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*Case Report*

# Langerhans cell histiocytosis in a 4-year-old boy with extensive bony lesions

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**Abstract:** Langerhans cell histiocytosis (LCH) is a rare benign disorder of unknown etiology with an estimated incidence of 4 to 5 cases per 100,000 persons per year. LCH can involve almost all parts of the body; however, sever extensive bone involvement is rare. The purpose of this report was to describe the case of a 4-year-old boy who presented with a history of a 2-month old fall injury. Physical examination revealed an angular deformity of the left proximal femur, torticollis, and limited motion of the cervical spine. A comprehensive skeletal survey, computed tomography (CT) scans of the chest, abdomen and pelvis as well as a bone scintigraphy were performed. Multiple lytic lesions of the skull, ribs, sternum, scapulae, spine, pelvis, humeri, femora, tibias and fibulas could be seen in the plain radiographs and CT scans. Bone scintigraphy revealed increased uptake of the technetium radioisotope in multiple bones. Malignant metastasis was excluded. Immunohistochemical staining and electron microscopy confirmed LCH. The patient was treated with systemic chemotherapy (vinblastine and prednisone). Twelve months later his symptoms subsided. The presented case revealed some very rare involvement sites for LCH such as the femoral epiphyses, vertebral plates, sternum, fibulas, and cervical spine. It is also very unusual to find so many involvement sites in one patient.

**Keywords:** Langerhans cell histiocytosis, pediatric, radiograph, computed tomography, pathology

## Introduction

Langerhans cell histiocytosis (LCH) is a rare benign disorder of uncertain etiology, which is characterized by a clonal proliferation of Langerhans cells [1]. LCH is probably an immune regulatory disorder as the most severe cases are found in patients with the most immature immune system. Usually children ages 1 to 3 are affected with an estimated incidence of 4 to 5 cases per 100,000 persons per year [2]. A unique rare case of extensive bone lesions of LCH is described in this report. The patient and the family members were informed that the data from this case would be submitted for publication. Consent was obtained. The Institutional Review Board of the Shengjing Hospital of the China Medical University approved the study.

## Case report

A 4-year-old boy presented to the Pediatric Orthopedics Department, Shengjing Hospital, China Medical University in Shenyang, China, with a history of a fall injury, which took place two months earlier and involved the left thigh. Physical examination revealed an angular deformity of left proximal femur, a torticollis, and limited motion of the cervical spine. A pelvis plain radiograph showed multiple lytic lesions in the pelvis and in the proximal regions of both femora, and a pathological fracture of the left proximal femur (**Figure 1A**). A comprehensive skeletal survey (**Figure 1B-G**), computed tomography (CT) scans of the chest, abdomen and pelvis (**Figure 2A-F**) and a bone scintigraphy (**Figure 3**) were performed in order to rule out other benign lytic lesions and metastatic tumors. Extensive lytic lesions of the skull, sternum, spine, pelvis, both humeri, femora, tibias and fibulas could be seen in the plain radiographs and CT scans. There were some lesions in the proximal diaphysis and metaphysis of the right radius and ulna. The radiographs of the left radius and ulna along with both hands and feet were normal. The CT scans showed multiple lytic lesions

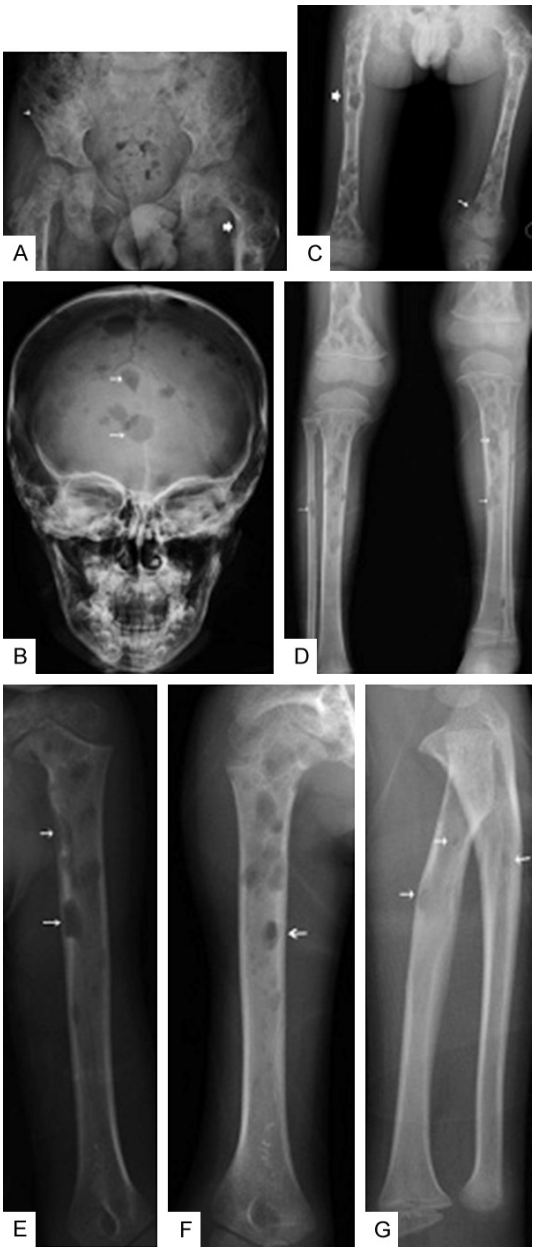


**Figure 1.** A. An anterior-posterior radiograph of the pelvis demonstrates extensive ill-defined lytic lesions in the pelvis and the proximal regions of both femora as well as a late-diagnosed (*thin arrows*). pathological fracture of the left proximal femur (*thick arrow*). B. An anterior-posterior radiograph of the skull shows multiple well-defined cranial defects of different sizes (*arrows*). C. An anterior-posterior plain radiograph of both femora shows multiple well-defined, diaphyseal and metaphyseal medullary lytic lesions with areas of breakthrough of the cortex (*thin arrow*) and thick layer of periosteal reaction (*thick arrow*). D. An anterior-posterior plain radiograph of the tibias and fibulas (*thin arrows*) shows multiple well-defined, diaphyseal and metaphyseal medullary lesions with periosteal reaction. E. An anterior-posterior plain radiograph of the left humerus shows multiple well-defined lytic lesions (*arrows*). F. An anterior-posterior plain radiograph of the right humerus shows multiple well-defined lytic lesions and a characteristic "hole-within-a-hole" effect (*arrow*). G. An anterior-posterior plain radiograph of the right ulna and radius shows multiple mild lesions in the proximal area of both bones (*arrows*).

of vertebral bodies of the cervical, thoracic, lumbar, sacral spine as in the ribs and sternum. The CT scans of the chest and abdomen showed no lesions in the lungs or in the gastrointestinal tract. There was no evidence of metastasis. Technetium bone scintigraphy revealed increased uptakes in the skull, sternum, ribs, scapulae, spine, pelvis, humeri, femora, tibias, and fibulas (**Figure 3**). The child was found to be anemic with a hemoglobin level of 73 G/L. The expansile lytic lesions of the skull, scapulae, and iliac bones were characteristic of flat bones involvement of LCH. Given the appearance of the lesions the most likely diagnosis was LCH.

A bone biopsy of the right iliac lesion was performed. Immunohistochemical staining showed histiocytes with cytoplasmic and membranous staining positive for CD-1a, CD-68, and S-100. Electron microscopic examination revealed Birbeck granules in the infiltrating cells (**Figure 4**). The immunohistochemical and ultrastructural features of the lesions were diagnostic of LCH.

Since the patient had the single-system multifocal type of LCH, he was treated with systemic chemotherapy (vinblastine and prednisone) without bone curettage. Twelve months later his symptoms subsided. This patient is now being followed in the outpatient clinic on a six month basis.

## Discussion

LCH, formerly known as histiocytosis X, encompasses three classic clinical syndromes: eosinophilic granuloma (localized benign form isolated to bone and often monostotic), Hand-Schuller-Christian disease (a chronic form with a classic triad of skull lesions, exophthalmos and diabetes insipidus, occurring between ages 1 and 5) and Letterer-Siwe disease (a fulminant form with disseminated lesions involving multiple visceral organs and occurring in children younger than 2 years of age) [3].

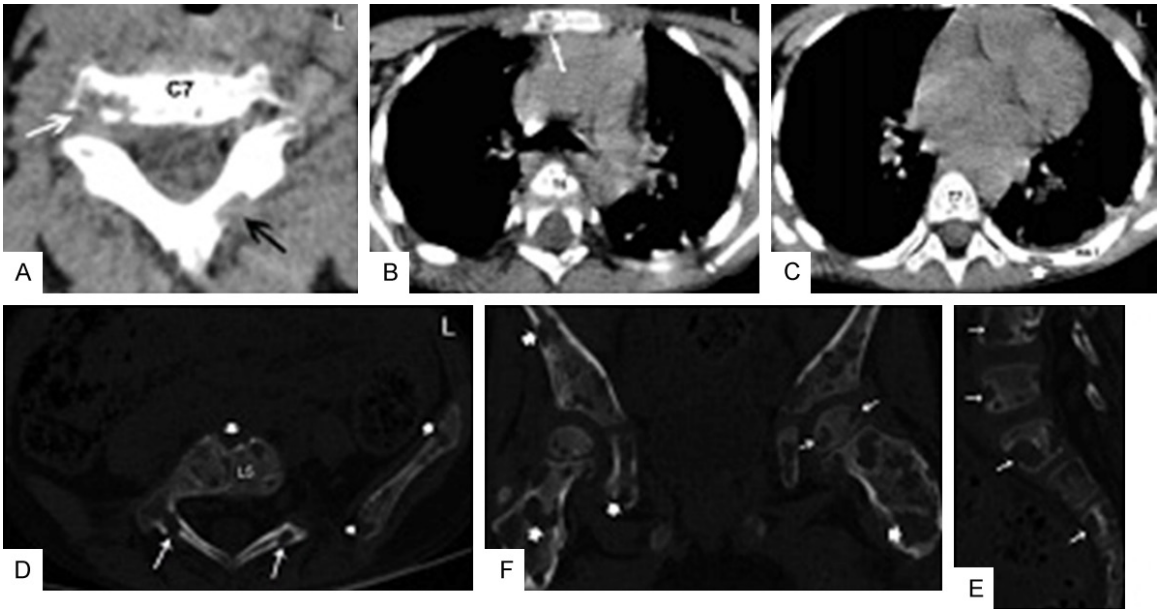


**Figure 2.** A. An axial CT image of the chest at C7 level shows lytic destruction of the vertebral body (*white arrow*) and the left vertebral plate (*black arrow*) of C7. Cervical spine is a rare location for LCH. B. An axial CT image of the chest at T5 level shows lytic destruction of the sternum (*arrow*). Sternum is a rare location for LCH. C. An axial CT image of the chest at T7 level shows lytic destruction of the left posterior rib 7 (*arrow*). D. An axial CT image of the pelvis at L5 level shows multiple lytic destructive lesions in the vertebral body of L5 and left ilium (*thick arrows*). The bilateral vertebral plates of L5 are also involved (*thin arrows*). The posterior spinal structures are very rare locations for LCH. E. A sagittal CT image of the pelvis shows multiple lytic destructive lesions of the vertebral bodies of L4, L5, and sacrum. The discs and soft tissue are not involved. F. A coronal CT image of the pelvis shows multiple lytic destructive lesions in both ilia, the pubes and both femora (*thick arrows*). The epiphyses are very rare locations for LCH (*thin arrows*).

The clinical manifestations of LCH are quite variable depending on the locations of the lesions. LCH can be localized to a single bone or multiple bones, or to a single system or multiple systems. LCH can involve almost all parts of the body, including the bone, skin, lung, liver, spleen, bone marrow and central nervous system; however, the skull and facial bones are most frequently involved. Symptoms in osseous LCH include local bone pain, night pain, soft tissue swelling, tenderness, pathologic fractures, headaches (skull lesions), proptosis (the greater wing of the sphenoid lesions), otitis media (mastoid lesions), floating teeth (maxilla and mandible lesions), and neck or back pain (spinal lesions) [4, 5]. The bony lytic destruction of the cervical spine can result in a torticollis and a limitation of motion of the cervical spine with disappearance of the cervical lordosis. The lytic lesions of the femur can result in pathological fractures (**Figure 1A**).

The imaging diagnosis of LCH has usually involved conventional radiographs because 80% of the cases have osseous lesions. The radiographic appearance depends on the site of involvement and the phase of the disease [3]. LCH usually appears radiographically as a well-defined medullary lucency, often with endosteal scalloping and local or extensive periosteal reaction. Rapidly growing lesions may have indistinct and hazy borders. A characteristic finding is a peculiar beveled contour of the lesion that produces a “hole-within-a-hole” effect (**Figure 1F**). In the skull, LCH typically produces one or more small punched-out areas that originate in the diploic space, expand and perforate both the inner and outer tables, and often contain a central bony density (button sequestrum) [6]. Lesions in the skull are round, oval (**Figure 1B**), or geographic if coalescent. Periosteal reaction and reactive sclerosis are absent in the skull vault.

CT has been helpful in the further delineation of osseous lesions by confirming disruption of the cortex, the extension of lytic lesions and soft-tissue involvement, particularly in the skull base, spine and pelvis where plain radiographs may not adequately demonstrate the lesions [7]. In the spine, LCH mainly involves the vertebral bodies with a predilection for the thoracic

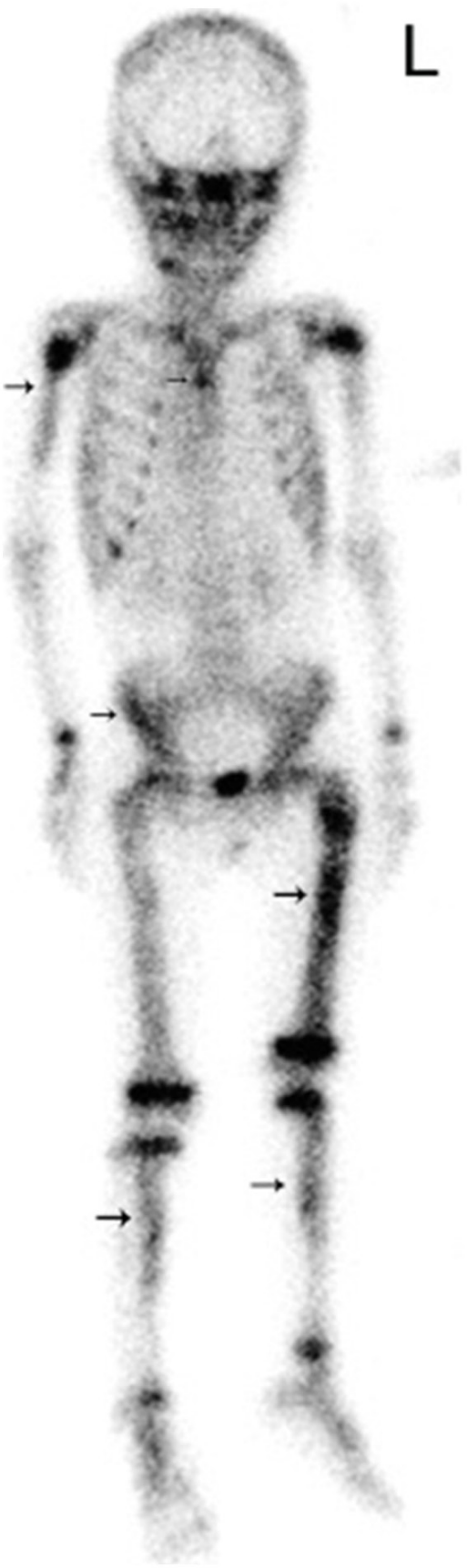


**Figure 3.** Technetium bone scintigraphy reveals increased uptakes in the skull, ribs, sternum, scapulae, spine, pelvis, humeri, femora, tibias, and fibulas (*arrows*).

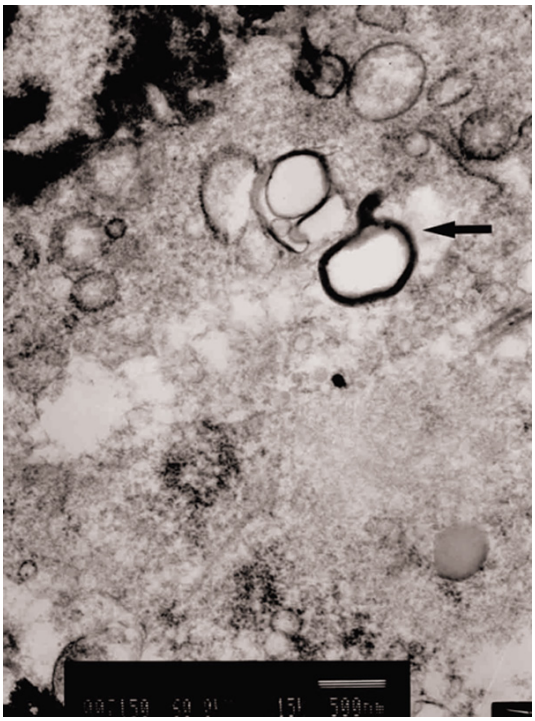

**Figure 4.** Electron microscopic examination reveals Birbeck granule in the infiltrating cells confirming the diagnosis of LCH (*arrow*).

spine followed by the lumbar (**Figure 2D**, **2E**) and cervical spines (**Figure 2A**). Involvement of the vertebral body may result in anterior wedging to near collapse with a characteristic "vertebra plana" appearance [3]. Involvement of the spinal posterior elements is less common [3] and can be seen in this case in the vertebral plate of C7 (**Figure 2A**) and L5 (**Figure 2D**). In flat bones, lytic lesions usually arise in the medullary space and extend to produce cortical destruction and periosteal reaction sometimes laminated. Flat bone involvement is common and lesions in the rib (**Figure 2C**), clavicle, and scapula may be expansile [5].

Magnetic resonance imaging (MRI) is most helpful in evaluating the skull, the central nervous system, bone marrow involvement, as well as soft-tissue mass or inflammation in LCH of the bone. Neural involvement most frequently involves the pituitary hypothalamic region, leading to diabetes insipidus and ante-

rior pituitary hormone deficiency [8]. MRI of the spine can demonstrate the preservation of disc space in LCH, thereby excluding vertebral osteomyelitis and tuberculous vertebral infection [3, 7]. In long bones, MRI shows the lesion to be in the bone marrow and is often ill-defined. The lytic lesion seen on plain radiographs and CT shows a hypointense signal on T1-weighted imaging and hyperintense signal on T2-weighted imaging. Healing lesions show a decrease in signal intensity on T2-weighted follow-up images, indicating gradual re-ossification of the osteolytic lesions, with resolution of the soft-tissue swelling [3]. MRI findings in LCH are nonspecific and may be simulated by osteomyelitis, osteoblastoma and Ewing sarcoma.

Bone scintigraphy in LCH has not been accepted universally as a routine diagnostic method because about 20% of bone lesions are not identified by bone scan [1]. Some lesions can be detected by radiographic skeletal survey and not be demonstrated by bone scintigraphy and vice versa. Patients with small stable lesions and patients undergoing chemotherapy may show a normal bone scan. However, small unstable lesions may be seen on bone scans very early on even when radiographs appear normal [3]. Rib, spine, and pelvic lesions are more easily missed on radiographs. The radiography is more cost-effective while bone scintigraphy is more sensitive [3].

Rare features of LCH, some of which were found in the patient, include lesions crossing a growth plate and involving an epiphysis (**Figure 2F**) or apophysis; lesions involving posterior spinal structures (**Figure 2A**, **2D**), sternum (**Figure 2B**), fibula (**Figure 1D**) or phalanges; intracortical and primary soft tissue lesions; lesions extending across a skull suture; presence of formation of a fluid/fluid level; localization of lesions in the cervical spine (**Figure 2A**); and soft-tissue calcification [3].

The treatment of LCH is still controversial. Many treatments have been described, which include topical steroids, intralesional injections of steroids, nonsteroid anti-inflammatory drugs, phototherapy, bone marrow allografting, stem cell transplantation, and chemotherapy. In general, radiation therapy is not recommended because it may predispose the patients to radiation-induced sarcoma around the irradiated field. Therapy depends on the severity of osseous involvement (single or multiple lesions), location and size of the lesions and presence or absence of systemic involvement [4]. Systemic chemotherapy was selected for our patient because of the extensive osseous involvement and has shown an excellent result.

The prognosis of LCH is variable and unpredictable. The prognosis of LCH depends primarily on the age of the patient and the extent of the disease. At presentation, children under 2 years old with vital organ involvement have a poorer prognosis and more significant morbidity and mortality than those older than 2 years with the localized form of the disease [3].

## Disclosure of conflict of interest

None.

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