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Case Report

Langerhans cell histiocytosis in an infant: a case report

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ABSTRACT

Langerhans cell histiocytosis is a rare non-malignant disease characterized by a clonal proliferation of pathological cells with the characteristics of Langerhans cells in single or multiple sites. A 7-month-old infant presented with continued fever and recurrent cough with progressive rash over the whole-body including palms and soles for over a month. On examination there was respiratory distress, generalized lymphadenopathy, hepatosplenomegaly and skin rash. The diagnostic workup for underlying causes showed ground glass opacity, pulmonary oedema and retroperitoneal lymphadenopathy on CT scans of thorax and abdomen respectively. The histopathology specimens of skin and lymph node biopsy further confirmed the suspicion of Langerhans cell histiocytosis. The patient was sent for treatment with vinblastine and prednisone to a higher centre. In this case report we highlighted the unusual presentations and prognosis of a child with Langerhans cell histiocytosis.

Keywords: Langerhans cell histiocytosis, Pneumonia, Infant, Lymphadenopathy

INTRODUCTION

Langerhans cell histiocytosis is a class I histiocytosis syndrome of dendritic origin. It is a rare disorder characterized by monoclonal proliferation of dendritic-cell related histiocytes (Langerhans cells), with a variable admixture of other cells, which form granulomas with proliferative and locally destructive behaviour. These histiocytes can cause subsequent infiltration of various organs.[1-4] LCH has a broad clinical spectrum ranging from localised disease, which may be benign and self-limiting, to life-threatening, disseminated disease.[5]

Clinical description

A 7 months old male was brought to us with complaints of fever and cough with a cold for 8 to 10 days. On taking a detailed history, the mother added complaint of rash for over a month which was insidious in onset, progressive, involving whole body, even palms and soles, non-bleeding and erupting in patches without any medications and also gave the complaint of abdominal distention over the last month with increased irritability.

The child was second born at term gestation, by vaginal delivery in a hospital setting with birth weight 3300 gm to non-consanguineous parents. There was no history of admission to a Neonatal intensive care unit (NICU). However, the child had a history of previous hospitalisation in the same hospital for cough and cold about 2 months back when congenital heart disease was also suspected and Echocardiography (ECHO) was advised. The ECHO was normal at follow up. The child was immunised appropriate for age as per national immunisation programme.

Physical examination showed an ill child with fever, mild tachypnoea (breathing rate 46/min), tachycardia (heart rate 145/min) and oxygen saturation in room air between 92 and 94%. With oxygen supplementation via nasal cannula

oxygen saturation was 97-98%. The child had diffused cutaneous lesions- scaly, papular, seborrheic dermatitis of the scalp, intertrigo in inguinal folds, oral mucosa covered with non-adherent white membrane appearing superficially like candidiasis and haemorrhagic papule and vesicles on the scalp, pinna, face, trunk and extremities including palms and soles (Figure 1).

The child had pallor but no icterus. Generalised lymphadenopathy of cervical (multiple, maximum 2×1.5 cm size), axillary (multiple, maximum 1.5×1 cm size) and inguinal (bilaterally, 1×1 cm size) regions were palpable. The respiratory system examination revealed crepitations in bilateral lung fields more in the upper zone than middle than lower zone. In gastrointestinal system examination, hepatosplenomegaly (liver being palpable 7.5 cm below right costal margin in mid-clavicular line and spleen upto 2 cm below left costal margin) was palpable and bowel sounds were normal. Cardiovascular system was normal with no murmur heard. Nervous system examination was appropriate for age with no developmental delay. Percussion findings of all systems were normal.

Management and outcome

Laboratory data revealed white blood cell count 10.6×10^9 /l (reference range $4.0\text{-}10.0\times10^9$ /l), haemoglobin 9.0 g /dl (reference range 11.3-14.1 g/dl), platelet count 221×10^9 /l (reference range $150\text{-}450\times10^9$ /l). Differential blood count: neutrophils 41%, lymphocytes 56%. Peripheral blood film showed dimorphic anemia with neutrophilic leucocytosis. Liver function tests and renal function tests were within normal range except for hypoproteinaemia. Urine examination was normal for reducing substances. The chest radiograph showed infiltrates and opacification of bilateral pulmonary fields- right more than left (Figure 1).

HRCT of chest revealed diffuse ground glass opacity in bilateral lung with picture of pulmonary oedema, bronchiectasis cavity in bilateral upper lobes and ill-defined soft tissue density with calcific changes in pre-vascular space suggestive of lymphadenopathy. CECT abdomen revealed hepatomegaly, bilateral inguinal lymphadenopathy and retroperitoneal lymphadenopathy. Skin biopsy demonstrated focal collection of reniform cells with grooved nuclei suggestive of Langerhans cell histiocytosis.

This compounded with the lymph node biopsy with a similar picture suggesting Langerhans cell histiocytosis helped in diagnosing the child. X-ray of skull and long bones was also done to rule out bone involvement. The child was then referred to the department of haemato-oncology in government hospital in Jaipur for further confirmation with immunohistochemistry (report not available) that would show S100+ and CD1a+ cells and for treatment with intravenous vinblastine and oral prednisone.[6] The child was planned for treatment as per 2009 Histiocyte Society guidelines for LCH protocol after confirmation with IHC. However, on follow-up via telephone, the child expired 2 days later on his way to the hospital in the ambulance.

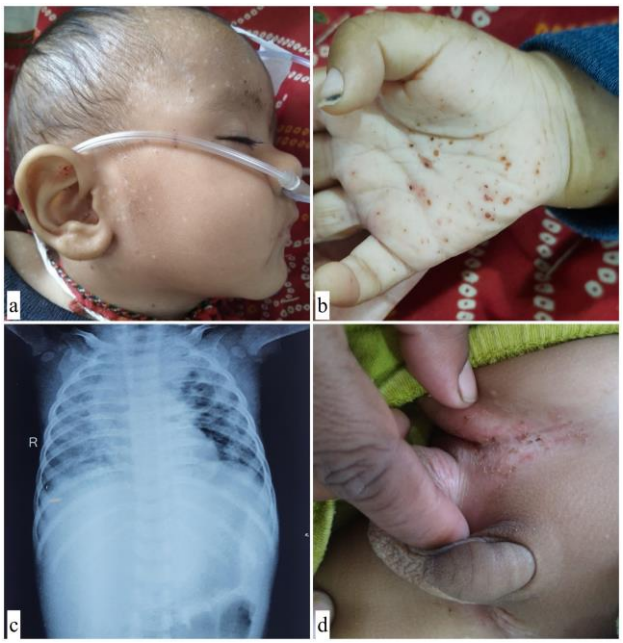

Figure 1: (a) Child with rash that is covering the face and pinna; (b) haemorrhagic papules present on the palm; (c) chest X-ray showing bilateral infiltrates; and (d) rash in inguinal folds.

DISCUSSION

Most often children are affected, with a peak incidence of 0.2-1.0/100,000 children per year from 1 to 4 years of age. Neonatal/congenital LCH is defined when it presents within the first 4 weeks of life (irrespective of age at diagnosis). LCH predominantly affects the skeletal system and skin, although central nervous system, thyroid and the so-called risk organs (liver, spleen and haematopoietic system) may also be affected.[7]

In 10-15% of patients, pulmonary infiltrates are found on radiography.[6] Pulmonary involvement is rarely the most predominant clinical manifestation. Of the patients with multisystem LCH without pulmonary abnormalities, 8.8% develop pulmonary LCH within the next year.[8] Isolated pulmonary LCH occurs in only 1% of the cases. Clinical presentation of symptomatic lung involvement in LCH in children is nonspecific, such as dyspnoea, cough, chest pain, fatigue, wheezing, and tachypnoea.

To obtain definite diagnosis, immunohistochemical demonstration of CD1a epitopes on the cell surface and/or demonstration of Birbeck granules in the cytoplasm by electron microscopy is required, in addition to conventional light microscopy (and positive staining for S100-protein). Once LCH is diagnosed, based on typical histopathological findings, stratification into single-system or multisystem disease is based on the number of organs involved.[6]

The course of the disease is unpredictable, varying from rapid progression and death, to repeated recurrence and recrudescence with chronic sequelae, to spontaneous regression and resolution.[9] Patients with localized disease have a good prognosis and may not require any treatment whereas for multisystem LCH, the Histiocyte Society recommends an intensive treatment during the first 6 weeks of therapy and continuation treatment thereafter.[10]

In children, prognosis mainly depends on two negative prognostic factors: risk organ involvement (dysfunction of liver, spleen and haematopoietic system) and poor response to initial treatment. Patients with risk organ involvement who do not achieve a response to initial treatment have a 75% risk of fatal outcome. In contrast, those who do respond to initial chemotherapy have an 88%-91% survival rate.[11]

This case report describes a young infant presenting with pneumonia and cutaneous manifestations as the first presenting signs of Langerhans cell histiocytosis. Although lung involvement develops in approximately half of the multisystem LCH patients, the clinical presentation is nonspecific and usually does not predominate. Skeletal involvement may occur later in life.

CONCLUSION

LCH is a rare disease with variable presentation which can make the diagnosis challenging. Most clinicians may only see a small number of cases in their career. We have referenced several case reports in the literature highlighting the heterogeneous nature of the disease to aid in prompt diagnosis as well as management. Prognosis can be good. In children, lung involvement is present in about 10-15% of all patients. Thus, LCH is an important differential diagnosis in diffuse lung disease.

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