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Thallium-201 uptake in Langerhans cell histiocytosis of bone

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Abstract A case in which there was thallium-201 (^{201}Tl) uptake in Langerhans cell histiocytosis (LCH) of the left femoral diaphysis is presented. The authors propose that ^{201}Tl scintigraphy is potentially useful in the diagnosis and follow-up of patients with LCH.

Case report

A 7-year-old boy presented with a 2-week history of left proximal thigh pain and progressive limping. A radiograph revealed a lytic lesion in the proximal left femur with associated periosteal reaction. Computed tomography (CT) showed cortical expansion, cortical disruption, and solid periosteal reaction (Fig. 1). Magnetic resonance imaging (MRI) demonstrated an intramedullary lesion that had broken through the cortex posteriorly, with associated marrow and soft tissue edema (Fig. 2).

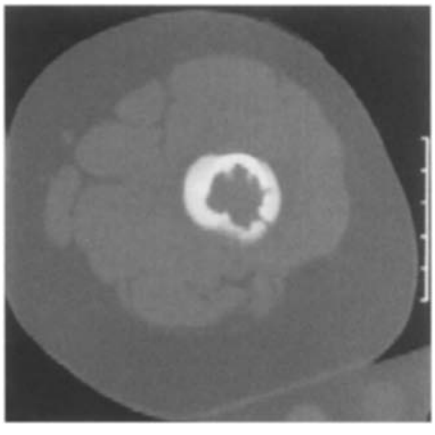

Fig. 1 Axial CT scan through the superior aspect of the lesion in the proximal left femur demonstrates cortical expansion, endosteal scalloping, and solid periosteal reaction

Thallium-201 (^{201}Tl) scintigraphy and technetium-99m methylene diphosphonate (^{99m}Tc-MDP) skeletal scintigraphy were performed prior to biopsy. Planar imaging performed 10 min following injection of 1.0 mCi ^{201}Tl (37 MBq) revealed increased uptake in the proximal left thigh (Fig. 3a). Single photon-emission computed tomography (SPECT) showed focally intense ^{201}Tl uptake in the proximal left femur and minimally increased uptake in the adjacent soft tissues (Fig. 4a). The dynamic and immediate static images obtained after injection of 6.0 mCi ^{99m}Tc-MDP (222 MBq) showed increased blood flow to the proximal left thigh and soft-tissue hyperemia. Planar imaging (Fig. 3b) and SPECT (Fig. 4b) performed 4 h after ^{99m}Tc-MDP administration demonstrated increased tracer localization corresponding to the periosteal new bone formation shown by CT. No other skeletal lesions were identified on spot images of the skeleton.

Excisional biopsy and curettage of the lesion were performed. Pathology revealed Langerhans cell histiocytosis.

Discussion

Langerhans cell histiocytosis (LCH), formerly called histiocytosis X, is a disease characterized by abnormal proliferation of Langerhans histiocytes and granuloma formation. The disease typically affects children and young adults. The skeleton is the most frequent site of

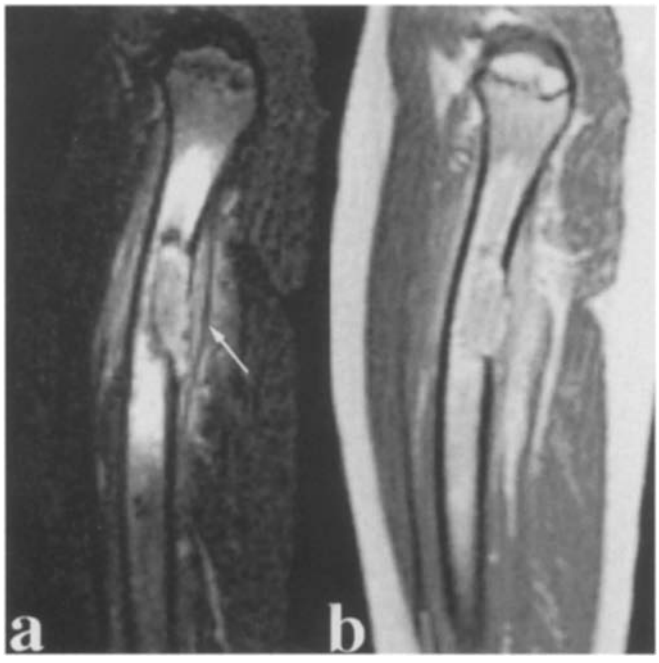

Fig. 2a,b Sagittal fast, short T1-inversion recovery image of the left femur (**a**) demonstrates an intramedullary mass that violates the posterior cortex and elevates the periosteum *(arrow)*. Sagittal gadolinium-enhanced T1-weighted image (**b**) obtained at the same level shows that the lesion enhances homogeneously without evidence of necrosis or abscess

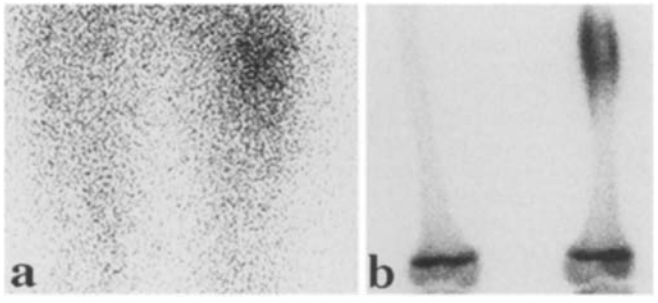

Fig. 3a,b ^{201}Tl scintiscan of the thighs (**a**) demonstrates abnormal uptake in the proximal left thigh. The delayed ^{99m}Tc-MDP image (**b**) reveals increased tracer uptake along the medial and lateral cortical margins of the proximal left femur

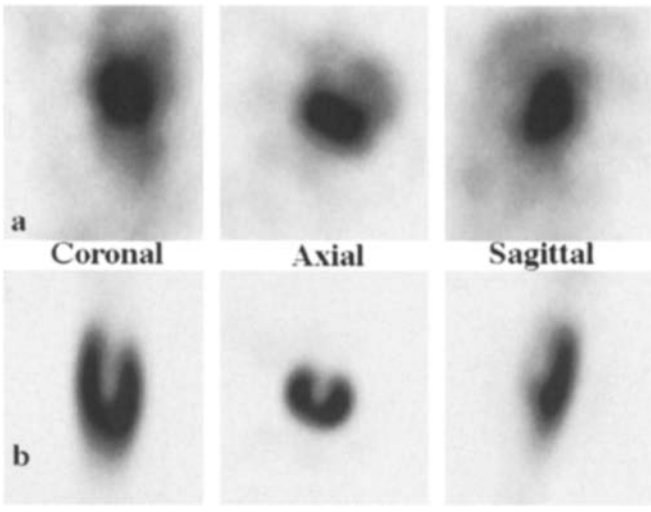

Fig. 4a,b ^{201}Tl SPECT (**a**) reveals focally intense uptake in the left femoral lesion. ^{99m}Tc-MDP SPECT (**b**) shows increased uptake along the medial, lateral, and posterior margins of the left femur, corresponding to the periosteal new bone formation demonstrated on CT

involvement, although any organ can be affected. In eosinophilic granuloma (EG), the most common clinical variant of LCH, involvement is limited to the skeleton. The less common variants, Hand-Schuller-Christian disease and Letterer-Siwe disease, are characterized by disseminated disease in skeletal and extraskeletal sites. Although classifying LCH into these syndromes may be less accurate than characterizing it solely by the extent of disease, these eponyms remain in common usage [1].

The radiographic skeletal survey is the most sensitive method for determining the presence and extent of skeletal LCH. Skeletal scintigraphy is also frequently utilized for this purpose. LCH has a variable appearance on skeletal scintigraphy: the majority of lesions are associated with increased tracer uptake in adjacent reparative bone, some appear as photopenic areas and some appear as photopenic areas with surrounding increased tracer uptake. A review of multiple published series indicated that skeletal scintigraphy is only 35–94 % as sensitive as plain-film radiography for the detection of the skeletal lesions of LCH. The authors of that review noted that in some of the series early-generation gamma cameras were used. Additionally, they pointed out that some authors compared scintiscans performed following therapy with plain films obtained prior to therapy [2]. The reported sensitivities may therefore underestimate the true sensitivity of skeletal scintigraphy for detecting osseous LCH. Complementary roles for skeletal scintigraphy and plain-film radiography in LCH are suggested by reports of lesions that are radiographically occult being detected scintigraphically, as well as the more commonly described converse situation [2].

Due to what are generally regarded as disappointing results with skeletal scintigraphy, attempts have been made to use other radionuclides in LCH patients. Gallium-67 imaging and ^{99m}Tc sulfur colloid bone marrow scintigraphy proved significantly less effective at demonstrating osseous LCH than both skeletal scintigraphy and plain-film radiography [3]. Successful immunolocalization of skeletal LCH lesions was achieved in five patients with disseminated LCH using indium-111-labeled murine monoclonal antibodies against CD1a Langerhans cell surface antigen [4]. The promise of

these results is tempered by the formation of human anti-mouse antibodies potentially limiting the ability to perform follow-up studies.

The potassium analog, ^{201}Tl, has been widely utilized as a myocardial perfusion agent in children and adults. Reports of ^{201}Tl uptake by a variety of neoplasms has led to its increasing application in oncologic imaging [5, 6]. ^{201}Tl uptake in tumors reflects tumor mass, cellular viability, metabolic activity, and, to a lesser degree, tumor vascularity [7].

In our patient, ^{201}Tl localization was noted in a histiocytic bone lesion of the left femur. One other case report describes ^{201}Tl uptake in a calvarial LCH lesion [8]. Skeletal scintigraphy in that patient, as well as in the one reported here, revealed a photopenic region with surrounding increased tracer uptake. In both patients, ^{201}Tl scintigraphy demonstrated focal tracer uptake; no central photopenia was observed. The difference between the ^{201}Tl and ^{99m}Tc-MDP scintigraphic appearances is consistent with ^{201}Tl localizing in sites of histiocytic proliferation and ^{99m}Tc-MDP localizing in sites of reparative bone formation.

This report, along with one other previous report of ^{201}Tl uptake in LCH, suggests that ^{201}Tl imaging may be useful in the initial evaluation of LCH patients. ^{201}Tl localization in the highly cellular sheets of Langerhans cells that characterize the early phase of LCH [1] is not surprising, based on the mechanism of ^{201}Tl uptake described above. ^{201}Tl imaging is also potentially applicable in the follow-up of LCH patients. Since ^{201}Tl does not localize in healing bone, it has proven useful in predicting the histologic response of osteosarcoma to chemotherapy [6]. A similar role may be possible in LCH, although the paucity of Langerhans cells in older LCH lesions [1] may be a limiting factor. Follow-up imaging was not done in our case, as complete excision had been performed.

We conclude that ^{201}Tl scintigraphy, by providing information additional to that obtained from other imaging studies, is a potentially useful tool for the evaluation of skeletal lesions in LCH. This hypothesis needs to be tested in a large prospective study.

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