

## Case Report

# A rare spine metastasis from an invasive esthesioneuroblastoma: a case report

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**Abstract:** A 66-year-old male patient presented with repeated epistaxis and sustaining nasal congestion was diagnosed with an ENB (Kadish grade C) after a nasal neoplasm biopsy in Oct 10, 2014. As an unresectable tumor assessed by CT scan, the patient received radiotherapy with prescribed dose of 40 Gy/20 f and one course of chemotherapy of VP-16 and cisplatin from Nov 2<sup>nd</sup>, 2014 to Sep 5<sup>th</sup>, 2014. However, he refused further treatment due to the release of symptom. Then disease progressed rapidly and the patient died of lung metastasis in May 27<sup>th</sup>, 2015. In Kadish grade C, 5 Year survival of ENB patient was 41-47%. The uniqueness of this case was after active chemoradiotherapy the patient died in 8 months since he was diagnosed.

**Keywords:** Esthesioneuroblastoma, spine metastasis, chemoradiotherapy

### Introduction

Esthesioneuroblastoma (ENB), also called olfactory neuroblastoma, is a rare malignant neoplasm arising from the olfactory epithelium of neural crest origin [1]. It always located in the superior nasal cavity in close proximity to the cribriform plate. Since the first description of ENB by Berger and Luc in 1924, less than 2,000 cases have been reported throughout the world. Because of its relative rarity, the medical literature that reporting ENB is limited to small, retrospective, single institution reports or case reports. Metastatic ENB to spine is extremely rare, with less than 20 cases reported worldwide [2] (**Table 1**). We present a male patient with widespread spinal metastases together with subcutaneous and anterior mediastinum metastasis, which occurred within 3 month after radiotherapy to the primary neoplasm, with no recurrence at the primary site.

### Case presentation

A 66-year-old man presented with repeated epistaxis and sustaining nasal congestion was

diagnosed with an ENB (Kadish grade C) after a nasal neoplasm biopsy in Oct 10, 2014 (**Figure 1A-C**). As an unresectable tumor assessed by MRI scan (**Figure 1D**), the patient received radiotherapy with prescribed dose of 40 Gy/20 f and one course of chemotherapy of VP-16 and cisplatin from 2014-11-02 to 2014-12-05. However, he refused further treatment due to the release of symptom. Then, disease progressed rapidly. In early February of 2015, he felt a pain and weakness in the right leg. On examination, decreased muscle strength was found on right lower extremity at grade 2 without paresthesia. Besides, there was a smooth, firm, mild tender skin swelling which measured 3x4 cm on lower right abdomen. A MR and CT scan identified multiple metastases in spine and the tumor also vigorously invaded musculi psoas major and spinal nerves (**Figure 2A-C**). The CT scan also demonstrated that a subcutaneous metastatic tumor and asymptomatic metastasis at anterior mediastinum (**Figure 2D-E**). Since March 9<sup>th</sup>, 2015, the patient received concurrent chemoradiotherapy. A total dose of 30 Gy/10 f was delivered to the lumbar vertebrae that were most invaded by the

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**Table 1.** Reported cases of ENB that metastasized to spine

Published Year	Metastatic sites	Reference
1958	Lumbar spine, cauda equine	[3]
1977	(Two patients) spinal cord	[4]
1979	Spinal cord	[5]
1980	Lumbar spine	[6]
1983	Spinal cord (epidural spine)	[7]
1986	Cauda equina (found at autopsy)	[8]
1986	Parasagittal cervical spinal cord	[9]
1991	Cauda equine	[10]
1993	Spinal cord (epidural spine)	[11]
1994	Cauda equina (leptomeningeal carcinomatosis)	[12]
2000	T5, T8	[13]
2002	Thoracic vertebrae	[14]
2002	T8 subarachnoid nodule; Multiple subarachnoid Nodules	[15]
2003	Intramedullary spinal cord (unknown level)	[16]
2003	T4, T5, T8 (on bone scan)	[17]
2005	Subdural C3-C7, L2-L4 (meningeal spread)	[18]
2006	Lumbar cord, cauda equine	[19]
2007	Thoracic and lumbar vertebrae, treated with RT	[20]
2007	Vertebral canal; cauda equina and filum terminale	[21]
2009	Thoracic intradural and extradural space	[22]
2011	C4-T1	[23]
2013	C5-6, T7-8	[2]
2015	Mutiple levels	[24]

tumor, while the chemotherapy was one course of paclitaxel liposome at the dose of 135 mg/m<sup>2</sup>. After this treatment, the subcutaneous mass disappeared and the pain in right leg was relieved. There was a remarkable improvement in neurological status of the right lower limbs, and patient was ambulatory within 2 weeks after radiotherapy. Unfortunately, liver function impairment (ALT: 235 µ/L, AST: 89 µ/L) occurred to him and delayed the subsequent chemotherapy and radiotherapy. Lung metastasis together with bilateral pleural effusions developed soon in April, 2015 (**Figure 3**). Disease progressed rapidly and patient died of lung metastasis on May 27<sup>th</sup>, 2015.

### Discussion

Esthesioneuroblastoma accounts for 2% of all intranasal tumors with an incidence of 0.4 cases per a million people [25]. Esthesioneuroblastoma can occur at any time, with peak occurrence reported in the second and sixth decade of life [14]. The tumors most commonly cause unilateral nasal obstruction (70%) and

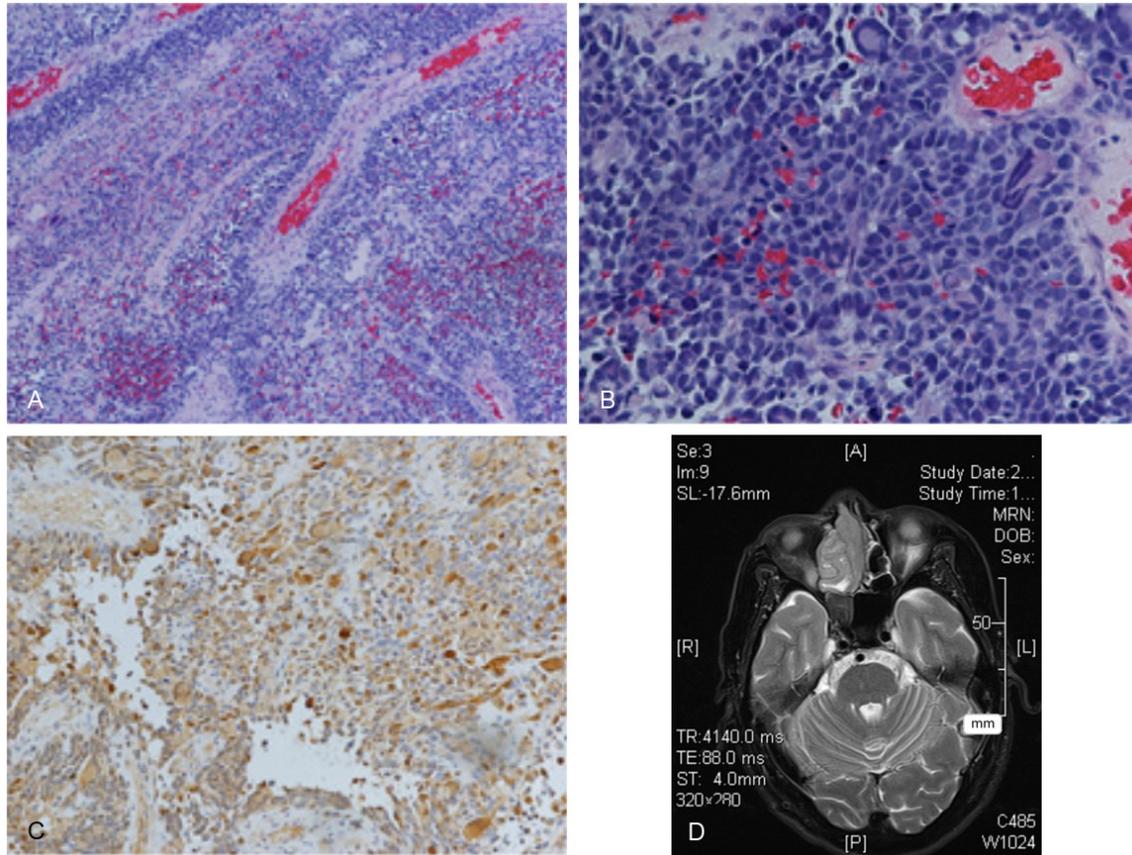
epistaxis (50%); less common signs and symptoms include headache, excessive lacrimation, rhinorrhea, and anosmia. The staging system proposed by Kadish *et al.* in 1976 [26] is still commonly used and modified by adds a fourth stage for patients with nodal or distant metastases [27]. ENB is also separated into four histological grades based on the degree of histological differentiation.

ENB shows varying biological activity, ranging from indolent growth to a highly aggressive neoplasm. The overall incidence of cervical nodal metas-

tasis reported in several large series ranges from 5 to over 30%. Many authors commented that, while most often occurring in the first 5 years, nodal metastases can develop over a very protracted time course. Distant metastasis occurs in poorly differentiated diseases at the rate of almost 8% with sites involved including lung, liver, eye, parotid, central nervous system (CNS), bone, adrenal gland, spleen, scalp, breast, ovary, aorta [28, 29].

Patients with ENB can achieve favorable long-term survival, even if disease is locally advanced. An analysis of the factors influencing survival and prognosis in patients with ENB 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 (stages A, B, C, and D, respectively) [30]. Patients who have undergone tumor resection for high-grade ENB mainly develop leptomeningeal metastasis whereas patients with low-grade ENB typically experience late locoregion-

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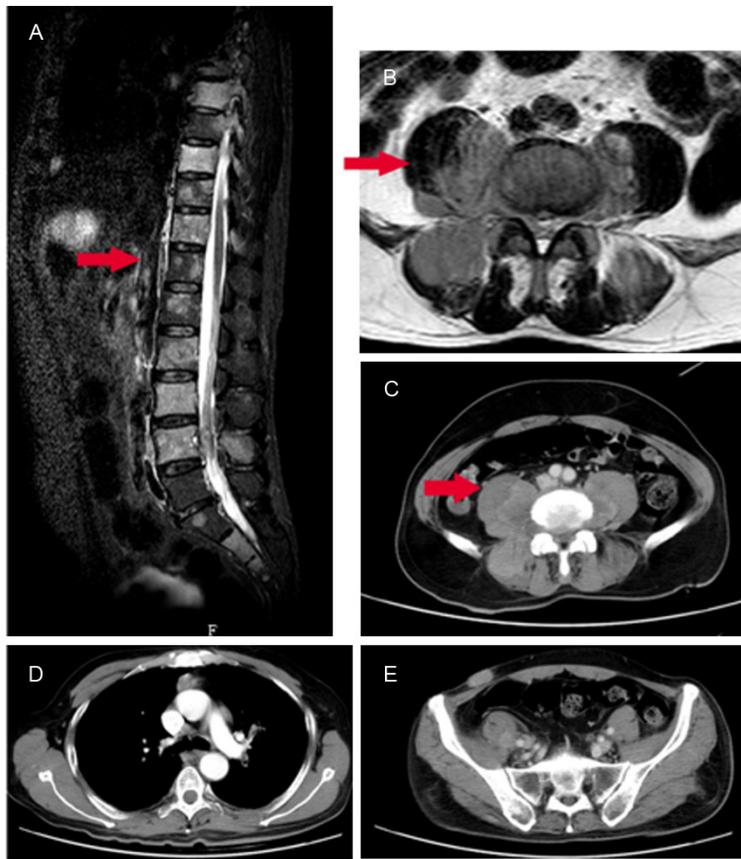
**Figure 1.** Pathological and MR manifestation of the primary tumor. (A) Low-powered photomicrograph showing proliferation of islands and cords composed of small cells displaying either basaloid or fusiform morphology, a thick collagenized cellularized stroma with little inflammatory infiltrate. (B) In detail, neoplastic cells with pleomorphic and hyperchromatic nuclei. (C) The tumor cells were positive for S100. Some positive expression was also observed in the stromal cells. (D) MR scan of the tumor (Haematoxylin-eosin, original magnification  $\times 100$  (A),  $\times 400$  (B); Immunohistochemical staining, original magnifications  $\times 200$ ).

al recurrence 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 ENB and 1.5 and 2.5 years for those with high-grade ENB, respectively [31]. Complete surgical resection of the tumor followed by radiation therapy is currently recognized as the optimal treatment for ENB. Although an effective routine therapeutic regimen has not been established, the addition of chemotherapy, using cisplatin, etoposide, adriamycin, vincristine, cyclophosphamide, or temozolomide is recommended for patients with recurrent or metastatic tumors [28].

Generally, ENB was considered as a mild malignancy with 5-year survival over 60% [14, 32]. In

the current case report, though the patient only received an inadequate primary treatment, no local relapse observed in the following 5 months. However, the patient developed multiple metastases quickly after primary treatment of the nasal tumor. Spine metastases which lead to nerve oppression caused the muscle weakness and limbs pain. However, asymptomatic metastasis at anterior mediastinum and subcutaneous developed simultaneously. The patient finally died of lung metastasis. The inadequacy of primary treatment with the interrupted chemoradiotherapy controlled the primary nasal tumor well but failed to prevent distant metastasis.

The spine is the most common site of osseous metastatic disease because of several patho-



**Figure 2.** Images of metastatic diseases. A. MR image indicated that multiple spine metastasis; B. MR image indicated that spine metastasis that invaded Psoas major muscle and erector; C. CT scan indicated that spine metastasis that invaded Psoas major muscle and erector; D. Metastasis at anterior mediastinum; E. Subcutaneous metastatic tumor.

physiologic factors, including the presence of vascular red marrow in adult vertebrae and communication of deep thoracic and pelvic veins with valveless vertebral venous plexuses. Pain and neurologic deficits resulting from these complications lead to impaired mobility, loss of functional independence, and overall decreased quality of life. In this case tumor cells may stimulate osteoblasts, which results in sclerotic metastases. The ENB cells grown dendrically and radially towards surrounding muscles. Tumor cells at vigorous growth responded well to radiotherapy. After radiotherapy, the patients achieved remission of symptoms and the CT scan showed relatively normal lumbar vertebrae without psoas major invasion.

No definitive consensus regarding the optimal treatment has been reached and considerable controversy exists over its optimal management, because of the rarity of this malignancy. Multimodality approach with a risk-adapted

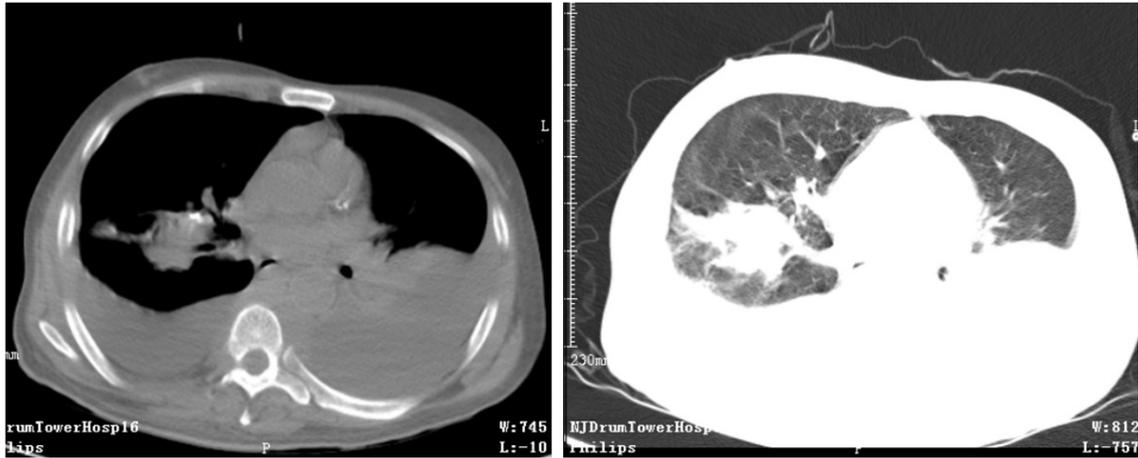
strategy is required to achieve good control rates while minimizing treatment related toxicity. In order to treat the primary tumor, surgical resection is the treatment of choice, particularly for locally contained low-grade tumours. Neoadjuvant radiotherapy appears to be helpful. Chemotherapy with cisplatin based regimens is helpful for high-grade malignancies. For the recurrent and metastatic tumors, a treatment involves radiotherapy and chemotherapy is recommended. Salvage surgery sometimes can improve quality of life and prolong survival together with radiotherapy. The reported case demonstrated a multiple metastasis even in the spine and extensive invasion to the surrounding muscles, indicating no indications of operation. The tumor metastasis to spine showed excellent response to radiotherapy. But, we do not think that the patient received benefit from chemotherapy because of the quick progression both in the spine and lung.

### Conclusion

Esthesioneuroblastoma is a normally slowly-developing but malignant tumor with high recurrence rates because of its anatomical position [33]. The present report refers to a rare case of ENB that developed a quick progression of multiple metastases with the spine together with surrounding muscle involved. The tumor demonstrated a vigorous growth and good sensitivity to radiotherapy. The case described in this article has lost the timing of the diagnosis of surgery, despite the aggressive chemotherapy and other comprehensive treatment, the disease was still rapid progressed, and died in 8 months since diagnosis.

### Disclosure of conflict of interest

None.



**Figure 3.** CT scan showed lung metastasis and pleural effusion.

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