Malignant Melanoma Arising From the Sphenoidal Sinus
—Case Report—

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Abstract

Malignant melanomas arising from the sella turcica or sphenoidal sinus with bilateral invasion of the base of the skull or cavernous sinus are extremely rare. Whether the sella turcica or sphenoidal sinus is the site of origin is difficult to determine based on neuroradiological findings. An 83-year-old Japanese female presented with headache as the initial symptom. She suffered rapid progression of bilateral obstruction of the nasal cavity, left nasal bleeding, and bilateral visual field defects. The preoperative diagnosis was pituitary adenoma, metastatic tumor, or malignant paranasal tumor. Biopsy was performed. The histological diagnosis was malignant melanoma. Postoperatively, the tumor progressed rapidly. She suffered several cranial nerve pareses and hypopituitarism. She died within 6 months. Tumors arising from the sphenoidal sinus cause obstruction of the nasal cavity or nasal bleeding first, and then cause cranial nerve pareses by invasion of the cavernous sinus. This sequence of clinical manifestations can be attributed to the anatomical relationships between the sphenoidal sinus, nasal cavity, and cavernous sinus. Differential diagnosis of the origin in the sella turcica or sphenoidal sinus appears to be relatively easy based on further observation of the clinical course and symptoms.

Key words: malignant melanoma, sphenoidal sinus, sella turcica

Introduction

Melanocytes are distinctive cells derived from the neural crest during the embryonic period, and are normally present in the skin, mucous membranes, pia mater, and uvea of humans. Melanocytes are the source of malignant melanomas, but intracranial melanomas, especially melanomas arising in the sella turcica, are rare.3,4,8,14,21 Primary malignant melanomas of the sphenoidal sinus are also rare,22 but may also arise in the nasal cavity and paranasal sinuses, and are difficult to differentiate from primary tumors of the sella turcica based only on neuroradiological findings.

We report a case of primary malignant melanoma arising from the sphenoidal sinus that manifested as a variety of cranial nerve symptoms and endocrinological symptoms.

Case Report

An 83-year-old Japanese female began to have headaches in mid-April 1997. Left nasal obstruction and left nasal bleeding started in early June, but she did not seek treatment. She developed right nasal obstruction, decreased visual acuity in her left eye, and superior temporal visual field defect in mid-June. About a week later she could only discriminate hand movements in front of her eye. She first noted haziness and decreased visual acuity in her right eye in late June. Her right visual acuity rapidly worsened over about 10 days, so she consulted the Department of Ophthalmology. Computed tomography (CT) demonstrated a mass lesion in the sella turcica and the sphenoidal sinus. The patient was then referred to our department.

Neurological examination showed bilateral anosmia, with uncorrectable visual acuity of 0.02 on the right and 0.00 on the left. Ophthalmoscopy revealed mild pale papilla bilaterally. Anisocoria was present
(right pupil 4 mm, left pupil 3 mm), and both the direct and indirect pupillary reflexes were absent. There was no impairment of ocular muscle movement and no ptosis. Sensory disorders were present in the distributions of the 1st and 2nd branches of the left trigeminal nerve, and the left corneal reflex was absent.

Peripheral blood studies showed a red blood cell count of \(344 \times 10^6\) cells/ml, hemoglobin 10.7 g/dl, and hematocrit 31.9%. Blood biochemistry studies were within normal limits. Tumor marker studies revealed no abnormalities in carcinoembryonic antigen, carbohydrate antigens 19-9, 125, and 15-3, squamous cell carcinoma-related antigen, \(\alpha\)-fetoprotein, and human chorionic gonadotropin. Urinalysis and testing for fecal occult blood yielded normal results. Endocrinological studies showed values within the normal range except for a prolactin (PRL) level of 51 ng/ml (normal range 2.5–20 ng/ml) and a thyroid-stimulating hormone (TSH) level of 0.03 mU/ml (normal range 0.23–4.0 mU/ml). TSH-releasing hormone, luteinizing hormone-releasing hormone, growth hormone-releasing hormone, and corticotropin-releasing factor hormone stimulation tests yielded normal results except for no response for TSH and PRL. Abdominal CT, abdominal ultrasonography, and upper and lower gastrointestinal tract endoscopy revealed no abnormal findings. No pigment deposition was observed in the epidermis anywhere in the body or in the oral mucosa or conjunctivae.

Skull radiography demonstrated extensive osteolytic and erosive changes in the sella turcica and the sphenoidal sinuses. CT demonstrated a mass occupying the sella turcica and sphenoidal sinus, with iso–high density mass invading the cavernous sinus bilaterally, with slight enhancement by contrast medium (Fig. 1). Magnetic resonance (MR) imaging showed a tumor with clearly defined boundaries occupying and extending from the sella turcica to the sphenoidal sinus. The tumor had expanded and grown laterally toward both cavernous sinuses, superiorly toward the suprasellar area and the anterior skull base, and posteriorly toward the clivus. We could not detect any normal pituitary gland. \(T_1\)-weighted MR imaging showed the tumor as a high intensity area with slight enhancement by gadolinium (Fig. 2). \(T_2\)-weighted MR imaging showed the tumors as a low intensity area. Cerebral angiography of the bilateral internal carotid arteries revealed lateral compression and narrowing in the \(C_1\) area, and \(A_1\) up. Feeders from the meningo-hypophyseal trunk at the \(C_3\) portion were observed bilaterally, but no tumor stain was detected. There were no feeders from the external carotid arteries.

The preoperative differential diagnosis included pituitary adenoma invading the sphenoidal sinus, metastatic brain tumor, and primary malignant paranasal sinus tumor arising in the sphenoidal si-

![Fig. 1 Preoperative computed tomography scan with contrast medium showing a mass in the sella turcica and sphenoidal sinus.](image)

![Fig. 2 Preoperative magnetic resonance images with gadolinium.](image)
nus or the ethmoidal sinus.

A biopsy procedure was performed through the transnasal approach on the left on July 15. The tumor had extended to the superior turbinate and middle turbinate, and its border was well defined. The nasal mucosa was congested. The bony floor of the sphenoidal sinus was involved by the tumor and was unclear. The tumor ranged from grayish-white to dark red in color, and part was black. The soft tumor contained necrotic tissue and was hemorrhagic. The tumor was removed piecemeal.

Routine histological and immunohistochemical staining of the biopsy specimen showed the small tumor cells had grown in a medullary pattern, and the nuclei contained abundant chromatin and varied greatly in size. Numerous mitotic figures and remarkable cell pleomorphism were observed. Massive necrosis was also present. Large amounts of brown pigment, thought to be melanin, were observed in the cytoplasm. The differential diagnosis was either malignant lymphoma or metastatic cancer, but much of the melanin pigments stained black with Fontana Masson stain, and immunohistochemical staining for HMB-45 was highly positive in the cytoplasm. S-100 protein and vimentin staining were also positive in the cytoplasm. In contrast, staining for cytokeratin, epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), LCA, L26, and UCHL-1 were negative in the tumor cells. The final histological diagnosis was malignant melanoma. The MIB-1-positive rate was 32%, and the proliferation activity of the tumor appeared to be high (Fig. 3).

The patient was elderly and was treated conservatively without adjuvant chemotherapy and radiation therapy. However, left oculomotor nerve paresis, thought to be due to tumor growth and cavernous sinus invasion, occurred in late June. In early August, right abducens nerve paresis developed, and by the middle of August, right oculomotor nerve paresis and left trochlear and abducens nerve pareses had occurred, and the patient was no longer able to move her left eye. Endocrinological symptoms also appeared. Diabetes insipidus was identified on August 30, and antidiuretic hormone supplemental therapy was started. Steroid hormone supplemental therapy was started on September 12, and thyroid hormone supplemental therapy on September 20. MR imaging showed tumor invasion of the upper pharynx and inferior clivus on September 24 (Fig. 4 left). CT revealed invasion of the bilateral orbits, indicating that the tumor was growing rapidly on October 22 (Fig. 4 right). The patient's general condition also deteriorated rapidly, and she died of multiple organ failure on November 4, after a total course of approximately 6 months. An autopsy was not performed.

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Discussion

The rate of occurrence of malignant melanoma in other countries is 4.5 persons per 100,000 population for Caucasians, 0.8 persons per 100,000 for blacks, and 0.38 persons per 100,000 for Japanese. Primary malignant melanoma is not rare in the nasal cavity or the paranasal sinuses, but malignant melanoma of the nasal cavity and paranasal sinuses constitutes a larger proportion of malignant melanomas in Japanese (8.8%) than in Caucasians (0.5–1.7%).

Primary malignant melanoma is more common in the nasal cavity than in the paranasal sinuses, with a ratio of 1:6.4:1. Primary malignant melanoma of the central nervous system comprises only 34 (0.1%) of the 50,260 cases in the Brain Tumor Registry of Japan. Malignant melanoma in the vicinity of the sella turcica is even rarer, with only five cases since 1963. Primary lesions of the sphenoidal sinus accounted for no more than one case, a reticulum cell sarcoma, 0.1% of 908 various malignant tumors. Only one previous case of primary malignant melanoma of the sphenoidal sinus has been reported.

Five cases of primary malignant melanoma of the sella turcica and two of the sphenoidal sinus, including our case, are summarized in Tables 1 and 2. CT of the previous case of primary malignant melanoma of the sphenoidal sinus showed the tumor as isodensity with strong enhancement. In our case, CT revealed iso–high density with slight enhancement. CT findings of primary intracranial malignant melanoma are not always the same, so the diagnosis cannot be based on the CT findings alone. Generally, CT shows high density with homogeneous enhancement with clearly defined boundaries. Our case is an exception.

$T_1$-weighted MR imaging showed the tumor as high intensity in all three cases, and $T_2$-weighted imaging showed low intensity except in the hemorrhagic case. Our case showed slight enhancement as observed on CT. $T_1$-weighted MR imaging visualized the lesion as high intensity with good enhancement by gadolinium, and $T_2$-weighted imaging showed low intensity in many cases of primary intracranial malignant melanoma. The $T_1$ and $T_2$ relaxation times are both shortened by the presence of free radicals, that are paramagnetic, in the melanin inside the malignant melanoma. These findings are important for the diagnosis, except in amelanotic melanomas which do not produce melanin, and also when there is intratumor bleeding.

Cerebral angiography showed evidence of vascular compression and faint tumor staining in the venous phase, but vascular compression and transient vascular blush have been observed in only two cases. Eleven cases of intracranial metastasis from malignant melanoma showed avascularity in seven cases, vascular blush in two cases, and no abnormal findings in the other two. Therefore, the cerebral angiographic findings are also very variable.

The differential diagnosis between malignant melanoma, malignant lymphoma, and metastatic tumor must be determined morphologically based on histological findings. Staining for EMA, GFAP, cytokeratin, LCA, L26, and UCHL-1 were not positive in tumor cells. Fontana-Masson and HMB-45 staining were strongly positive in the cytoplasm. Fontana-Masson and HMB-45 are specific for malignant melanoma, and so are reliable for the differential diagnosis.

Skull radiography demonstrated extensive bone destruction in the sella turcica area on admission in our patient. Baseline hormone studies showed mildly elevated PRL, so pituitary adenoma causing hyperprolactinemia due to PRL-inhibitory factor inflow obstruction was considered. We could exclude drug-induced hyperprolactinemia. Furthermore, metastatic tumor in the vicinity of the sella turcica.
Table 1  Summary of cases of sella turcica malignant melanoma

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Age/ Sex</th>
<th>Initial symptoms</th>
<th>Clinical courses</th>
<th>CT</th>
<th>MR imaging</th>
<th>Angiography</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neilson and Moffat (1963)</td>
<td>62/M</td>
<td>RA, pneumonia (incidental disease)</td>
<td>hypothorituitarism (DI)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Scholts and Sz (1976)</td>
<td>54/M</td>
<td>It visual dist.</td>
<td>headache; bil II, paries;</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Copeland et al. (1980)</td>
<td>37/F</td>
<td>rt visual dist.</td>
<td>hypothorituitarism (DI)</td>
<td>—</td>
<td>—</td>
<td>transient blush</td>
<td>—</td>
</tr>
<tr>
<td>Chappell et al. (1960)</td>
<td>35/F</td>
<td>oogomenorrhea, galectorrhoea, headache</td>
<td>hypothorituitarism (DI)</td>
<td>—</td>
<td>T1: high intensity, T2: low intensity</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Aubin et al. (1997)</td>
<td>47/M</td>
<td></td>
<td>hypothorituitarism (DI)</td>
<td>T1: high intensity, T2: high intensity</td>
<td>intratumoral hemorrhage</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

CT: computed tomography, DI: diabetes insipidus, dist.: disturbance, MR: magnetic resonance, RA: rheumatoid arthritis, T1: T1-weighted image, T2: T2-weighted image, —: unknown data.

Table 2  Summary of cases of sphenoidal sinus malignant melanoma

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Age/ Sex</th>
<th>Initial symptoms</th>
<th>Clinical courses</th>
<th>CT</th>
<th>MR imaging</th>
<th>Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shinbori et al. (1968)</td>
<td>67/F</td>
<td>headache</td>
<td>isodense with good enhancement</td>
<td>—</td>
<td>faint stain</td>
<td></td>
</tr>
<tr>
<td>Present case</td>
<td>83/M</td>
<td>headache</td>
<td>iso-high density with moderate enhancement</td>
<td>T1: high intensity, T2: low intensity</td>
<td>transient blush</td>
<td>—</td>
</tr>
</tbody>
</table>

CT: computed tomography, DI: diabetes insipidus, Gd: gadolinium-diethylenetriaminepenta-acetic acid, MR: magnetic resonance, T1: T1-weighted image, T2: T2-weighted image, —: unknown data.

or the sphenoid sinus was considered as the patient was elderly. However, no abnormal findings were detected by various studies of the entire body. Consequently, metastatic lesion was eliminated. We could not detect any normal pituitary gland by MR imaging. So, the site of origin was difficult to identify as the sella turcica or the sphenoidal sinus based on the neuroradiological studies alone, but some insight into the differential diagnosis can be gained by comparing the clinical manifestations (Tables 1 and 2).

Headache caused by hemorrhage was the initial symptom in one patient, but the initial symptom was visual field disturbance in two patients with primary tumor in the sphenoidal sinus, and endocrinological manifestation in the other patient. Later in the course, hormonal manifestations developed in four of the five patients, particularly diabetes insipidus. Few cranial nerve symptoms were observed other than those involving the optic nerve, except cranial nerve symptoms thought to be due to invasion of the cavernous sinus, but these developed fairly close to the terminal stage. In contrast, the initial symptom was headache in the two patients with the primary lesion in the sphenoidal sinus, including our own. Otorhinolaryngological symptoms had developed, such as nasal obstruction, anosmia, and nasal bleeding, before a month had elapsed. Later, cranial nerve symptoms and endocrinological symptoms had occurred, so that differentiation from pituitary adenoma became difficult. However, the development of various cranial nerve symptoms relatively soon after the initial symptoms seems to be characteristic of cavernous sinus invasion. The cavernous sinus area is anatomically often in contact with the surface of the sphenoidal sinus when mucous membrane loss or the bone thinning or loss has occurred so the tumor can rapidly invade the cavernous sinus area.

Malignant melanoma arising from the ethmoidal sinus should also be considered in the differential diagnosis. Two cases of primary ethmoidal sinus malignant melanoma occurred among 39 cases of malignant melanoma involving the nasal cavity and paranasal sinus, two cases of primary ethmoidal sinus malignant melanoma were included in 43
cases, and two cases in 25 cases. In Japan, five cases of primary ethmoid sinus malignant melanoma were found among 143 cases of malignant melanoma involving the nasal cavity and paranasal sinus. In no case has the tumor invaded the skull base and caused several cranial nerve pareses. Tumors arising from the ethmoid sinus tend to grow and invade into the nasal cavity and maxillary sinus, so whether the tumor has arisen from the sphenoidal sinus or ethmoidal sinus is not easy to differentiate.

The differential points can be summarized as follows. When the tumor arises in the sella turcica area, visual field disturbances or endocrine symptoms often occur as the initial symptoms or in the initial stage. Cranial nerve symptoms are more likely to develop as a result of invasion of the cavernous sinuses. When the tumor arises in the sphenoidal sinus, headache is the most common initial symptom, and nasal bleeding and anosmia are observed in the early stage. Cranial nerve symptoms may develop as a result of invasion of the cavernous sinuses in the early stage.

References

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