

# Liver Involvement in Langerhans' Cell Histiocytosis

## A case report

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### Abstract

Langerhans' cell histiocytosis (LCH) (Histiocytosis X) is a rare disease of unknown cause characterized by oligoclonal proliferation of Langerhans cells. It occurs mostly in children and young adults and involves one or more body systems such as bone, hypothalamus, posterior pituitary gland, lymph nodes, liver or various soft tissues. The diagnosis is always made by a histological approach.

A 3.5-year old male child with LCH involving multiple systems, including the skin, lungs, liver with clinical signs of diabetes insipidus. The patient was diagnosed following a skin biopsy that revealed infiltration of Langerhans cells. This case report would increase the awareness of pediatricians about the multisystem involvement in LCH.

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### Introduction

Langerhans' cell histiocytosis (LCH) (Histiocytosis X) is a clonal proliferative disorder of the Langerhans cells.<sup>1,2</sup> The disease is rare, with an annual incidence of approximately 2-5 per million per year and a peak incidence at 1-4 years of age<sup>3</sup>. It may manifest at any age, with males being affected more frequently than females. The clinical presentation may be variable, either solitary disease of the bone, or severe multivisceral involvement (lung, bone, liver, spleen, lymph nodes, hypothalamus, pituitary gland, gastrointestinal tract, etc.). Liver involvement occurs mainly in multisystem involvement cases and usually presents as a part of a disseminated process. Among children with LCH (especially in children younger than 5 years old), liver involvement is relatively frequent, even though it is often overlooked. The diagnosis is based on cytology or histology in combination with immunohistochemical tests for S100 protein expression.

### Case report

A 3.5-year-old child was admitted to the department of Pediatric Gastroenterology & Nutrition of Bangabandhu Sheikh Mujib Medical University with history of not growing well, scaly skin lesion over scalp, chest, upper abdomen and back of the body with abdominal distension

in association with polydipsia (2 l fluid per day), polyuria and 8 months history of jaundice. He has no history of fever, contact with TB patient, blood transfusion, any surgery or dental procedure, family history of liver disease, respiratory distress or bone pain. Physical examinations revealed skinny ill appearing patient with mild pallor and icterus. He has scaly skin lesion over chest, upper abdomen, scalp and back of body. He is a febrile, BCG mark present, stigmata of CLD absent. On anthropometric measurement, the child is severely wasted, stunted and underweight. Systemic examination revealed an enlarged liver. The laboratory data showed mild anemia (Hb: 9.6 g / dl), markedly raised ESR (125 mm in 1<sup>st</sup> hour), evidence of cholestasis (S. bilirubin: 7.3 mg/ dl, Direct bilirubin: 3.5mg/dl, S. ALT: 478 U/L, S. alkaline phosphatase : 2360 U/L). Central Diabetic Insipidus is diagnosed as his serum osmolality was 305 mosm/l (> 300 mosm/L) and urine osmolality was 89 mosm/ l (< 300 mosm/l) before giving DDAVP and after giving DDAVP urine osmolality became 187 mosm/l (> 2 fold of baseline). Abdominal ultrasonography revealed heterogenous echotexture of the liver with calcification. There was no lytic bone lesion of skull or spine on radiological examination. The chest X-ray film detected miliary opacities over both lung fields. MRI of brain showed no abnormality of hypothalamic- pituitary region.

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Bone marrow puncture showed no abnormality. Skin biopsy was done for confirmation of diagnosis of Langerhans' cell histiocytosis which showed collection of langerhans histiocytes in superficial dermis. The patient was referred to hematological department for specific management.

Treatment started with 1<sup>st</sup> course of chemotherapy (vinblastine 6 mg/m<sup>2</sup> intravenous bolus and prednisone 40 mg / m<sup>2</sup>/day orally) and for diabetes insipidus, DDAVP nasal spray (10µg/day) started after consultation with pediatric nephrology department. But after starting the treatment, patient party denied to continue the treatment and decided to take the child to abroad for further management. Regarding prognosis of this patient, as liver involvement is associated with high mortality rate, if treatment could be continued in this patient, chance of 3 year survival was only 51%.



Fig 1 : patient



Fig 2 : Chest X-ray showing miliary opacity in both lung fields

## Discussion

Langerhans' cell histiocytosis (LCH) is a rare proliferative disorder of the Langerhans cells.<sup>1,2</sup> The term encompasses the formerly known entities of histiocytosis X that included Letterer Siwe disease, Hand Schuller Christian disease and eosinophilic granuloma. However, little is yet known about the etiology and pathogenesis of LCH .

It occurs mostly in children and young adults, with males being affected more. Reported patient was also a male child of 3.5 years. The clinical presentation may be variable, and the course of the disease may show extreme case-to-case variation. The clinical course and outcome depend 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.

Although the rate of liver involvement is much lower than that in most other organs in LCH patients, it is relatively common in -

disseminated LCH representing 40% to 60% of the cases. In a review of 348 cases, the French Langerhans' Cell Histiocytosis Study Group found liver involvement in 10.1% of patients during the initial episode, rising to 14.4% in subsequent episodes<sup>1</sup>. The latest monocentric pediatric study reported a 15.6% rate of liver involvement among 217 cases<sup>11</sup>. Braier et al. report an 18% incidence of liver involvement in patients with multisystem LCH<sup>12</sup>. Therefore, liver involvement is probably more common than previously recognized. It is vital to aware the possibility of liver involvement once the diagnosis of LCH was established in children.

Liver involvement in children with LCH typically presents with hepatomegaly, abnormal liver enzymes, or jaundice, associated with multiorgan involvement. Reported patient also had jaundice, hepatomegaly with liver dysfunction. Diabetes insipidus together with the liver parenchymal infiltration and the cholestatic pattern of liver tests and pulmonary involvement found in reported patient raised the suspicion of a granulomatous disease such as histiocytosis X, but other diagnosis like disseminated TB was also considered which was excluded.

The definitive diagnosis is always based on histological examinations and confirmed by immunohistochemical tests. But unfortunately in this patient histological analysis of liver tissue was not done because patient party denied to do so. Skin biopsy was done which showed collection of langerhans histiocytes in superficial dermis.

However, because the pathophysiology of Langerhans cell histiocytosis is only poorly understood, treatment approaches remain empirical, and the response to treatment is seldom predictable<sup>13</sup>. When the liver is affected, treatment is aggressive due to the progressive irreversible damage due to cholestasis<sup>1</sup>.

The extent of the disease has a significant effect on the course of the disease and on its prognosis. Multivisceral forms are associated with a 4-year survival rate of 60-80%<sup>11</sup>.

## Conclusion

Liver involvement in LCH is not that much uncommon in children. So regular clinical and biochemical liver evaluation must be performed onwards to screen every LCH children from the time of the initial diagnosis and during the follow-up. Awareness of the varieties of ways that the disease can manifest itself and the wide spectrum of possible organ involvement is vital for pediatricians and radiologists who encounter this disease.

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