Metastatic neuroblastoma to the mandible in a 3-year-old boy: a case report

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ABSTRACT

Although neuroblastoma is a relatively common malignancy of childhood and its dissemination to distant organs is often seen, metastasis to the mandible is rare. A 3-year-old boy which a mandibular soft tissue mass was the initial presenting symptom of disseminated neuroblastoma is reported. The results of biopsy were inconclusive and the differential diagnosis from the imaging studies included lymphoma, soft tissue sarcoma, and osteosarcoma. A metastatic work-up disclosed neuroblastoma of the adrenal gland origin with osseous and bone marrow metastases. Urinary catecolamines were also increased. Regarding the widespread features of the tumor and lack of adequate treatment at this stage of disease, a palliative chemotherapy was conducted, and the patient died one month after starting treatment. This case illustrates that neuroblastoma at a young age, with bone metastases and bone marrow involvement are predictive of the poor outcome of the disease. Therefore, detecting early stage metastasis is one of the essential factors for improving treatment of neuroblastoma patients.

Key words: *Neuroblastoma, metastasis, mandible.*

INTRODUCTION

Neuroblastic tumors are a heterogeneous group of embryonal tumors derived from the neural crest cells. Neuroblastoma accounts for 10-15% of all childhood malignancies. The median age at diagnosis is 22 months, and more than 95% of cases are diagnosed by 10 years of age (1).
Histologically, the International Neuroblastoma Pathology Committee (2) proposed three basic morphologic patterns: neuroblastoma (NB), ganglioneuroma (GN) and ganglioneuroblastoma (GNB). These tumors have a variety of clinical behaviors, from spontaneous regression or differentiation to early metastasis and death (2,3). Neuroblastoma is the most immature and undifferentiated form (of the three) with a high propensity to metastasis. Dissemination to bones, skull and lymph nodes has been well described (4,5). However, an unusual presentation such as the mandible is rare.

In this paper, we report a rare case of an adrenal neuroblastoma with metastasis to the mandible. We discuss clinicopathologic features, biologic behaviour and prognostic factor of neuroblastoma.

CASE REPORT

A 3-year-old boy was referred to our department for diagnosis and treatment of anaemia, generalised bone pain, a swelling of the left mandible (Fig. 1) with teeth displacement. Empiric treatment of symptoms failed to control the continuing pain and the progressively enlarging intraoral mass. (Fig 2)
On clinical examination, the patient was found to have a firm, non-tender, and fixed mass on the left body of the mandible. The buccal mucosa overlying the mass was erythematous, swollen and extended to the occlusal surfaces of the mandibular molars. This was associated with mild (left) facial asymmetry. Multiple enlarged cervical lymph

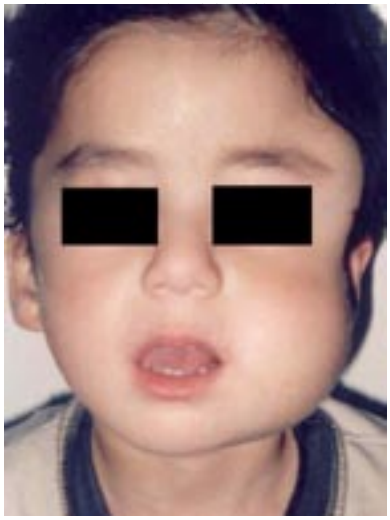

Fig. 1. Swelling of the left facial side

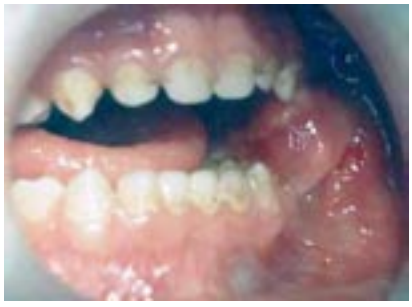

Fig. 2. Intraoral view revealed the left involvement of the mandible

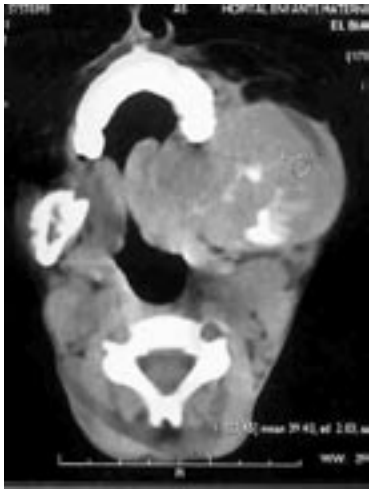

Fig. 3. CT scan showing extension of a mass in the left side of the mandible with a clear osseous destruction.

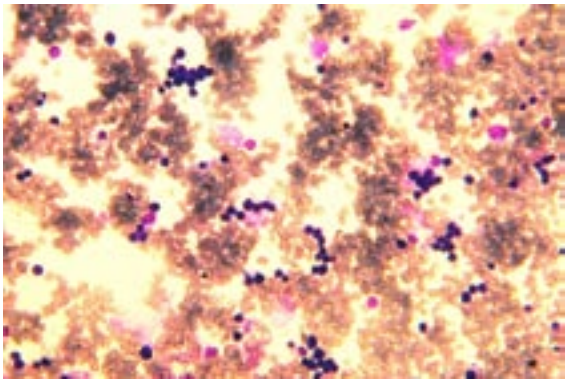

Fig. 4. Photograph of bone marrow infiltrate composed of small, round, blue cells with occasional rosettes

Computed tomography scans revealed invasion of the left mandibular bone with lytic destruction measuring 4,6×4,9 cm with involvement of the masseter and the lateral pterygoid muscles and extension into the infratemporal fossa (Fig 3). A fine needle aspiration biopsy of the tumor was performed twice, but both specimens were inconclusive.

At the time of his admission, there were also some laboratory abnormalities: hemoglobin (Hb) 7,5 g/dl, Mean corpuscular volume (MCV) 63 μm3, platelet count (PLT) 250x10^9/l, Glutamyl oxaloacetic transaminase (GOT) 106 I.U/l, Glutamyl pyruvic transaminase (GPT) 220 I.U/l, and α-fetoprotein (ALP) 196 I.U/L. Urinary homovanillic acid (HVA) was increased to 35 mg/day.

Given these findings, a metastatic work-up was performed to assess the location and extent of both primary and metastatic lesions. Ultrasound abdominal radiography identified a 8,9×6,6×7,8 cm nonhomogenous left adrenal tumor, and paraaortic lymph nodes in close proximity were enlarged. Further radiographs and osseous scintigraphy imaging of the whole body disclosed additional metastases to the orbit, the frontal sinus wall and left knee. Bilateral bone marrow aspirates revealed metastatic NB (Fig 4). Based on these findings, the tumor was classified as stage IV disease according to the International Neuroblastoma Staging System INSS (chromosomal and molecular work up were not available)

In consideration of the poor prognosis and lack of adequate treatment at this stage of disease, a palliative chemotherapy was started. The patient died at home 1 month after initiation of this therapy.

DISCUSSION

Neuroblastoma is the most common extracranial pediatric solid tumor and the most common neoplasm in infancy. This embryonal neoplasm which takes the form of a lump or mass may arise in any site where elements of the sympathetic nervous system exist. This solid tumor usually originates in the tissue of the adrenal gland (80%), the mediastinum (15%) and less than 5% will present in the head and neck region (6,7).

Considering the age of the patient, the rapid onset of mandibular enlargement together with radiographic features of bone destruction, differential diagnoses include lymphoma, soft tissue sarcoma, osteosarcoma, primitive neuroectodermal tumor (PNET), a central malignancy of odontogenic origin, or a metastatic tumor. According to the International Neuroblastoma Staging System INSS (8) the diagnosis of NB can be made by either characteristic histopathologic evaluation of tumor tissue or by the presence of tumor cells in bone marrow aspirate. Elevation of urinary levels of vanyllylmandelic acid (VMA) and homovanillic acid (HVA), dopamine, serum ferritin and serum levels of neuron specific enolase can help to confirm the diagnosis (3,9).

Based on several clinical series, 50% to 60% of patients with NB present with disseminated disease (stage IV), a finding that is more likely in patients over 1 year of age (1,2,8,10).

Table 1. International Neuroblastoma Staging System (INSS) (8)

Stage	Description
I	Localized tumor with complete gross excision, with or without microscopic residual disease; representative ipsilateral lymph nodes negative for tumor microscopically
IIA	Localized tumor with incomplete gross excision; representative ipsilateral nonadherent lymph nodes negative for tumor microscopically
IIB	Localized tumor with or without complete gross excision with ipsilateral nonadherent lymph nodes positive for tumor; enlarged contralateral lymph nodes must be negative microscopically
III	Unresectable unilateral tumor infiltrating across the midline, with or without regional lymph node involvement; localized unilateral tumor with contralateral regional lymph node involvement; midline tumor with bilateral extension by infiltration (unresectable) or by lymph node involvement
IV	Dissemination of tumor to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs (except as defined for stage 4S)
IVS	localized primary tumor (as defined for stage 1, 2A, or 2B), with dissemination limited to skin, liver, and/or bone marrow (<10% tumor) in infant younger than 1 year of age

Metastases to bone marrow and bones have been described in disseminated forms of NB (7,11). Two patterns of marrow disease can be observed: diffuse type and nodular type (12). Bone marrow metastases occur initially in the bone marrow sinusoids where tumor cells adhere and extravasate to bone marrow parenchyma, resulting in the formation of nodular lesions in the medullary cavity. The nodular lesions eventually progress to diffuse lesions after proliferation and gradually enlarge to erode cancellous bone and invade the bone cortex, resulting in bone metastases (12). The bone marrow involvement in our case at the time of the initial presentation and multiple osteolytic lesions argue strongly for a metastatic origin of the mandibular tumor.

Because of the extreme heterogeneous characteristics of NB, several prognostic factors have been identified, among them patient age, tumor stage, tumor histology and genetic abnormalities (2,7,13). Surgery alone is adequate therapy for most cases of early stage disease (6). Chemotherapy in conjunction with radiation therapy appears to have a cure rate of up to 68% for intermediate risk disease (stages IIB, III and IV-S disease) (1,14). In contrast, patients with high risk disease (age >1 year, stages II and III with N-MYC amplification, all patients with stage IV) show progression and have poor clinical outcome (2,15). (Table 1)

CONCLUSION

Neuroblastoma with metastases to unusual locations, such as the mandible, presents a diagnostic problem. However, symptoms such as systemic illness, bone pain and unexplained teeth displacement in a child should raise suspicion of a malignant metastatic tumor. Metastatic work up by radiography, bone marrow biopsy and laboratory investigations (eg, catecholamines) are helpful in detecting early stage metastasis which is the essential factor for improving treatment of neuroblastoma tumors.

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