

Imaging of Osseous Lesions in Langerhans Cell Histiocytosis (LCH)

Research Article

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Abstract

Introduction: Langerhans Cell Histiocytosis (LCH) is a rare condition resulting from idiopathic proliferation of histiocytes and can affect any organ but is more often seen in bone, lung, skin, lymph nodes and endocrine glands. This paper is aimed at analyzing the imaging patterns of osseous involvement in cases of LCH.

Material and methods: It is a retrospective analysis of 18 histopathologically proven cases of LCH with osseous involvement done at our institute over the last 5 years.

Results: Of the total patients, 13 were males. Most were aged less than 10 years old. The bones involved were skull (n=9), long bones (n=6), vertebrae (n=5), pelvis (n=3), rib (n=1) and clavicle (n=1). Enhancement of soft tissue component was seen in 10 cases. Radiological features depend on site of involvement and phase of disease. Early phase lesions are lytic poorly defined. Lamellated periosteal reaction along with pathological fracture was noted in some. Later, the lesions became more clearly defined with sharp border. Chronic lesions were sclerotic. In our study, involvement of clavicle and posterior element of vertebrae and more affection of cervical than thoracic spine are unusual findings.

Conclusions: Though LCH is common in children less than 2 years, it can occur at any age. Skull involvement is the most common site for bony lesions. Unusual sites like clavicle may be involved. We observed that cervical spine is frequently affected and posterior element involvement is also not uncommon. Full skeletal survey with appropriate imaging is recommended after an initial diagnosis.

Keywords: Langerhans cell Histiocytosis; Eosinophilic granulomas; Hand schuler christian disease; Letterer disease

Introduction

Langerhans Cell Histiocytosis (LCH), previously referred as Histiocytosis X, is a clonal non-neoplastic disorder in which there is idiopathic proliferation of histiocytes resulting in focal or systemic manifestations. There can be painful swelling and sometimes

pathological fracture can occur. Depending on its location and spread to adjacent tissues, the symptoms like proptosis, otitis media, hearing loss, spinal cord compression, loose tooth or Diabetes Insipidus (DI) can be the presenting feature [1]. It is a rare disorder with a reported Incidence of 2-5 cases per million per year in young adults <15 years and 1-2 cases per million per year in adults. It accounts for less than

5% of all primitive bone tumors [2]. It can affect any organ but is more often seen in bone, lung, skin, ln, ears, endocrine glands (except adrenal and gonads, pituitary gland, thymus), CNS, GIT, liver, spleen, bone marrow and blood [3].

Three variants-Eosinophilic Granuloma (EG), Hand Schuler Christian disease (HSC) and Letterer disease (LS) are described based on the pattern of presentation, but a distinction among these three entities is not always possible on clinic-radiological manifestations alone. EG often has bone involvement; single bone involvement is more common than poly-ostotic. In HSC multiple bones and multiple organs (skin, soft tissue, lymph node, liver, thymus and lung) are involved. A clinical triad - calvarial defect, exophthalmos and DI is a recognized pattern in HSC. LS Disease presents with multi organ involvement and is progressively fatal [4]. This paper is aimed at analysing the imaging patterns of osseous involvement in cases of Langerhans cell Histiocytosis, in view of its rarity.

Material and Methods

It is a retrospective analysis of 18 histopathologically proven cases of LCH with osseous involvement done at our institute over the last 10 years. The database of the cases including the histopathologically and imaging reports were retrieved and analyzed.

Results

We analyzed 18 cases of histopathologically proven LCH. Of them 13 were males. Most of them (n=12) were aged less than 10 years old; 3 were in age range of 11 to 20 years and 3 were more than 20 years old. The site of occurrence and the bony lesions are depicted in the Table 1. The bones involved were skull (n=9), long bones (n=6), vertebrae (n=5), pelvis (n=3), rib (n=1) and clavicle (n=1). Enhancement of soft tissue component was seen in 10 cases.

Radiological Features

In children, the osseous involvement is seen in 75-90 % of cases of LCH. Skull is the most common site affecting more than half. About 30% lesions occur in long bones. Other sites that are generally involved include vertebrae, pelvis, ribs and mandible. Hands and feet are uncommon sites of involvement. Multiple bone involvement in the same patients may be seen in 18-30% cases [5]. In study of 47 adults the jaw was the primary site in 30% followed by skull in 21% cases [6].

Table 1

Site	Number involved	Remarks
Skull	9	
Long bones	6	Femur- 4; Ulna- 2
Vertebrae	5	Cervical- 4; Dorsal-3; Lumbar- 2 Collapse of vertebrae in all cases Single vertebra involved in one case ; multiple vertebrae in others
Pelvis	3	
Rib	1	
Clavicle	1	

Radiological features depend on site of involvement and phase of disease. Early phase lesions are lytic poorly defined (Figure 1). Lamellated periosteal reaction may occur along with pathological fracture. Continuous periosteal reaction, cortical thickening are features of less aggressive lesion (Figure 1). Later, the lesions become more clearly defined with sharp border. Sometimes expanded appearance may be due to pre-existing soft tissue or due to lamellated peri-osteal reaction. Chronic lesions may resolve completely or may become sclerotic (Figure 2).

Skull

It is the skull that is most frequently involved and frontal bone is the commonest site. Skull was involved in 9 out of 18 (50%) of our cases. Parieto-temporal bone is the most common site in our observation (Figure 2). Skull lesions are lytic with endosteal scalloping cortical thinning. They are typically round or ovoid, measuring from 1 to 4 cms with well-defined non-sclerotic margin giving punched-out appearance (Figure 2). Uneven destruction of inner and outer table results in bevelled edge or double contour. Lytic lesion may contain a fragment called button sequestrum which refers to a piece of devitalized bone separated from surrounding bone (Figure 2). Button-sequestrum sign is specific for LCH. The number and size of skull lesions may increase with confluent areas resulting in geographic skull (Figure 3). Lesions may be associated with soft tissue which is isodense in T1 and hyper in T2 W images.



Figure 1: AP radiograph of femur reveals permeative lytic lesion in proximal femur with adjacent periosteal reaction in 5 years old male child and radiograph of femur of another 5-year-old male shows irregular ill-defined lytic lesion in diaphysis of femur with periosteal reaction.

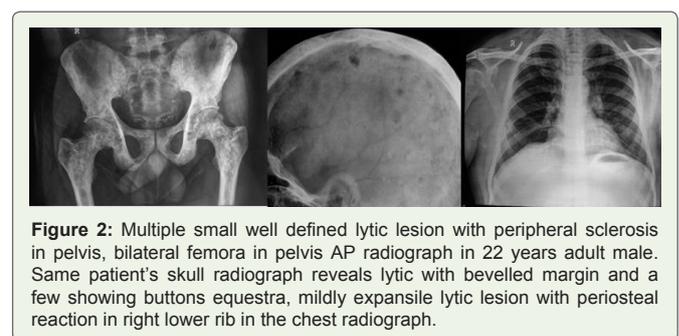


Figure 2: Multiple small well defined lytic lesion with peripheral sclerosis in pelvis, bilateral femora in pelvis AP radiograph in 22 years adult male. Same patient's skull radiograph reveals lytic with bevelled margin and a few showing buttons equestra, mildly expansile lytic lesion with periosteal reaction in right lower rib in the chest radiograph.

Homogenous enhancement is seen in CT and MRI (Figure 4). Sometimes adjacent dural enhancement may be observed on MRI. The differentials include epidermoid and dermoid for a single lesion and when multiple lesions are present, it has to be differentiated from metastatic neuroblastoma [7,8].

Mandible

Typical lesion can cause ‘floating teeth’ appearance when it has to be differentiated from periodontal disease, hyperparathyroidism, metastases, multiple myeloma, ameloblastoma, osteomyelitis, lymphoma, alveolar squamous cell carcinoma or Ewing’s sarcoma (Figure 5) [9].

Flat bones

Rib involvement produces geographic moth-eaten or permeative pattern of lysis (Figure 2). It is sometimes associated with soft tissue

involvement and may be associated with pathological fracture. Periosteal reaction is seen in pelvic bone lesion (Figure 4). Surrounding zone of sclerosis and well defined rim is seen in pelvic lesion, which is not seen in other flat bones. Scapular lesion appears as large irregular lytic area with little or no sclerosis. Expansile permeative lytic lesions occur in clavicle and when there is destruction of cortex, abundant periosteal reaction is observed (Figure 6). The common differentials may be considered are osteomyelitis and small round cell tumors [10].

Vertebra

LCH involvement of vertebra is known to occur in 10-18% of pediatric spinal tumor [11]. Thoracic vertebrae are more commonly involved (54%) than lumbar (35%), which is more than cervical vertebra (11%) (Figure 7) [12]. In contrast, majority of our cases have cervical (n=4) followed by dorsal (n=3) followed by lumbar vertebra (n=2). Solitary vertebra involvement occurs in 10% cases. Vertebral involvement was single level in 1 case and multiple in 4 of our series (Figure 7). Vertebral body is more involved and posterior elements

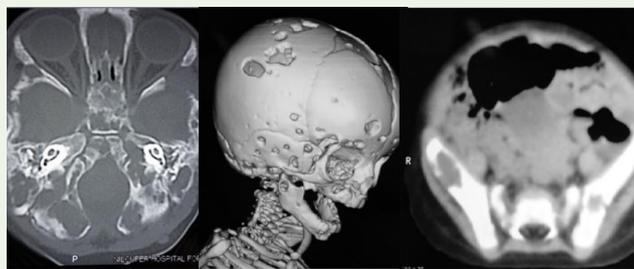


Figure 3: Axial CT in bone window at base of skull depicts multiple geographic lytic lesions in all the bones and 3D reconstruction demonstrates the lesions clearly and the lesion in right iliac. Sagittal reconstruction reveals multiple vertebrae are involved and posterior elements are also affected along with the vertebral bodies which is rare.

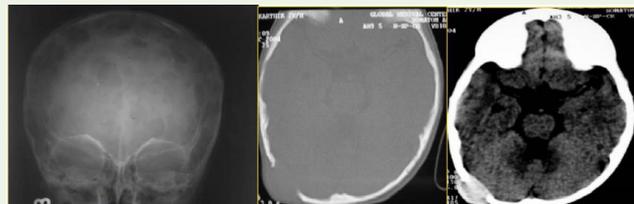


Figure 4: AP skull radiograph of 2 years M child reveals multiple lytic lesions in bilateral frontal, temporal, parietal bones and contrast enhanced axial CT of another 2-year-old child shows lytic lesion with bevelled margin in bone window and contrast enhanced soft tissue in soft tissue window.

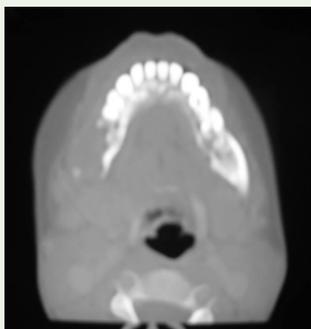


Figure 5: CT axial image of mandible in bone window shows focal lytic lesion of right mandible in a 4 years male child.

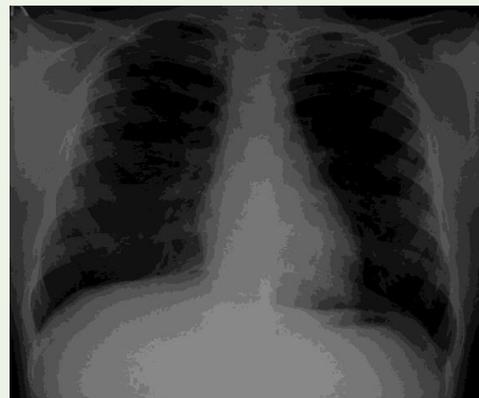


Figure 6: Chest radiograph reveals lytic lesion of left clavicle at medial end in a 23 years M.



Figure 7: Lateral radiograph and T2W sagittal MRI images reveal collapse of D8, D11 vertebrae, axial T1W MRI reveals soft tissue, epidural component and involvement of posterior elements.

are rare [13]. Involvement of posterior elements was observed in 3 of our 5 cases of spinal involvement which is unusual (Figures 7,8).

The initial lesion may be lytic. Typically solitary, well defined with scalloped vertebral body. Alternatively the body of vertebra may be abnormally flattened. The intervertebral disc a little widened or is normal. Gradually vertebral collapse gives vertebra plana or 'coin on edge' appearance. Typical vertebral plana is reported in only 40% of LCH (Figure 8). It is more common in children [14,15].

Cervical lesion usually involves core of vertebral body with lytic lesion while in thoracic and lumbar area, there is more tendency for collapse. The collapse may be symmetrical or asymmetrical. Vertebra plana with sclerosis, coarsening of trabecular pattern and 'bone within bone' appearance of intra body osseous lesion are common features. Soft tissue component may be seen (Figure 7). Disc spaces are preserved. Vertebral height may be restored spontaneously or after treatment. Sometimes affected vertebra reverts to an almost normal configuration [16].

Long bones

Long bone involvement is seen in 30% cases, like our series showing 6 out of 18 (30%). In long bones femur is the most common site as in the present series (n=4) followed by tibia and humerus (Figure 1). Diaphysis is the most common site of long bone involvement. A well-defined lytic lesion with or without sclerotic margins is the classical appearance. Metaphysis can also be affected and rarely may extend to growth plate to involve epiphysis. Pure epiphyseal lesions are rare. Endosteal scalloping, cortical thinning, intra cortical tunneling, widening of medullary cavity are the most frequent changes that are noted (Figure 9). Sometimes lesion may be permeative and mimics malignancy. Sometimes lesion penetrates the cortex and extends to adjacent soft tissue (Figure 10). The endosteal scalloping appears as budding appearance in CT and MRI (Figure 10). Periosteal reaction may be aggressive or may be absent. Periosteal reactions may occur with or without pathological fracture. It may be thin, intermediate or more solid form and may be circumferential (Figure 1). At this stage it has to be differentiated from osteomyelitis, Ewing's sarcoma or lymphoma (Figure 9). Sclerosis is noted with treatment with more defined margin and lesion may even disappear. Sometimes lesions may be mixed lytic and sclerotic due to chronicity with elements of healing [8].

Unusual Skeletal Changes

Unusual sites are epiphysis, trans-physeal plate extension, button

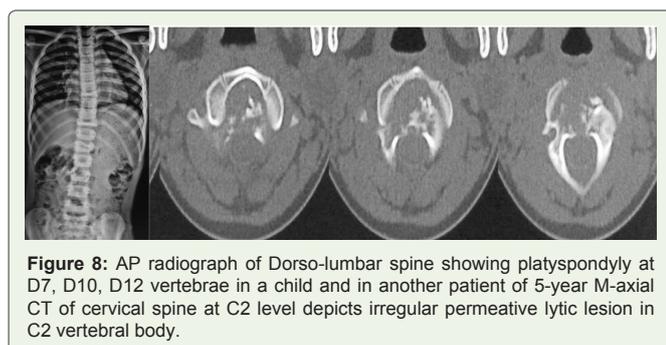


Figure 8: AP radiograph of Dorso-lumbar spine showing platyspondyly at D7, D10, D12 vertebrae in a child and in another patient of 5-year M-axial CT of cervical spine at C2 level depicts irregular permeative lytic lesion in C2 vertebral body.



Figure 9: 8-year-old female presented with a lesion in meta-diaphysis with intracortical tunneling of upper end of ulna in AP radiograph and permeative expansile lytic lesion with periosteal reaction in upper metaphysis of femur mimicking round cell tumor in another female child confirmed to be LCH on HPE.



Figure 10: Radiograph of 18 months old child revealing expansile permeative pattern of lytic lesion in metaphysis of ulna. T1W, STIR axial MRI scan show the lesion along with soft tissue component and budding appearance is well seen due to endosteal scalloping.

sequestra in extra cranial sites, dural extension of vertebral lesion, involvement of clavicle, posterior arch, small bones of hands and feet [17]. In our study, involvement of clavicle and posterior element of vertebrae, more affection of cervical spine than thoracic spine and extra-skeletal affection are unusual findings.

Poor Prognostic Factors

Presentation before two years, poly-ostotic (>3bones), bone lesion spreading to adjacent soft tissue, hepato-splenomegaly and bone marrow involvement are considered as poor prognostic signs [18].

Role of Imaging Work Up

Most of bony lesions are detected by radiographs and had been used conventionally for several years. Radionuclide bone scan typically shows 'hot' spot and nuclear scan may reveal additional lesions in complex sites. CT and MRI are done for better delineation of the lesions. CT is particularly helpful in confirming periosteal reactions and cortical erosion. It facilitates the evaluation of skeletal areas difficult to assess by radiographs such as skull, facial bones and pelvic bones. MRI is most suited for assessment of involvement of paravertebral soft tissue. PET-CT is for localization of multiplicity of lesions and for treatment response. The activity of lesions can be assessed by MRI or PET scanning [19].

Treatment

EG may resolve spontaneously and resolution is unaffected by mode of therapy. Surgery, Radiation, Chemotherapy, steroids either alone or in combination are tried. Surgery is indicated when neurologic affection is found.

Conclusion

Though LCH is common in children less than 2 years, it can occur at any age. Skull involvement is the most common site for bony lesions. Unusual sites like clavicle may be involved as seen in one of our cases. Though it is described in literature that thoracic spine is affected more commonly, we observed that cervical spine is frequently affected and posterior element involvement is also not uncommon. Enhancing soft tissue is also commonly observed. After initial diagnosis in a case of LCH, it is crucial to find out if there is a single or multiple lesions for which full skeletal survey with appropriate imaging is recommended.

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