prevent complications such as infection and cosmetic deformity. Up to 25% of nasal glial heterotopias have a fibrous stalk that extend towards the skull base.^{17,18}

Neoplasms

Juvenile nasopharyngeal angiofibroma (JNA)

JNA tumors are benign, highly vascular and locally aggressive. JNAs are thought to arise from the pterygoid canal and may extend laterally to the pterygopalatine fossa (PPF) and/or infratemporal fossa (ITF), medially into the nasal cavity,¹⁹ superiorly to the middle cranial fossa, and inferiorly to the buccal, masseteric, and other deep spaces of the neck (Fig. 1B). Patients are generally adolescent males who present with severe recurrent epistaxis and nasal obstruction. Biopsy in the clinic is not recommended due to their vascularity, and pre-operative imaging is essentially pathognomonic. Several staging systems are described and based on the extent of disease including imaging and clinical examination.^{20,21} Snyderman et al.²⁰ created an endoscopic staging system that considered residual vascularity from the internal carotid artery following embolization of external carotid tributaries. The authors found the route of skull base extension and residual vascularity provided better prediction of immediate morbidity, strongly correlating with blood loss, requirement for multiple procedures, and residual or recurrent tumor.

JNAs occur exclusively in males, as their growth requires androgenic hormonal input. Such hormonal factors are under active investigation, as JNAs express estrogen, progesterone, and androgen receptors.^{22,23} Beta-catenin, a coactivator of androgen receptors, and vascular endothelial growth factor (VEGFR-2) are overexpressed in JNAs.²⁴ Androgen receptor antagonists have achieved partial regression of disease.²⁵ The effectiveness of Bevacizumab, a monoclonal antibody that inhibits vascular endothelial growth factor A, has also been explored.²⁶

Nonetheless, JNAs remain a surgical disorder. Endoscopic surgery has superseded traditional open approaches, with similar or improved outcomes. Pre-operative embolization 24- to 48- hours before surgery should be considered to decrease intra-operative blood loss. Residual disease can be treated with either revision surgery or radiation. Rowan et al.²⁷ found that of the 34 patients in their series, 33 underwent an exclusively endoscopic surgical approach,

with six (18%) requiring planned staged operations. Ten patients (29%) had residual disease, and three (9%) underwent further surgical resection.

Rhabdomyosarcoma

Sinonasal rhabdomyosarcoma is a rare malignancy with poor outcomes, as patients often present with advanced disease and rapid onset of symptoms (Fig. 1C).²⁸ In a recent retrospective review of 16 patients with sinonasal rhabdomyosarcoma, positive prognostic factors included age under 18 years, and the embryonal or botryoid subtypes. The alveolar subtype was found to be a very poor prognostic factor,²⁹ with increased likelihood of regional and distant metastases, higher recurrence rates, and decreased survival. Multimodality treatment, which often includes surgery, radiation, and chemotherapy, is associated with the best survival outcomes.³⁰ Optimal surgery aims for primary resection with negative margins, which can limit radiation therapy, though this is not achievable when tumors extend intraorbitally or intracranially.³¹ Continued endoscopic surveillance after completion of treatment may identify recurrent or persistent disease, though the survival benefit of surveillance is unclear.²⁸ Five-, 10-, and 20-year disease-specific survival rates for all subtypes combined are 60.2%, 46.1%, and 20.6%, respectively.³²

Pituitary adenomas

Compared to the adult population, pituitary adenomas are rare in children. They account for approximately 3% of all intracranial neoplasms in children and 5% of all pituitary adenomas.³³ Functional pituitary adenomas are more common than non-functional adenomas in children, with prolactinomas and adrenocorticotrophic hormone-secreting tumors being most commonly encountered, followed by growth hormone-secreting and non-secreting tumors.³³ Symptoms often result from compression of nearby structures, manifesting as visual loss or headache. While prolactinomas are typically managed with dopamine agonists, other secreting adenomas or tumors causing mass effect warrant surgery. When possible, the endoscopic transphenoidal approach is preferred over an open transfrontal approach as the endoscopic approach has been shown to lead to a significantly decreased length of stay and hospital costs in children with pituitary adenomas.³⁴ In a literature review of 37 publications regarding pediatric pituitary adenomas examining 1284 patients, surgical cure was achieved in 65% of patients. Complications included pituitary insufficiency (23%), permanent visual dysfunction (6%), chronic diabetes insipidus (3%), and post-operative cerebrospinal fluid (CSF) leak (4%).³³ Patients younger than 10 years of age are more likely to have complications including post-operative hydrocephalus, panhypopituitarism, and diabetes insipidus.³⁴

Rathke's cleft cyst

Rathke's cleft cyst is a benign cystic lesion located in close proximity to the pituitary gland. These cysts are ectopic remnants of Rathke's pouch, with the minority of these

tumors diagnosed in childhood.³⁵ These cysts are often found incidentally, most often identified in imaging studies obtained for patients with recurrent headaches, visual changes, or endocrine pathology. On MRI, a Rathke's cleft cyst is non-enhancing and often has an intracystic nodule with high signal intensity on T1-weight images.³⁶ The majority of pediatric Rathke's cleft cysts are followed with observation, especially if discovered incidentally.³⁷ Surgery is indicated when there are significant or progressive symptoms related to the cyst, increasing cyst size, or diagnostic uncertainty.³⁸ Surgery involves fenestration and aspiration of the cyst with partial or complete removal of the cyst wall.³⁹ Post-operative diabetes insipidus can occur in approximately 20% of patients.^{35,40}

Craniopharyngiomas

Craniopharyngiomas are benign tumors that arise from the epithelial remnants of Rathke's pouch. Despite being the most commonly diagnosed benign tumor in the sellar and suprasellar region in the pediatric population, craniopharyngiomas are rare tumors with a reported incidence of 300–400 new cases per year in the United States.⁴¹ These tumors frequently have both a solid and cystic component with a propensity to recur years after resection. Craniopharyngiomas pose distinct surgical dilemmas and can result in serious morbidity.⁴² Patients with craniopharyngiomas typically present with endocrine deficits, visual changes, and occasionally mental status changes due to mass effect secondary to their anatomic location or hydrocephalus.

To reduce the likelihood of craniopharyngioma recurrence, gross total resection (GTR) is desired though not necessarily practical in all instances, particularly in larger tumors or tumors with significant supradiaphragmatic extension. In a recent case series of 45 consecutive pediatric patients undergoing endoscopic transsphenoidal resection, 20 patients required revision surgery. The authors found GTR was more likely in patients undergoing primary surgery (98%) compared to the revision surgery group (75%). Among the patients in which GTR was achieved, 12% experienced tumor recurrence with a mean follow-up of 7.8 years. In the primary surgery cohort, 80% of patients had worsening of pituitary function and 83% developed diabetes insipidus. In the repeat surgery cohort, 100% of patients developed these complications.⁴³ The authors concluded that GTR should be the goal for the first surgical attempt, although this goal must be carefully weighed against the risk of hypothalamic injury, which can have serious endocrine and neuro-cognitive morbidity. Patel et al.⁴⁴ similarly found post-operative pituitary dysfunction and diabetes insipidus in 63.6% and 46.7% of a cohort of 16 pediatric patients undergoing endoscopic craniopharyngioma resection. Fear of hypothalamic injury may cause surgeons to consider debulking or subtotal resection with post-operative radiation as major complication including post-operative CSF leak and death rates can occur in 19% and 12.5% of cases, respectively.⁴⁴ Alalade et al.⁴ reported that GTR was achieved in 45% of patients, while subtotal resection, near-total resection, or biopsy was performed in the remaining patients to avoid

hypothalamic injury. Due to the potential severe complications following GTR, many centers have advocated for limited surgery with postoperative radiation therapy.⁴⁵ They have demonstrated equivalent long-term tumor control rates comparing GTR and limited surgery with radiation therapy, but with reduced postoperative surgical and endocrine complications. Injuries to the hypothalamic and pituitary axis can cause significant morbidity, particularly in the pediatric population due to their extended life expectancy following resection and long-term surveillance with testing of pituitary function and serial MRI scans is necessary due to the high incidence of recurrence and complications.⁴⁶

Chordoma

Chordomas are malignant lesions that have locally destructive behavior and relatively low metastatic potential (Fig. 1D).⁴⁷ Still, metastases to the lung, bone, soft tissue, lymph nodes, liver, and skin have been reported in up to 65% of patients, especially those with advanced disease.⁴⁸ Chordomas arise from an embryologic remnant of the notochord. With clival chordomas, the most common presenting symptom is abducens nerve palsy.⁴⁹ Both CT and MRI are often obtained. Optimal outcomes often require a combination of surgical resection followed by radiotherapy. Chemotherapy may be an option in select cases.⁵⁰ Radiation or radiation with chemotherapy may be considered in recurrent or persistent disease.⁵¹ In patients under 5 years-old, a worse prognosis is observed. Clival chordomas appear to be at a particular high risk for post-operative CSF leak.⁵² In a recent retrospective review, Rassi et al.⁴⁹ found that long-term overall and progression-free survival was achievable with gross total resection and proton-beam therapy.

Fibro-osseous lesions

There are three primary fibro-osseous lesions that occur in the pediatric population: osteomas, fibrous dysplasia, and juvenile ossifying fibromas. Osteomas are rare benign bony tumors that occur in the paranasal sinuses. Most paranasal sinus osteomas are slow-growing, found incidentally, and often asymptomatic. Symptoms may occur as the osteoma grows,⁵³ and surgery is generally reserved for the symptomatic patient.

Fibrous dysplasia is a benign fibro-osseous disorder that can involve any areas of the skull base in the pediatric population. These are often diagnosed by radiographic imaging,⁵⁴ which shows a ground glass appearance of the bone on CT. Fibrous dysplasia grows slowly but may result in headaches, visual disturbance, nasal obstruction, or obstructive sinusitis. In a recent retrospective review of 14 patients aged 2–18 years old, endoscopic GTR was achieved with single-stage surgery in 10 patients (71%), while two patients (14%) required a second surgery,⁵⁵ with a low complication rate.

Juvenile ossifying fibromas are rare, benign fibro-osseous lesions that can involve the paranasal sinuses and skull base and grow rapidly.⁵⁶ Complete removal of this tumor is required due to its aggressive and locally

destructive course.⁵⁷ In a small case series of 11 patients undergoing endoscopic transnasal resection, ten patients were cured following surgery after mean follow-up of 25.8 months.⁵⁸

Skull base reconstruction

Skull base reconstruction in the pediatric population remains challenging, even with the increased utilization of vascularized flap repair.^{59–62} Post-operative CSF leak rates remain higher than adult counterparts, regardless of the repair technique.⁵² Initial concerns about the utility of the nasoseptal flap in the pediatric population have been shown to be unfounded, as the multiple studies support adequate coverage and pedicle length.^{63,64} Lack of sphenoid pneumatization in the pediatric population does not appear to impede gross total resection or increase complications.⁶⁵

Conclusion

Pediatric sinonasal and skull base lesions include a diverse range of pathology best addressed by an experienced multidisciplinary team. A comprehensive understanding of pediatric skull base anatomy, surgical techniques, and reconstructive principles is critical for successful outcomes.

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Declaration of Competing Interest

None.

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