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Musculoskeletal

Langerhans cell histiocytosis of bone in an adult: A case report

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ABSTRACT

Langerhans cell histiocytosis (LCH) may clinically manifest in a variety of ways due to its ability to involve nearly every organ system. LCH may present as a single bone lesion, skin rash, or as invasive disseminated disease and occurs typically in the pediatric and adolescent population, affecting both males and females. Independent of its clinical presentation and severity, LCH lesions share the common histology of $CD1a^{+}/CD207^{+}$ dendritic cells along with an inflammatory infiltrate, and, based upon improved scientific understanding, is now classified as a myeloproliferative neoplasm. We present a case report of an adult diagnosed with LCH of the pelvis.

Case presentation

A 54-year-old white man presented to an outside hospital emergency department for acute low back pain, flank pain, constipation, and left buttock pain radiating into his left thigh. He had no history of trauma to the area or an inciting event. His medical history was significant for psoriatic arthritis treated with Humira and a history of melanoma in situ. He underwent a computed tomography (CT) scan of the abdomen and pelvis with and without intravenous contrast along with a noncontrast CT of the lumbar spine, which revealed a 2.5-cm well-circumscribed osteolytic bone lesion involving the left ilium with a narrow zone of transition. There was no discernible periosteal reaction or extraosseous soft tissue mass identified (Fig. 1). Laboratory workup (complete blood count, complete metabolic panel, and urinalysis) were within normal limits.

A bone scan was also performed and revealed abnormal focal intense radiotracer activity in the left iliac bone adjacent to the sacroiliac joint. Focus of radiotracer uptake in the right tibia was related to a prior fracture. Mild uptake in bilateral knees and ankles were also identified and may have been degenerative in nature or related to prior trauma (Fig. 2). The patient was subsequently referred to our institution for further evaluation.

On presentation to our institution, physical examination was significant only for mild tenderness to palpation of his left ilium.

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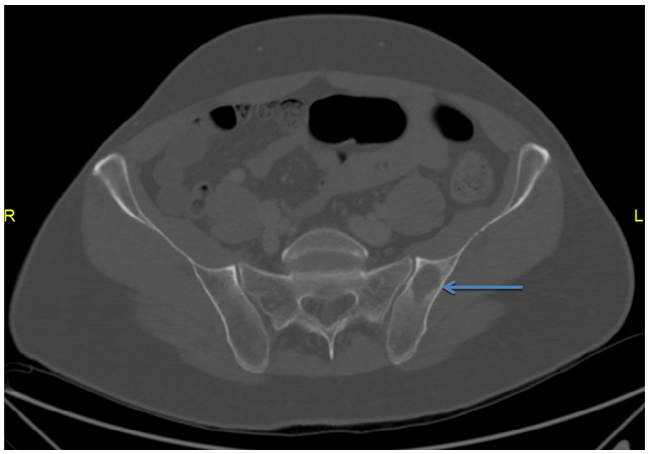

Fig. 1 – Axial CT scan demonstrates a geographic osteolytic lesion of the posterior left iliac bone, with subtle areas of marginal sclerosis. Also demonstrated is intramedullary sclerosis of the adjacent bone, likely reactive in nature. CT, computed tomography.

There was no palpable soft tissue mass, lymphadenopathy, or other site of pain.

The patient underwent a magnetic resonance imaging (MRI) of the pelvis which demonstrated an oval-shaped approximately 2.5-cm intramedullary lesion within the posterior left iliac bone centered at the level of the sacroiliac joint, corresponding to the osteolytic seen on prior CT scan. The lesion demonstrated slight T1 hyperintense signal to muscle, moderate T2 hyperintense signal and avid enhancement after the administration of intravenous contrast (most notable along the periphery). Edema-like signal on T2-weighted imaging adjacent to the lesion was suspected to represent reactive marrow edema (Figs. 3, 4, and 5).

Given the patient's age, the highest concern was for metastatic disease. Other considerations included plasmacytoma or osteomyelitis. The MRI findings were nonspecific and therefore a CT-guided biopsy with an 11-gauge Osteo-Site M2 bone biopsy needle was performed (Fig. 6). Two fine-needle and one core biopsy specimen were obtained. This revealed only minute fragments of bone and significant hemorrhage, thus an open biopsy was scheduled.

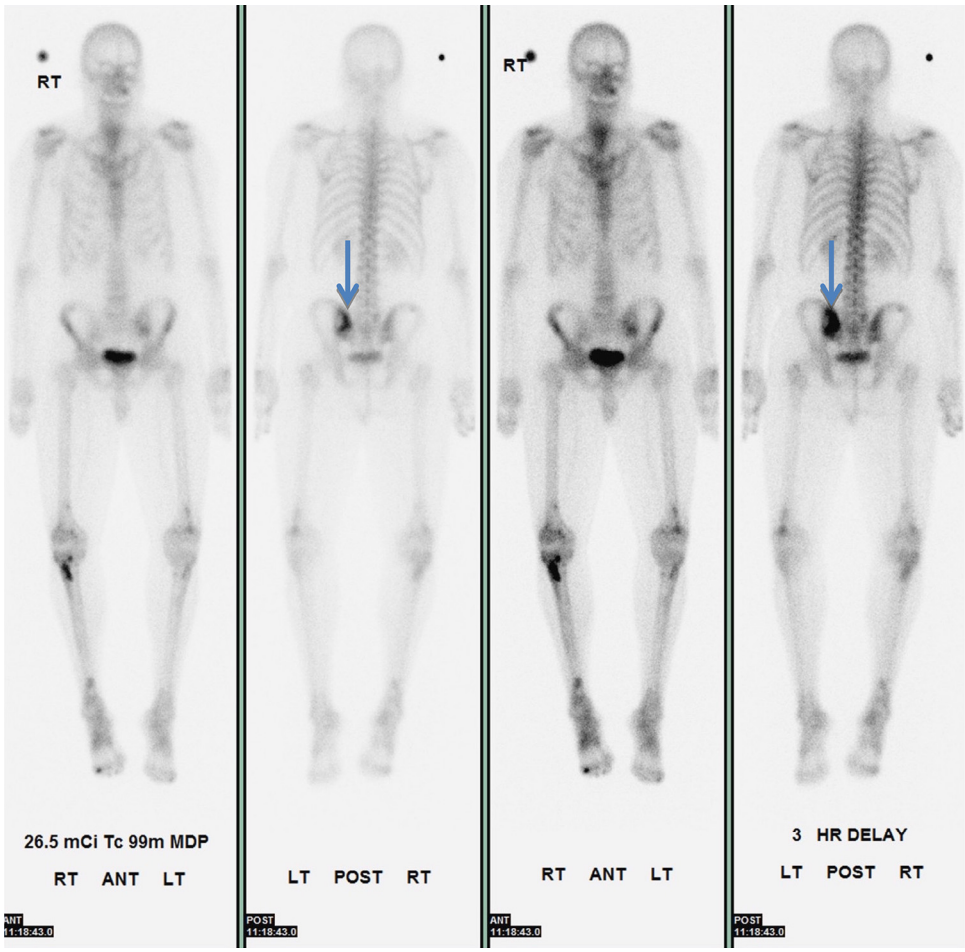

Fig. 2 – Bone scan demonstrates increased radiotracer activity of the left iliac bone adjacent to the sacroiliac joint, corresponding to abnormality on CT. Intense radiotracer activity is also noted in the right proximal tibia from prior fracture and elsewhere within both knees and ankles, not relevant to the current discussion but possibly degenerative/posttraumatic in etiology. CT, computed tomography.

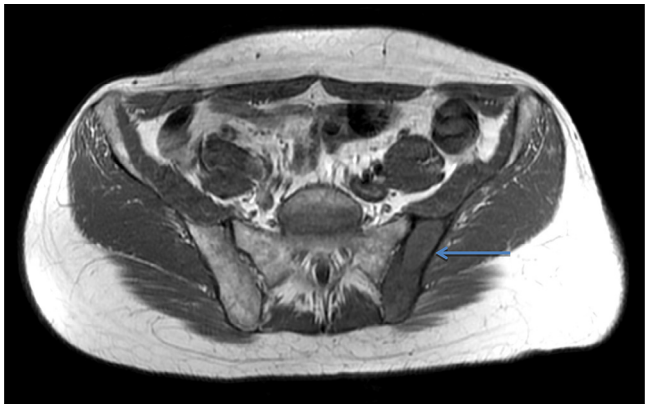

Fig. 3 – Axial T1-weighted non–fat-saturated MRI image demonstrates a slightly T1 hyperintense lesion of the posterior left iliac bone. MRI, magnetic resonance imaging.

Subsequent open biopsy histologic examination revealed fragmented bone with variably sized fragments of tissue demonstrating a lesion composed largely of lymphocytes and macrophages admixed with oval-shaped cells with grooved or indented nuclei with fine chromatin, inconspicuous nucleoli, and slightly eosinophilic cytoplasm. Occasional plasma cells and rare eosinophils were present in a background of fibrous stroma (Figs. 7 and 8). These oval-shaped cells were positive for S100, CD1a, and langerin, the phenotypic profile of Langerhans cells (Fig. 9). Based on the histomorphology and immunohistochemical findings, a diagnosis of Langerhans cell histiocytosis (LCH) was rendered (Figs. 7, 8, and 9).

The patient followed-up 2 months later for repeat MRI (Fig. 10), which demonstrated a stable appearing left iliac bone lesion with new postsurgical changes overlying the posterior subcutaneous soft tissues status post interval biopsy.

Clinically he did not complain of pain or numbness in his extremities and had returned to normal activity.

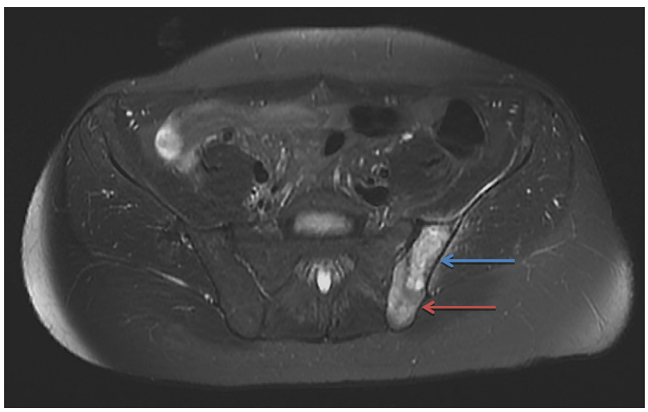

Fig. 4 – Axial T2-weighted fat-saturated MRI image demonstrates a moderately hyperintense left iliac bone lesion at the level of the sacroiliac joint (blue arrow), with suspected adjacent reactive marrow edema (red arrow). MRI, magnetic resonance imaging.

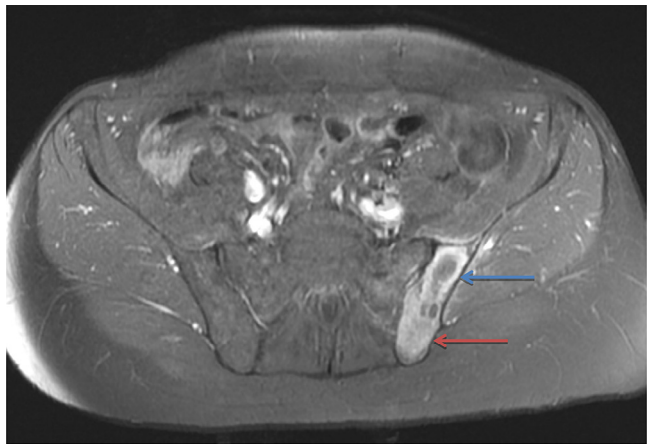

Fig. 5 – Axial T1-weighted fat-saturated postcontrast MRI image demonstrates intense enhancement along the periphery of the lesion (blue arrow) with suspected enhancing reactive marrow edema posterior to the lesion (red arrow). MRI, magnetic resonance imaging.

Discussion

We present a case of a 54–year-old man who presented with left buttock pain which led to initial imaging evaluation with CT scan of the abdomen and pelvis and lumbar spine with subsequent bone scan and MRI. Ultimately, the lesion was found to be consistent with LCH following open biopsy. This rare presentation of LCH in an adult deserves further discussion and review.

LCH is known to affect predominantly a pediatric population. Several reports approximate 90% of patients who present with localized skeletal LCH are between 5 and 15 years of age, with an average age of onset of 10-14 years [1,2]. In his series of adult patients with LCH, Baumgartner et al [3] finds, in comparison to children, that LCH tends to limit itself to a few organ

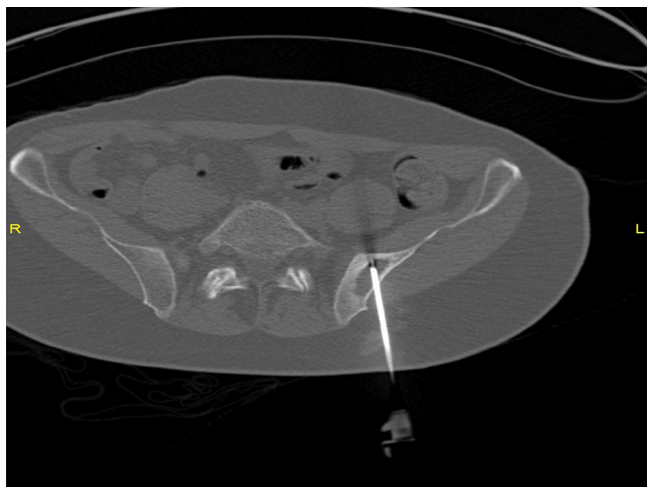

Fig. 6 – CT-guided biopsy of the left iliac bone lesion. CT, computed tomography.

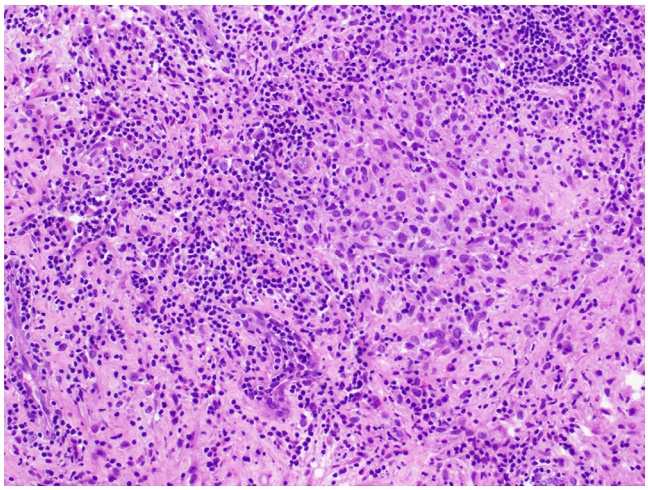

Fig. 7 – 20× H&E LCH biopsy: Langerhans cell histiocytosis. Population of Langerhans cells are seen, with surrounding small lymphocytes and occasional plasma cells and eosinophils. H&E, hematoxylin and eosin.

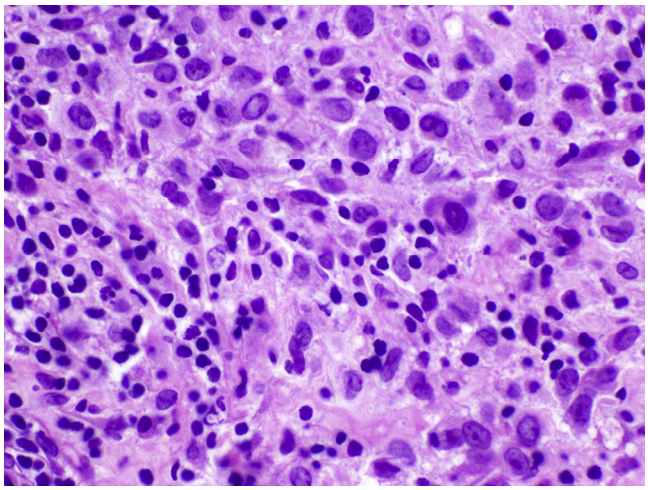

Fig. 8 – 60× H&E LCH biopsy: Langerhans cell histiocytosis. Typical cytologic features are seen, with many nuclei containing nuclear grooves, folding, or indentations with inconspicuous nucleoli. H&E, hematoxylin and eosin.

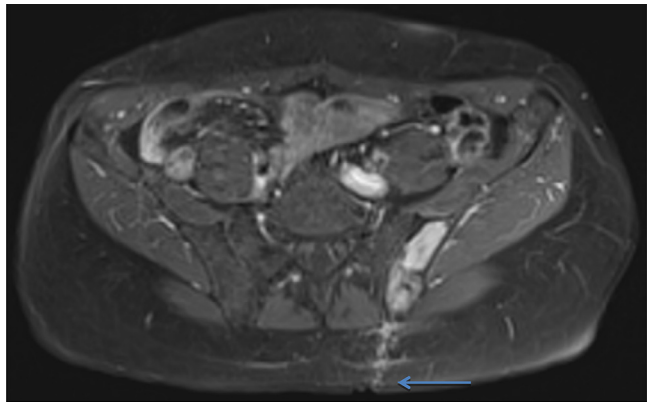

Fig. 10 – Axial T2-weighted fat-saturated (top) and axial postcontrast fat-saturated (bottom) images demonstrate a stable left iliac lesion with new overlying postbiopsy changes within the subcutaneous soft tissues (blue arrow).

systems, in particular the bones and lungs. According to DeCandido [4], approximately 10% of cases occur in patients over the age of 40 years, and only approximately 12% of lesions occur in the pelvis. Although no published data exist specifically evaluating the prevalence of osseous LCH over the age of 50, the disease should be considered exceedingly uncommon in this age group. The International Registry of the Histiocyte Society published a report evaluating 274 adult patients diagnosed with LCH and found a mean age of onset and diagnosis in men and women of 33 years (standard deviation 15 years) and 35 years (standard deviation 14 years), respectively, suggesting that the disease is very rare over the age of 50 [5].

Arkader et al. evaluated 79 children diagnosed with primary musculoskeletal LCH over a 3-decade period and found the natural history for most lesions to be that of gradual healing, with curettage and grafting occasionally indicated to accelerate healing [6]. Although the only way to definitely know whether or not the iliac lesion in our patient was present during childhood would be to have prior imaging as a child, given the natural history of pediatric osseous LCH to heal over time, it would be reasonable to assume that the lesion in our patient arose de novo as an adult rather than persisting from childhood.

LCH is a complex disease processes that has had slow progress with regard to understanding its pathogenesis and treatment. In the year 1868, Paul Langerhans discovered the

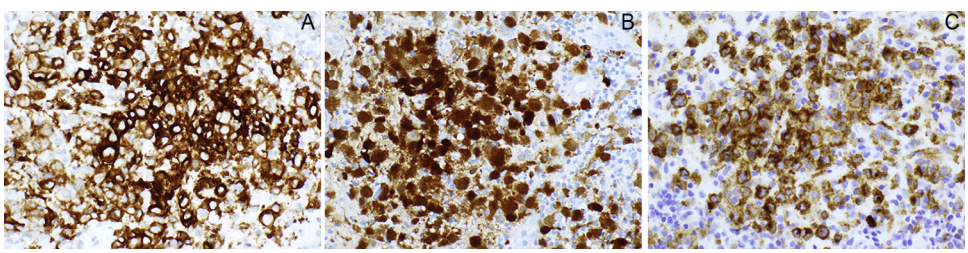

Fig. 9 – (A) 40× CD1a LCH biopsy: CD1a shows membrane positivity. (B) 40× S100 LCH biopsy: S100 shows nuclear and cytoplasmic expression. (C) 40× Langerin LCH biopsy: Langerin shows granular and cytoplasmic staining. LCH, Langerhans cell histiocytosis.

epidermal dendritic cells that now bear his name [7]. However, the Birbeck granule, which is the ultrastructural hallmark of the Langerhans cell, was not identified until the 1970s by Nezelof [8].

Prior to the 1950s, 3 classic presentations of disease were recognized: Letterer-Siwe disease, a somewhat gruesome presentation of LCH that occurred in young children with multisystem involvement (skin, lung, liver, spleen, and bone); Hand-Schuller-Christian disease, a milder disease process noted in older children manifested by lesions in bone, tooth loss, exophthalmos, central diabetes insipidus, and growth hormone deficiency; eosinophilic granuloma, involving one or more osseous structures and demonstrating the best prognosis. In the 1950s, Lichtenstein noted that all of the above diseases demonstrated a common histologic appearance and hypothesized that these diseases are not distinct entities, but must possess a common cell origin [9]. To convey that the above disease processes stem from a common cell origin, the term histiocytosis X was created. The "X" was meant to represent the unknown but common cell origin. Until Nezelof's discovery of the Birbeck granules, which are associated with langerin ($CD207^+$), LCH was referred to as histiocytosis X. The newer name (LCH) emphasizes the histogenesis of the condition by specifying the type of lesional cell and removes the connotation of the unknown ("X") because its cellular basis has now been clarified [10].

The radiologic manifestation of LCH is wide and varied, similar to its clinical presentation, most commonly identified in children but occasionally in adults. Osseous lesions are the most common radiographic appearance of LCH, seen in approximately 80% of patients and may affect any bone, with a predilection for the flat bones, commonly manifesting in the skull but also seen in the mandible, ribs, pelvis, and spine. Although long bone involvement is more common in children, isolated flat bone involvement is more commonly seen in adults and is consistent with the case report findings described above. In the flat bones, one of the more common imaging findings (particularly in the iliac bone) is that of a lytic lesion with a sclerotic rim and surrounding sclerosis. This is concordant with the CT scan findings of our patient. On MRI these lesions often demonstrate T2 hyperintense signal and enhancement after the administration of intravenous contrast, also consistent with findings in our case report. Skeletal scintigraphy often shows increased uptake at the site of disease, as in our case. However, false-negative results on scintigraphy have been reported in older lesions and therefore correlation with radiographs, CT, or MRI is necessary [11].

The imaging findings of LCH are nonspecific with differential diagnostic considerations (depending on patient age), including metastasis, plasmacytoma, unicameral and aneurysmal bone cysts, and chondromyxoid fibroma among other disease processes [11]. Song et al. evaluated the radiologic presentation of several adult patients with LCH and found some distinguishing factors that may help differentiate LCH from more common entities such as metastasis and multiple myeloma. Patients with multiple myeloma commonly present with punched-out lytic lesions, fractures, and rarely sclerosis as opposed to patients with LCH. Similarly, metastatic lesions oftentimes present with cortical destruction, bony remodeling, fractures, and a permeative appearance, unlike LCH. LCH may also be confused with fibrous dysplasia radiographically. However, the authors note that fibrous dysplasia typically demonstrates a ground-glass appearance, whereas LCH does not, and they also found that LCH presented oftentimes with additional findings such as marginal sclerosis, septa, and endosteal scalloping [12].

Although the radiologic findings of LCH in an adult are nonspecific, this diagnosis may be considered in a patient presenting with an isolated osteolytic flat bone lesion demonstrating marginal and surrounding sclerosis, increased T2 signal, and enhancement on MRI with or without uptake on skeletal scintigraphy.

The management of LCH depends on the organ system(s) involved. In patients with isolated skeletal LCH, as in our patient, treatment may consist of curettage and corticosteroid injections [13]. Superimposed radiation may also be considered [1].

In conclusion, while LCH in the adult population is uncommon, it should be kept in mind in a patient presenting with one or more osteolytic lesions.

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