OLFACTORY NEUROBLASTOMA WITH NASAL AND SUPRASELLAR EXTENSION : A CASE REPORT

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Abstract : We report the case of a patient with an olfactory neuroblastoma which occupied the sphenoid sinus with nasal and suprasellar extension. Presenting symptoms included diminished visual acuity in the right eye. Computed tomography (CT) and magnetic resonance (MR) imaging demonstrated a tumor that had destroyed most of the sphenoid sinus, extending to the nasal cavity and suprasellar region. The patient underwent surgery via a fronto-temporal approach. An extensive review of the literature revealed approximately 300 cases of olfactory neuroblastoma, however, only two of these cases involved the sphenoidal region. This tumor is not thought to be derived from the olfactory neuroepithelium, but rather from neural crest tissue surrounding the sphenoid sinus.

Key words : Olfactory neuroblastoma, Sphenoid sinus, Neural crest, Olfactory neuroepithelioma, Olfactory neuroepithelium, Magnetic resonance imaging

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INTRODUCTION

Olfactory neuroblastoma is a rare malignant tumor arising from the olfactory region. The first cases was described by Berger in 1924¹⁾; since then approximately 300 cases have appeared in the literature²⁾. With the exception of a few isolated cases which involved the nasopharynx, maxillary sinuses, or intracranial regions, all other primary tumors originated high in the nasal cavity, occurring in the roof of the nasal cavity in the region of the cribriform plate. Only two tumors in the sphenoidal region have been reported^{3,4)}, without details related to tumor origin. The following report describes a case of sphenoidal olfactory neuroblastoma.

CASE REPORT

In February, 1993, a 66-year-old women was admitted to the hospital for a right visual disturbance that had persisted for 1 year.

Examination. General physical examination revealed high blood pressure. The patient exhibited reduced visual acuity in the right eye due to optic nerve atrophy. The remainder of her neurologic examination was unremarkable. Endocrinological laboratory examinations showed normal LH, FSH, and thyroxin concentrations. The patient demonstrated normal response of THS, PRL, LH, and GH to a triple load test with thyrotropin-releasing hormone, LH-releasing hormone, and insulin. Serum cortical and urinary 17-OHCS concentrations were with normal limits.

Additional laboratory studies revealed a slightly elevated serum concentration of neuron-specific enolase (NSE) (14.8ng/ml, normal range : 0.0-10.0ng/ml). The urinary excretion of vanillylmandelic acid (VMA) was 6.8mg day (normal range 3.0-5.0). Olfactory nerve function was intact. A neoplasm with a rough surface was located in the nasal septum obstructing the right nostril. Biopsy was performed via the nasal cavity. The histological examination revealed

olfactory neuroblastoma. Plain films of the sinuses revealed opacification of the sphenoid sinus with bony destruction, however, the ethmoid sinus appeared intact.

Computed tomography (CT) demonstrated a large tumor involving the nasal cavity, sphenoid sinus, and intracranial region, which was homogeneous and of high density. Post contrast CT revealed homogenous enhancement.

The mass appeared isointense to the gray matter on T1- and T2-weighted MR images, and was markedly enhanced by gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA). Sagittal MR through the midline demonstrated tumor breaching the sphenoid sinus, and extended extra axial intracranial tumor (Fig.1). Angiography revealed that the tumor was fed by both external carotid arteries. Scintigraphy performed 24 hours after injection of I-123 metaiodobenzyl guanidine (MIBG) showed abnormal uptake by the tumor.

Fig.1. Sagittal, T1-weighted magnetic resonance (MR) image with Gd-DTPA enhancement, demonstrating a soft-tissue mass that completely opacifies the sphenoidal sinus with nasal and suprasellar extension.

Operations. The tumor, exposed via a right frontotemporal craniotomy, was grayish red. It was composed of a soft portion removed with suction and a fibrous fixed portion. The tumor was located between both optic nerve and internal carotid artery. Tumor had destroyed the anterior portion of the middle cranial base. No dura mater in the temporal base was visible. The suprasellar tumor was partially removed, and the markedly elevated right optic nerve was decompressed.

Postoperative course. CT and MR imaging showed residual tumor mass involving the sphenoid sinus, nasal cavity, and suprasellar region. In May 1993, chemotherapy was initiated with intravenous cyclo-

phosphamide (1000mg), vincristine (1.5mg), and cisplatin (70mg). Following this therapy, she received 60Gy of irradiation to the primary lesion bilaterally. In August 1993, a second course of combined chemotherapy was administered, and in October, a third. After three course of chemotherapy, tumor regression was achieved which has since been maintained. Though the patient requires therapy for the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), she has returned to her activities of daily living with some support. There is no evidence of recurrence during a follow up period. However, about 2.5 years from the onset, she died of unknown disease.

Pathologic Findings. Tumor in the cranial and nasal cavities was composed of ill-defined, round to oval cells with relatively hyperchromatic nuclei. Lobular architecture was present, and a focal fibrillar area was identified (Fig.2A). Neither Flexner-type rosettes nor Horner-Wright rosettes were observed. These cells also did not exhibit mitotic or necrotic figures.

Immunostaining of the tumor cells revealed immunoreactivity for synaptophysin, neurofilament protein (68-160kDa), chromogranin, S-100, and Ber-EP4, but not for GFAP, keratin, vimentin and EMA. Synaptophysin immunoreactivity was observed in tumor cell bodies and in the fibrillar area. Cells immunoreactive for neurofilament protein also were distributed throughout the tumor, showing some differences in the reaction products between the two polypeptides. Staining for the 68-kDa polypeptide was weakly positive in the cell processes, but rarely present in the cellbodies. On the other hand, staining of the 160-kDa polypeptide was well demonstrated in both the cell bodies and processes (Fig.2B).

A relatively large number of tumor cells were shown to be immunoreactive for chromogranin. Immunoreactivity for the S-100 protein was restricted to the margin zone of regions of alveolar architecture, adjacent to the vascular stroma (Fig.2C).

GFAP, EMA, vimentin and keratin (AE1/AE3) were not detected immunohistochemically in any of the materials examined.

On electron microscopic examination, neither junctional nor synaptic complexes were identified. A prominent features was the limited presence of dense core vesicles, ranging from 100 to 250 nm in diameter, scattered mainly in the cytoplasm processes (Fig.3). Ciliated structures, basal bodies, and microvilli were not detected in any tumor cells.

Fig.2. A : Photomicrograph showing tumor composed of ill-defined cells. A focal fibrillar area is present. Mitoses are not visible. (H.E. stain, $\times 60$)
 B : Photomicrograph showing some tumor cells, immunoreactive for NFP (160-kD). ($\times 240$)
 C : Photomicrograph showing immunohistochemical staining for S-100. ($\times 120$)

DISCUSSION

Cytogenetic Considerations

There are several theories regarding the cytogenesis of olfactory neuroblastomas. The most widely accepted theory involves the olfactory neuroepithelium because of its morphologic similarity to the tumor cells and its favored location for the neoplasm.

However, this theory has been questioned following the recognition that some olfactory neuroblastomas illustrate immunohistochemical and ultra structural similarities to conventional neuroblastoma which are

Fig.3. Electron micrograph demonstrating dense, core vesicles ranging from 100 to 250 nm in diameter. Bar = $1\mu\text{m}$

of neural crest origin^{5~7}). Thus, their cytogenesis remains a matter of debate.

Hassoun et al.⁸(1981) and Takahashi et al.⁹ (1987) have documented olfactory neuroepitheliomas composed of compact lobules with tubular arrangements. Ultrastructurally, those tumors have consisted of two cell types, both devoid of neurosecretory granules and reminiscent of the sensory neurons and sustentacular cells of the olfactory epithelium. They concluded that their cases corresponded to a rare variant, the olfactory neuroepithelioma, which is a true tumor of the neurosensory system originating from the neuroepithelium. This differs from the olfactory neuroblastoma which is generally considered to be of neural crest origin.

In 1993, the World Health Organization (WHO) divided olfactory neuroblastomas into two groups; olfactory neuroblastomas and olfactory neuroepitheliomas¹⁰.

Two cases of olfactory neuroepithelioma reported by Takahashi. et al.⁹ and Banerjee. et al.¹¹ include the results of immunohistochemical studies. These olfactory neuroepitheliomas demonstrated immunoreactivity for an epithelial antigen (keratin) as well as a neurogenic antigen (NSE, and S-100). There also are some reports on the immunohistochemical features of olfactory neuroblastoma. Frieson. et al.¹² examined 11 cases of neuroblastoma using NFP 200-kD, SY, NSE, chromogranin, S-100, GFAP, keratin, EMA, MAP-2, and Class 3 B-Tubulin with the following results; NSE 11/11(+), S-100 8/11(+), NFP 200-kD 8/11(+), chromogranin A 10/11(-), GFAP 10/11(-), vimentin 10/11(-), and keratin (AE1/AE 3) 11/11(-), EMA 11/11(-). Takahashi. et al.⁷ have reported a case of olfactory neuroblastoma with immunoreactive for NFP 200-kD and NSE. Immunostaining for GFAP, keratin and S-100 was negative.

In addition, Du et al.¹³ have reported a case of olfactory neuroblastoma immunoreactive for NSE and S-100, but for keratin or desmin. These results suggest

that olfactory neuroblastomas are generally immunoreactive for neurogenin antigens (NFP 200-kD, SY, NSE, S-100, and chromogranin), but not for epithelial antigens (vimentin, keratin, and EMA).

The most noteworthy result in the current study was the presence of immunoreactivity for S-100 protein; S-100 protein positivity was found mostly in peripheral dendritic cells and their cytoplasmic processes extending into the intercellular spaces between tumor nests and vascular stroma.

Choi and Anderson^{14,15)} immunohistochemically examined 12 cases of olfactory neuroblastoma for the presence of the S-100 protein. Elongated tumor cells immunoreactive for S-100 were clearly demonstrated at the margins of the tumor nodules in all cases. Immunoelectron microscopy revealed that these tumor nodules were completely surrounded by a basal lamina and composed of membrane-bound-granule-bearing main cells and elongated S-100 positive margin cells. Thus, our findings are in close agreement with those of Choi and Anderson in several ways.

The S-100 protein was first isolated from bovine brain by Moore¹⁶⁾. Schwann cells in the peripheral nervous system, satellite cells in the sympathetic ganglia, and sustentacular cells of the adrenal medulla are all reactive for S-100 protein^{17,18)}. They are widely dispersed collections of specialized neural crest cells that arise in association with the segmental or collateral autonomic ganglia throughout the body, including the adrenal medulla, the vagal bodies, and the juglotympatic and intercarotid bodies.

Our ultrastructural and immunohistochemical findings strongly suggest that the present tumor, an olfactory neuroblastoma, is actually the neoplastic counterpart of the neuroblast, or is likely of neural crest origin.

CT and MR imaging Characteristics

Previous reports have described the CT and MR imaging characteristics of olfactory neuroblastomas. With the exception of a few isolated cases, all other neuroblastomas have originated high in the nasal cavity, in the region of the cribriform plate.

In the report by Li et al.¹⁹⁾ MR imaging in 5 patients with typical olfactory neuroblastomas was performed. All of these cases of olfactory neuroblastoma originated in the nasal cavity and involved the ethmoid sinus. In 5 cases, the tumors extended to the anterior skull base. Schroth et al.²⁰⁾ reported the MR studies of 15 patients with olfactory neuroblastoma. In all cases the tumors arose in the superior nasal cavity and extended into the ethmoid sinus. To our knowledge, there has been only two cases of this lesion localized to the sphenoid sinus.

Burke et al.³⁾ reviewed eight cases of olfactory neuroblastoma. One of them involved the rare primary presentation of a lesion in the sphenoid sinus-clivus region. In this pre-CT era, pneumoencephalography demonstrated partial opacification of the sphenoid sinus, with a lytic lesion in the posterior dorsum sellae and an extradural mass along the clivus compressing the prepontine cistern. The remaining seven patients had radiograph showing opacification of the nasal cavity as well as ethmoid and maxillary sinuses.

Sarwar⁴⁾ reported the case of a patient with a sellar-parasellar olfactory neuroblastoma visible plain radiographs and tomograms, appearing as a calcified lesion in the sellar and parasellar regions, with slight extension into sphenoid sinus. The olfactory region was normal. Five years later, CT demonstrated a multilobular, partially calcified lesion in the sellar and parasellar regions.

Thus, patient may represent the first reported case of a sellar-parasellar olfactory neuroblastoma demonstrated on MR imaging.

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