Malignant Peripheral Nerve Sheath Tumor in the Anterior Skull Base Associated With Neurofibromatosis Type 1

—Case Report—

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Abstract

A 36-year-old man presented with a tumor in the anterior skull base manifesting as headache and visual disturbance. Neurofibromatosis type 1 (NF-1) was identified in early childhood in the patient, and also in his father. Subtotal excision of the tumor was performed, leaving the portion extending outside of the cranium. The histological diagnosis was malignant peripheral nerve sheath tumor. Local radiotherapy was instituted postoperatively. Facial paralysis and dysphagia appeared 7 months after the first operation. Magnetic resonance imaging revealed new lesions in the lateral ventricle and around the brainstem. These tumors were also subtotally excised, but the patient died 10 months after the first operation. The tumor very likely originated from the meningeal branch of the trigeminal nerve. Treatment of such tumors developing inside the cranium should include the widest resection possible, followed by irradiation of the entire neuraxis including the spinal cord to inhibit dissemination through the cerebrospinal fluid. Treatment should be started as quickly as possible if the tumor is associated with NF-1, because of the poor prognosis associated with this condition.

Key words: malignant peripheral nerve sheath tumor, anterior skull base, neurofibromatosis type 1

Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are malignant tumors developing from cells present in the peripheral nerve tissue, and account for about 10% of all cases of malignant tumors arising from soft tissues.⁶⁾ Most cases of this type of tumor are associated with neurofibromatosis type 1 (NF-1),²⁵⁾ and often develop in deep-seated nerves, such as the ischial nerve and spinal nerves.^{5,6,12)} Intracranial MPNST is extremely rare, with only 24 cases reported to date.^{1-4,8,9,11,13-23,26,27,29)} The tumor originated in the trigeminal nerve or the acoustic nerve in most of these cases. Accordingly, the lesion is generally located mainly in the middle cranial fossa and the cerebellopontine angle. We encountered a case of MPNST associated with NF-1 which was located mainly in the anterior skull base.

Case Report

A 36-year-old man presented with a 4-month history of occasional headache. The headache became worse and his vision deteriorated on the left. He consulted the outpatient clinic of our hospital. Cranial computed tomography (CT) revealed a tumorous lesion located mainly in the anterior skull base and extending bilaterally. His past medical history included the diagnosis of NF-1 in early childhood. His father also had NF-1. He was admitted to the hospital.

Physical findings on admission included multiple café-au-lait spots and neurofibromas on the trunk and all four extremities. Neurological examination revealed left anosmia, reduced field of vision on the left to around 30-cm motus manus, and bilateral papilledema. Preoperative magnetic resonance (MR) imaging revealed a heterogeneously intense mass lesion, about 6 cm in diameter, located mainly in the anterior skull base on the left. The tumor had displaced the left frontal lobe upward and backward, and extended into the parasellar area, inside

Fig. 1 A: Preoperative axial T₁-weighted magnetic resonance (MR) image with gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) showing a mass lesion, about 6 cm in diameter, in the anterior skull base on the left. The lesion was heterogeneously enhanced, and extended contralaterally. B: Preoperative sagittal T₁-weighted MR image with Gd-DTPA showing the tumor displaced the left frontal lobe superiorly and posteriorly. The tumor extended posteriorly towards the sella turcica, and inferiorly into the orbit and ethmoidal sinuses. C: Preoperative coronal computed tomography scan showing the upper wall of the ethmoidal sinuses displaced inferiorly by the tumor, and a bone defect in the inner lateral wall of the orbit.

Fig. 2 Left internal carotid angiograms showing the left anterior cerebral artery deviated to the right and superiorly, and the left middle cerebral artery deviated to the left. Supply came from the frontopolar artery, orbitofrontal artery, and posterior ethmoidal artery. A: anteroposterior view, B: lateral view.

the orbit and into the ethmoidal sinuses (Fig. 1A, B). Preoperative CT revealed the upper wall of the ethmoidal sinuses displaced inferiorly by the tumor, and a bone defect in the inner lateral wall of the orbit (Fig. 1C). Left internal carotid angiography showed supply from the frontopolar artery, orbitofrontal artery, and posterior ethmoidal artery (Fig. 2). Left external carotid angiography showed

no obviously abnormal findings.

Tumor resection was performed via a bilateral frontal craniotomy. The tumor was encapsulated and yellowish brown, elastic and soft, and bled easily on touch. The extra-axial tumor had grown from the anterior skull base as if lifting the frontal lobe. Although the border of the tumor was relatively clear, marked adhesion to the dura of the anterior skull base was noted. The tumor was subtotally excised, leaving the portion extending into the orbit and the ethmoidal sinuses.

Histological examination revealed an intricate palisade alignment of long, narrow cells. Evidence of necrosis was present around these cells (Fig. 3A). Cells with nuclear atypia and mitotic figures were observed (Fig. 3B). Immunohistochemical staining showed the tumor cells included sporadic positive staining for the S-100 protein (Fig. 3C). However, the tumor cells were negative for epithelial membrane antigen, keratin, and glial fibrillary acidic protein (data not shown). The histological diagnosis was MPNST.

Postoperatively, local radiotherapy (60 Gy) was given, mainly to the tumor excision site and the surrounding area. The postoperative course was uneventful and the patient was discharged. Seven months after the first operation, the patient developed left facial paralysis, followed by dysarthria, dysphagia, left abducens nerve paralysis, and right

Fig. 3 Photomicrographs of the surgical specimen. **A:** Fusiform cells are observed in a close palisade alignment, and necrosis is present in the surrounding area. Hematoxylin and eosin stain, $\times 100$. **B:** The cellular borders are obscure and the tumor cells have fusiform or oval nuclei. Mitotic figures are present in the cells. Hematoxylin and eosin stain, $\times 400$. **C:** Immunohistochemical staining shows the tumor cells exhibit uneven and sporadic positive reaction for the S-100 protein (arrows). $\times 400$.

Fig. 4 T₁-weighted magnetic resonance images with gadolinium-diethylenetriaminepenta-acetic acid obtained 7 months after the first operation. **A:** Coronal image showing a mass lesion, about 3 cm in diameter, in the left cerebellopontine angle. **B:** Axial image showing a mass, about 1 cm in diameter, in contact with the left lateral ventricular wall.

hemiparesis. MR imaging revealed a mass, about 3 cm in diameter, in the left cerebellopontine angle and the anterior surface of the cerebellopontine region, and a mass, about 1 cm in diameter, within the left lateral ventricle (Fig. 4). The patient was again admitted to the hospital.

Resection of the tumor was performed via a left suboccipital craniotomy. A tumor adhering to the choroid plexus near the foramen of Luschka and displacing the lower cranial nerves and pons was subtotally excised, except for the portion adhering to the pons. The histological diagnosis was the same as of the first tumor. The symptoms improved postoperatively, but the tumor grew again within a short time, and the patient died 10 months after the first operation. Autopsy was not performed.

Discussion

The origin of the intracranial MPNST in our case was mainly in the anterior skull base but could not be identified precisely from the perioperative findings. Benign peripheral nerve sheath tumor in the anterior skull base may arise from the meningeal branch of the trigeminal nerve, anterior ethmoidal nerve, olfactory tract, or the olfactory bulb.²⁸⁾ In our case, the tumor was assumed to arise from the meningeal branch of the trigeminal nerve, because of the location mainly within the cranium, the mode of bone destruction suggesting progression from inside towards the outside of the skull, marked dural invasion, and displacement of the olfactory nerve upward by the tumor.

MPNSTs are associated with an extremely poor

prognosis. Local recurrence is observed in 54% of cases, distant metastasis to the lungs and bone in 65% of cases, and the 5-year survival rate is 34%.¹²⁾ The treatment is basically aimed at radical resection, including as much of the surrounding normal tissues as possible, followed by adjuvant radiotherapy administered postoperatively. Chemotherapy apparently has no effect.²⁴⁾ Possible dissemination through the cerebrospinal fluid should also be taken into consideration. In our case, cerebrospinal fluid dissemination was suspected based on the fact that the lateral ventricle was opened during the first operation, and also on the postoperative findings of MR imaging and perioperative findings during the second operation. Dissemination was observed near the jugular foramen or around the spinal cord in three of the 24 cases of intracranial MPNST previously reported.^{8,14,27)} Therefore, precautions during the procedure of tumorectomy as well as postoperative irradiation of the entire neuraxis including the spinal cord are recommended.

The tumor was associated with NF-1 in three, including our case, of all the cases of intracranial MPNST.^{21,27)} Compared with cases of MPNST not associated with NF-1, the age of onset tends to be lower in cases of the tumor associated with NF-1 (mean age, 29.4 years with NF-1, 46.5 years without NF-1), and the prognosis is believed to be worse.⁵⁾ Moreover, NF-1 was present in about half of the rare cases of benign peripheral nerve sheath tumor becoming malignant.¹⁰⁾ These results are easily explained if the mechanism underlying the onset of NF-1 is inactivation of the tumor suppressor gene due to a gene defect.⁷⁾ Thus, regular follow up of NF-1 patients and early institution of radical surgery are essential for improved outcome after treatment for MPNST associated with NF-1.

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