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Ectopic primary olfactory neuroblastoma of the maxillary sinus

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ABSTRACT

Olfactory neuroblastoma (ONB) is a rare malignant tumor. Although the vast majority of cases arise in the nasal cavity, ONB is rarely reported in ectopic locations. We report a case of ONB in the maxillary sinus. A 63-year-old woman presented with left-sided nasal obstruction and epistaxis. Magnetic resonance imaging showed a nonenhancing left maxillary sinus tumor. Histologic sections showed ONB, Hyams grade IV, invading bone, skeletal muscle, and adjacent fibroadipose tissue. It is essential to be accurate when diagnosing sinonasal tumors because the differential diagnosis is broad, and one must consider the possibility of ectopic ONB, although it is rare. The behavior of ONB and other neuroendocrine tumors of the sinonasal region is quite different, and there are varied approaches to treatment. Therefore, an accurate diagnosis as well as correct grade and stage must be assigned.

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1. Introduction

Olfactory neuroblastoma (ONB), or esthesioneuroblastoma, is a rare malignant tumor first described in 1924 by Berger and Luc [1]. ONB accounts for 3% of all intranasal tumors [2]. It is usually found in the upper nasal cavity and commonly extends to the ethmoid sinuses, orbit, and anterior skull base [3]. ONB has an even age distribution and occurs equally in male and female individuals [2,4,5]. The most common symptoms related to ONB are nasal obstruction (70%), epistaxis (40%), headache, nausea, cervical lymphadenopathy, and facial swelling [3]. However, symptoms may be subtle and mimic those of inflammatory or infectious disease, delaying diagnosis [6].

Olfactory neuroblastoma arises from the olfactory neuroepithelium in the olfactory rim of the nasal cavity [2]. It is considered to be an intermediary between a pure neural neoplasm and a neuroendocrine epithelial tumor [7]. The cell type from which ONB arises has yet to be definitively identified, however [6]. Histologically, ONB is composed of cells with small round nuclei and punctate chromatin arranged in nests or sheets in a neurofibrillary stroma. Classically, this tumor has Flexner-Wintersteiner and Homer Wright rosettes. The tumor cells exhibit staining that is diffusely positive for neuroendocrine immunohistochemical markers such as neuron-specific enolase, chromogranin A, and synaptophysin.

Although the vast majority of ONBs arise in the nasal cavity, it is very rarely reported in locations without olfactory neuroepithelium. These locations include the sphenoid sinus, sellar region, anterior ethmoids, petrous apex, pituitary gland, and nasopharynx [3,8–13]. We report herein on a case of ONB arising from an ectopic location: the maxillary sinus.

2. Case report

The patient is a 63-year-old white woman with a medical history of breast cancer who underwent radiation therapy and chemotherapy in 2006 and presented 2 years prior with sinus symptoms and superficial cellulitis over the left maxilla. The cellulitis responded to treatment with antibiotics. The patient was asymptomatic until 4 months ago when she presented to our institution with a left-sided nasal obstruction, minimal epistaxis, and left-sided facial tenderness.

Her computed tomography findings included left maxillary sinus soft-tissue thickening that was hypermetabolic on a positron emission tomography scan. At the anterior margin of the sinus cavity, she has a nodular focus of intense activity (12 mm; standard uptake value, 9.8). Magnetic resonance imaging displayed a lesion along the left posterior maxillary alveolar ridge that extended posteriorly into the retrotuberosity region and possibly behind the left maxillary sinus (Fig. 1A). She has no evidence of nodal disease.

The patient underwent a left total maxillectomy with left selective lymph node dissection. Gross examination of the maxillectomy specimen revealed a soft, tan, glistening, partially necrotic mass measuring $3 \times 3 \times 1$ cm that appeared to erode the bone within the maxillary sinus but did not involve the buccal pad or skeletal muscle.

Examination of histological sections of this maxillary sinus lesion demonstrated it to be a high-grade ONB (Hyams grade, IV/IV) invading through bone and into adjacent fibroadipose tissue and skeletal muscle (Fig. 1B-D). The soft tissue and bone margins were negative for tumor involvement. Also, we did not identify lymphovascular or perineural invasion. Twenty-six regional lymph nodes were negative for metastasis.

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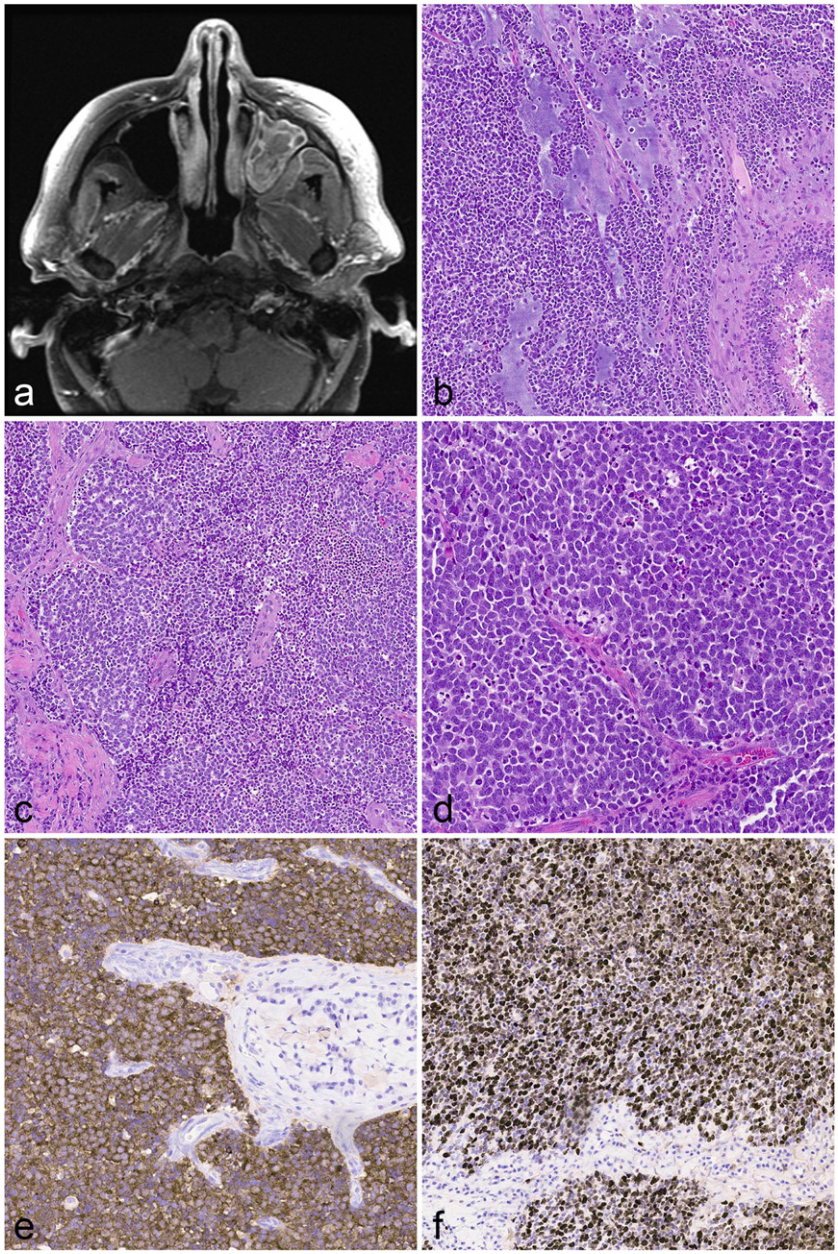

Fig. 1. (a) Magnetic resonance image of the patient showing a nonenhancing tumor behind the left maxillary sinus. (b) Histological (hematoxylin and eosin) section of the ONB showing a submucosal tumor (B; lower right corner, sinonasal mucosa; magnification 4×) (c) that is composed of cells with small round nuclei and punctate chromatin arranged in nests or sheets and rosettes (d) with increased mitotic figures and apoptotic bodies (magnification 10×) with increased (magnification 4×). (e) The tumor is diffusely immunoreactive with anti-synaptophysin antibody, (f) whereas the proliferation rate is very high (Ki-67 90%; magnification 10×).

Immunohistochemical studies demonstrated the tumor cells to be strongly and diffusely positive for synaptophysin (Fig. 1E); focally positive for chromogranin; and negative for pan-keratin, CAM5.2, cytokeratin 18, leukocyte common antigen LCA, and S-100. The tumor had 30 mitoses per 10 high-power fields, which were highlighted by a phosphohistone H3–positive immunohistochemical stain. The Ki-67 proliferation rate was greater than 90% (Fig. 1F).

3. Discussion

Although authors have reported more than 1000 cases of ONB arising within the superior nasal cavity, they have very rarely reported cases of ONB arising within an ectopic location. Reported ectopic locations of ONB have included the sphenoid sinus (n = 5), sellar region (n = 2), nasopharynx (n = 2), pituitary gland (n = 2), maxillary sinus (n = 2), floor of the nose (n = 1), inferior meatus of the nasal cavity (n = 1), and anterior ethmoids (n = 1) (Table 1) [3,8–19].

The evidence that ONB can very rarely arise at ectopic locations calls into question the exact location and cell type of origin for ONB. This is a controversial topic. The most likely cell type and site of origin seem to be basal neural cells and the olfactory mucosa, respectively [2,20–22]. Other suggested locations include the ectodermal olfactory placode, autonomic ganglia in the nasal mucosa or olfactory epithelium, Jacobson's organ, Loci's ganglion, and sphenopalatine ganglion [2,3,21]. Also, authors proposed a neuronal or neural crest origin owing to the presence of neural elements in ONB cells [23]. However, ectopic ONB arises in locations that do not normally have olfactory neuroepithelium. The tissue that gives rise to ectopic ONB has yet to be determined; possible sources include ectopic cell rests, Jacobson's organ, persistent terminal ganglion cells, and sympathetic/parasympathetic autonomic ganglia in the sinuses [3].