

Case Report

Langerhans Cell Histiocytosis: Literature Review & Case Report

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Abstract: LCH is a disorder of unknown cause, characterized by an abnormal proliferation of histiocytes. The disease has a predilection for children, although LCH may occur in adults. The basic histopathological findings are identical in the three well established clinical syndromes (*eosinophilic granuloma*, *Hand-Schüller-Christian disease*, *Letterer-Siwe disease*). Knowledge of the spectrum of clinical features and radiological appearances will facilitate early diagnosis. The radiographic skeletal survey is the cornerstone of the initial imaging evaluation for *Langerhans cell histiocytosis* because it allows the detection of bone lesions, which occur in most children affected by the disease. To accurately detect *Langerhans cell histiocytosis* at an early stage, radiologists must recognize the significance of individual clinical and laboratory findings as well as the relevance of imaging features for the differential diagnosis.

Keywords: Histiocytosis, Langerhans Cell, Histiocytosis-X, Letterer-Siwe Disease, Hand Schüller Christian Disease

INTRODUCTION

The disorder was first described on the basis of purely clinical observations more than a century ago, after the Langerhans cell was detected by the medical student Paul Langerhans in 1865 [1]. Over the years, the terms *eosinophilic granuloma*, *Hand-Schüller-Christian disease*, and *Letterer-Siwe disease* were devised to denote the most common clinical manifestations within a broad spectrum of divergent disease patterns (from localized to multifocal involvement) with increasing degrees of severity. In 1953, Liechtenstein observed that the underlying component of all these manifestations was the histiocyte. This observation was followed by the recognition of the many separately defined syndromes as a single disease entity: *histiocytosis X* (X being the unknown etiologic factor [1]).

In 1985, the Writing Group of the Histiocyte Society established a histiocytosis classification system based on distinct pathologic criteria and on the clinical evolution of disease. Under the definitive name *Langerhans cell histiocytosis*, the disease was designated as class I of the histiocytic disorders [2]

Langerhans cell histiocytosis (LCH) presents a diagnostic challenge because it may manifest with a heterogeneous spectrum of lesions, ranging from a single bone lesion to multisystem disease. The clinical course and outcome vary, depending on the patient's age, the distribution and extension of the lesions, and the degree of organ dysfunction present at the time of initial diagnosis [3,4,5]. Fatal outcomes occur most often in very young children (younger than 2 years) with multisystem involvement, for which aggressive therapy is warranted [5,6,7]. Treatment generally consists of multiagent chemotherapy and

immunosuppressant therapy. However, because the pathophysiology of *Langerhans cell histiocytosis* is only poorly understood, treatment approaches remain empirical, and the response to treatment is seldom predictable [6].

The annual incidence of *Langerhans cell histiocytosis* is reported to be between 2.6 and 5.4 cases per million children in the general population. The peak age at initial diagnosis is from 1 to 3 years, but the disease may manifest at any age [1,3,4]. Boys are more often affected than girls [1,5].

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CASE REPORT

A 4yrs old, male patient presented in orthopedics OPD of our institute with complaints of pain in back and knee, cutaneous lesions resembling seborrheic dermatitis involving the scalp, face and trunk. On examination there was tenderness in dorsal spine and knee. There was no history of trauma. Patient was referred to our department for X-ray knee and spine. X-ray knee revealed lytic defects with non-sclerotic margins and endosteal scalloping in metaphysis of lower end of bilateral femur and metaphysis and diaphysis of bilateral tibia. (Figure-1,2). X-ray spine revealed collapse of multiple vertebral bodies, characteristic "vertebra plana" appearance (Figure-3). A skeletal survey was advised. X-ray skull revealed multiple, lytic lesions with non-sclerotic, scalloped margins, likened to a map described as the "geographical skull" (Figure-4). X-ray elbow

showed multiple,lytic defects in long bones with endosteal scalloping-described as ‘hole-within-hole’ appearance(Figure-5). X-ray Chest showed lytic lesions affecting multiple ribs(Figure-6). On basis of characteristic osseous lesions a diagnosis of *Langerhans cell histiocytosis* was made.



Fig.1:Radiograph of bilateral knee-A.P. view.Lytic lesions with non-sclerotic,scalloped margins in metaphysis of lower end femur and upper end tibia.



Fig.2: Radiograph bilateral leg-A.P.View. Lytic lesion with scalloped margins meta-and diaphysis of bilateral tibia.



FIG. 3a FIG. 3b
Fig.3: Radiograph of dorsal spine.A.P. view(a,b). Collapsed bodies of D10 and L1 vertebra- ‘vertebra plana’.



Fig.4: Radiograph skull-lateral view.Multiple,lytic lesion with non-sclerotic, scalloped margins with a maplike configuration- ‘Geographical skull’

DISCUSSION

Little is yet known about the etiology and pathogenesis of *Langerhans cell histiocytosis* [7],despite the steady accrual of epidemiologic data [3,4,5]. There is no evidence that the disease originates in a malignant neoplastic process [2],and no underlying viral or genetic cause has been identified. To date, the most likely theory postulates a histopathologically benign, primarily reactive, and probably immunologically mediated process [9,10]. The X in the older term *histiocytosis X* reflects the earlier lack of understanding of the disease etiology and the underlying pathophysiologic process, whereas the current term *Langerhans cell histiocytosis* reflects the more recent recognition of the central role of the Langerhans cell in the disorder, as well as the definition of specific morphologic, immunohistochemical, and clinical criteria for diagnosis [10].

Historically, this disease was termed *eosinophilic granuloma* when only bone lesions were present,*Hand-Schuller-Christian disease* when there was triad of bone lesions,diabetes insipidus and exophthalmos,and *Letterer-Siwe disease* when children,usually less than 2years old,had disseminated disease marked by wasting,generalized lymphadenopathy,hepato-splenomegaly,anaemia and sometimes pancytopenia [11].

Solitary *LCH* may occur in any bone,although there is a predilection for the flat bones,with more than half of skeletal lesions occurring in skull,mandible,ribs and pelvis [12].Calvarial lesions are common and tend to have sharp borders with involvement of the inner and outer tables of the skull, resulting in a beveled edge appearance [13].In skull the lesions frequently coalesce to produce widespread irregular defects usually likened to a map and described as the ‘geographical skull’ (14).Lesions in the mandible and maxilla begin round the tooth roots,so that the teeth,which are never affected,remains dense and appear to ‘float in

air'(14).Solitary lesion in the spine may collapse,partially or completely,the later presenting the classical appearance of 'vertebra plana' [14,15].The most common affected site is the thoracic spine.During the phase of collapse,the wall of the affected vertebral body tend to bulge laterally and paravertebral soft tissue shadows may be evident.The disc spaces on either side remain intact and may even be widened.The differential diagnosis of vertebra plana includes relative rarities of Ewing's tumour,metastasis from neuroblastoma,benign osteoblastoma,haemangioma,aneurismal bone cyst,atypical tuberculous focus and Calve's disease[8,14].Osteolytic lesion with non-sclerotic margins may develop in the scapula,ribs and pelvis.Any portion of the ilium may be affected in solitary or multifocal bone involvement.The supra-acetabular portion is most frequently involved.The iliac wings,iliac bone adjacent to the sacroiliac joints and ischiopubic rami are other common sites of pelvic *LCH*.

Approximately 25-35% of monostotic lesions occur in the long bones,most commonly the femur, followed by humerus and tibia.Most lesion arise in diaphysis(58%),metaphysis(28%),or metadiaphysis(12%).Epiphyseal lesions are rare(2%).Solitary lesion of short tubular bones of the hands and feet are distinctly uncommon[23]. In the long bones,endosteal scalloping,cortical thinning,intracortical tunneling and widening of medullary cavity are common radiographic findings [13].Initially *LCH* arising in long bone produces an area of poorly defined medullary destruction.Defects may enlarge and erode endosteal cortex causing endosteal scalloping.Confluent lesion imparts 'hole-within-hole'appearance.Later,well defined lytic defects are seen.A sharply defined, sclerotic margins indicate a more mature lesion.With healing lesion may appear sclerotic or may completely disappear with little or no deformity [12].Although the presence of vertebra plana.beveled lytic,map-like skull lesion or floating teeth may suggest the diagnosis,imaging findings are often non-specific.

Osteomyelitis,Ewing sarcoma,leukemia,lymphoma and metastatic neuroblastoma should be considered in the differential diagnosis for many of the individual bone lesion[13],especially those involving the long bones and pelvis.Venous lakes,arachnoid granulations,parietal foramina,epidermoid cyst and haemangioma may be considered as possible causes of lytic skull lesions[13]. To accurately detect *Langerhans cell histiocytosis* at an early stage, radiologists must recognize the significance of individual clinical and laboratory findings as well as the relevance of imaging features for the differential diagnosis.

CONCLUSION

LCH is a disorder of unknown cause,characterized by an abnormal proliferation of

histiocytes.The disease has a predilection for children,although *LCH* may occur in adults.The basic histopathological findings are identical in the three well established clinical syndromes (*eosinophilic granuloma,Hand-Schuller-Christian disease,Letterer-Siwe disease*).Prognosis depends on age of presentation and extent of vital organ involvement.Knowledge of the spectrum of clinical features and radiological appearances will facilitate early diagnosis.

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