Case Report

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Osseous Manifestation of Systemic Mastocytosis in a Paediatric Bone Scan: A Case Report

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Abstract

Systemic mastocytosis is a rare disorder of the mast cells with a wide spectrum of clinical manifestations depending on the organs involved.

We report a case illustrating the role of Tc-99m hydroxyl diphosphonate (HDP) to assist in diagnosing systemic mastocytosis in a 4-year-old girl who presented right thigh pain and intermittent fever. She initially presented with right thigh pain. The findings of the radiograph of the lower limbs were unremarkable. MRI of the right femur showed heterogenous intramedullary signal within the right femur, involving the diaphysis and metaphyseal region. Based on the radiographs and MRI changes, the differential diagnosis of disseminated acute osteomyelitis was made. Bone scan with Tc-99 hydroxy diphosphonate (HDP) performed showed diffuse skeletal uptake involving the appendicular and axial skeleton. Bone biopsy of the femur showed presence of mast cell infiltration.

Diagnosing systemic mastocytosis remains challenging due to the contradictory results of available imaging modalities. When interpreting a focal or diffuse uptake on bone scintigraphy, systemic mastocytosis should be considered, particularly in the paediatric age group.

Keyword: Systemic mastocytosis, Tc-99m bone scintigraphy

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Introduction

Systemic mastocytosis is a rare clonal disorder of the mast cells that are characterized by pathologically increased proliferation of mast cells that commonly involve the skeletal system. Symptoms of systemic mastocytosis are often non-specific, more so in the pediatric setting. Bone pain may be the first and only manifestation of the disease. Due to the latent course of the illness, the diagnosis of bone marrow infiltration may be delayed or initially misdiagnosed. We report a case illustrating the role of Tc-99m hydroxyl diphosphonate (HDP) bone scintigraphy to facilitate early diagnosis in systemic mastocytosis.

Case Report

A 4-year-old girl presented with the right thigh pain and intermittent fever over the previous 2 months. She sustained a fall in the bathroom and was initially treated for a soft-tissue injury. One month after the fall, she presented again with progressively worsening right thigh pain and left thigh pain. At the time of evaluation, the patient had a limping gait, however, no swelling or skin changes

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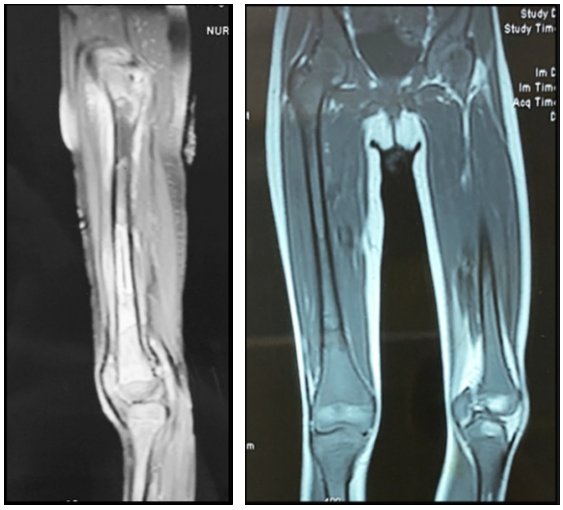

Figure 1: T1W shows (a) sagittal image of the right femur (b) coronal image of bilateral hip shows heterogeneously enhancing irregular locule at distal physis of the right femur, periosteal reaction, and surrounding edema.

were seen over either thigh. Both hips had a full range of motion with no neurological deficit.

Radiographs of the lower limbs were unremarkable. Subsequently, she developed fever raising the suspicion of infection. Her blood studies show anemia, thrombocytopenia, leukocytosis, and hypoalbuminemia with raised C-reactive protein.

Magnetic resonance imaging (MRI) of the right femur showed heterogeneous intramedullary signal within the right femur, involving the diaphysis and metaphyseal region, not extending beyond the epiphyseal plate. There was a heterogeneously enhancing irregular locule at the distal physis of the right femur and regular periosteal reaction with associated surrounding soft-tissue edema (Fig. 1). A few rim-enhancing medullary lesions were seen in the proximal left femur (metadiaphysis), head and neck of the left femur, left ilium, and left sacral alar. In view of the plain radiographs and MRI changes, the diagnosis of disseminated osteomyelitis was made and the patient was treated with IV cloxacillin.

Despite completing a 2-week course of antibiotic, the condition of the patient deteriorated with worsening lower limb pain and high-grade fever. Bone scintigraphy with Tc-99 HDP demonstrated diffuse skeletal involvement seen at the left humerus, sternum, right scapula, L5 vertebra, bilateral hemipelvis, bilateral femur, and the right tibia/fibula (Fig. 2).

Due to the appearances seen on imaging, bone marrow biopsy of the right femur was performed. The histologic sections with toluidine stain showed mast cell infiltration in the right femoral marrow, confirming the diagnosis of systemic mastocytosis.

The patient was treated with a short course of oral corticosteroid (prednisolone). However, she presented with a clinically palpable fullness in the right hypochondrium with the right periorbital swelling and generalized bone pain.

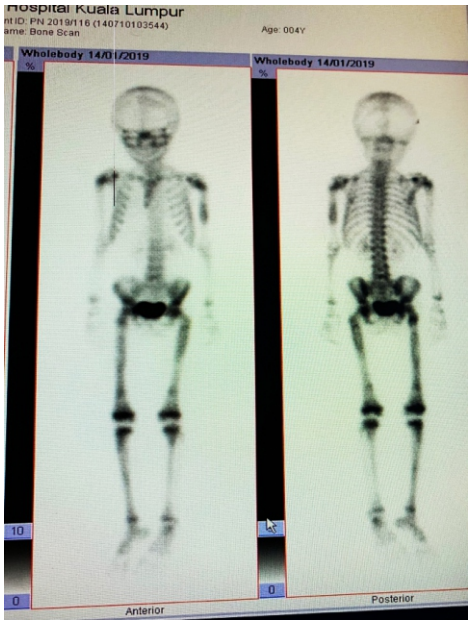

Figure 2: Tc-99m HDP hole body planar images shows multiple foci of HDP-avid bone lesions at the midshaft to proximal shaft of the left humerus, sternum, right scapula, L5 vertebra, bilateral hemipelvis, bilateral femur and right tibia/fibula.

Laboratory investigation revealed suppressed hematopoiesis resulting in bicytopenia with platelet of 34.0 × 109/L and hemoglobin of 6.2 g/dL. Computed tomography (CT) of the brain, thorax, and pelvis revealed extensive permeative bone changes at the base of skull, orbit, clivus, and sphenoid bone associated with a soft-tissue component in the left parietal convexity, multiple vertebrae, bilateral femur, and pelvic bones. There was a right suprarenal mass measuring 2.8 cm × 2.8 cm × 3.4 cm with several enhancing lobulated para-aortic and a paravertebral mass.

A repeat bone marrow trephine biopsy and immunophenotypic analysis revealed a non-hematopoietic malignancy with bone marrow infiltration, negative for CD 45 and CD 117. The patient was started on chemotherapy; however, she showed poor response and died from progression of the disease.

Discussion

Systemic mastocytosis is a rare clonal disorder of the mast cells that are characterized by pathologically increased proliferation of mast cells that commonly involve the skeletal system [1]. Mast cells are derived from hematopoietic stem cell progenitors and play an important role in the in the recruitment of leukocytes and tissue repair. Tissue infiltration by mast cells results in release of other substances involved in hypersensitivity reactions such as histamine, serotonin, heparin, prostaglandin, proteases, and tumor necrosis factor-alpha [2].

Mastocytosis is more common in children than adults. About

55% of pediatric cases present in the first 2 years of life, 10% occur in children younger than 15 years of age, and 35% in those over the age of 15 years [3].

The clinical manifestation is variable, ranging from asymptomatic to highly aggressive mastocytosis. In aggressive systemic mastocytosis, proliferation of mast cells can lead to organ failure and patients can show clinical signs and symptoms such as bone pain, osteolytic or sclerotic bone lesions, fractures, hepatosplenomegaly, cirrhosis, and lymphadenopathy [4].

The disease usually has an indolent course but it can be associated with hematological malignancies such as myelodysplastic or myeloproliferative syndrome or acute leukemia. In a study large muticenter series, Pieri et al. reported that up to 32% of patients with aggressive mastocytosis evolved into acute leukemia [5].

The gold standard for diagnosing bone involvement in systemic mastocytosis is through bone histopathology. The disease categorization and prognosis are based on bone marrow biopsy and aspirate [6]. Based on the WHO criteria, multifocal aggregates of mast cells (>15) observed in sections of bone marrow biopsy are considered a major criterion and presence of abnormal mast cell morphology (>25%) in bone marrow or other extracutaneous organs; or atypical mast cells (>25%) in bone marrow aspirates are considered minor criteria for diagnosing systemic mastocytosis [2].

Other diagnostic work-up includes a full blood count that may reveal thrombocytopenia, leukocytosis, and eosinophilia and increased plasma or 24 h urine histamine excretion. The osseous changes are contributed by mast cell mediators such as histamine which stimulate fibroblastic activity leading to osteoid formation and osteosclerosis. Excess production of heparin, prostaglandin, and proteases increases bone resorption and degradation of bone matrix resulting in the formation of lytic lesions, osteopenia, and osteoporosis. Tumor necrosis factor-alpha also influences the function of osteoblasts and osteoclasts [2].

Osteopenia and osteoporosis were found to be the most common presentations followed by osteosclerosis or mixed pattern. Diffuse demineralization or osteopenia occurs more commonly in young patients or older patients, with fractures seen up to 16% in this group [2]. Systemic mastocytosis with osteosclerosis is associated with more aggressive disease [2].

Role of Imaging

Radionuclide scan with Tc-99m HDP is a useful non-invasive method that is more sensitive than radiographs for the detection of skeletal involvement in systemic mastocytosis [1]. Patterns of osseous uptake on bone scintigraphy include unifocal, multifocal, and diffuse. The previous studies have shown a sensitivity of 79% in detecting systemic mastocytosis [6].

Although bone scintigraphy is sensitive, the patterns of sclerotic seen in this case were non-specific and in this age group, the differential diagnoses to consider included extensive primary bone tumor, skeletal metastasis secondary to malignancy, renal osteodystrophy, diffuse osteomyelitis, Langerhans histiocytosis, and Ribbing's disease [2].

Lawrence et al. reported on a prospective series of 46 patients focusing on bone marrow pathology. The degree of uptake and number of lesions seen on the bone scan did not correlate with prognosis. As the disease progresses, there is a general shift from focal to diffuse abnormalities reflecting increasing bone marrow involvement [6].

Bone involvement on radiography can be seen in approximately 70% of patients with systemic mastocytosis [6]. In our case, there was no significant abnormality noted on radiographs of the lower limbs. Radiographs abnormalities may be diffuse or circumscribed. Lytic lesions can be 4–5 cm in diameter surrounded by a "halo sclerosis" [6]. Sometimes, diffuse osteopenia may be the only finding seen on radiographs. In predominantly sclerotic systemic mastocytosis, diffuse or focal pattern of increased trabeculations and thickness of the cortex with or without narrowing of the marrow can be appreciated on radiographs, however, these findings are often non-specific.

Multidetector CT has been shown to be more sensitive for the detection of bone marrow abnormalities than radiographs [2]. Additional information includes cortical thickness and the associated narrowing of marrow space which can be missed on conventional imaging.

Finally, little is known about the role of fluorodeoxyglucose (FDG) positron emission tomography/CT in systemic mastocytosis [2]. A case series by Zettinig et al. reported normal FDG distribution findings in areas of osteolytic lesions and the mild increased activity in cortical bone and marrow spaces was non-specific [4].

Conclusion

The diagnosis of systemic mastocytosis remains challenging due to the non-specific presentation and ambiguous results of conventional imaging methods. Considering this, bone scintigraphy is a non-invasive imaging modality that is a useful and sensitive initial test to facilitate early diagnosis.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil; **Source of support:** None

References

1. Arrington ER, Eisenberg B, Hartshorne MF, Vela S, Dorin RI. Nuclear medicine imaging of systemic mastocytosis. J Nucl Med 1989;30:2046-8.

2. Fritz J, Fishman EK, Carrino JA, Horger MS. Advanced imaging of skeletal manifestations of systemic mastocytosis. Skeletal Radiol 2012;41:887-97.

3. Frieri M, Quershi M. Pediatric mastocytosis: A review of the literature. Pediatr Allergy Immunol Pulmonol 2013;26:175-80.

4. Zettinig G, Becherer A, Szabo M, Uffmann M, Dudczak R, Valent P. FDG positron emission tomography in patients with systemic mastocytosis. AJR Am J Roentgenol 2002;179:1235-7.

5. Pieri L, Bonadonna P, Elena C, Papayannidis C, Grifoni FI, Rondoni M, et al. Clinical presentation and management practice of systemic mastocytosis. A survey on 460 Italian patients. Am J Hematol 2016;91:692-9.

6. Chen CC, Andrich MP, Mican JM, Metcalfe DD. A retrospective analysis of bone scan abnormalities in mastocytosis: Correlation with disease category and prognosis. J Nucl Med 1994;35:1471-5.

7. Lawrence JB, Friedman BS, Travis WD, Chinchilli VM, Metcalfe DD, Gralnick HR. Hematologic manifestations of systemic mast cell disease: A prospective study of laboratory and morphologic features and their relation to prognosis. Am J Med 1991;91:612-24.

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