Case Report

Oral & Maxillofacial Manifestations In Pediatric Esthesioneuroblastoma—Report of a Case and Review of Literature

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Abstract: *Esthesioneuroblastoma (ENB) is a rare, malignant neoplasm arising from the olfactory epithelial cells, with only approximately 100 pediatric cases being reported in the literature since its original description in 1924. As a result of its origin high in the nasal cavity, most patients have nonspecific symptoms, precluding early diagnosis and leading to the development of locally advanced disease that usually has been found to involve the orbital cavity, paranasal sinuses, and anterior cranial fossa in children. The purpose of this paper was to report a rare case of pediatric esthesioneuroblastoma diagnosed following the patient's dental complaints, wherein local invasion of the tumor into the maxillofacial region was noticed before its extension into other vital structures. (Pediatr Dent 2011;33:261-4) Received September 17, 2009 / Last Revision January 31, 2010 / Accepted February 10, 2010*

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Esthesioneuroblastoma (**ENB**) is an uncommon malignant neoplasm arising from the nasal vault, possibly from neuroectodermal cells of the olfactory placode. This condition was first described in the French medical literature by Berg et al., in the year 1924 under the name esthésioneuroépithéliome olfactif.[1] Ever since, numerous terms have been used to denote this condition, which include: olfactory neuroblastoma; olfactory neuroepithelioma; stesioneuroblastoma; esthesioneuroepithelioma; and olfactory esthesioneuroblastoma.

The origin of ENB has been widely debated and has been attributed to the uncontrolled proliferation of neuroepithelial cells of the olfactory placode, sympathetic fibres (ganglionic loci of the nervus terminalis) in the anterior portion of the nasal cavity, sphenopalatine ganglion, and organ of Jacobson.[2] The fact, however, that the tumor cells express hASH1 (the human homologue of the Drosophila achaete-scute gene, which is expressed in immature olfactory neurons and is required for their development) favors their olfactory epithelial origin.[3,4]

The most common presenting complaint in pediatric patients is progressive nasal obstruction. Other common complaints include ophthalmologic complications, such as proptosis, ophthalmoplegia, and even visual loss due to local extension of tumor, epistaxis, lacrimation, rhinorrhea, and anosmia. Involvement of paranasal sinuses may result in frontal headache and diplopia.[2] Mobile tooth, nonhealing extraction sites, long-standing ulcerations and ill-fitting dental prosthesis are common dental complaints.[5] Magnetic resonance imaging (**MRI**) and computerized tomography (**CT**) imaging reveal the presence of a nasal mass filling the nasal cavity. Advanced disease may be associated with opacification, erosion of the sinuses, bony erosion of the orbits, and cribriform plate with intracranial extension.[6]

ENB has been reported to account for only 3% of all malignancies of the sinonasal tract, with a rare incidence of 20% to 25% diagnosed in patients younger than 20-years-old.[7] A 17-year retrospective cohort analysis (1991 - 2006) conducted at the Massachusetts Eye and Ear Infirmary and Massachusetts General Hospital studied pediatric patients diagnosed with a malignancy that arose within the nasal cavity. In this analysis, ENB was found to be the second most common malignancy (25%) arising from the nasal cavity in children.[8] This study also involved a comparison of this institution-specific patient group with a similar cohort of patients (<19 years and diagnosed with primary nasal cavity cancer) extracted from the national Surveillance Epidemiology and End Results (SEER) database between the years 1973 and 2002. In this nationwide group of patients, ENB was found to be the most common primary nasal malignancy diagnosed in pediatric patients (28%).[8] The vicinity of the nasal cavity and the greater chances of a malignant tumor arising from this region to involve the oral and maxillofacial region explain the great need on the part of pediatric dentists to understand ENB's oral and maxillofacial presentations.

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The purpose of this paper was to present a unique case of a 10-year-old girl who was diagnosed with unilateral esthesioneuroblastoma, along with her oral and maxillofacial manifestations.

Case report

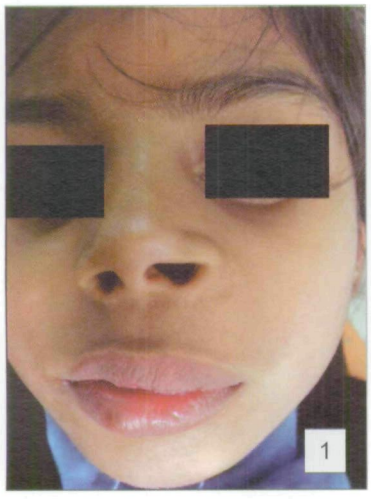
A 10-year-old girl of Indian origin reported to the pediatric dental wing of CSM Medical University, Lucknow, Uttar Pradesh, India, with the chief complaints of persistent pain in the "upper front teeth associated with a swelling of the middle portion of the face." Dental pain preceded the swelling and the patient was given over-the-counter medications by her mother for a 1-week period to suppress her dental pain until a swelling was detected 2 weeks prior to the first visit of the patient to the author's department. The swelling progressed rapidly to attain the size and form as shown in Figure 1, and there was no history of fever, nasal congestion, epistaxis, or weight loss in the recent past. The general health and mental status of the patient were normal with a noncontributory medical history. The patient was of normal height but underweight for her age (below the 25th percentile) vs normal children of a similar race.[8]

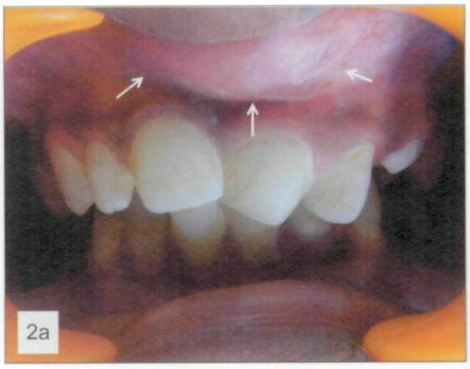
On examination, a unilateral, diffuse, firm swelling with indistinct edges and mild tenderness was observed in the left middle third of the face extending between the base of the nose and dentoalveolar portion of the anterior maxilla. The ala and lateral surface of the left nose appeared distended due to the underlying growth. The skin overlying the lesion was stretched, normal in color, and freely movable over the lesion.

Intraorally, a firm, nonfluctuant mass resulting in bicortical expansion of the anterior maxilla with obliteration of the vestibule in relation to the central incisors could be observed (Figure 2). The overlying mucosa was normal, with no ulceration or erythema. There was crowding of the permanent maxillary anterior teeth with tipping of the crown portions of the central incisors and left lateral incisor toward the midline. Grade 1 mobility could be detected in these teeth with mild tenderness on percussion. Normal responses were elicited from the permanent maxillary anterior teeth when tested for their pulp vitality.

Panoramic radiographs revealed the presence of a radiolucent lesion between the roots of the permanent maxillary central incisors, which was associated with severe displacement of the roots of the central incisors and left lateral incisor (Figure 3). CT imaging revealed the presence of an expansile soft tissue lesion filling the left nasal cavity with infiltration of the inferior turbinate and causing mass effect over the nasal septum (Figure 4a). The interface of the lesion with the medial wall of the maxillary antrum was well maintained. Inferiorly, the lesion was seen to breach the maxillary cortex and also evoke a "sunray type" of periosteal reaction (Figure 4b). No abnormalities were detected in the brain parenchyma or paranasal sinuses.

Aspiration of the lesion was nonproductive. An incisional biopsy was performed under local anesthesia, in the vestibular





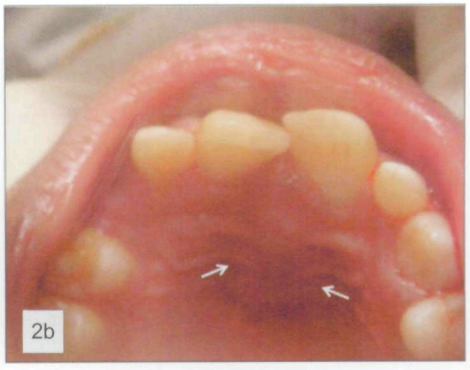


Figure 1. Frontal view of patient showing a naso-maxillary swelling with distention of left side ala and lateral half of nose.

Figure 2. (a) Intraoral facial view depicting obliteration of vestibule (white arrows) and abnormal orientation of tooth #s 8, 9 and 10. (b) Intraoral palatal view showing the palatal extension of swelling (white arrows).

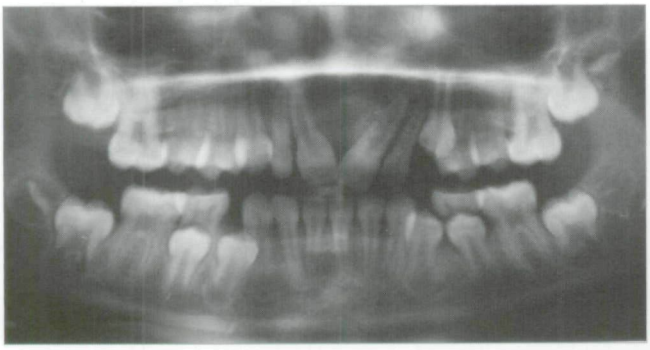
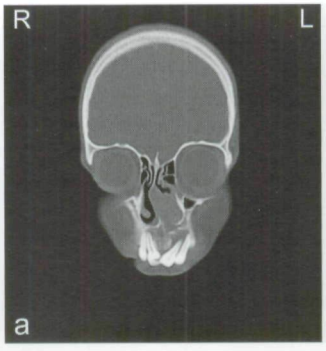


Figure 3. Panoramic radiogragph of patient showing displacement of tooth #s 8, 9 and 10.



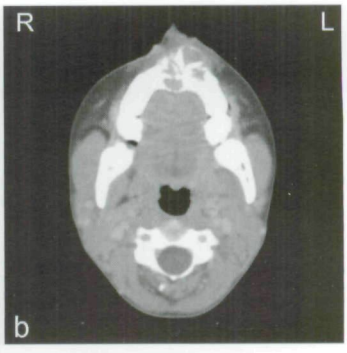


Figure 4. (a) CT images showing an expansile soft tissue lesion causing mass effect over the nasal septum and displacing tooth #s 8,9 and 10, (b) and breach in the maxillary cortical plates.

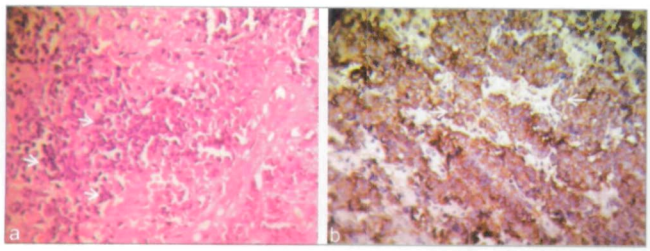


Figure 5. (a) Hematoxylin & Eosin stained view (400x) of histopathological specimen showing nests of small round cells (white arrow) with scant cytoplasm and hyperchromatic nuclei separated by eosinophilic stroma. (b) Immuno-histochemically, the cytoplasm of round cells (white arrow) are seen (400x) to express neuron specific enolase.

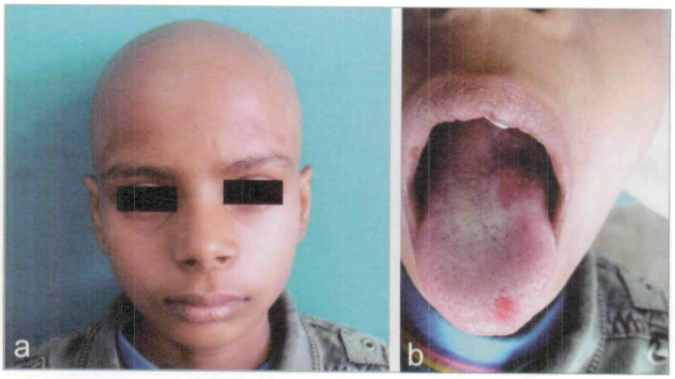


Figure 6. (a) Post chemotherapy. Frontal view of patient suggestive of reduction in tumor mass. (b) Reddish inflamed surfaces of tongue indicative of chemotherapy induced mucositis.

region adjacent to the permanent maxillary central incisors to determine the definite diagnosis. Histopathological examination revealed the presence of anaplastic, hyperchromatic small cells with round to oval hyperchromatic nuclei, at different stages of mitosis and scant cytoplasm in an eosinophilic fibrillary intercellular background material (Figure 5a). Immunohistochemical staining revealed positivity for neuron specific enolase (NSE) (Figure 5b) and negativity for desmin, vimentin, CD 99, S-100, and common leukocytic antigen. These histological features were consistent with the diagnosis of ENB.

The patient was then referred to the oncology section of the pediatrics department, CSM Medical University, Lucknow where appropriate chemotherapy was instituted. The patient received a combination of cisplatin, adriamycin, cyclophosphamide, and etoposide during the first cycle, following which a reduction in tumor mass could be evidenced clinically, on extraoral examination (Figure 6a). No alterations in the size and extent of tumor, however, could be detected intraorally. The patient had developed focal reddish inflamed surfaces on the dorsal surface of her tongue, suggestive of chemotherapy-induced mucositis (Figure 6b).

Topical chlorhexidine and lignocaine gels were prescribed for the same before meal times and benzydamine oral rinses (Tantum Oral Rinse, Elder Pharmaceuticals Ltd, Mumbai, India) three times daily during the course of chemotherapy. The patient, however, did not maintain her appointments for oral checkup and discontinued her chemotherapy after the first cycle. Efforts to contact the parents through the mobile number they provided remained unsuccessful. Similarly, mails sent to the patient's residential address were unanswered. Moreover, efforts on the part of the local health supervisors to locate the patient's residential address also were fruitless.

Discussion

Cancers of the nasal cavity are locally aggressive,[8] and the vicinity of dental structures increases the likelihood of their involvement. Pediatric ENB is a rare entity, with only approximately 100 cases reported so far in the literature.[9] No standard treatment plan for its management has been devised, which can once again be attributed to its rarity, as no institution would treat more than a few patients diagnosed with ENB each year.[4] The results of a recent retrospective cohort analysis of Benoit et al., however, reflected the strong bias toward soft tissue sarcomas in children and confirmed ENB to be an important diagnostic entity, especially in children.[8] Moreover, no cases have been reported so far highlighting the oral and maxillofacial findings in pediatric patients affected by ENB.

Nasal obstruction and ophthalmologic symptoms appear to be the common presenting complaints in most of the pediatric patients. But our case was unique, in that dental pain associated with facial swelling was the chief complaint, which is not widely reported in the literature. The cause of dental pain in this patient could be related to the pressure imposed on the apical root surfaces of the incisors by the tumor mass coupled with the alveolar bone loss around these teeth. Or, the case may be neuralgic in origin, due to impingement of apical nerve fibres supplying the tooth.[10] In spite of the reported aggressive nature of these tumors, the root surfaces of the central incisors were not resorbed by the tumor mass—instead, they were severely displaced.

ENB can be distinguished from Ewings sarcoma (rare within the nasal cavity and paranasal sinuses) by the lack of CD99 and myc -2 immunostaining. Rhabdomyosarcoma, a relatively common malignant tumor arising from the nasal cavity in children, can be distinguished by the lack of cross-striated cells (rhabdomyoblasts) and an absence of immunostaining with desmin and vimentin. Non-Hodgkin's lymphoma can be distinguished by the lack of common leukocyte antigen immunostaining. Thus, the pathological distinction of ENB from other malignant tumors requires proper correlation of clinical findings along with immunohistochemical stainings. The demonstration of HASH gene expression could become the diagnostic procedure of choice in the future.[11] Common maxillofacial conditions associated with divergence of permanent maxillary central incisor roots, such as nasopalatine cyst, can be easily distinguished via history (lack of rapid progression) and clinical findings (involvement of the nasal cavity and PNS).

Traditional teachings have propagated the use of craniofacial resection along with follow-up radiotherapy as the main stay of treatment in pediatric ENB,[12,13] although recent

reports of successful neoadjuvant chemotherapy have been encouraging.[10,14-16]

Although ENB is a rare entity, it needs to be considered as part of the differential diagnoses in pediatric patients presenting with rapidly progressive lesions in the nasal and maxillofacial region. This case report detailed the clinical, radiographic, and histological features that led to the diagnosis of ENB in a pediatric dental patient, with special emphasis on the oral findings. Further studies involving retrospective analyses of health records of ENB patients to identify the dental and maxillofacial changes are required to better understand the maxillofacial manifestations in this condition.

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