Case Report

Langerhans' Cell Histiocytosis-A Case Report

Diagnostic Challenge in A $2^1/_2$ Years Age Girl: A Cliniceo-Radio-Pathological Correlation

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Reporting a case of Langerhans Cell Histiocytosis in a pediatric patient.

CASE REPORT:

A 2_ years old child was brought to this hospital with a history of fever associated with failure to thrive since the age of 16 months. The past and family history was noncontributory. She was a full term baby and immunized as per EPI and her infancy.

On examination, she was a stunted, wasted and irritable child. She had cervical lymphadenopathy and features of gingivitis. There was evidence of BCG scar. She had erythematous rashes on the palm, sole and abdomen. Chest and CVS examination was normal. Per abdomen examination revealed palpable liver 3cm and spleen 2cm below costal margin.

On investigation, the blood count including platelet was within normal range but the ESR was elevated (ESR-38mm/1st hr). Blood and urine chemistry revealed normal findings. Mountoux skin reaction was within normal limit, Gastric aspirate for AFB was negative. Her chest X-Ray showed miliary shadows (Fig1) distributed throughout the lung fields. With this background information of clinical findings, investigation reports and chest radiograph features several possibilities in terms of etiologic categories were thought of. The most likely condition in this case was put in favor of miliary tuberculosis. Other differential diagnosis like histoplasmosis, viral infections, Loeffler's pneumonia and Langerhans' cell histiocytosis were also considered.

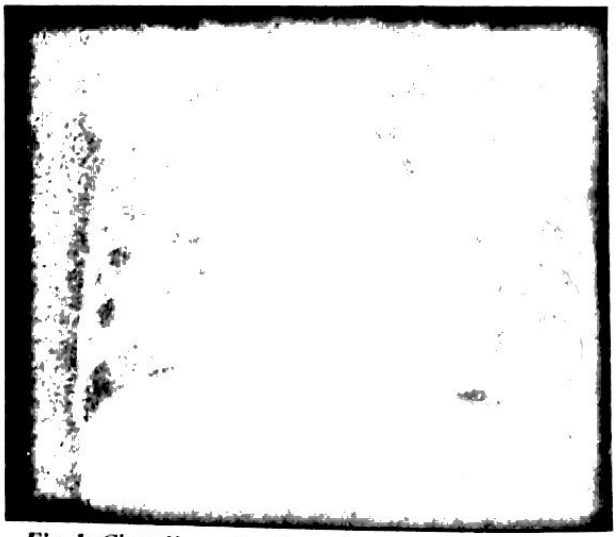

***Fig. 1:** Chest X-ray showing miliary shadows distributed throught the lung field*

X-Ray skull was suggested. This showed multiple lytic defects of varying sizes without marginal sclerosis on the frontal and parietal bones (Fig2). Again, some form of chronic infection and metastasis could not be ruled out. Further, ultrasound abdomen was carried out which revealed hepatosplenomegaly. Skeletal survey including X-ray pelvis, spine and long bones were taken. Again

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some striking features in x-ray pelvis were appreciated. There were multiple lytic defects with marginal sclerosis on both innominate bones (Fig3).

Fig: 2

Fig: 3

***Fig: 2& 3** showing multiple lytic defects of varying sizes on frontal and parietal bones*

***Fig: 4** x-ray showing multiple lytic defects with marginal sclerosis*

Taking into account the plain radiograph features HRCT chest was carried out and it showed miliary nodular and reticulonodular densities in all the zones. CT-scan head was performed and this revealed multiple lytic lesions of different sizes as also observed in plain X-ray.

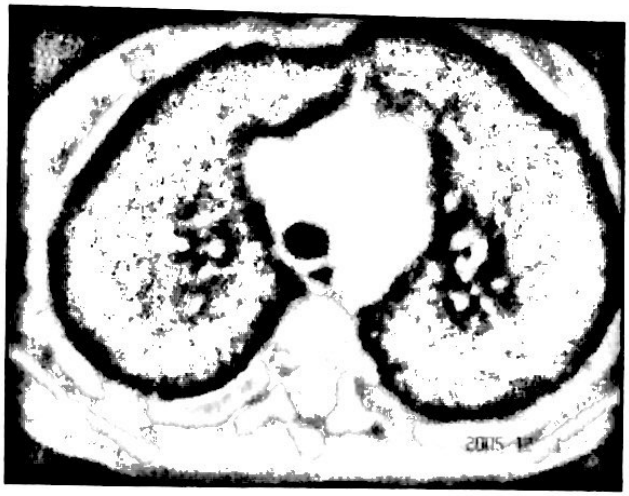

***Fig:5** HRCT chest showing miliary nodular and reticulonodular densites*

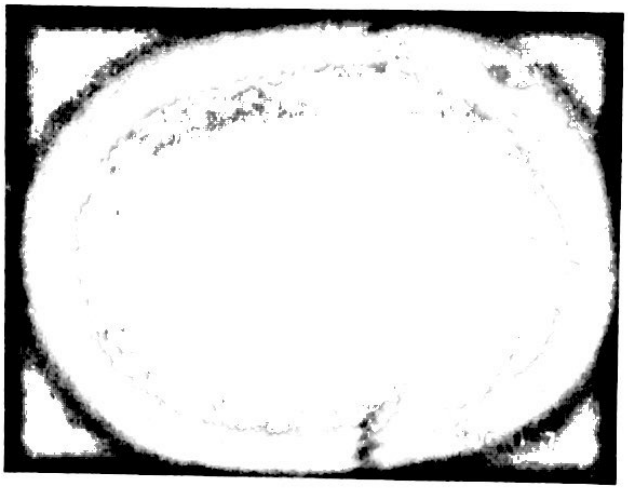

***Fig: 6** CT head*
(bone window showing lytic defect on vaul)

Now, at different stages of making diagnosis the strong possibility of Langerhans' cell histiocytosis couldn't be excluded though it could be a rare diagnosis in this paediatric age with such features.

Therefore, histopathology was planned. Before that, FNAC from enlarged lymph nodes suggested the features of xanthogranulomatous reaction. The biopsy from skull lesion revealed increase in the foamy histiocytes along with few eosinophils-consistent with Langehans' cell histiocytosis (Letterer-sewe disease). Immunohistochemistry done on the tissue showed S-100 to be strongly positive which further enhances the diagnosis of LCH.

Discussion

In this patient a diagnosis of LCH with multisystem involvement consistent with Letterer-Sewe Disease was made on the basis of cytologically confirmed skull vault lesions in addition to clinicoradiological evidence of multisystem LCH with skin rashes, gigivitis, lymphadenopathy, hepatosplenomegaly, failure to thrive and miliary shadows in radiographs of chest. In the absence of imaging of skull radiographs and skeletal survey, the differential diagnosis would include miliary tuberculosis, histoplasmosis, viral infection and metastasis. However, imaging in this patient showed characteristic features of LCH in skull and pelvis radiographs. To our knowledge, this is an example of LCH, which could have been missed if only clinical features which was in favor of tuberculosis in this endemic region was considered and if skull radiographs hadn't been suggested.

Multisystem LCH presents most commonly in childhood and has an annual incidence of 4 to 4.5 per million. It arises from a clonal proliferation of histiocytes, which are similar to the Langerhans cell family in that they express Class I CD1a antigen but are immature. LCH in children has been grouped under class I histiocytosis syndrome based on HPE findings, which demonstrate Langerhans' cell with Birbeck granules and or CD1 positivity on immunohistochemistry. Depending on their degree of differentiation these cells can produce cytokines, which are felt to be directly responsible for some of the pathological lesions of LCH such as bone resorption and lung fibrosis. Other lesions such as those in the central nervous system are caused by direct infiltration by abnormally proliferating histiocytes.

Though it is a variable disease in childhood, accurate diagnosis is very much important for facilitating progress in treatment. The prognosis appears to depend on the presence or absence of other risk-organ involvement. So, practical categorization as proposed by Histiocyte Society is important. Pathology in multisystem involvement in children includes skeleton in 80%, skin in 50%, lymph node in 30%, liver and spleen in 20%, lung in10-15% and pituitary/hypothalamus in 10% cases. Findings on imaging in skeleton show characteristic patterns, however, extremely variable appearance on skeleton which can represent a benign as well as malignant skeletal lesions. They can be with well defined or ill defined, lytic or sclerotic, permeative or geographic lesions associated with or without periosteal reaction with or without apparent expansion and with or without soft tissue mass. The lesions in skull are characteristically lytic with bevelled edge whereas in other sites they may represent different phases of healing like some are lytic and some have sclerotic margin. In contrast to skeletal features, findings usually follow a predictable interstitial pattern from miliary shadows to start with followed by reticulonodular lesions then formation of cystic or bullous lesions leading to the complication of pneumothorax. Lung involvement in Langerhans cell histiocytosis (PLCH) is rare in childhood but occurs most commonly in children with multisystem (MS) LCH in contrary to isolated finding in adults.

Our case demonstrates miliary shadows in chest radiographs with coexistent skeletal involvement namely in skull and pelvis. Interstitial patterns in lung fields including miliary shadows in the background findings of multiple system involvement in a child of less than 5 years should raise the possibility of LCH though miliary TB could be the first consideration.

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