CASE REPORT

LANGERHAN CELL HISTIOCYTOSIS: A CHILD PRESENTING WITH NINE MONTHS HISTORY OF FEVER

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We report a case of Langerhan Cell Histiocytosis in a three and a half years old child. The child presented with history of low grade fever, off and on for 9 months. There was 2 months history of progressive pallor and 5 days history of epistaxis. Blood complete picture revealed pancytopenia and the patient was referred to a paediatric oncologist. Initial diagnosis of acute lymphoblastic leukaemia (ALL), Lymphoma and disseminated Tuberculosis (TB) was made on basis of initial investigations. Coetaneous involvement occurred 7 months later along with Diabetes Insipidis, bone changes and pulmonary involvement.

Keywords: Fever, Langerhan cell histiocytosis, lymphoma, cutaneous
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INTRODUCTION

Langerhan Cell Histiocytosis (LCH) is a rare disorder, primarily affecting children with a male predominance, in which multiple organs are involved by the accumulation of reactive histiocytes. The pathogenesis remains to be fully explained.

Diagnosis is based on finding reactive histiocytes in organ involved. Treatment varies from individual to individual according to extent of involvement. Langerhan Cell Histiocytosis society treatment guideline (LCH-II protocol) is applied in treatment of children.

CASE REPORT

Our patient a $3^1/_2$ year old boy, resident of Gujrat, was referred to Combined Military Hospital Rawalpindi with 9 months history of low grade fever, 2 months history of progressive pallor and 5 days history of epistaxis.

Blood complete picture showed Haemoglobin Hb of 2.6g/dl, platelet count was 5000, and WBC count was 4.6. Patient was referred to paediatric oncologist where he was transfused Red Cell Concentrate and Platelets. Bone marrow aspiration and trephine was done the next day, which showed chronic granulomatous infiltrate. Ultrasound abdomen showed hepato-splenomegaly.

There was past history of polydipsia and polyuria for which he was being given desmopressin nasal spray. MRI brain showed no structural abnormality. Lymph node biopsy was done and a differential of acute lymphoblastic leukaemia (ALL), Lymphoma and disseminated TB was made. The patient was under investigation to confirm the diagnosis, while symptomatic treatment with blood and platelet transfusions was being given.

During this he developed eryhthematous rash. He was referred to dermatology department. Examination showed papular greasy erruption in seborrhoeic areas of scalp, retroauricular spaces and back involving groins, with petechiae at the periphery (Figure-1). Initial diagnosis of Langerhan Cell Histiocytosis was made, while Acute Graft versus host disease was kept in differential. Liver enzymes,

Prothrombin time and partial thromboplastin time were normal. Skeletal survey showed multiple lytic lesions in skull and right supra acetabular region (Figure-2). Chest X-ray showed non homogenous shadowing of lungs (Figure-3), but there were no respiratory symptoms or complaints.

Bone marrow biopsy was repeated and S100 and CD1a markers were applied, which were positive. A final diagnosis of multisystem Langerhan Cell Histiocytosis was made. Patient was treated with chemotherapy as per LCH Guidelines June 2010,

Vinblastine 6 mg/m^2 weekly for 6 weeks, Prednisone 40 mg/m^2 in three divided doses for 4 weeks, Sucralfate as gastro-protective and PCP prophylaxis was given with cotrimoxazole. Patient responded well to the treatment, his fever settled and skin lesions improved.

Blood counts started improving after 3 weeks of treatment, with an Hb of 7.8 and a platelet count of 63,000.

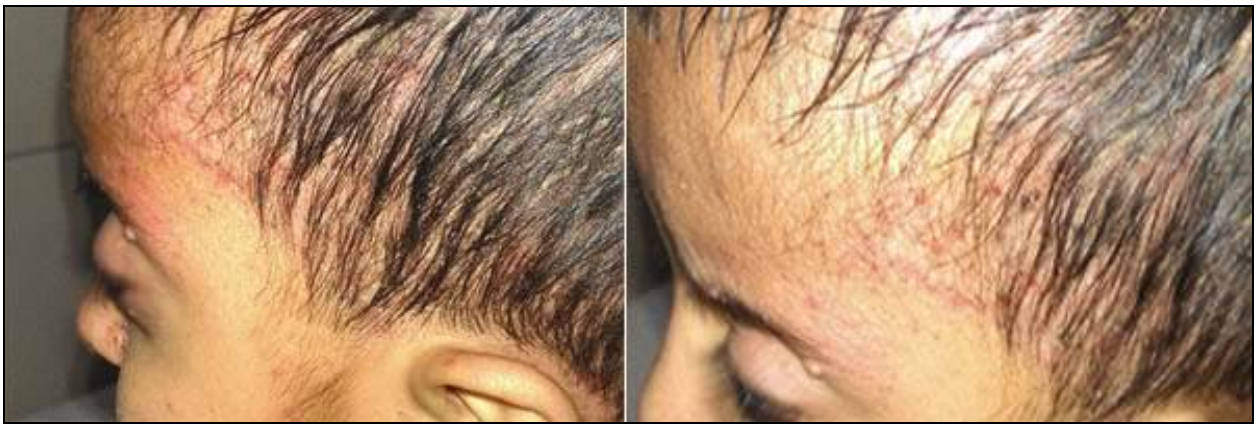

Figure-1: Greasy eruption in seborrhoeic areas

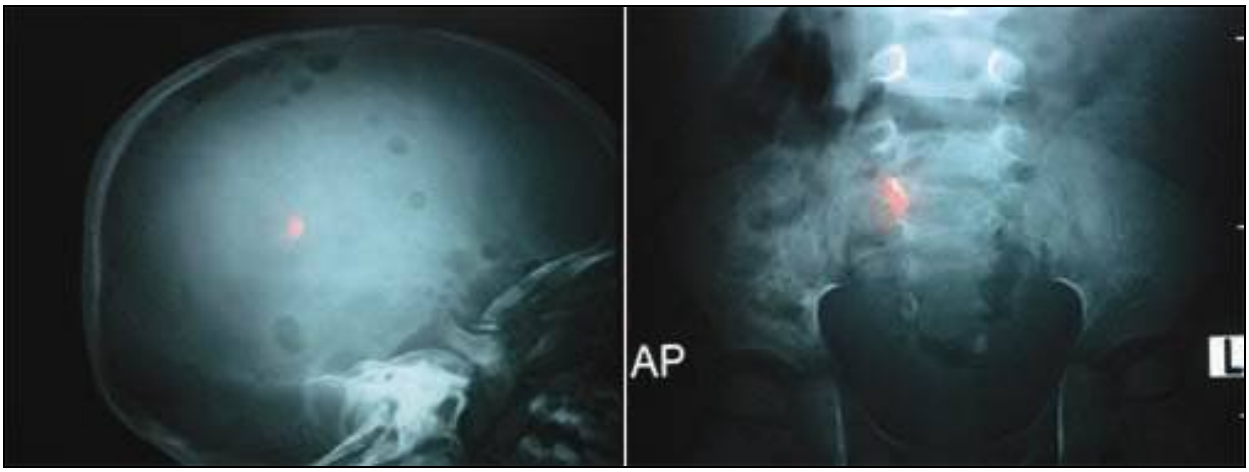

Figure-2: Multiple lytic lesions in skull and right supra acetabular region

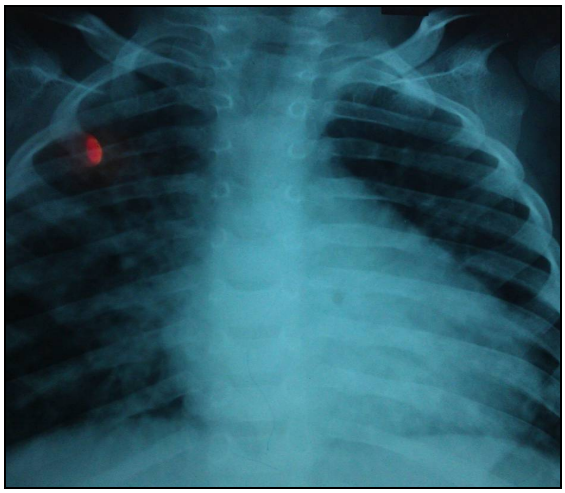

Figure-3: Chest X-ray showing non-homogenous shadowing of lungs

DISCUSSION

Histiocytosis is a group of diseases which are characterized by accumulation of reactive histiocytes in various organs of the body. LCH is an uncommon condition, which affects children more commonly as compared to adults , with a male predominance. The exact pathogenesis is not known. Promonocytes are derived Neutrophil/Macrophage colony forming unit, in the blood they circulate as monocytes and then they enter various tissues as histiocytes. The exact mechanism of accumulation of histiocytes in tissues is unknown; it is thought that abnormal populations of T cells secrete cytokines which attract normal histiocytes to organs involved.[1] The effects of reactive histocytes are as per their function; they secrete endogenous pyrogens causing fever, they stimulate osteolclast activating factor leading to lytic bone lesions, they cause cytophagocytosis leading to anaemia, thrombocytopenia and leucopenia.[2] Tissue damage is also caused by cytokine production.

The organs involved in decreasing order of frequency are the skeleton, skin, lungs or lymph nodes. Painful swelling of the bones is the most common presenting feature and it may be augmented by the presence of involvement of adjacent soft tissue, skin and mucosa.[3] Diabetes Insipidis is the most common presentation of CNS involvement. Bone marrow involvement leads to pancytopenia,

which when severe causes splenomegaly. Liver involvement causes hepatomegaly and ascites. LCH involving the lungs primarily is relatively rare and is seen in young adults.

A presumptive diagnosis is based on histopathological appearance of skin biopsy; probable diagnsosis is based on marker studies (s100, peanut agglutinin and alpha mannosidase). A definitive diagnosis is made when lesional cells express CD1 or exhibit Birbeck granules on electron microscopy.[2]

Treatment varies from patient to patient as per involvement of various organs of the body. If only skin is involved, then usually no treatment is required. When treatment is required for skin involvement, then the first line therapy is topical steroids, while PUVA and topical nitrogen mustard are second line. For single bone lesions, intra-lesional steroids are used. For multi organ disease, some suggest systemic steroids as the first line therapy, while some suggest single agent chemotherapy.[4,5] Several studies have shown that multi drug chemotherapy sustained over a long period provides maximum benefit and fewer relapses.[5] Currently LCHIII protocol is being used for treatment in children with multi-organ involvement.

All of the above mentioned features were seen in our case. Fever as a presenting symptom of LCH is very rare and to our knowledge only three such cases have been mentioned in literature.[1,6,7] Our case differs from the previous case reports in that our patient was a child of three years whereas the previous case reports were of adult patients and neonate. Our patient was being worked up on the working differential of ALL, lymphoma and Disseminated TB. The suspicion of LCH only arose after the onset of purpuric rash which arose after blood transfusions; with Acute GVHD secondary to transfusion being the differential. The delay in diagnosis was primarily because of PUO for 9 months being the main presenting complaint.

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