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Pathology

LANGERHANS CELL HISTIOCYTOSIS – A RARE CASE REPORT

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ABSTRACT Langerhans cell histiocytosis is rare, clonal, and likely neoplastic proliferation of neoplastic Langerhans cells. Mainly occurs in childhood (< 30 yrs) and more in males. Most commonly site being skull. We present a case of 4yr old male child who presented with complaint of painful swelling in lower right arm for 3 months. The child was unable to move his left forearm. On examination, a tender bony swelling was felt at lower end of right humerus. X-ray revealed a lytic lesion. FNAC was performed by 22 gauge needle. Diagnosis of Langerhans cell histiocytosis was rendered which was confirmed by histopathological examination of biopsy tissue from the representative area. Thus, FNAC is valuable is valuable in making primary diagnosis of Langerhans cell histiocytosis.

KEYWORDS : Langerhans cell Histiocytosis, clonal, neoplastic, Langerhans cells, lytic.

Introduction- Langerhans cell histiocytosis is rare, clonal, and likely neoplastic proliferation of neoplastic Langerhans cells. Langerhans cells are derived from bone marrow, circulate freely from skin to regional lymph nodes.[1] Langerhans cell histiocytosis (LCH) affects patients from the neonatal period to adulthood, although it appears to be more common in children aged 0-15 years.[2]The incidence appears to be 3-5 cases per million children, and 1-2 cases per million adults.[3]The disease has gone by several names, including –HandSchüller–Christian disease, Abt-Letterer-Siwe disease, Hashimoto-Pritzker disease(a very rare self limiting variant seen at birth) and histiocytosis X, until it was renamed in 1985 by the Histiocyte Society.[1] LCH is clinically divided into three groups: unifocal, multifocal unisystem, and multifocal multisystem.[4] Pulmonary Langerhans Cell Histiocytosis (PLCH) is a unique form of LCH in that it occurs almost exclusively in cigarette smokers.[5] Gene BRAFV600E mutations are seen in some cases of Langerhans Cell Histiocytosis.[6]The cornerstone of diagnosis in LCH includes identification of the characteristic clinical features, but also requires corroborating histopathological and immunohistochemical findings.[7] Prognosis is dependent on a variety of factors, including the age of onset, the number of organs involved, the degree to which normal function of the organs is affected and the rate of disease progression.[8]

Case Presentation-

We present a case of 4yr old male child who presented with complaint of painful swelling in lower right arm for 3 months. The child was unable to move his left forearm. There was history of trauma 8 months back without any fracture. On examination, a tender bony swelling was felt at lower end of right humerus and there were no signs of inflammation, fever, or any other swelling or skin lesions. X-ray revealed a lytic lesion. (Figure 1).

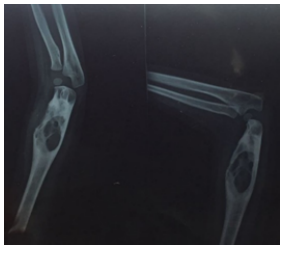

Fig. 1

FNAC Findings-

FNAC was performed by 22 gauge needle. Diagnosis of Langerhans cell histiocytosis was rendered. Microscopically, aggregates of large histiocytes with nucleus displaying grooves and folding (coffee bean nucleus) and eosinophilic cytoplasm along with admixture of inflammatory cells, mainly eosinophils.(Figure 2).

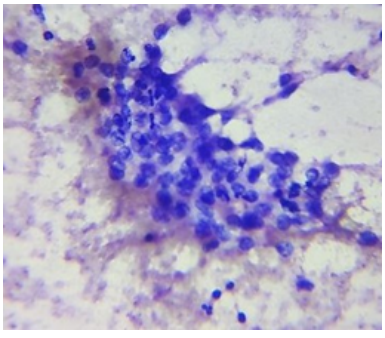

Fig 2

Histopathological Findings-

Gross- Specimen consists of multiple greyish white soft to firm tissue pieces altogether measuring 3.5 x 3 cm.

Microscopic Findings- H&E stained sections show sheets of histiocytic cells which are ovoid cells with longitudinal groove and eosinophilic cytoplasm. These are mixed with inflammatory cell infiltrate comprising of eosinophils, lymphocytes.(Figure 3).

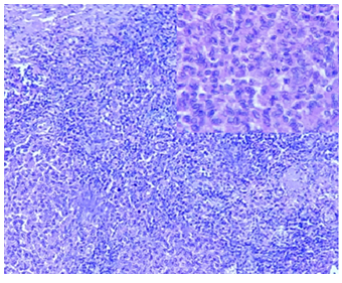

Figure 3 showing microscopic features in low power (10x) with high power (40x) in inset.

Results-
Diagnosis of Langerhans Cell Histiocytosis was made.

DISCUSSION-
Clinically and histologically the histiocytoses comprise a diverse group of proliferative disorders characterized by the infiltration and accumulation of histiocytes and other effector cells of the immune system within various tissues. The generic term "histiocyte" refers to several types of cells including: monocytes/macrophages, dermal/interstitial dendritic cells and Langerhans cells.[9] Histiocytes are critical cells of the immune system: macrophages primarily act as scavenger cells that process antigens whereas LCs serve primarily as antigen presenting cells. In the past, there had been a great deal of confusion as to how to classify the histiocytoses since the exact ontogeny was not completely understood. However, with the advent of immunohistochemical stains, the Histocyte Society proposed reclassification of these disorders based upon the predominant cell type in the infiltrate. This initial classification system included: Langerhans histiocytosis (Class I), non-Langerhans cell histiocytosis (Class II), and malignant histiocytosis (Class III).[10] As more information has become available, a revised classification schema was proposed and includes: dendritic cell disorders, macrophage-related disorders, and lastly, malignant histiocytic disorders.[11]

The prevalence of LCH seems to be higher among whites than other races. The incidence of LCH is greater in males than in females, with a male-to-female ratio of 2:1.[12]The incidence appears to be 3-5 cases per million children, and 1-2 cases per million adults.[3]We are presenting a case of 4 yr old male child.

LCH may affect a single or a multitude of different organs. Most commonly it involves the bone, lung, central nervous system, liver, thymus, skin, and lymph node. The extent and severity of the disease may vary widely, and it could range from benign and self-limiting to lethal.[13]

LCH is clinically divided into three groups: unifocal, multifocal unisystem, and multifocal multisystem.[4] Unifocal LCH, also called Eosinophilic Granuloma, is a slowly progressing disease characterized by an expanding proliferation of Langerhans Cells in various bones. It can be a monostotic (involving only one bone) or polyostotic (involving more than one bone) disease.[14] The most common sites differ depending on the patient's age. In children, the most frequent sites of involvement are the skull (40%), femur, rib, vertebra, and humerus.[15]In contrast, the primary sites of bone involvement in adults in one study were jaw (30%), skull (21%), vertebra (13%), pelvis (13%), extremity (17%), and rib (6%).[3] In this case humerus is involved. It typically has no extraskeletal involvement, but rarely an identical lesion can be found in the skin, lungs, or stomach. When found in the lungs, it should be distinguished from Pulmonary Langerhans cell hystiocytosis—a special category of disease most commonly seen in adult smokers.[16]

Seen mostly in children, multifocal unisystem LCH is characterized by fever, bone lesions and diffuse eruptions, usually on the scalp and in the ear canals. 50% of cases involve the pituitary stalk, leading to diabetes insipidus. The triad of diabetes insipidus, exopthalmos, and lytic bone lesions is known as the Hand-Schüller-Christian triad. Peak onset is 2–10 years of age.[17]

Multisystem LCH, also called Letterer-Siwe disease, outlines the involvement of two or more organ systems with or without organ dysfunction and can further be divided into low-risk and high-risk according to involvement of high-risk organs such as liver, spleen, lung and hematopoietic system that predisposes to higher mortality.[18] It is mostly seen in children under age 2, and the prognosis is poor: even with aggressive chemotherapy, the five-year survival is only 50%.[17]

LCH provokes a non-specific inflammatory response, which includes fever, lethargy, and weight loss. Organ involvement can also cause more specific symptoms. The most frequently seen symptom in both unifocal and multifocal disease is painful bone swelling. Osteolytic lesions can lead to pathological fractures.[19]

The histiocyte society has established a set of guidelines to assist in the diagnosis, and study of LCH includes complete physical and hematological examination along with liver function tests, urine osmolality, and bone marrow examination. For a definitive diagnosis, a complete skeletal radiographic survey and chest radiography is also necessary.[20] The varied clinical presentation of Langerhans cell histiocytosis can make diagnosis difficult. The clinical and radiographic findings frequently are not specific enough to determine the diagnosis. Some patients may have an elevated erythrocyte sedimentation rate and patients with disseminated disease frequently have anemia. There are no diagnostic laboratory studies, and in many instances biopsy is necessary to establish the diagnosis.[21] In the present case, the blood investigation showed increased ESR rate and reduced hemoglobin. Bone lesions caused by Langerhans cell histiocytosis vary from focal sharply defined areas of bone lysis to diffuse osteopenia and can resemble lesions caused by a wide variety of metabolic, infectious and neoplastic diseases. The natural history varies from a benign disorder that resolves spontaneously to a progressive fatal disease. In general, the younger the individual at the time of onset of the disease, the poorer the prognosis and the more extensive the disease.[22]

As LCH does not give any pathognomonic clinical and radiographic features, the diagnosis of LCH is based on microscopic examination of obtained biopsy specimen from the bony lesions. The histopathological pattern demonstrates a diffuse infiltration of large pale staining mononuclear cells that resemble histiocytes with indistinct cytoplasmic borders and rounded or indented vesicular nuclei. The number of eosinophils vary and are typically interspersed among the histiocytes along with the presence of Plasma cells, lymphocytes, and multinucleated giant cells.[23] The presence of Langerhans cells is necessary for diagnosis.

Conclusion-
FNAC is valuable is valuable in making primary diagnosis of Langerhans cell histiocytosis as the microscopic features are characteristic and the findings are well supported by histopathological correlation.

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