Neuroblastoma metastasized to the mandible and the spinal extradural regions

A case report

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Abstract

Neuroblastoma (NB) metastasized into the mandible and spinal extradural region was rarely reported. We present a case with metastatic NB to the mandible and the spinal extradural regions. The patient received chemotherapy using NB 97 regimen and was tumor free after 8 months, but 9 months after the treatment, the patient presented with lower limb paralysis and persistent pain in maxillofacial region as well as swelling in the left mandibular area. Metastasis to the mandible and the spinal extradural regions was diagnosed based on the spinal and maxillofacial magnetic resonance imaging. Radiotherapy with a density of 2 Gy per day was given via a linear accelerator. The total dose of the intraspinal occupying lesion was subject to radiotherapy with a regimen of 30 Gy (10 fractions). For the management of the maxillofacial pain, tumor in the maxillofacial region was subject to a density of 10 Gy and soft tissue tumefaction was eliminated after a density of 50 Gy, and the maxillofacial appearance was much better than before. Finally, the patient died from tumor progression 2 years after diagnosis for NB.

Abbreviations: CT = computed tomography, INRG = International Neuroblastoma Risk Group, INSS = International Neuroblastoma Staging System, MRI = magnetic resonance imaging, NB = neuroblastoma.

Keywords: metastasis, Neuroblastoma, radiotherapy

1. Introduction

Neuroblastoma (NB) derived from neural crest cells of the adrenal medulla or sympathetic ganglia is responsible for 15% of cancer-related death in children. In clinical practice, the criterion standard for NB diagnosis is histology based on biopsy.[1] The symptoms were usually related to the location of the primary or metastatic lesions, such as malaise, abdominal mass and pain, back pain, fever, anemia, and weight loss. Currently, the treatment of NB is depending on the staging by International Neuroblastoma Risk Group (INRG), and usually involves a combination of surgery, chemotherapy, and/or radiation.[2] Unfortunately, many patients showed poor outcome after the treatment due to metastasis. NB metastasis via both hematogenous and lymphatic routes may spread to a variety of locations including lymph nodes, bone marrow, cortical bone, dura, the orbits, liver, and skin.[3] However, rare cases with NB metastasized into the mandible and spinal extradural region have been reported. In this case, we report a child suffering from metastatic NB to the mandible and the spinal extradural areas.

2. Case presentation

A 4-year-old female child presented to the Pediatric Department of our hospital due to anemia lasting for 1 month. Abdominal ultrasonography revealed a medium echo area measuring 68.8 × 44.5 × 76.8 mm. Abdominal computed tomography (CT) showed a mass (6.8 cm in size) with irregularly shape in the right adrenal gland. The thickness of the renal parenchyma was not even. Chest CT showed pleural effusion and thickening, as well as thoracic bone destruction.

Right adrenal gland biopsy and bone marrow biopsy were carried out to establish a definitive histological diagnosis, which revealed poorly differentiated NB. Stage IV NB was diagnosed based on the histology, INSS, or INRG. Hematoxylin and eosin staining revealed dense proliferation of small round tumor cells with sparse cytoplasm and hyperchromatic nuclei (Fig. 1).

For the treatment, chemotherapy was given using German NB 97 regimen which was consisted of 6 cycles of chemotherapy with some dose reductions (cisplatinum 24 hours 40 mg/m² per day days 1–4 [96 h], etoposide 24 hours 100 mg/m² per day days 1 to 4, vindesine 1 hour 3 mg/m² per day 1; doxorubicine 4 hours, 30 mg/m² per day, days 6–7) to complete within 5 months according to the previous description.[4] Meanwhile, abdominal surgery was performed to remove tumor remnants, followed by radiotherapy...
Afterwards, the patient received 3-month maintenance chemotherapy (cyclophosphamide oral 150mg/m² per day for days 1–7; 4 cycles). Eventually, complete remission was obtained.

The patient is tumor-free after 8-month-follow up. Nevertheless, 9 months after the treatment, the patient presented with lower limb paralysis and persistent pain in maxillofacial region as well as swelling in the left mandibular area. She presented to our department with progressive paraparesis, urinary retention, and hypoesthesia. Her muscle strength was fair to good in the upper extremities but nonexistent in all muscles of the lower extremities at admission. Lower limb reflexes were pathologically brisk. Spinal magnetic resonance imaging (MRI) revealed a dorsal epidural mass from T6 to T8 levels (Fig. 2A). Axial imaging was obtained using MRI. Maxillofacial MRI displayed longer T1 signals together with whole tumor inhomogeneous enhancement and destruction of the cortical bone (Fig. 3). On this basis, the patient was diagnosed with metastasis to the mandible and the spinal extradural regions.

After taking the previous treatment dose and the organs at risk into consideration, radiotherapy with a density of 2Gy per day was given via a linear accelerator (6 MV photons). For the management of intraspinal tumor, the total dose of the intraspinal occupying lesion was subject to radiotherapy with a regimen of 30 Gy × 10 fractions. To relieve the maxillofacial pain, the tumor in the maxillofacial region was subject to a density of 50 Gy × 25 fractions. The maxillofacial pain disappeared after a density of 10 Gy and soft tissue tumefaction was eliminated after a density of 50 Gy, and maxillofacial appearance was much better than before (Fig. 4). MRI indicated a sharp decrease of tumor size after a density of 30 Gy in spinal extradural region (Fig. 2B). Finally, the patient died from tumor progression 2 years after diagnosis for NB.

### 3. Discussion

Dissemination of NB to bones, skull, and lymph nodes has been well described[5,6]; however, rare cases showed involvement in the head and neck region.[7,8] In this case, we presented a rare case of an adrenal NB with metastasis to the mandible and spinal extradural regions.

The incidence of the disease was 10.5 per 1 million children aged <15 annually.[9] Localization and histopathological characteristics may vary among NB patients.[9] The disease is known for its wide variety of clinical manifestations. NB metastasis by both hematogenous and lymphatic routes and my spread to a wide variety of locations including lymph nodes, bone marrow, cortical bone, dura, the orbits, liver, and skin.[3] Moreover, mandible and spinal metastasis is rare in general. In this study, a literature review was performed to summarize the cases of mandible metastasis, together with the treatment regimen and outcome (Table 1).[3,8,10–16]

Up to now, no approved standard guidelines have been established for treating NB. The treatment of NB is mainly...
depending on the surgery, radiation therapy, chemotherapy, bone marrow transplantation, and immunotherapy.[17–19] In the literature review, 14 cases with NB metastasized to the mandible region were included, and the treatment was highly depending on the chemotherapy, surgery and radiotherapy. In this case, the patient showed metastatic NB to the mandible and the spinal extradural areas, and radiotherapy is a treatment option for the disease after taking the previous treatment dose and the organs at risk into consideration.

In this case, we reported a case of metastatic NB to the mandible and the spinal extradural areas. The radiotherapy may serve as a treatment option. In future, further studies are needed to validate the efficiency of radiotherapy in the NB metastasis to the mandible and the spinal extradural areas.

**Author contributions**

Conceptualization: Hui Xu.
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**Software:** Kai Xin.
**Supervision:** Kai Xin.
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**Correction**

This article originally published incorrectly under the article type Observational Study and has since been corrected to Case Report.

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