

## Case Report

# Neonatal Langerhan's Cell Histiocytosis; Early Presentation with Delayed Diagnosis

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### ABSTRACT

Neonatal Langerhan's cell histiocytosis (LCH) is a rare disease which presents in the first four weeks of life with skin manifestations; although the diagnosis may be delayed till other organ involvement becomes apparent. We describe a four-month-old male infant who presented with skin lesions in the neonatal period

and was diagnosed later, when involvement of lymph nodes, liver, spleen and bone became apparent. Due to the possibility of clinically unapparent involvement of other organ systems in neonatal LCH, thorough clinical, laboratory and imaging studies are mandatory for a comprehensive evaluation of all cases on presentation.

KEY WORDS: Langerhan's cell histiocytosis, neonatal, skin lesions

### INTRODUCTION

Langerhan's cell histiocytosis (LCH) is a rare disorder with diverse clinical presentations and prognosis<sup>[1]</sup>. Its incidence is 2-5/1,000,000/year and is slightly more prevalent in boys<sup>[2]</sup>. Previously called Histiocytosis X, it was renamed LCH to differentiate it from reactive and neoplastic causes of histiocytosis<sup>[3]</sup>. LCH includes eosinophilic granuloma, Hand-schuller Christian and Letterer-Siwe disease<sup>[4]</sup>. Neonatal LCH is defined as LCH presenting within the first four weeks of life irrespective of the age at diagnosis. Incidence is estimated as 1-2/1,000,000/year<sup>[5]</sup>.

Baseline evaluation for a newly diagnosed patient requires search for all possible sites of involvement<sup>[6]</sup>. Treatment modalities of chemotherapy, radiotherapy, surgical intervention or combination of all these depends on the extent of the disease<sup>[7]</sup>.

We present a male infant who had skin manifestations in the neonatal period and was diagnosed as LCH at four months of age only when involvement of other organ systems became apparent.

### CASE REPORT

A four-month-old male infant from Srilanka who was said to be previously well until the parents noticed a neck swelling, low grade fever and pallor one week before presentation. He had history of multiple skin lesions appearing within the first month of age all over his body and face. He was a product of full term normal delivery,

from non-consanguineous parents. There were no perinatal problems. He has a healthy elder brother. There was no family history of malignancy or blood diseases.

The patient on examination was alert, conscious, thriving well, but febrile and pale. There was bilateral proptosis more pronounced on the left and marked bilateral swelling of the neck. His growth parameters were at the 10<sup>th</sup> centile for age. Skin examination revealed wide spread vesiculopustular lesions especially prominent on the forehead, scalp, trunk and groin, together with dry scaly hypopigmented patches scattered all over the body (Fig. 1).

There was marked bilateral cervical lymphadenopathy with enlarged bilateral axillary and inguinal lymph nodes to a lesser extent. These nodes were all firm, non-tender, with no signs of overlying inflammation.

Chest examination showed tachypnea, mild subcostal retraction with bilateral equal air entry and no added sounds. Cardiovascular examination was normal. Liver was 3 cm and spleen 1 cm below their respective costal margins. There were no other masses felt on abdominal examination. Apart from mild hypotonia and head lag his CNS examination was normal.

Basic blood investigations showed normochromic normocytic anemia, with normal white blood cells and platelets. Blood chemistry, liver, renal functions, plasma and urine osmolality as well as coagulation studies were normal. In view of his extensive

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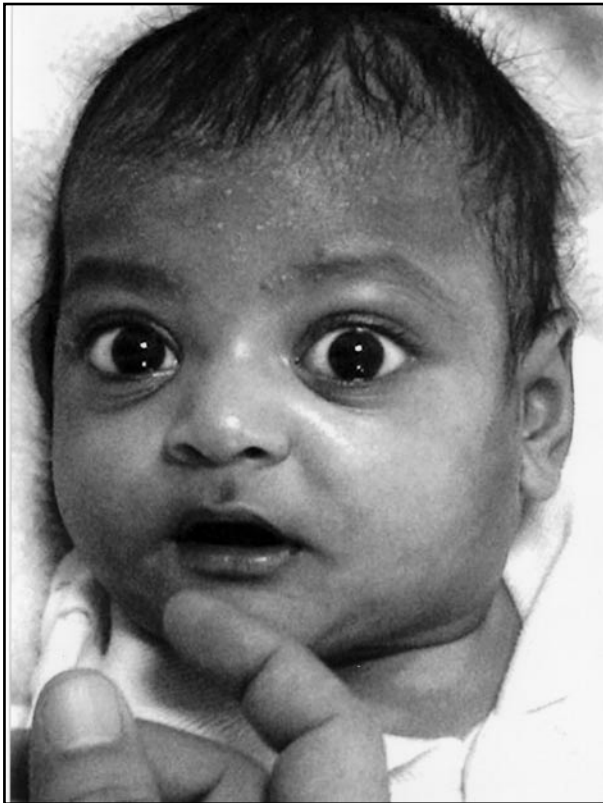


Fig. 1: Vesiculo-pustular skin lesions on the forehead, multiple hypopigmented lesions on the neck, bilateral proptosis, and cervical lymphadenopathy



Fig. 3: CT chest showing extensive fibro-nodular infiltrations of both lung parenchymas

skin lesions with marked lymphadenopathy and hepato-splenomegaly LCH was suspected. A plain skull radiograph was done which showed multiple punched out osteolytic lesions (Fig. 2).

Chest X-ray showed a widened mediastinum while CT chest revealed large multinodular anterior mediastinal mass with bilateral hilar lymph nodes



Fig. 2: Plain skull X- ray showing multiple punched out osteolytic lesions



Fig. 4: CT head showing marked left eye proptosis with bone erosion

and extensive fibro-nodular infiltration of both lung parenchymas (Fig. 3).

There were also multiple osteolytic lesions in both scapulae and thoracic cage. CT abdomen showed diffuse hepato-splenomegaly with enlargement of the celiac, iliac and inguinal lymph nodes. Osteolytic lesions of the iliac bones and vertebrae were seen. CT head showed normal brain tissue, multiple osteolytic lesions of the skull base and left sphenoid wing and soft tissue swelling compressing and displacing the left optic nerve medially (Fig. 4).

Extensive infiltration of the upper neck and retropharyngeal space with multiple soft tissue nodules and osteolytic lesions of the jaw were seen. Lymph node, skin, and bone marrow biopsies were rejected by his father at that time only to be done in Srilanka where the father took his child. Bone marrow biopsy done there revealed a hypoplastic marrow. Lymph node excision biopsy showed infiltration with mononuclear and multinuclear Langerhan's cells with numerous eosinophils.

Special stain S 100 was positive.

He received two doses of vincristine and oral steroids. He was brought back to Kuwait where he was referred to the pediatric oncologist; he was treated as a case of LCH with multiorgan involvement. He received two cycles of vinblastine injections and oral steroids but unfortunately died of an intercurrent infection during the above treatment four months after diagnosis.

## DISCUSSION

The variability in the presentation of neonatal LCH contributes to the frequent delay in diagnosis. When cutaneous involvement is the only obvious presenting sign 6-12 months may be required to determine the ultimate extent of the disease.

Typical cutaneous lesions in neonatal LCH are scaly erythematous, seborrheic like eruptions of brown to red papules especially prominent in intertriginous zones. Superficial ulcerations may occur. Weeping lesions may suggest eczema.

Sarah *et al*<sup>[8]</sup> followed up 19 cases in a retrospective validation cohort study who presented (as in our case) with skin lesions in the neonatal period and were subsequently diagnosed as LCH upon involvement of other organs. As in our case the most common initial skin lesions in their patients were crusted vesiculo-pustules. Those lesions were misdiagnosed as chronic dermatitis or as part of an infectious process. Twelve of the 19 patients had multisystem disease and two of them subsequently died.

When the diagnosis of neonatal LCH is suspected a comprehensive workup for systemic disease evaluation should be done. This includes careful physical examination as well laboratory and radiological investigations.

In a retrospective study done by Minkov<sup>[5]</sup>, in which he studied 61 patients who presented in the neonatal period, only 20 cases were diagnosed within the first four weeks of life. Diagnosis was established later in the remaining 41 cases with median time from initial presentation to diagnosis being two months (range = 0 days - 23 months). In another retrospective study, in which the group of patients presented between 0-6 months of age, the

average time for diagnosis was about six months<sup>[9]</sup>. Because of this delay in diagnosis, the true incidence of congenital/neonatal LCH may be expected to be higher.

A comprehensive evaluation of all cases is essential. Treatment depends on the extent of the disease, age at diagnosis, and presence of organ dysfunction. As in our case, most patients receive a combination of corticosteroids and chemotherapeutic agents (usually vinblastine or etoposide)<sup>[1]</sup>. Widely accepted prognostic factors are age, extent of organ involvement, and presence of organ dysfunction at diagnosis<sup>[10]</sup>. Awareness about the variety of ways this disease can present itself and its wide spread organ involvement is vital for all pediatricians who encounter this disease.

## REFERENCES

1. Gadner H, Grois N, Arico M, *et al*. A randomized trial of treatment for multisystem Langerhan's cell histiocytosis. *J Pediatr* 2001; 138:728-734.
2. Kilborn TN, Teh J, Goodman TR. Paediatric manifestations of Langerhans cell histiocytosis: a review of the clinical and radiological findings. *Clin Radiol* 2003; 58:269-278.
3. Cochrane LA, Prince M, Clarke K. Langerhan's cell histiocytosis in the paediatric population: presentation and treatment of head and neck manifestations. *J Otolaryngol* 2003; 32:33-37.
4. Jubran RF, Marachelian A, Dorey F, Malogolowkin M. Predictors of outcome in children with Langerhans cell histiocytosis. *Pediatr Blood Cancer* 2005; 45:37-42.
5. Minkov M, Prosh H, Steiner M, *et al*. Langerhans cell histiocytosis in neonates. *Pediatr Blood Cancer* 2005; 45:802-807.
6. Lipton JM, Arceci RJ. Histiocytic disorders. In: Hoffman R. *Hematology: basic principles and practice*. 4th edition. Florida, Churchill Livingstone; 2005, 857-867.
7. Kusuma Kumary P, Priyakumari T, Chellam VG, James FV, Nair MK. Langerhans cell histiocytosis in children less than 2 years of age. *Indian Pediatr* 1999; 36:29-36.
8. Stein SL, Paller AS, Hout PR, Mancini AG. Langerhans cell histiocytosis presenting in the neonatal period: retrospective case series. *Arch Pediatr Adolesc Med* 2001; 155:778-783.
9. Rivera-Luna R, Alter-Molchadsky N, Cardenas-Cardos R, Martinez-Guerra J. Langerhans cell histiocytosis in children under 2 years of age. *Med Pediatr Oncol* 1996; 26:334-343.
10. Minkov M, Grois N, Heitger A, Potschger U, Westermeier T, Gadner H. Response to initial treatment of multisystem Langerhans cell histiocytosis: an important prognostic indicator. *Med Pediatr Oncol* 2002; 39:581-585.