Case Report

Lytic and sclerotic (mixed) vertebral metastasis in ganglioneuroblastoma

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ABSTRACT

The clinical presentation of ganglioneuroblastoma is highly variable and it is not uncommon to see metastasis at presentation. Bone is the second most common site of metastasis in neuroblastoma. Neuroblastoma cells usually activate osteoclasts and form osteolytic lesions. Here, we describe a patient who presented with back pain. On evaluation, X-ray and positron emission tomography-computed tomography showed mixed lytic and sclerotic vertebral metastasis, and subsequently diagnosed as ganglioneuroblastoma.

Keywords: Ganglioneuroblastoma, metastasis, neuroblastoma, positron emission tomography-computed tomography

INTRODUCTION

Neuroblastoma is the most common childhood extra-cranial solid tumor which includes neuroblastoma, ganglioneuroblastoma, and ganglioneuroma. It is an embryonal malignancy of the autonomic nervous system arising from neuroblast. The clinical presentation is highly variable and it is not uncommon to see metastasis at presentation. Next to bone marrow, bone is the second most common site of metastasis in neuroblastoma.[1] An osteoblastic lesion caused by neuroblastoma has not been described previously in English literature. Here, we describe a patient of ganglioneuroblastoma who presented with back ache and imaging showed mixed lytic and sclerotic vertebral metastasis.

CASE REPORT

A 13-year-old girl presented with a history of abdominal distension, back ache, and loss of appetite and weight of 3 months' duration. Her medical history was otherwise unremarkable. On examination, an ill-defined mass of 10 cm × 8 cm size was palpable in the right hypochondrial region, extending 7 cm below the right costal margin and medially up to the umbilical region. Ultrasonography of the abdomen revealed a large, heterogeneous mass of 18 cm × 16 cm × 16 cm size arising from the right adrenal, infiltrating the right lobe of liver, and displacing the right kidney inferolaterally.

Fine-needle aspiration cytology (FNAC) of the adrenal mass showed clusters of malignant cells forming rosettes in an eosinophilic fibrillary background with high nuclear cytoplasmic ratio. In addition, scattered ganglion cells with eccentric-placed nuclei and prominent nucleoli were also present and features were consistent with ganglioneuroblastoma [Figure 1].

The 24-h urinary vanillyl mandelic acid VMA level was 5.4 mg/24 h (normal is < 7 mg/24 h). Radiography of the lumbo-sacral spine showed mixed lytic and sclerotic lesion involving the L3 vertebrae [Figure 2] and confirmed by computed tomography (CT) soft tissue with bone window [Figure 3]. To assess the extent of neuroblastoma and metastasis, PET-CT was done. It showed [Figures 4a and b] increased uptake in the right adrenal and liver areas with metastatic involvement of L3 vertebrae. These imaging findings and FNAC reflected the diagnosis of ganglioneuroblastoma; stage IV (vertebral and liver metastasis). The patient was treated with intravenous zoledronic acid[2] and carboplatin, vincristine, etoposide, and cyclophosphamide[3] based chemotherapy regimen.

DISCUSSION

Ganglioneuroblastoma is a neuroendocrine tumor arising from neural crest element of the sympathetic nervous system. The most common site of origin is the adrenal gland, followed by nerve tissues in the neck, chest, abdomen, or pelvis. It is a disease exhibiting extreme heterogeneity from an asymptomatic mass to widely disseminated disease or both. Age and stage of the

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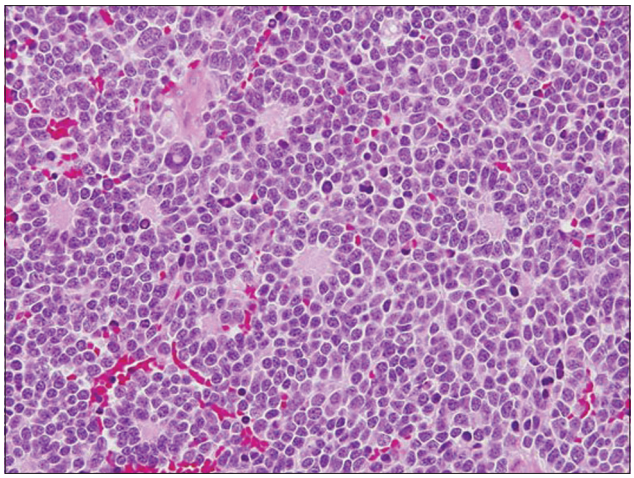

Figure 1: Fine-needle aspiration cytology of the adrenal mass showed clusters of malignant cells forming rosettes in an eosinophilic fibrillary background

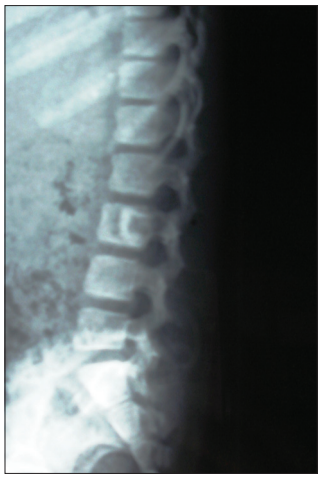

Figure 2: X-ray of lumbosacral spine showing lytic and sclerotic (arrow mark) vertebral metastasis

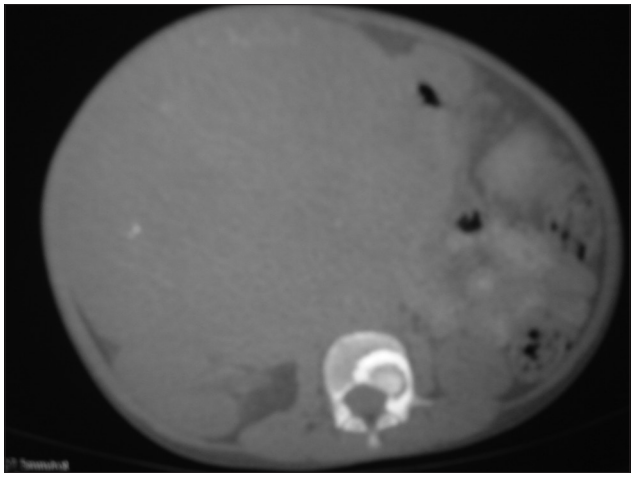

Figure 3: Computed tomography soft tissue window showing lytic and sclerotic metastasis of L3 vertebrae

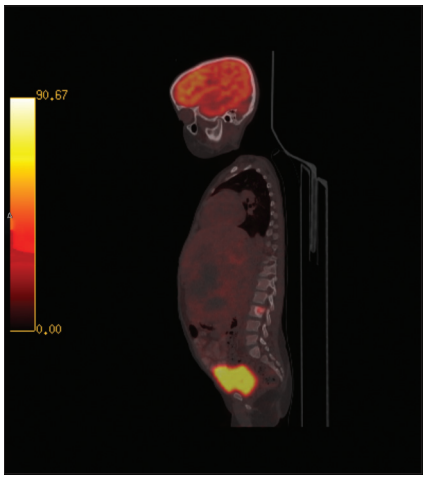

Figure 4a: PET computed tomography showing hyper metabolic mass lesion with metastatic involvement of L3 vertebrae

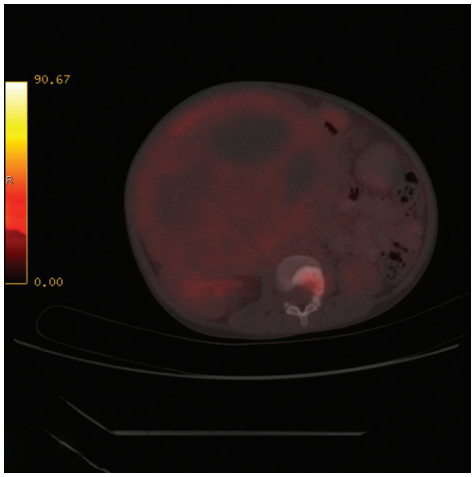

Figure 4b: FDG uptake in a mixed lytic and sclerotic lesion of L3 vertebra

disease are important prognostic factors and are used for risk stratification and treatment assignment. After bone marrow, bone is the second most common site of metastasis in neuroblastoma.

Bone metastasis in malignancy is arbitrarily classified into osteolytic and osteoblastic on the basis of the type of cells that are predominantly activated. There are multiple pathways by which neuroblastoma cells can activate osteoclasts to form osteolytic lesions. The major mechanism of osteoclast activation by neuroblastoma is via the production of receptor activator of nuclear factor kappaB ligand (RANKL).[4] In the absence of RANKL, neuroblastoma cells activate osteoclasts by interleukin-6, a potent osteoclast activating factor, secreted by bone marrow mesenchymal stem cells. The mechanisms of osteoblastic metastasis and the factors involved are unknown in neuroblastoma. Tumor production of growth factors, such as platelet-derived growth factor, insulin-like growth factor, and adrenomedullin, has been implicated in osteoblastic bone metastases.[5] Endothelin-1 (ET-1) has been implicated in osteoblastic metastasis from breast and prostate cancer. It stimulates the formation of bone and the proliferation of osteoblasts in bone organ cultures.[6] Dickkopf-related protein 1 (Dkk1), a secreted inhibitor of the Wnt signaling pathway is recently implicated in suppressed bone formation of multiple

myeloma. In osteoblastic disease, ET-1 stimulates osteoblast activity by decreasing autocrine production of the negative regulator Dkk1.[7]

Take home message

Bone is the second most common site of metastasis in ganglioneuroblastoma. Neuroblastoma cells can activate both osteoclast and osteoblast and produce mixed lytic-sclerotic vertebral metastasis. Zoledronic acid may be a promising agent for prevention of further metastasis.

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