A maxillary sinus tumor in an adolescent girl

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A 12-year-old girl was referred to the Department of Oral and Maxillofacial Surgery, Wuhan Union Hospital, on February 20, 2011, with a 1-month history of a painless, progressively enlarging mass on the left palate. The patient had no history of trauma, infection, tumors, or radiation. She had no noteworthy family history or past history. The swelling was noted by her parents.

On general physical examination, the patient appeared healthy, well nourished, and in no acute distress. Intraoral examination revealed a firm, nontender, fixed mass (3 × 2 cm) on the left hard palate (Figure 1). The overlying mucosa had a reddish hue without ulceration. The patient did not demonstrate lymphadenopathy or masses in the neck. Chest radiograph and abdominal ultrasound scans were normal. Routine laboratory evaluation was found to be well within normal limits. Plain radiography showed complete opacification of the left maxillary sinus, and the inner and outer walls of the maxillary sinus were no longer visible.

Magnetic resonance imaging (MRI) showed an enhanced mass in the left maxillary sinus, ethmoid sinus, sphenoid sinus, nostril, and orbital cavity (Figure 2). An axial contrast-enhanced T1-weighted image showed widespread enhanced lesion in the left maxillary sinus, with the inner wall and a portion of the outer wall of the maxillary sinus showing damage (Figure 2, *A*). The coronal contrast-enhanced T1-weighted image showed the enhanced mass involving the left nasal cavity (Figure 2, *B*). The sagittal T2-weighted image showed a high-intensity tumor involving the left maxillary sinus, ethmoid sinus, sphenoid sinus, and maxillary alveolar bone (Figure 2, *C*).

DIFFERENTIAL DIAGNOSIS

Based on the clinical and radiographic presentation, aggressive lesions in maxillary sinuses that should be considered in the differential diagnosis are embryonal rhabdomyosarcoma, olfactory neuroblastoma, nasopharyngeal carcinoma, inverted papilloma, mesenchymal chondrosarcoma, Ewing's sarcoma, osteosarcoma, and Burkett's lymphoma.

Rhabdomyosarcoma (RMS) is a rare malignant mesenchymal tumor that arises from the cells committed to a skeletal muscle lineage. RMSs are histologically classified into embryonal, alveolar, botryoid, and pleomorphic subtypes. Embryonal RMS accounts for 6% of all malignancies in children younger than 15 years, with the common age group younger than 10 years,[1] but also occurs in adolescents and young adults. Embryonal RMS is slightly more common in males than in females by a ratio of approximately 1.3:1.0. The orbit, paranasal sinuses, soft tissues of the cheek, and the neck are the most frequent locations in the head and neck region.[1] In the present case, the age of the patient, the location, and clinical appearance suggest embryonal RMS as our working diagnosis.

Olfactory neuroblastoma (ONB) is an uncommon malignant neuroectodermal nasal tumor arising from the specialized sensory neuroepithelial olfactory cells. It comprises about 2% of all sinonasal tract tumors, with an incidence of approximately 0.4 per million population. ONB may occur at any age, but a bimodal age distribution in the second and sixth decades of life is most common, without a gender predilection. The common location for ONB is the upper part of the nasal cavity, including the superior nasal concha, the upper part of septum, the roof of nose, and the cribriform plate of the ethmoid bone. The major clinical symptoms are unilateral nasal obstruction (70%), epistaxis (50%), headache, pain, excessive lacrimation, rhinorrhea, anosmia, and visual disturbances.[2-4] MRI findings, however, showed that the lesion occurred in the left maxillary sinus.

Nasopharyngeal carcinoma (NPC) is a squamous cell carcinoma arising from the epithelial lining of the nasopharynx that can rarely involve the maxillary sinus. NPC is one of the most common malignancies among

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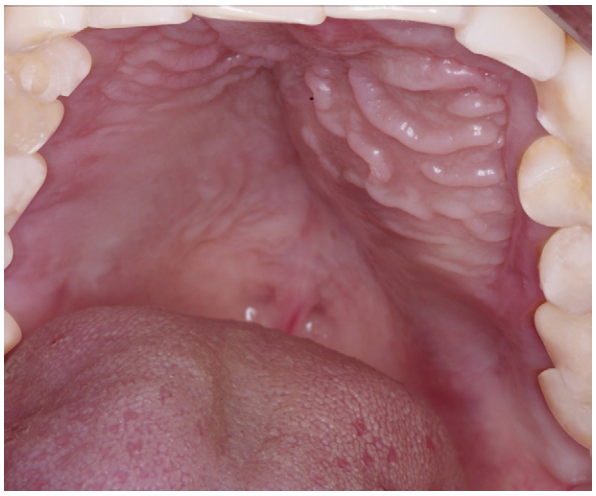

Fig. 1. Clinical appearance of the mass on the left hard palate.

men in certain areas of South China, Southeast Asia, and North Africa.[5] NPC, however, is rare in children, with only 5% to 12% of cases of NPC occurring in patients 30 years or younger. NPC presents most commonly as a unilateral neck mass in 50% to 70% of patients, from cervical lymph node metastases. Eustachian tube obstruction may produce persistent unilateral hearing loss or otitis media. Other clinical features include a bloody nasal discharge, nasal obstruction, and headaches.[6]

Inverted papilloma is a benign epithelial tumor that arises from the mucous membrane of the nasal cavity and paranasal sinuses. Paranasal involvement most frequently affects the maxillary and ethmoidal sinuses. Inverted papilloma constitutes 0.5% to 0.4% of primary nasal tumors and occurs most frequently in patients in their fifth and sixth decades and with male predominance in these lesions. Patients typically present with nasal obstruction, epistaxis, or nasal discharge.[7]

Mesenchymal chondrosarcoma (MC) is an infrequent neoplasm involving bone and soft tissue. This rare variant of chondrosarcoma accounts for up to 3% to 9% of all chondrosarcomas and has high predilection for the head and neck region. The maxillary anterior alveolus is the most common site. MC occurs more commonly in the second and third decades of life. There is no gender predilection. The most common clinical presentation of MC of the jaws is a painless mass or swelling.[8,9]

Among the primary malignant tumors of bone, we considered small cell osteogenic sarcoma, Ewing's sarcoma, and Burkett's lymphoma in our differential diagnosis. Osteosarcomas are the most common primary malignant bone tumors, although lesions of the jaw are uncommon, representing about 4% of the osteosarcomas.[10] Osteosarcoma occurs over a wide age range,

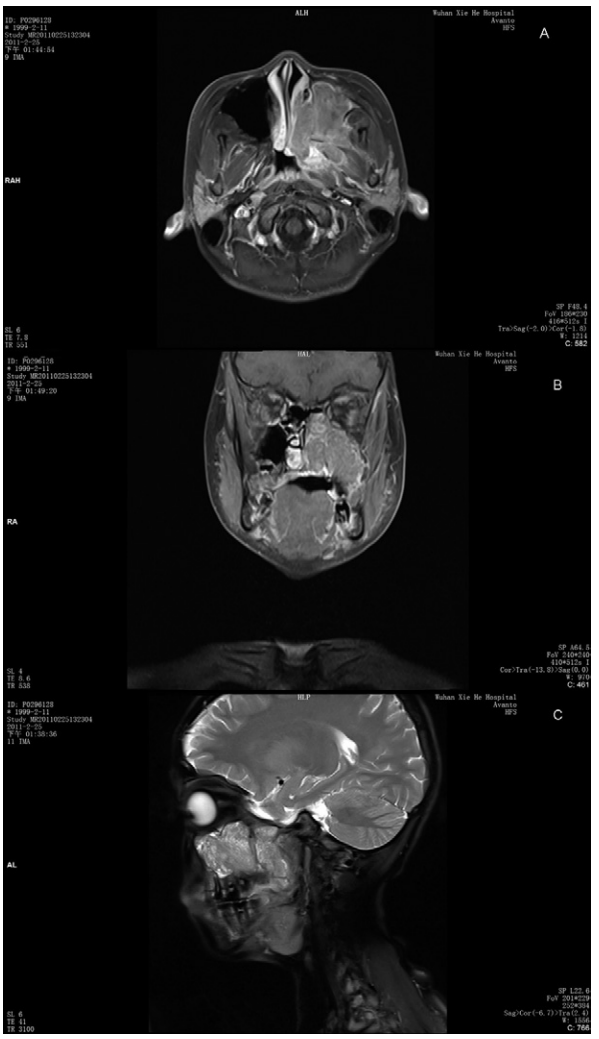

Fig. 2. **A,** An axial contrast-enhanced T1-weighted image showed widespread enhanced tumor in the left maxillary sinus with damage to the inner wall and a portion of the outer wall of the maxillary sinus. **B,** The coronal contrast-enhanced T1-weighted image showed the enhanced mass involving the left nasal cavity. **C,** The sagittal T2-weighted image showed a high-intensity tumor involving the left maxillary sinus, ethmoid sinus, sphenoid sinus, and maxillary alveolar bone.

with a peak in the fourth decade of life. Small-cell osteogenic sarcoma is a rare variant of osteosarcoma. It accounts for 1% of all osteosarcomas. The chief clinical features are swelling, pain, and ulceration.[11] Radiologically, the findings may include radiolucency, radiopacity, or a mixture of both, with poorly-defined irregular margins. Ewing's sarcoma is the second most common primary bone tumor in childhood. It accounts for 4% to 6% of primary malignant bone tumors, with only 1% to 4% in the head and neck region. The tumor is rarely seen before the age of 5 and after the age of 30, with its peaks in the second decade of life. This tumor is slightly more common in males. The 2 most common

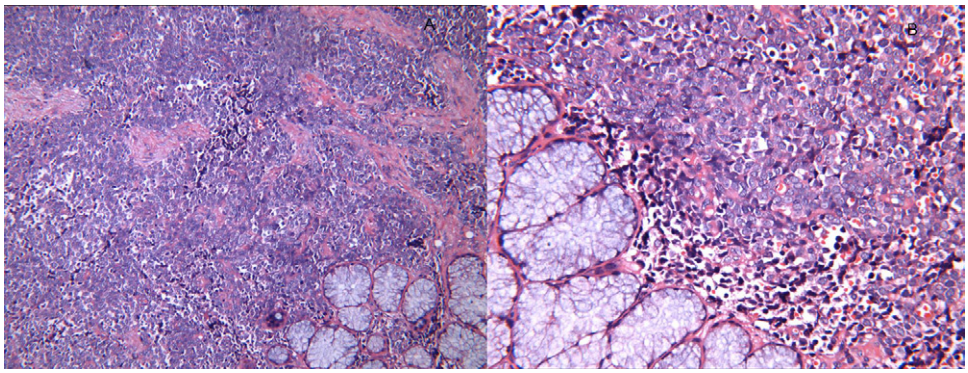

Fig. 3. Photomicrograph showing compactly arranged small, round tumor cells with vesicular nuclei and scanty cytoplasm (hematoxylin and eosin, original magnification ×200 [**A**] and ×400 [**B**]).

primary sites in the head and neck region are the mandible and skull base, followed by the orbit and nasal cavity, with or without the paranasal sinuses.[12-14] Burkett's lymphoma is usually found in the pediatric population and accounts for 3% to 5% of all lymphomas. In the head and neck region, Burkett's lymphoma usually presents as a painless mass, with facial swelling, nasal obstruction, and cervical lymphadenopathy. The clinical symptoms may vary depending on the site of involvement.

Based on the clinical and MRI features, prevalence, location, and age, we made a presumptive diagnosis of an embryonal RMS.

DIAGNOSIS AND MANAGEMENT

An incisional biopsy of the protruding mass in the oral cavity was done before a definitive operation. Light microscopic analysis showed that the tumor comprised an almost uniform population of small round cells with scant cytoplasm and hyperchromatic nuclei (Figure 3). Nuclei were round to ovoid with smooth nuclear contours, exhibited fine salt-and-pepper''–like chromatin, and nuclear molding. Scattered necrosis with apoptotic cell debris was diffusely present. There were numerous mitotic figures. Immunohistochemistry for a number of markers was conducted, using both positive and negative controls for each assay. Analysis of the specimen showed a CD99-positive tumor (Figure 4) that also positively stained for synaptophysin (Syn) (Figure 5), and the neuroendocrine markers CD56 and Ki-67. Tests for S-100, desmin, pancytokeratin (PCK), CD45, MyoD1, TdT, and chromogranin A (CgA) were all negative. Cytogenetically, EWS-FLI1 fusion transcript was detected by reverse transcriptase–polymerase chain reaction (RT-PCR). Based on these findings, the lesion was diagnosed as primitive neuroectodermal tumor of the maxillary sinus.

An extensive left maxillectomy was scheduled to be performed on this patient to remove the tumor. Concerned about the treatment effect and destruction of contour of her face after the operation, the parents of the little girl abandoned the operation and she was referred to the tumor center of our hospital for further treatment. Twenty-three fractions of radiation were undertaken after chemotherapy; however, clinical deterioration was observed 3 months after the initial diagnosis and the patient died 2 months later.

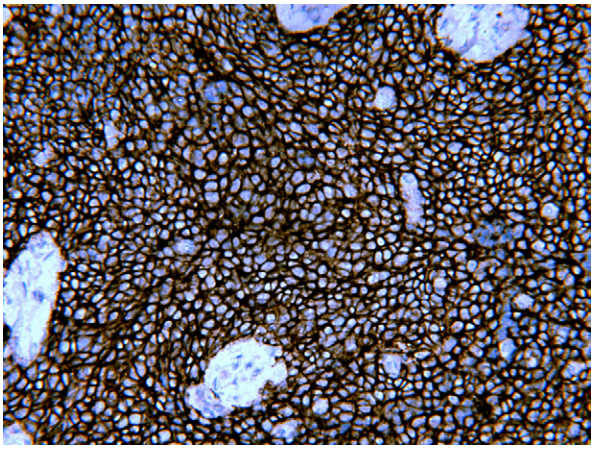

Fig. 4. Tumor cells showing intense membrane-associated staining with CD99 (MIC2) (immunohistochemical staining, original magnification ×400).

DISCUSSION

Primitive neuroectodermal tumor (PNET) comprises small round cells and develops mainly in the central nervous system of children and young adults. PNET outside the central nervous system is called peripheral primitive neuroectodermal tumor (pPNET).[15] pPNETs arise in many places throughout the body, with the chest wall, larynx, abdomen, and pelvis being the most common primary sites.[16] pPNET can occur in the head and neck region, and the most common location is the orbit, although it may be found in the larynx, maxilla,

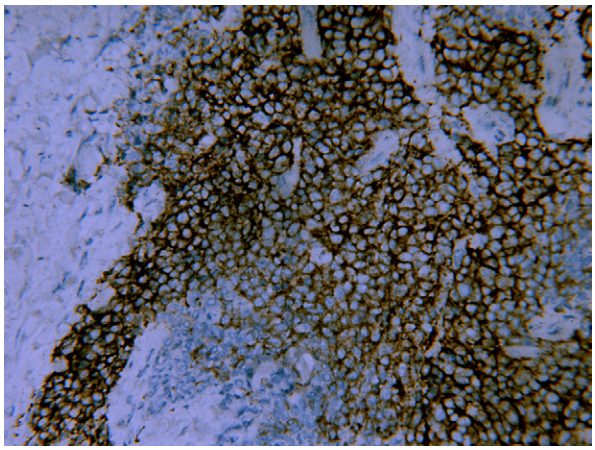

Fig. 5. Tumor cells displaying immunoreactivity for synaptophysin (immunohistochemical staining, original magnification ×400).

mandible, both minor and major salivary glands, and paranasal sinuses.[14,17-24] In this case, the location was in the maxilla, which is an unusual location, with fewer than 10 cases reported in the English-language literature. These tumors are seen predominantly in children and young adults. The age range is from 20 months to 49 years (average age, 20.9 years). There is no apparent sex predilection. The patients usually present with a painless mass in the maxillary region and constitutional symptoms. All patients are treated with chemotherapy, radiotherapy, and surgery; however, the clinical course of all these patients is almost always grim.[24-28] The clinicopathologic features in 9 patients with PNETs in the maxilla are summarized in Table I.

Because of the rarity and the difficulties in pathologic diagnosis, the frequency of pPNET in the head and neck region varies among different studies. In a large series, 23% or 42% of the pPNET presented in the head and neck region, but in other series, the rates were lower.[29] pPNET occurs mostly in children and adolescents without gender predilection.[18]

A rapidly enlarging, often painful mass is the most frequent clinical presentation. Depending on the sites of involvement in the oral maxillofacial region, additional signs and symptoms may include nasal obstruction, epistaxis, paresthesia, loss of teeth, and ulceration of the overlying mucosa. Tumor of the maxillary sinus might not be detected until the lesion protrudes into the nasal cavity and oral cavity, which can cause nasal obstruction, epistaxis, and destruction of the palate. Metastases may be the initial presentation. This patient was referred to the hospital with a painless, progressively enlarging mass on the left palate for 1 month. There was no nasal obstruction, epistaxis, or deformation of facial contour. She did not demonstrate lymphadenopathy in the neck.

Primary malignant tumors of the maxillary sinuses are rare in children. They must be carefully evaluated when bone destruction occurs on its walls and neighboring structures, such as the ethmoid sinus, sphenoid sinus, and orbital cavity. MRI and plain radiography are widely used in clinics and are essential for the evaluation of the tumor margins and anatomic relations. The planning of the appropriate treatment modality will require these radiographic studies. In this case, the MRI findings showed that the orbital cavity and other important structures were involved by the tumor, and radical extensive resection of maxilla would need to be performed to remove the tumor. In addition, MRI can also be used to evaluate tumor metastasis and spread to surrounding tissues. MRI findings can provide useful information in clinical differentiation between pPNETs and other tumors[30,31]; however, it is very difficult to make a definite diagnosis by MRI examination only.

pPNET is also considered a part of the PNET–Ewing's sarcoma family. Immunohistochemical and cytogenetic studies suggest that these tumors have a common origin. The tumors show histologic and immunohistochemical evidence of neuroectodermal differentiation. Cytogenetic studies have shown similar abnormalities in Ewing's sarcoma and PNET cells: mainly, the t(11; 22) (q24; q12) translocation. The EWS-FLI1 fusion transcript can be detected in 80% to 90% of the PNET–Ewing's sarcoma family by RT-PCR.[32] This genetic anomaly can be recognized by the CD99 antibody. Therefore, positive CD99 staining is highly sensitive for PNET. However, CD99 staining is not specific for PNET. Many other tumors, such as lymphoblastic lymphoma, can also stain positive for CD99.[33] Features for diagnosis of the pPNET include (1) well-defined histologic evidence of Homer-Wright or Flexner-Wintersteiner rosettes, (2) immunoreactivity to 2 or more neural markers, and/or (3) electron micrographic evidence of neural differentiation and neurosecretory granules.[1] The presence of Homer-Wright rosettes is the most helpful histologic feature for the diagnosis of pPNET, but some pPNETs do not show this feature, as with this patient.[33] In this case, the tumor cells were stained positive for CD99, CD56, and Syn. S-100, desmin, PCK, CD45, MyoD1, and CgA were all negative. The final diagnosis was pPNET according to the positive and helpful negative immunohistochemistry results.

PNET progresses rapidly and often metastasizes at the time of diagnosis. At present, there is no consensus on the choice of therapeutic modality. The major prognostic factors include tumor site, tumor volume, and the presence of metastasis. When a pPNET is encountered, a multidisciplinary treatment protocol should be planned. An aggressive surgical resection, if it is pos-

Table I. Clinicopathologic features in 9 patients with PNETs in the maxilla

Authors	*Age, y*	*Sex*	*Clinical presentation/duration*	*Positive IHC staining*	*Treatment*	*Follow-up*	*Disease status*
Slootweg et al.[20]	10	M	Painless enlargement of the left anterior maxilla/3 mo	ND	StR, RT	2 mo	NED
Bown et al.[21]	12	M	Swelling in the right maxillary region	NSE	TR, StR, RT, ChT	15 mo	AWD
Filiatrault et al.[22]	11	F	Partial obstruction of the right nostril/6 mo	NSE	ChT, RT	10 mo	AWD
Shah et al.[23]	42	M	Swelling in the left maxillary region/1 y	NSE	PR, RT, ChT	9 mo	DOD
Ibarburen et al.[24]	1	F	Swelling in the left maxillary region	ND	ChT, PR	3 y	AWD
Alobid et al.[25]	23	F	Unilateral left-sided nasal obstruction, rhinorrhea/2 mo	CD99, NSE, CgA, S-100, vimentin, Syn	RT, ChT	59 mo	NED
Sun et al.[26]	49	F	Painless, enlarging mass on the right palate/6 mo	CD99, vimentin NSE, CgA	TR, RT	3 mo	NED
Mohindra et al.[27]	8	M	Swelling on right side of the face, associated with protrusion of the right eye/ 4 mo	CD99, vimentin	ChT	First post-RT follow-up	AWD
Hormozi et al.[28]	28	F	Swelling in the left maxillary region/1 y	CD99, vimentin, S-100	TR, StR, RT, ChT	3 y	NED

AWD, alive with disease; *CgA,* chromogranin A; *ChT,* chemotherapy; *DOD,* dead of disease; *F,* female; *IHC,* immunohistochemistry; *M,* male; *ND,* no data; *NED,* no evidence of disease; *NSE*, neuron-specific enolase; *PR,* partial resection; *RT,* radiotherapy; *StR,* subtotal resection; *Syn,* synaptophysin; *TR,* total resection.

sible, should be performed owing to their malignant and progressive character. Chemotherapy or radiotherapy should also be performed to treat residual disease and to prevent recurrence.[20,21,23,24,26,28] For patients who have unresectable tumors or who reject surgery, radiotherapy and chemotherapy are the remaining alternative modalities,[22,24,25,27] but they are not effective when used. PNETs are known to be very aggressive, and have a tendency for recurrence and metastasis. In general, survival rates for 2 and 3 years are about 65% and 56%, respectively.[25] Because of the high recurrence rates, patients must be followed closely to identify tumor recurrence as early as possible, and to decrease the rate of metastasis. If pPNET in the maxillary sinus is limited, radical maxillectomy in the initial stage may afford a better prognosis; however, in this case, MRI findings showed an enhanced mass in the left maxillary sinus, with involvement of the left ethmoid sinus, sphenoid sinus, nostril, and orbital cavity. Unfortunately, this patient did not respond to chemotherapy or radiotherapy. The tumor grew rapidly, and the girl died. In conclusion, although treatment protocols for these tumors are not well established, a successful treatment generally, including a well-developed strategy consisting of radiotherapy, chemotherapy, and surgery that will act to remove the primary tumor as well as any distant metastases would probably offer the patient the best chance at long-term survival.

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