Olfactory Ensheathing Cell Tumor: Case Report

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ABSTRACT

Subfrontal schwannomas, sometimes referred to as olfactory groove schwannomas, are rare tumors (34 cases reported to date). Despite the name and several theories proposed in the literature, there is no officially recognized description of the tumor's cell origin. Yasuda proposed the concept of an olfactory ensheathing cell (OEC) tumor in 2006. Olfactory ensheathing cells are glial cells that ensheath the axons of the first cranial nerve. Microscopically, both olfactory ensheathing cells and Schwann cells have similar morphological and immunohistochemical features. However, immunohistochemically olfactory ensheathing cells are negative for Leu7 and Schwann cells positive. A 30-year-old woman presented with a subfrontal, extraaxial, enhancing tumor, and underwent gross total resection. Immunohistochemical reactivity data suggested a schwannoma (positive for S-100 and negative for epithelial membrane antigen). However, the tumor was negative for Leu7. Accordingly, our final diagnosis was that of an OEC tumor. Subfrontal schwannoma immunohistochemical staining, if negative for Leu7, is indicative of an OEC tumor. It is possible that schwannoma-like extraaxial tumors at the anterior skull base are OEC tumors, which negative Leu7 staining can confirm.

KEYWORDS: Olfactory ensheathing cell tumor, olfactory ensheathing cell, subfrontal schwannoma, olfactory groove schwannoma, Leu7

Schwannomas are benign, slow-growing, nerve-sheath tumors that arise from Schwann cells. Intracranial schwannomas without association of cranial nerves account for less than 1% of surgically treated schwannomas of the central and peripheral nerve system. Furthermore, intracranial schwannomas in the subfrontal region are rare (34 cases have been reported in the literature to date).¹⁻¹¹ Despite these case reports, subfrontal schwannoma cell origin has not been determined. Few hypotheses have been proposed because it

is thought that there is no Schwann cell surrounding the olfactory groove.^{5,9,12-15}

In 2006, Yasuda proposed the concept of an olfactory ensheathing cell (OEC) tumor.¹⁶ OECs have been found in the nerve-fiber layer of the olfactory bulb and along the primary olfactory pathway of normal adult animals and humans. They are specialized glial cells that surround the olfactory sensory axons in the nose and are similar to Schwann cells in terms of appearance when illuminated and under electron microscopy, as well as

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immunohistochemical staining.^{17,18} We report a case of a subfrontal tumor ultimately diagnosed OEC tumor and describe its origin.

CASE REPORT

Clinical Presentation

A 30-year-old woman presented at our institution with a history of headache that had continued for several months. On examination, it was found that she had no neurological deficits, except for right anosmia. Magnetic resonance (MR) imaging demonstrated a heterogeneously enhancing mass lesion, about 4-cm in diameter, in the frontal base. Three-dimensional computed tomography of the skull showed erosion of the cribriform plates (Fig. 1).

Technique and Intervention

A bilateral frontal craniotomy was performed, and tumor was located in the intradural, extraaxial space attached to the right cribriform plate. The bony structure around both cribriform plates was eroded, while the left olfactory bulb was intact, and the right olfactory bulb was not located. Tumor was completely removed and the bone defect repaired by a periosteal flap.

Histological Examination

Paraffin-embedded 4 μ m tumor sections were fixed in 10% formalin. Sections were stained for the presence of epitopes recognized by the anti-S-100 antibody (Dako, Santa Barbara, CA) (1:100), the anti-epithelial membrane antigen (EMA) antibody (Dako) (1:5), and the anti-Leu7 antibody (Becton and Dickinson, Mountain View, CA, USA) (1:100), using the labeled streptavidin-biotin (LSAB) method. The LSAB method comprised a Ventana I-VIEW DAB Universal Kit (biotin-labeled immunoglobulin, peroxidase-labeled streptavidin, 3-3'-diaminobenzidine tetrahydrochloride, H₂O₂, and copper

sulfate) and a specialized instrument (BenchMark XT, Ventana). Sections were pretreated with proteinase K (Dako) prior to Leu7 staining. Staining controls were performed using normal mouse serum in place of specific antiserum (data not shown).

Microscopically, tumor cells formed patterns of compact fascicular Antoni A areas with palisading nuclei (Fig. 2A). Tumor-cell immunohistochemical reactivity was positive for S-100 protein (Fig. 2B) and negative for both EMA (Fig. 2C) and Leu7 (Fig. 2D). A positive Leu7 control reaction stained at the same time as the patient material was not included. However, after pathological diagnosis, we again performed tumor Leu7 and EMA staining and staining of an autopsy specimen (peripheral nerve and dura matter). The tumor specimen remained negative for Leu7 and EMA, and the autopsy materials were positive for Leu7 and EMA (data not shown).

With the exception of the negative reaction for Leu7, pathological findings were compatible with a schwannoma. It is possible that immunohistochemical reactivity data are indicative of an atypical schwannoma. However, immunohistochemical reactivity data that are positive for S-100 but negative for EMA and Leu7 are characteristic of an OEC. Therefore, our final pathological diagnosis was that of an OEC tumor.

Postoperative Imaging

Postoperative MR images demonstrated total tumor excision (Fig. 3). The patient was discharged with no new neurological deficit; however, olfactory function was not restored.

DISCUSSION

According to past reports, subfrontal schwannomas are occasionally described as olfactory schwannomas or olfactory groove schwannomas. To date, 34 case reports have been published.¹⁻¹¹ Tumor characteristics include

Figure 1 (A) Axial and (B) sagittal view of T1-weighted MR images with gadolinium showing a subfrontal tumor with heterogeneous enhancement. (C) Three-dimensional computed tomography scan of the anterior skull base demonstrates erosion of bilateral cribriform plates.

Figure 2 Photomicrographs demonstrate arrangement of spindle cells (A: H&E stain $\times 100$). Tumor immunoreactivity was positive for S-100 protein (B: $\times 400$), and negative for both EMA (C: $\times 400$) and Leu7 (D: $\times 400$).

the following: male dominance, a younger age than most patients with vestibular schwannomas, nonspecific initial symptoms, frequent rate of hyposmia, and good prognosis (Table 1).

Tumor origin is puzzling, and several hypotheses have been proposed. Developmental theories suggest that either mesenchymal pial cells transform into ectodermal Schwann cells or the tumor develops from

Figure 3 (A,B) Postoperative MR images with gadolinium enhancement showing no residual tumor.

Table 1 Summary of Schwannomas at the Olfactory Groove

Demographics	
Gender (male: female)	22:12
Age range years (mean)	14 to 63 (31.8)
Indications	Number of cases
Initial symptom	
Headache	13
Seizure	12
Others	7
Unknown	2
Olfaction	
Normal	15
Abnormal	13
Unknown	6
Enhancement on MR imaging	
Heterogeneous	18
Homogeneous	7
No enhancement	1
Unknown	8
Attachment	
Olfactory groove or cribriform plate	19
Skull base	8
Others	3
Unknown	4
Prognosis	
Excellent	33
Death	1*
Recurrence	0

*Death due to postoperative hypothalamic shock.

aberrant neural crest cells within the central nervous system (CNS).^{5,12,14} Nondevelopmental theories presume that intracranial schwannomas arise from Schwann cells that are normally present in adjacent structures, such as the perivascular nerve plexus,¹³ the meningeal branch of the trigeminal or anterior ethmoidal nerves innervating the anterior cranial fossa and olfactory groove,⁹ or the fila olfactoria, which is known to acquire a Schwann-cell sheath that extends ~0.5-mm beyond the olfactory bulb.¹⁵ Furthermore, Fuller et al¹⁹ reported in adult human brain the presence of an additional cranial nerve (the nervus terminalis or cranial nerve zero) identified bilaterally as a microscopic plexus of unmyelinated, peripheral-nerve fascicles in the subarachnoid space covering the gyrus rectus of the orbital surface.

The notion of an OEC tumor was first proposed by Yasuda et al¹⁶ in 2006. OECs are specialized glial cells that surround the olfactory sensory axons in the nose. They have properties of Schwann cells in that they promote and assist in the growth of axons.²⁰ They are unique among the glia in that they reside both inside and outside the CNS, in the olfactory bulb and olfactory nerve, respectively.²¹ OECs are responsible for successful regen-

eration of olfactory axons throughout the life of adult mammals. Several clinical trials worldwide have been initiated that use autologous transplantation of olfactory tissue containing OECs into the damaged spinal cord of humans.^{22,23} Both OECs and Schwann cells express p75 neurotrophin receptor, S-100, and glial fibrillary acid protein in vitro.^{24,25} Therefore, it is difficult to distinguish OECs from Schwann cells. Bianco et al²⁶ reported that OECs were negative and Schwann cells were positive for Leu7. Yasuda et al¹⁶ also noted that OEC tumors and schwannomas shared similar hematoxylin and eosin (H&E) staining characteristics and identical immunohistochemical reactivity for S-100 and EMA stain; the exception, however, was that OEC tumors were negative and schwannomas were positive for Leu7.

In the case we present, tumor immunohistochemical reactivity was positive for S-100 and negative for both EMA and Leu7. Therefore, our final diagnosis was that of an OEC tumor. However, according to Johnson et al,²⁷ 20% of schwannomas are negative for Leu7. Thus, in our case, a diagnosis of an "atypical" schwannoma cannot be excluded. There are few subfrontal schwannoma case reports that note Leu7 staining has been undertaken. We advocate for further studies involving immunohistochemistry, molecular biology, and electron microscopy to provide more data on tumor origin and definition. If Leu7 staining were performed for subfrontal schwannomas, most cases could, potentially, prove to be negative. Our case report, based on the negative Leu7 result, suggests and has convinced us that subfrontal schwannomas should be defined as OEC tumors.

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