

Multidisciplinary approach to children with sinonasal tumors: A review

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ABSTRACT

Sinonasal tumors in children are rare and difficult to manage. These tumors can be broadly categorized into congenital or acquired and benign or malignant. The tumors mainly arise from the mucosa, cartilage, or bone of the nasal cavity and may occupy areas of the nasal septum, turbinates, osteomeatal complex, sinuses, and nasopharynx. The management of pediatric sinonasal tumors is challenging, especially in cases of malignancy. Malignant tumors pose a treatment dilemma because most such tumors tend to be aggressive and carry a poor prognosis. Multiple complications associated with the primary disease or treatment may occur, and such complications need to be fully addressed to provide optimal care. In most cases, a multidisciplinary team approach will offer the best possible outcome for children with sinonasal tumors.

KEYWORDS

Benign tumor, Chemoradiation, Endonasal endoscopic surgery, Malignant tumor, Sinonasal tumor, Surgery

Introduction

Pediatric head and neck tumors account for 3% to 5% of all tumors, and identification of such tumors is important because each tumor has different management approaches and outcomes. Pediatric sinonasal tumors have distinct epidemiologic, clinicopathologic, and prognostic differences compared with adult sinonasal tumors. Sinonasal tumors in pediatric patients are rare and can be benign or malignant in nature (Table 1). These tumors may arise from the nasal cavity mucosa and its cartilaginous structures. Most are nonepithelial tumors. Benign sinonasal tumors include papilloma, hemangioma, leiomyoma, fibroma, and angiofibroma. Most malignant sinonasal tumors are of the sarcomatous type; others include lymphoma, olfactory neuroblastoma, and primitive neuroectodermal tumors. Rare tumors include Ewing's sarcoma, fibrosarcoma, malignant fibrous histiocytoma,

nasopharyngeal carcinoma, thyroid carcinoma, and salivary gland carcinoma.

The diagnosis of sinonasal tumors is often delayed because of their subtle symptoms. Most cases are diagnosed at an advanced disease stage. These advanced sinonasal tumors are clinically significant because they occupy the head and neck region territory, interfering with critical functions such as breathing, speech, articulation, mastication, and deglutition. The anatomical structures in children are also substantially different from those in adults, adding challenges and difficulties in the management of pediatric sinonasal tumors.

Rhabdomyosarcomas are distributed almost evenly throughout the different sinonasal sites, whereas most olfactory neuroblastomas are located in the nasal cavity. Sarcoma is more commonly seen in the maxillary sinus. In

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TABLE 1 Most common types of benign and malignant tumors in children

Benign Tumor	Malignant Tumor
Congenital mass (glioma, encephalocele, teratoma)	Rhabdomyosarcoma
Sinonasal Polyp	Non Hodgkin's Lymphoma
Hamartoma	Primitive Neuroectodermal tumor PNET
Hemangiomas	Nasopharyngeal carcinoma
Leiomyoma	Salivary gland carcinoma
Dermoid cyst	Thyroid carcinoma

TABLE 2 Characteristics of children with benign versus malignant masses

Features	Benign tumor	Malignant tumor
Duration of symptoms	Long history of sinonasal symptoms	Short history of worsening sinonasal symptoms
Change of mass size	Slow increase in size	Rapid and progressive increase in size
Nasal obstruction	Present	Present
Sinusitis symptoms	Present	Absent
Epistaxis	Absent	Present
Constitutional symptoms	Present	Present
Loss of appetite and loss of weight	Absent	Present
Feeding problems	Present	Present
Failure to thrive	Absent	Present
Developmental delay	Absent	Present
Distant metastases	Absent	Present

terms of grading, Chung et al¹ reported that the distribution of the tumor grade among their patients was as follows: grade IV, 37.3%; grade II, 25.3%; grade III, 22.7%; and grade I, 14.7%. Most children present with advanced disease, which is challenging to treat, tends to have more significant sequelae, and carries a poor prognosis. Both the patient and his or her immediate family members must be thoroughly counselled on the disease and its extent, the required treatment, and the complications that may arise during both treatment and follow-up.

Children tend to have a longer life span; thus, an effective and optimal treatment should be instituted from the very beginning (at the very first presentation) to ensure less morbidity and a good quality of life. Both the patient and parents need to be fully informed and actively involved in making decisions regarding all diagnostics, procedures, and plans for subsequent treatment. Numerous complications may arise, either directly due to the primary disease or indirectly due to treatment-related factors. These complications include disturbances of breathing, olfaction, and mastication and failure to thrive as a consequence of the primary disease. Adverse effects of chemoradiation include nausea, vomiting, mucositis, hyperpigmentation, neutropenia, renal toxicity, alopecia, fatigue, and hematotoxicity. These complications significantly impair children's quality of life.

Most patients require a multidisciplinary team approach involving plastic surgeons, otolaryngologists, neurosurgeons, neuroradiologists, pediatric

anesthesiologists, and a rehabilitation team. The rehabilitation team should comprise physical, speech, and swallowing therapists and social rehabilitation experts and should work in concert to provide the best care to patients and their family members.

Clinical presentation

Pediatric sinonasal malignancies are rare, heterogeneous tumors that usually carry a poor prognosis. The clinical presentation depends on the type, nature, origin, and location of the mass (Table 2). The symptoms may include nasal blockage, epistaxis, nasal discharge, external nose deformity, mouth breathing, feeding difficulties, and failure to thrive. Apart from the initial presentation, the patient may also present with symptoms and signs caused by adverse effects of the treatment. Patients with a sinonasal mass may develop complications including failure to thrive, developmental delay, and physical handicap. Breathing, olfaction, swallowing, and mastication may be affected, and these problems need to be fully addressed by the management team.

The age distribution varies depending on the type of lesion, but it generally ranges from 2 to 15 years. Both male and female patients are equally affected. In a study by Sengupta et al,² malignant lesions were found predominantly in children aged >5 years (69.81%), and the highest incidence occurred in those aged 10 to 12 years (47.17%). Malignant tumors were found with decreasing frequency in children aged 6 to 9 years

(22.64%), 2 to 5 years (18.87%), and 0 to 1 year (11.32%).² The overall male: female ratio was 1.78: 1.00; for thyroid carcinoma and neuroblastoma, however, the sex ratio was equal. Chung et al¹ reported similar findings; their patients' mean age at diagnosis was <10 years, and a slight male predilection was found. The most common site of pediatric sinonasal malignancies is the nasal cavity, followed by the maxillary sinus and ethmoid sinuses. The most common type of pediatric sinonasal malignancy is rhabdomyosarcoma, followed by olfactory neuroblastoma, sarcoma, and squamous cell carcinoma.

These nasal tumors are frequently life-threatening when active and persistent bleeding from a progressive sinonasal carcinoma occurs. Such cases require emergent judicious attention from clinicians and family members, especially when newborns and infants are affected. Most children with sinonasal tumors present with symptoms of nasal obstruction, nasal discharge, epistaxis, sinusitis, diplopia, facial numbness, and headache. For these patients, a detailed history should be obtained from the parent and/or guardian. The assessment should also focus on how the symptoms are affecting the child's function, growth, feeding, and sleep pattern.

The clinical presentation of benign tumors may differ from that of malignant tumors. However, most patients have subtle or no symptoms. Children with malignant tumors may present with nasal obstruction, facial swelling, ophthalmic complaints, rhinorrhoea, epistaxis, rhinosinusitis, and chronic upper respiratory tract infections, which are nonspecific and can be easily mistaken for more common conditions. Some children with malignant tumors present at a late stage of the disease, and such tumors can be locally aggressive. In 10-year single-institution study by Zevallos et al,³ the authors encountered 44 cases of pediatric sinonasal malignancies, and sarcoma was the most common pathology. The paranasal sinuses are commonly affected, including the maxillary sinus (45%), ethmoid sinus (25%), nasal cavity (16%), sphenoid sinus (7%), and nasopharynx (4%). In contrast, another study showed that lymphoma was the most common malignancy of the nasal cavity and sinuses in the pediatric population.²

Among benign tumors, congenital nasal masses are common and include gliomas, encephalocoeles, germ cell tumors, teratomas, and dermoid cysts. These benign congenital tumors can be immediately diagnosed at birth based on the clinical and imaging findings. Ancillary tests can be performed to attain the final diagnosis and include blood sampling, amniocentesis, and prenatal ultrasound. Inflammatory conditions such as sinusitis and polyposis can also be seen in the pediatric population and can mimic a benign tumor because the symptoms are often similar. In particular, children with polyposis often present with significant nasal obstruction, nasal discharge,

mouth breathing, and disturbed performance, all of which may also be presenting symptoms of benign sinonasal tumors. A thorough clinical examination and detailed investigation are imperative to attain the correct diagnosis. The subsequent treatment must be tailored to the specific condition to avoid unnecessary complications.

The most common presentations of sinonasal masses are nasal obstruction, rhinorrhoea, hyposmia, and headache. Intermittent epistaxis is a feature of malignant masses. External deformity of the nose and cheek is more common in patients with neoplastic polypoid lesions but can also be seen in patients with longstanding non-neoplastic polyps that develop at an early age. Unilateral presentation is seen in almost half of cases. Non-neoplastic inflammatory polyps are usually unilateral and single, while allergic polyps are usually bilateral and multiple.

Gliomas are classified into three categories based on their location: intranasal (30%), extranasal (60%), and combined (10%). Gliomas may rarely advance into the orbit, frontal sinus, oral cavity, or nasopharynx. Intranasal gliomas present as a pale mass in the nasal cavity with protuberance from the nostril. The base most often originates from the lateral wall near the middle turbinate and occasionally from the nasal septum. In contrast, extranasal gliomas present as firm, noncompressible, smooth masses that appear anywhere from the nasal tip to the nasal glabella.⁴

Teratomas are the most common germ cell tumors of childhood and consist of tissues from each of the three embryonic germ layers. They are mostly benign, although malignant transformation has been infrequently described. Teratomas of the head and neck account for <5% of all teratomas. They are most commonly found in the cervical region and nasopharynx. Occurrences have also been described in other regions of the head and neck, such as the brain, orbit, and oropharynx. However, presentation of a teratoma as an isolated intranasal mass is extremely rare.⁵

Other benign tumors include encephalocoeles, which are accompanied by other anomalies in most patients. Frontoethmoidal encephalocoeles typically present as nasal broadening or a blue, pulsatile, reducible mass near the nasal bridge that transilluminates. They may be seen at the glabella, over the nose, or on the forehead. Such masses are often noted early in life because of the resultant deformity and may be misdiagnosed as a cavernous hemangioma, polyp, or hypertelorism. However, the correct diagnosis is crucial because these lesions may cause cerebrospinal fluid rhinorrhoea or recurrent meningitis. They tend to enlarge with crying, the Valsalva manoeuvre, or compression of the jugular veins.

The presence of constitutional symptoms is useful in identifying suspicious malignant sinonasal tumors because

these tumors produce exuberant hormones and cytokines that cause inflammatory reactions and release mediators that are responsible for fever, loss of appetite and weight, metabolite derangement, lethargy, and cachexia. The attending clinician should carefully assess all of the patient's symptoms, and proper investigations and imaging studies should be performed to ensure early attainment of the correct diagnosis.

Methods of diagnosis

Diagnosing a sinonasal mass in a pediatric patient is challenging because of the presence of multiple patient-related factors and because the diagnostic procedures and investigations themselves may cause harm and adverse effects in the patient. The risks and benefits of all procedures and investigations must be judiciously considered before being conducted on these patients because some procedures may do more harm than good. The primary intention is to attain the correct diagnosis and administer proper treatment without causing serious complications. It is imperative to consider all of the patient's characteristics together with the clinical examination findings to arrive at a correct final diagnosis. This process is supplemented by investigations and procedures such as imaging, biopsy, and measurement of blood and other laboratory parameters (Figure 1).

Symptoms such as nasal obstruction in neonates and children less than 2 years of age must be properly diagnosed; this is particularly important in neonates, who exhibit a strong preference for nasal breathing. Severe nasal obstruction at that age thus has a great clinical impact and, like choanal atresia, may even be life-threatening if not treated immediately after birth.⁶ The most thorough possible clinical examination should be performed. Flexible endoscopy can be safely performed in almost all children, including neonates, because of the availability of small-calibre and angled endoscopes. The children may need to be comforted and counselled together with their parents. These procedures in infants and neonates can be performed under sedation or general anesthesia, especially if a tissue biopsy is required to achieve a pathological diagnosis.

An intranasal mass in a newborn often triggers consideration of a congenital midline nasal mass such as a nasal encephalocoele or nasal glioma. This is especially true when the mass arises from the roof of the nasal cavity. Preoperative magnetic resonance imaging (MRI) and computed tomography (CT) are therefore essential to identify any intracranial extensions or bony skull base defects suggestive of a nasal encephalocoele. This is because treatment is vastly different and would require a multidisciplinary team involving the expertise of a

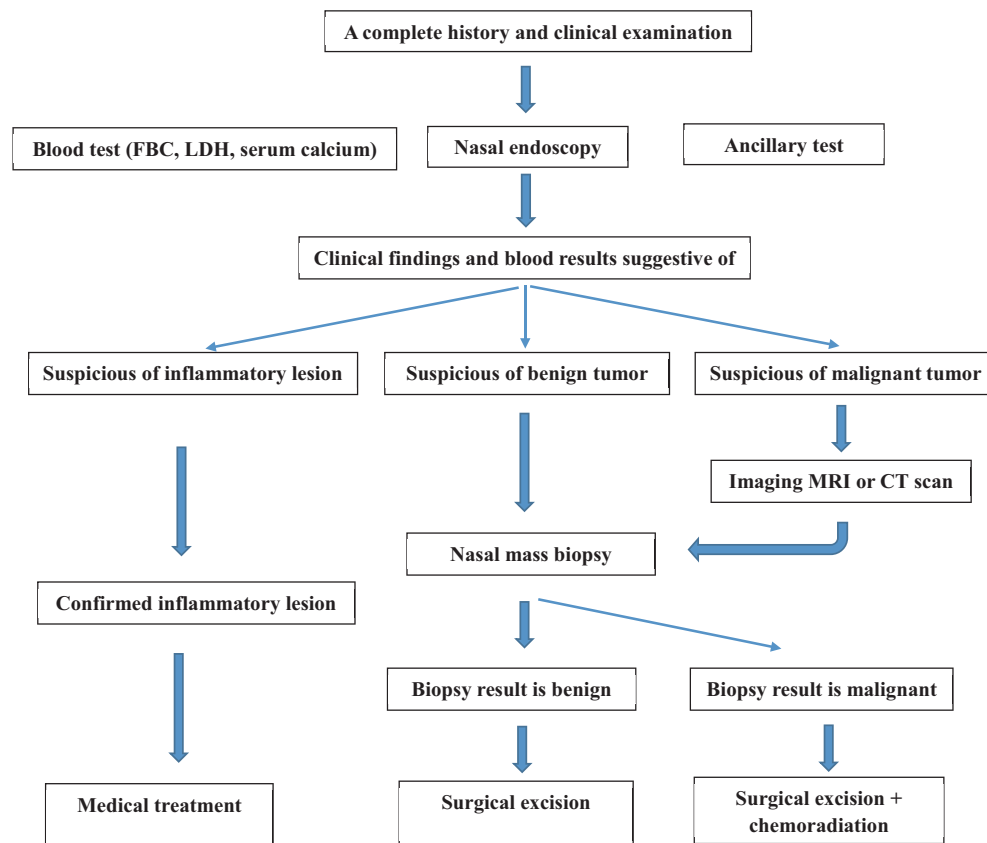


FIGURE 1 Flow diagram of diagnosis and treatment of pediatric sinonasal tumors. FBC, full blood test; LDH, lactate dehydrogenase.

neurosurgeon.⁵

Cancer of the nasal cavity in children is particularly challenging because of the often nonspecific symptoms and characteristically advanced degree of local destruction at presentation. Tumors of the nasal cavity are often initially misdiagnosed as sinus disease and treated empirically because their symptoms mimic those of other inflammatory nasal diseases. Treatment failure or the onset of new symptoms eventually prompts a further diagnostic workup, which reveals the true underlying pathology.⁷

One of the important investigative modalities is imaging, including CT, MRI, and scintigraphy. Selection of the imaging technique depends on myriad factors such as the patient's age, the availability of some modalities, the location of the mass, and the need for sedation or anesthesia. CT and MRI are complementary examinations, and although MRI is now the preferred examination for evaluating many of these lesions, CT may be necessary to further assess bone changes. Caution is always recommended when considering the use of CT in children because of the potentially increased risk of carcinogenesis from ionizing radiation. CT evaluation of most head and neck lesions is performed with the administration of contrast material, and images are best evaluated when they are reformatted to include three planes in both soft tissue and bone algorithms. MRI sequences that are ideal for assessing nasal lesions include multiplanar thin-section (high-resolution) T1-weighted imaging, T2-weighted imaging with fat saturation, contrast-enhanced T1-weighted imaging with fat saturation, and diffusion-weighted imaging.⁸

Most tumor types that arise in the nasal area are indistinguishable on the basis of clinical and radiographic features. Surgical biopsy is necessary for a histopathologic diagnosis, with particular reliance on molecular studies and special staining for immunohistochemical markers. These techniques allow the definitive diagnosis of both rhabdomyosarcoma and esthesioneuroblastoma as well as the differentiation of esthesioneuroblastoma from other neuroendocrine entities. An early molecular analysis suggested that esthesioneuroblastoma is a member of the Ewing sarcoma/primitive neuroectodermal tumor family.⁷

CT in conjunction with MRI is used to evaluate congenital craniofacial masses. CT is useful for detection of osseous defects, the bony anatomy, and the interorbital distance. Three-dimensional CT is superior and demonstrates the entirety of the skull base defect. An enlarged foramen caecum, bifid crista galli, or frontal bone defect indicates an intracranial connection. MRI helps to visualize the contents within the sac and reveals brain abnormalities. A soft tissue mass in connection with the subarachnoid space is seen on MRI if an encephalocele is present. The lesion is isointense relative to grey matter with most MRI sequences, but it may be hyperintense with T2-

weighted sequences because of gliosis. Because both studies are costly, some clinicians recommend using MRI as the initial imaging study. In patients with possible meningoencephalocoeles, digital angiography or magnetic resonance imaging should be performed to evaluate the vascular structures. Biopsy is always contraindicated because of the persistent intracranial connection.⁴

The diagnosis of sinonasal tumors in the pediatric population requires judicious consideration because most procedures are invasive and have a risk of unwanted complications. Repeated tissue samples and blood must usually be collected, and the children often must also undergo several imaging procedures before the final correct diagnosis is achieved. A tissue biopsy is required in all cases suspected of malignancy based on clinical findings and other ancillary test results. Acquiring a nasal mass biopsy from children almost always requires sedation; in contrast, such biopsies in adults can be easily performed on an outpatient basis.

Apart from the above-described diagnostic procedures, the management of pediatric sinonasal tumors also entails long-term surveillance for all children diagnosed with malignancies of the nasal cavity. Pediatric soft tissue sarcomas have a high recurrence rate, while recurrence of esthesioneuroblastoma has been reported after a disease-free period of 17 years. Serial physical examinations and imaging studies should be continued well into adulthood to detect recurrence and initiate salvage therapy in a timely manner.

Management

A multidisciplinary team approach with multimodal therapy is the best overall approach for pediatric sinonasal tumors. The multidisciplinary team should comprise a core team of pediatricians, oncologists, otorhinolaryngologists, maxillofacial surgeons, neurosurgeons, and plastic reconstructive surgeons and an ancillary team of radiologists, pathologists, anesthesiologists, physiotherapists, and nutritionists; such a team setup allows for more comprehensive treatment and rehabilitation than does a single-disciplinary approach. Multimodal treatment comprises endoscopic and open surgery with reconstruction, radiotherapy, and chemotherapy. An endoscopic approach is preferred for benign tumors; however, more extensive benign tumors with intracranial and orbital involvement may require a combined endoscopic and open surgical approach. For some malignant tumors, surgery is the primary treatment and may be used as a single modality or combined with radiochemotherapy. Small malignant tumors can be treated by an endoscopic or open surgical approach. Postoperative radiochemotherapy may be required for locoregional control and treatment of distant metastasis. Radiotherapy or chemotherapy is the primary treatment for certain tumors.

Benign tumors

A sinonasal inverted papilloma is a benign but locally invasive tumor. It has a low incidence in children. The recommended approach is endoscopic resection. A sinonasal inverted papilloma presents similarly to a nasopharyngeal angiofibroma, with unilateral recurrent epistaxis, nasal blockage, and mass formation.⁹ Another facial tumor that should be considered in children is a myxoma. Patients as young as 20 months have been reported to develop this tumor.¹⁰ Myxomas should be differentiated from malignant sarcomas because multimodal therapy consisting of surgery, irradiation, and chemotherapy is required for sarcomas. A myxoma is an aggressive tumor, and complete resection is recommended. Involvement of the maxillary sinus may require partial maxillectomy.

A sinonasal schwannoma is a rare intranasal tumor. The tumor site is the ethmoid and may extend to the skull base and orbit.¹¹ The mainstay of treatment is endonasal endoscopic resection. Complete tumor resection will ensure a favourable outcome. Nasal chondromesenchymal hamartoma is a rare sinonasal benign tumor in children that may present with orbital and skull base involvement.¹² Endonasal endoscopic resection is also the mainstay of treatment for this tumor.

Malignant tumors

Sinonasal malignancies in children include carcinomas, sarcomas, and esthesioneuroblastomas. The most common tumor site is the maxillary sinus, and most of these tumors are rhabdomyosarcomas.³ Primary surgery includes endoscopic resection and open surgical resection. Squamous carcinomas, adenoid cystic carcinomas, and salivary gland malignancies are treated by open surgical resection with adjuvant radiotherapy. The outcomes among patients with carcinomas, sarcomas, and esthesioneuroblastomas are not significantly different; previous research has shown that the overall survival, disease-specific survival, and recurrence are the same.³

Non-Hodgkin's lymphoma is the most common childhood head and neck cancer. The paranasal sinuses are the second most common primary site of non-Hodgkin's lymphoma in children after the cervical lymph nodes.¹³ The most common histological variant is diffuse large B-cell lymphoma. The clinical presentation depends on the site and histology. Low-grade tumors present as a sinonasal mass associated with nasal blockage with or without cervical lymphadenopathy. High-grade tumors tend to have more aggressive signs and symptoms such as epistaxis, persistent ulcers, and soft tissue and bony destruction. The primary treatment is chemotherapy with or without radiotherapy. Both modalities may achieve remission in two-third of patients. The prognosis remains poor, however, with a 5-year survival rate of 30% for all

types.¹³

A multidisciplinary approach to childhood meningioma is required because of its extensive involvement of the orbit, paranasal sinuses, midface, and anterior skull base. Combined open surgical resection such as a transcranial and transfacial approach may be required.¹⁴ Ewing's sarcoma is a highly aggressive malignant tumor that originates from the primitive neuroectodermal cells. It commonly occurs in early childhood or adolescence. Ewing's sarcoma has two forms: skeletal and extraskelatal manifestations.¹⁵ It is extremely rare in the sinonasal tract. Unilateral nasal obstruction, anosmia, and intermittent epistaxis are some of the clinical presentations of this tumor, which may mimic other conditions. The histopathological finding of small and round cells is highly suggestive of the tumor. Surgery, radiotherapy, and chemotherapy are the mainstays of treatment.

Sinonasal chondrosarcomas in children are rare. Early diagnosis and surgical treatment are associated with a favourable outcome.¹⁶ Wide surgical excision by either an external or endoscopic approach is the recommended management. Although the outcome does not differ between the external and endoscopic approach, the disease-free interval is longer with the endoscopic approach. Death may result from uncontrollable local disease caused by involvement of critical intracranial, neural, or vascular structures.

Discussion

When a child presents with a sinonasal mass, the differential diagnoses can be extensive and confusing, especially to clinicians who are unaccustomed to managing such cases. Treatment may be delayed and may not be optimal. Management of such a case by a multidisciplinary team allows for the best overall care in terms of prognosis and outcome. A holistic approach to management that involves parents and caregivers should be implemented from the start. Because the experience can be traumatic for both children and their parents/caregivers, expression of empathy will increase the likelihood of cooperation and compliance with treatment.

Diagnostic approach

The diagnosis should be differentiated according to congenital and acquired causes based on the patient's clinical symptoms and examination findings. Further confirmation of the diagnosis may be obtained by blood tests, imaging, and biopsy when required. Biopsy may not be necessary if sufficient information has been obtained from less invasive methods such as blood tests or imaging. Unilaterality and bilaterality can sometimes indicate the nature of the masses. A history of slow or rapid growth can help to determine the aggressiveness of the mass. A midline versus lateral location may also be helpful for the

diagnosis.

Management approach

The appropriate treatment depends on the cause of the tumor. Treatment of a benign tumor may be straightforward, but it can become challenging when critical structures are involved. Benign but aggressive tumors that can recur, such as an inverted papilloma, can pose a dilemma when the recurrence becomes more frequent and extensive. Constant vigilance with regular monitoring and tumor surveillance may ensure earlier detection and thus allow for prompt treatment. The treatment of children with sinonasal masses requires an understanding of their anatomy, physiology, and growth process. Treating a child's anatomy as that of a 'miniature adult' could well be a common fallacy made by physicians. When dealing with masses that require surgical intervention, the form and function of the involved structures should be considered. Reconstruction is always necessary to minimize morbidity and ensure optimal cosmesis.

Conclusions

A multidisciplinary approach offers the best management strategy in ensuring optimal and comprehensive care for any child with a sinonasal tumor. Parents and caregivers play an important role in management and should also play an active role in the decision process. The prognosis depends on the type of pathology and timing of treatment. An early-stage malignancy may respond to the primary treatment and has a better outcome.

CONFLICT OF INTEREST

All authors declare no conflicts of interest.

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