

Non-contiguous Meningeal Recurrence of Olfactory Neuroblastoma: A Case Report and Literature Review

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Olfactory neuroblastoma is an uncommon malignant tumor of neural crest origin arising from the olfactory epithelium of the superior nasal cavity. There are some reports of local recurrence or continuous extension along the olfactory epithelium to the central nervous system, but non-contiguous distant meningeal metastasis without local recurrence at the primary site is rare. We report a case of non-contiguous meningeal recurrence of olfactory neuroblastoma presenting as a giant frontal mass. A 66-year-old woman was admitted with a left nasal intranasal localized tumor without cranial extension and gross total removal was achieved. Pathological examination showed olfactory neuroblastoma and radiation therapy was added in a limited region of the removal cavity. Radiological follow-up continued for 10 years and there was no local recurrence. Sixteen years after radiation therapy, the patient found a slight frontal mass gradually growing. Magnetic resonance imaging revealed an enhanced mass lesion of 7 cm in thickness and 9 cm in diameter associated with marked thickness of the frontal bone, intradural cystic mass compressing the bilateral frontal lobe, and no local recurrence. A second operation was performed followed by radiotherapy and we diagnosed non-contiguous meningeal recurrence of metastatic olfactory neuroblastoma. Olfactory neuroblastoma is a locally aggressive tumor. Although metastasis of this tumor has been reported, non-contiguous spread to the dura is rare. Understanding the route of remote metastasis and careful evaluation after primary treatment are needed to avoid misdiagnosis and treatment delays.

Keywords: olfactory neuroblastoma, leptomeninges, recurrence

Introduction

Olfactory neuroblastoma is an uncommon neoplasm that arises from the olfactory epithelium in the nasal cavity near the cribriform plate. It accounts for 2–6% of intranasal tumors and has an incidence of 0.4 per million.^{1–3)} The metastatic behavior

of olfactory neuroblastoma is largely based on small retrospective studies because of the rarity of this tumor.⁴⁾ The incidence of neck metastases at presentation is approximately 5–8%.⁵⁾ The probability of developing subsequent recurrence in neck nodes has been reported to be 20–25%.⁵⁾ Although local recurrence or direct extension along the olfactory epithelium and metastasis to the central nervous system has been reported, non-contiguous meningeal metastasis is quite rare.^{6,7)} To our knowledge, there are only 16 cases in 4 reports of remote leptomeningeal metastasis of olfactory neuroblastoma. We report a case of non-contiguous meningeal metastasis of olfactory neuroblastoma without local recurrence at the primary site presenting with a giant frontal mass and discuss clinical characteristics with a literature review.

Case Report

A 66-year-old woman felt a left nasal obstruction and was diagnosed with a nasal olfactory tumor in the Department of otolaryngology. The lesion was removed and pathological examination showed olfactory neuroblastoma. Radiological examination demonstrated that the lesion did not extend into the intracranial and skull base and that it was limited to the nasal cavity (Figs. 1A and 1B). Intraoperative findings demonstrated that tumor limited intranasal cavity and did not extend to skull base bone and dura. Intranasal tumor was completely removed at the initial surgery. Radiation therapy was added in the limited region of the removal cavity. Irradiation area did not include the skull base bone and dura. Radiological follow-up continued for 10 years and there was no local recurrence. However, the patient found a slight frontal mass 16 years after radiation therapy and the frontal lesion gradually grew. She was admitted to our department with a complaint of loss of motivation and enlargement of the frontal swelling mass (Fig. 2A). Computed tomography demonstrated a tumor mass lesion of 7 cm in thickness and 9 cm in diameter associated with marked thickness of the frontal bone and intradural cystic mass compressing the bilateral frontal lobe (Fig. 2B). Magnetic resonance image revealed an enhanced mass of the frontal lesion including the cystic walls and high vascularity associated with marked brain edema (Figs. 2C and 2D). The superior sagittal sinus was occluded by the tumor invasion (Fig. 2D). She also had an asymptomatic parietal mass lesion, which was thought to be meningioma because the lesion was homogeneously enhanced round shape mass without any change in size and shape. The differential diagnosis of the frontal mass lesion was multiple meningioma, bone tumor,

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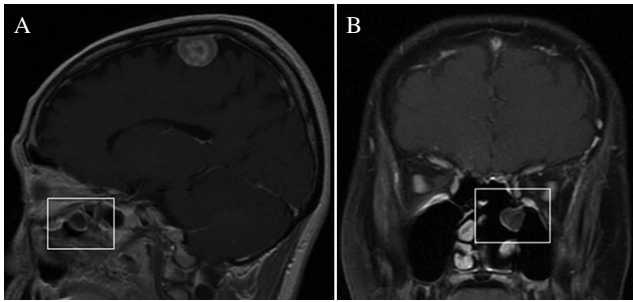


Fig. 1 Magnetic resonance imaging showed intranasal limited tumor mass without the anterior skull base invasion at initial treatment [T₁-weighted images. (A); sagittal view, (B); coronal view, white square].

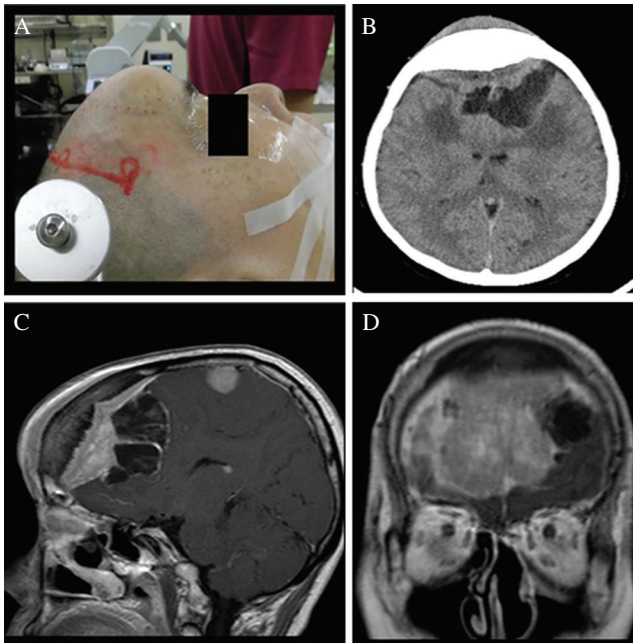


Fig. 2 Preoperative photograph of the lateral view at the remote meningeal recurrence shows a frontal swelling mass (A). Computed tomography demonstrated a tumor mass lesion of 7 cm in thickness and 9 cm in diameter associated with marked thickness of the frontal bone and intradural cystic mass compressing the bilateral frontal lobe with brain edema (B). Magnetic resonance imaging revealed an enhanced mass of the frontal lesion including the cystic walls in the subcutaneous layer, frontal bone, and dura matter protrusive to the bilateral frontal lobe [T₁-weighted images. (C); sagittal view, (D); coronal view].

and remote meningeal recurrence of the nasal olfactory neuroblastoma. Otolaryngological examination showed no local recurrence of the treated nasal lesion. Systemic evaluation on enhanced computed tomography showed no lymphatic and bony recurrence and metastatic lesion. Gross total removal of the frontal mass was achieved. The lesion originated from the frontal convexity dura matter, which extended to the frontal bone and bilateral frontal lobe. Bony mass invaded into the subcutaneous layer with high vascularity. A dural lesion extended to the superior sagittal sinus, was occlusive, and protruded the frontal lobe with multiple cysts. The subcutaneous lesion and thickened bone mass were totally removed. The invasive lesion into the dura and cystic mass were detached

from the frontal lobe and resected from the anterior superior sagittal sinus. The frontal dural defect was repaired with artificial dura and the frontal bone was repaired with a titanium plate. Pathological examination revealed metastatic olfactory neuroblastoma that was markedly immunopositive for synaptophysin and neuron-specific enolase in tumor cells (Fig. 3). The mib-1 labelling index was 20%. Her consciousness level and willingness loss gradually recovered after the surgery. Radiation therapy of a total of 50.4 Gy was added for the frontal skull base around the removal cavity. She was discharged without neurological deficit after radiation therapy.

Discussion

Because of the aggressive nature and high recurrence rate of olfactory neuroblastoma, adjuvant radiotherapy and chemotherapy have evolved and could increase the overall and disease-free survival rates.^{8,9)} Banuchi et al.⁴⁾ reported that the overall survival for all patients was 85% at 5 years and 75% at 10 years from their retrospective analysis of 57 cases. The current understanding of the metastatic behavior of nasal olfactory neuroblastoma is largely based on small retrospective studies because of the rarity of this tumor. Systemic metastases occur in 10–30% of patients, usually by

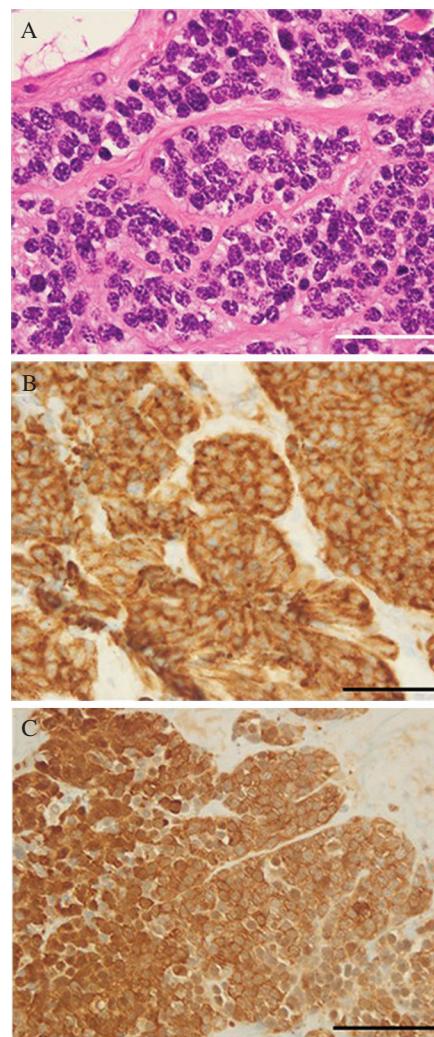


Fig. 3 Pathological examination revealed metastatic olfactory neuroblastoma [Hematoxylin and eosin staining in (A), bar; 40 µm]. Immunohistochemical staining of synaptophysin (B) and neuron-specific enolase (C) were markedly immunopositive in tumor cells (bar; 40 µm).

hematogenous and lymphatic spread,^{10,11} and distal central nervous system metastasis from leptomeningeal dissemination is an extremely rare sequela with a grave prognosis.¹² The incidence of neck metastases at presentation is approximately 5–8%.⁵ However, the probability of developing subsequent recurrence in neck nodes has been reported to be 20–25%.⁵ Similarly, the incidence of distant metastases at presentation is about 7%.^{13,14} The cumulative incidence of distant metastasis was 39% at a median time of 40 months. Patients who presented with Kadish stage C or D had a significantly increased risk of distant failure compared with those at stage A or B.⁴

Distant non-contiguous intracranial metastasis of nasal olfactory neuroblastoma is rare and only 16 cases has been reported. Jiang et al.⁷ reported 10 cases of distant non-contiguous olfactory neuroblastoma. All 10 patients were treated initially with craniofacial resection followed by radiation. Gross total resection was achieved in eight patients. The median time to dural metastasis was 73.0 months from the time of primary tumor resection and the median overall survival was 133.9 months. Nine patients first manifested with dural metastasis in the peri-Sylvian region. One patient presented with bilateral peri-Sylvian dural-based lesions. One patient demonstrated additional lesions along the anterior third of the falx. Five patients developed additional dural-based lesions.

Kim et al.⁶ reported a case of remote recurrence in the parietal convexity mimicking a meningioma, the primary site of which was in the cribriform plate and ethmoid sinus with intracranial extension. The metastatic lesion was located in the parietal meninges, not in the peri-Sylvian area with dural tail sign. They discussed that dissemination of tumor cells occurs mainly by arterial circulation.¹⁵ Sgouros and Walsh¹⁶ found a relationship between dural metastasis and the external carotid artery. In addition, retrograde dissemination through the venous system without valve or lymphatic circulation can result in metastasis.¹⁵ Several theories described the pathophysiologic mechanism of distant dural invasion. Alternatively, an outward extension of an underlying cortical-based metastatic lesion can directly infiltrate overlying dura.¹⁷ One case report hypothesized that tumor cells may gain entry through the ependymal epithelium into

the cerebral spinal fluid (CSF).¹¹ This study showed dissemination of metastatic tumor cells preferentially target large CSF cisterns, including lumbar and pontine cisterns, with the most dependent region, the cauda equina, the most frequent site of metastasis of all spinal cord lesions. Despite the risk of tumor cells gaining access into the subarachnoid space during surgery, tumors within the cistern and gravity-dependent lumbar CSF regions were not observed.^{7,11}

In our case, the metastatic lesion was located in the frontal convexity dura matter, which was associated with no local nasal recurrence and no continuous extension of the nasal lesion. The frontal mass invaded into the frontal bone and subcutaneous layer with marked enhancement and another enhanced mass in the remote parietal convexity. Additionally, the primary nasal site was classified into Kadish stage A at initial treatment and no local recurrence was observed for 16 years. Therefore, we considered this lesion as a multiple meningioma. However, the dural lesion had a thickened nodular shape with multiple cystic components; a rare case of remote recurrence of olfactory neuroblastoma was considered and the nasal primary lesion was evaluated repeatedly in the Department of Otolaryngology. There was no local recurrence. A remote intracranial metastasis was diagnosed at a maximum of 84 months in previous reports. Our case had the longest interval from initial treatment to detection (Table 1). There was a possibility that the lesion was in a state of rest of cell cycle after the initial treatment. Mechanism of long term resting state is unclear in brain tumors.¹⁸ Recent report shows that Notch and WNT signaling pathway relates to cell cycle and re-activation of proliferation cycle in meningioma and astrocytoma.¹⁸ Expression of these signaling factors might contribute to predict future recurrence and be useful as a marker of cell proliferation. Mechanism of remote metastasis is also unclear. Dural metastasis due to direct invasion from intranasal lesion to skull base cannot explain our case. Some hypotheses have been reported that dissemination of tumors cells through arterial circulation and retrograde dissemination through the venous system might occur remote metastasis.^{15,16} Subcutaneous extension was also rare compared with that of previous cases (Table 1). The frontal convexity dura was the origin of the metastatic

Table 1 Distant non-contiguous intracranial metastasis of nasal olfactory neuroblastoma

Author	Journal, Year	Cases	Age	Location	Interval from initial treatment	Initial treatment	Extension
Chamberlain ¹⁹	Cancer, 2002	3	51, 56, 47	Convx; 2, Base; 1	51 M, 27 M, 84 M	GTRx2, STR1 + radiation + chemotherapy	Dural x3, subcutaneous x1, spine x1
Sivakumar et al. ²⁰	Surg Neurol Int, 2015	2	48, 48	Convx; 2	6 Y, 6 Y	Craiofacial resection + radiation	Dural x3, spine x2
Jiang ⁷	J Neurooncol, 2016	10	-	Sylvian; 9, Falx; 1	73.03 M (median)	Craniofacial resection	Dural x10
Kim ⁶	World Neurosurg, 2016	1	56	Convx; 1	5 Y	GTR + radiation	Dural
Present case	-	1	66	Convx; 1	16 Y	Endoscopic total resection	Dural, subcutaneous

Convx: convex, GTR: gross total removal, M: month, STR: sutotal removal, Y: year.

lesion in our case. There was no direct invasion into the frontal base from the nasal primary lesion and no intracranial operative procedure was performed at the primary resection. We hypothesized that dural migration of tumor cells through arterial circulation might cause non-contiguous metastasis and the tumor aggressively grew extensively to both the intradural side and trans-osseous subcutaneous side.

We experienced a rare case of non-contiguous remote meningeal metastasis of olfactory neuroblastoma without local recurrence of the primary lesion which presented with a giant frontal mass lesion 16 years after the treatment of the initial nasal localized lesion.

Conflicts of Interest Disclosure

We have no potential conflict of interest.

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