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Case Report

Olfactory neuroblastoma followed by emergency surgery for symptomatic intradural spinal metastasis: A case report

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Abstract

Background: Olfactory neuroblastoma (ONB) is a rare, aggressive tumor of the nasal cavity. It may invade the paranasal cavities and anterior skull base locally but may also metastasize to the cervical lymph nodes, lungs, or distant central nervous system.

Case Description: Here, we report a case of ONB in which emergency surgery was performed for intradural spinal metastasis (ISM). The patient was a 52-year-old male who underwent surgery for ONB. The tumor extended from the nasal cavity to the intracranial space and was resected completely. After radiotherapy (60 Gy), the patient was discharged without any neurological deficit except anosmia. Seven months after the surgery, he consulted our department because of progressive tetraparesis. Cervical magnetic resonance imaging demonstrated an intradural spinal mass involving C5–T2 and necessitating emergency surgery. The tumor was resected subtotally followed by 58 Gy whole-spine irradiation. The patient's neurological symptoms improved, however, paralysis of the right upper and both the lower limbs remained. During the 4 months between the spinal surgery and his death, there was no further motor deterioration in any of his four extremities.

Conclusion: This case demonstrates the need to be aware of potential ISM in the follow-up of patients with ONB. The early detection of ISM by spinal MRI is crucial to ensuring good palliative care.

Key Words: Myelopathy, olfactory neuroblastoma, spinal metastasis, surgery

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INTRODUCTION

Olfactory neuroblastoma (ONB) is a rare malignant intranasal neoplasm that originates from the neural crest cells of the olfactory epithelium.[3,4,19] The tumor is locally aggressive and local recurrence is common. Intracranial recurrence is in most cases limited to the cribriform plate and/or frontal regions.[3,4] Between 10 and 30% of the patients with ONB develop metastases, typically in the cervical lymph nodes[3] but also in the lungs, viscera, long bones, pelvis, and breast.[4,19,20] Although ONB is rare, 15 cases of intradural spinal metastasis (ISM) from ONB have been reported.[1,4,5,9,12,14-18,21-24,26] Here, we report a recent case in which a patient, previously operated on for ONB, underwent emergency surgery for progressive

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paralysis due to ISM. This case and the accompanying literature review demonstrate the importance of proper long-term postoperative management of patients with ONB.

CASE REPORT

A 52-year-old man complained of nasal stuffiness along with bleeding, headache, and vomiting. He was referred to our department after magnetic resonance imaging (MRI) showed an enormous mass occupying the nasal and paranasal cavities and extending into the bilateral frontal base [Figure 1a and b]. No neurological deficit other than anosmia was identified. The tumor spread beyond the nasal cavity and paranasal sinuses, and was therefore classified as stage C based on the modified Kadish clinical staging system [Table 1a].[13] Total removal of the tumor was achieved surgically, using a transnasal approach in combination with a bilateral front basal craniotomy [Figure 1c and d]. The dura along the anterior skull base was opened partially and the cranial base was reconstructed using the pericranial flap. Histological examination of the tumor demonstrated proliferating tumor cells with large, oval nuclei containing prominent nucleoli. Scattered necrotic changes, nuclear fission, and Homer–Wright rosettes were identified. These findings were consistent with Hyams grade III ONB [Table 1b].[6] No neurological deficit other than olfactory analgesia was observed after surgery, however, the patient suffered from meningitis caused by cerebrospinal fluid rhinorrhea that developed 1 week postoperatively. Because complete eradication of the rhinorrhea and meningitis required 9 weeks of treatment, radiation therapy was started 10 weeks after the surgery. Large-field irradiation of the resected area, from the nasal cavity to the frontal lobe, was administered with a total of 60 Gy in 30 fractions. The patient was discharged 17 weeks after the surgery and was followed-up on an outpatient basis. At the time of discharge, whole-body enhanced computed tomography (CT) revealed no apparent distal metastasis or tumor recurrence.

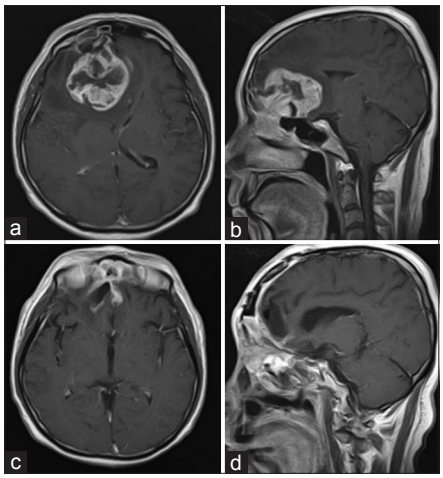

Figure 1: Axial (a) and sagittal (b) T1-weighted Gd-enhanced magnetic resonance imaging (MRI) on admission, showing a contrast-enhancing sinonasal mass with intracranial extension through the cribriform plate into the anterior cranial fossa. Postoperative axial (c) and sagittal (d) T1-weighted Gd-enhanced MRI demonstrating complete removal of the sinonasal and intracranial tumor

At 24 weeks postoperatively, the patient noted numbness in both upper limbs, which gradually worsened. He was readmitted 25 weeks after the surgery because of rapidly deteriorating symptoms. Neurological findings on readmission revealed tetraparesis, hypesthesia, and hypoalgesia below C6, hyperreflexia of both legs, and urinary incontinence. CT and MRI revealed an intradural lesion compressing the spinal cord along its right ventral aspect at C5 through T2 [Figure 2a-d]; MRI of the head showed no evidence of tumor recurrence. In view of the diffuse nature of the disease, it was decided to

Table 1: Clinical staging (a) and grading (b) of olfactory neuroblastoma based on the modified Kadish staging system and Hyams' grading system

Stage	Extent of tumour
A	Tumour confined to the nasal cavity
B	Tumour involves the nasal cavity plus one or more paranasal sinuses
C	Extension of tumour beyond the sinonasal cavitiesand into paranasal sinuses. Involvement of cribriform lamina, orbit, skull-base, or intracranial cavity
D	Cervical lymph node or neck involvement or distant metastasis

Microscopic features	Grade I	Grade II	Grade III	Grade IV
Pleomorphism	−	+	++	+++
Lobular architecture	+	+	+/−	+/−
Neurofibrillary matrix	+++		+/−	−
Rosettes	+	+	+/−	+/−
Mitoses	−	−	+	+++
Necrosis	−	−	+	+++

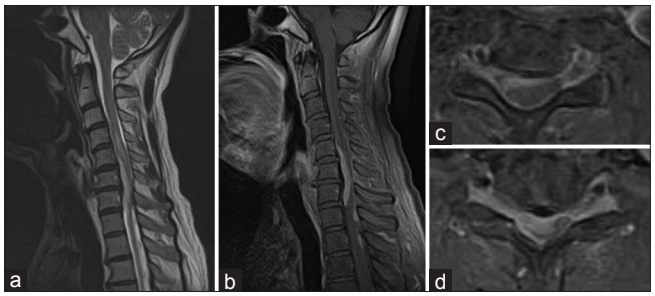

Figure 2: Magnetic resonance imaging on second admission. The T2-weighted images (WI) (a) and Gd-enhanced T1-WI (b) sagittal images show multiple intradural lesions between C3 and Th4. Gd-enhanced axial T1-WI images reveal compression of the spinal cord along its right ventral aspect at C4/5 (c) and C5/6 (d)

surgically relieve the compression by the tumor to avoid complete tetraplegia. A laminectomy from C4 to T3 was performed. Intraoperative findings confirmed the absence of tumor in the epidural space. However, under the arachnoid membrane, the tumor compressed the spinal cord along its right ventral aspect. Because the tumor adhered to the spinal surface and was entangled in several nerve roots, it was removed but not completely. A dural plasty was then performed with a Gore-Tex® membrane to avoid restriction of the subdural space. The tumor was histologically diagnosed as ONB, consistent with the first operation [Figure 3a and b]. After surgery, his urinary incontinence promptly improved. Paralysis of the right upper and both lower limbs remained but seemed to be improving. Residual tumor was seen on MRI performed 1 week after the surgery but the spinal cord was well decompressed [Figure 4a-d]. Whole-spine irradiation of 58 Gy in 29-Gy fractions was started 1 week postoperatively. MRI after irradiation no longer revealed residual spinal tumor, but shortly after spinal irradiation, the patient became progressively lethargic. Brain MRI showed multiple leptomeningeal enhanced lesions. General malaise and anorexia followed and the patient developed bilateral pneumonia, which caused his death 16 weeks after the surgery for ISM and 41 weeks after the first operation. During the time before his death, there had been no further deterioration in the motor weakness of his four extremities.

DISCUSSION

Approximately 2% of all sinonasal tract tumors are ONBs, corresponding to an incidence of approximately 0.4 per million population.[8,22] ONB may occur at any age (2–94 years), with a bimodal age distribution in the second and sixth decades of life and without a predilection for males vs. females.[21] The tumors most commonly cause unilateral nasal obstruction (70%) and epistaxis (50%); less common signs and symptoms include headache, excessive lacrimation, rhinorrhea, and anosmia.[3,4,19] The tumor typically arises from the olfactory epithelium and then invades locally, within the nasal cavity, concurrent with its spread through the cribriform plate into the cranial cavity, resulting in a dumbbell-shaped tumor.[3,4,19] The staging system proposed by Kadish *et al*. in 1976 is still commonly used[8] but it has been criticized for its lack of prognostic value and because it does not include metastatic spread. The modified Kadish staging system adds a fourth stage for patients with nodal or distant metastases [Table 1a].[13] ONB is also separated into four grades based on the degree of histological differentiation [Table 1b].[6] An analysis of the factors influencing survival and prognosis in patients with ONB showed that the most important factor influencing outcome is the extent of disease at diagnosis. Jethanamest *et al*. reported that survival at 10 years correlated with extent of disease according to the modified Kadish staging system (83, 49, 39, and 13% for stages A, B, C, and D, respectively).[7] In addition, the two recognized forms of ONB, low and high-Hyams grade, differ in their natural histories and outcome, and are regarded as distinct entities. Patients who have undergone tumor resection for high-grade ONB mainly develop leptomeningeal metastasis whereas patients with low-grade ONB typically experience late locoregional recurrence.[11] After a median follow-up of 9.6 years, the median disease-free survival (DFS) and overall survival (OS) were 5.4 and 20.5 years in patients with resected low-grade ONB and 1.5 and 2.5 years for those with high-grade ONB, respectively.[11]

Complete surgical resection of the tumor followed by radiation therapy is currently recognized as the optimal treatment for ONB. Although an effective routine therapeutic regimen has not been established,[2,10] the addition of chemotherapy, using cisplatin, etoposide, adriamycin, vincristine, cyclophosphamide, or temozolomide is recommended for patients with recurrent or metastatic tumors.[1,25] Hyams grade is indicative of both the prognosis and the response to chemotherapy.[3,16] Among patients with ISM, long-term survival after chemotherapy administered in combination with laminectomy or radiation has been

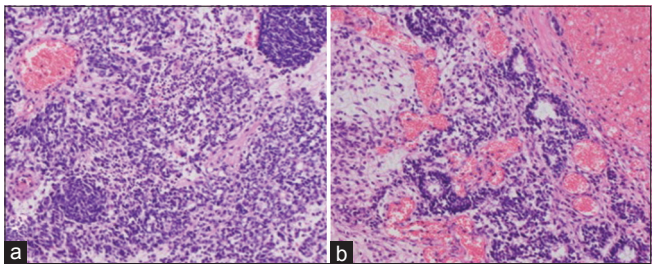

Figure 3: Photomicrographs of the spinal tumor. The hematoxylin and eosin-stained sections show tumor cells predominantly arranged in a densely growing pattern, scattered necrotic changes, nuclear fission, and Homer–Wright rosettes (a: ×100, b: ×200). These findings are consistent with Hyams grade 3 olfactory neuroblastoma and with the pathological findings of the first surgery

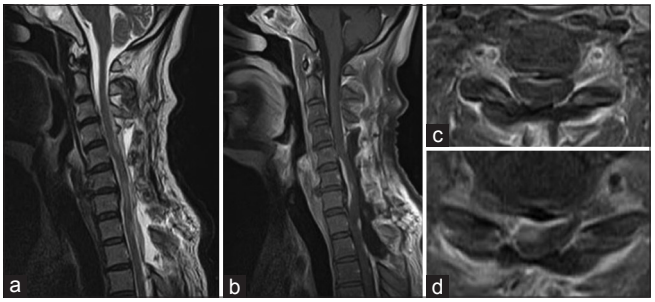

Figure 4: Magnetic resonance imaging performed 1 week after the surgery. The T2-weighted images (WI) (a) and Gd-enhanced T1-WI (b) sagittal images demonstrate residual tumor. Gd-enhanced T1-WI axial images at the level of C4/5 (c) and C5/6 (d) show the decreased compression of the spinal cord

Table 2: Reported cases of olfactory neuroblastoma with spinal metastasis

Author (year)	Age (years)/ sex	Primary tumor			Spinal metastasis				Prognosis after presentatin (months)
		mKS	HG	Treatment	level	Metastatic latency (months)	symptom	Treatment	
Riemenschneider *et al*. (1958)	67/M	-	-	RT	Lumbar, Cauda equina	5	no	-	6
Daly *et al*. (1980)	47/M	C	-	RT	Lumbar	16	-	Laminectomy + RT	21
Carpentier *et al*. (1986)	75/F	C	IV	RT	Cauda equina	12	Sensory dist in LE	RT+dexamethasone	24
Willen *et al*. (1986)	20/F	C	-	Total resection +RT+chemotherapy	Cervical	1	Sensory dist in UE	RT+chemotherapy	4
Ranjan *et al*.(1986)	56/M	A	-	Total resection + RT	Thoracic	48	Sensory dist in LE	Laminectomy	-
Perkkio *et al*. (1991)	5/F	A	-	Total resection	Lumbar, Cauda equina	1	Sensory dist in LE	RT+chemotherapy	14m
Louboutin *et al*. (1994)	76/F	C	-	RT	Lumbar, Cauda equina	6	Sensory dist in LE	RT+chemotherapy	9
Tsuchiya *et al*. (2000)	35/M	C	II	Total resection	Thoracic	8	no	RT	15
Murakami *et al*. (2005)	37/M	C	II	Total resection	Cervical, Thoracic	36	no	Laminectomy + RT	96
Mori *et al*. (2007)	49/M	C	III	Total resection	Lumbar, Cauda equina	180	Lumbago	Laminectomy + RT	-
Arnold *et al*. (2009)	64/M	C	II-III	Total resection + RT	Thoracic	132	Hand clumsiness	Laminectomy + RT+ chemotherapy	>156
Rao et al. (2011)	59/M	C	II-III	Total resection + RT	Cervical, Thoracic, Lumbar	216	Hand clumsiness	Laminectomy + chemotherapy	>230
Tripathy *et al*. (2012)	27/M	C	II	Total resection	Thoracic, Lumbar	12	Paraparesis	Laminectomy + chemotherapy	>18
Shirzadi *et al*. (2013)	54/M	C	-	Total resection + RT	Thoracic	156	Sensory dist in LE	Laminectomy + chemotherapy	192
Sivakumar *et al*. (2015)	48/F	D	-	Total resection +RT	Thoracic, Lumbar	72	no	Laminectomy+ chemotherapy	>108
Present case	52/M	C	III	Total resection +RT	Cervical, Thoracic	6	Tetraparesis	Laminectomy + RT	10

RT: radiation therapy, mKS: modified Kadish Stage, HG: Hyams grade, UE: upper extremities, LE: lower extremities

reported [Table 2].[1,8,21-23] Despite the small number of published cases and the lack of a consensus in opinion, chemotherapy might have been an option in our patient who had modified Kadish C and Hyams grade III disease.

Motor weakness did not progress in our patient between spinal surgery and his death. However, ISM was not detected until it caused neurological symptoms. Thus, microsurgical resection of ISM should be considered in selected cases. Patients with rapidly worsening neurological deficits, no evidence of widespread organ metastasis, and a life expectancy of at least a few months should be considered for tumor resection.

Although ONB is a rare malignant tumor, 15 cases of associated ISM have been reported [Table 2],[1,4,5,9,12,14-18,21-24,26] with leptomeningeal dissemination recognized especially in high-grade ONB.[9,11,22] Although ISM has been reported as a rare pathophysiology of ONB patients,[9,17,21,22] these observations highlight the need for increased awareness of it in the postoperative follow-up of ONB patients to help in an earlier recognition of disease spread. In these patients with early-stage ISM, better palliation without spinal surgery may be achieved by spinal irradiation. However, in some patients, ISM was first detected more than 10 years after treatment of the primary ONB and in patients with modified Kadish A tumors.[15,16] Accordingly, ONB patients should be observed carefully for longer than 10 years postoperatively, even if the primary lesion was confined to the nasal cavity or paranasal sinus.[17]

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Conflicts of interest
There are no conflicts of interest.

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