

Langerhans Cell Histiocytosis in a Neonate Presenting with Skin-only Disease: Case Report and Review of the Chinese Literature

JR PAN, TM YUAN, LH CHEN, HM YU

Abstract

Langerhans cell histiocytosis is a comparatively rare disease in the neonatal period. We report a case of Langerhans cell histiocytosis in a neonate with only haemorrhagic vesiculopustular skin lesions and insidiously developed multisystemic involvement of dermal, digestive, respiratory, and skeletal systems. We also review three cases of neonates with Langerhans cell histiocytosis reported in the Chinese-language medical literature. Any cutaneous involvement in neonates with Langerhans cell histiocytosis may indicate aggressive multisystemic disease and have a very poor prognosis; therefore skin biopsies should be performed in neonates with complicated cutaneous lesions as early as possible and careful observation should be applied to newborns with cutaneous Langerhans cell histiocytosis which should be treated as a multisystemic disease.

Key words

Dermatology; Multisystem; Neonatal

Introduction

Langerhans cell histiocytosis (LCH) is a rare disease characterised by proliferation and accumulation of pathological Langerhans cells. The minimum incidence of LCH is estimated to be 8.9 per million children per year.¹ We report a case of LCH in an otherwise thriving neonate presenting with only rash and insidiously developed multisystemic involvement. We also review three cases of neonates with LCH reported in the Chinese-language medical literature between 1999 and 2012.

Case report

A 4-day-old female neonate was admitted to our department due to a haemorrhagic vesiculopustular eruption that had been observed immediately after birth. The infant appeared well except for haemorrhagic vesicopustules on the face, the trunk and extremities, including the palms and soles within the first 24 hours after birth. The patient was started empirically on intravenous penicillin and external mupirocin on the first day after birth in the local hospital, but the haemorrhagic vesicles did not remit. Her parents were unrelated. There were no hereditary disorders or unexplained infant deaths in family history.

On physical examination, the infant appeared vigorous with normal vital signs. Diffuse haemorrhagic vesicopustules and overlying pustules were found on the skin (Figure 1), mostly concentrated in the areas of palms and soles, and the rest of the examination was normal.

Her white blood cell count was 9260/μL (57.2% neutrophils). The haemoglobin level was 199g/L and the platelet count was 168000/μL. C-reactive protein was 12 mg/L. Serum electrolytes, alanine aminotransferase, aspartate transferase, serum urea nitrogen, creatinine, MB isoenzyme of creatine kinase and coagulation studies were all within normal limits. No microorganisms were found

Department of Neonatology, Children's Hospital, Zhejiang University School of Medicine, Zhugan Xiang 57, Hangzhou 310003, People's Republic of China

JR PAN (潘佳容) MD
TM YUAN (袁天明) MD
LH CHEN (陳理華) MD
HM YU (俞惠民) MD

Correspondence to: Dr HM YU

Received April 26, 2013

in the blood culture. An abdominal ultrasound scan was negative. A skeletal survey was performed to rule out systemic involvement; the result was that there was some mild erosion among long bones.

A haemorrhagic vesicle from the left crus was taken for biopsy. Histopathological examination demonstrated an infiltrate of large cells with pale cytoplasm and reniform nucleus, staining positive for S100 and CD1a (Figure 2). Thus the diagnosis of LCH was established.

After admission, intravenous injection of cefotaxime was empirically applied. Intravenous injection of vancomycin was given on the 9th day after admission because of significant increase in the C-reactive protein value. The C-reactive protein value got higher with time, which reached 105 mg/L on the 15th day after admission. The rash slowly regressed during the first week of hospitalisation, while some new rashes reappeared from the second week. The

patient got a fever from the eleventh day after admission. Despite fever and vomiting the patient's general condition was good. The patient was finally discharged on the 17th day after admission because the parents refused to continue the therapy. Evidence of progression was found in the more than 3-month clinical follow-up of this patient, including fever, anaemia, emaciation and dyspnoea.

Literature Review

With 3 powerful Chinese medical journal search engines (cqvip.com, wanfangdata.com, and cnki.net), a Chinese-language medical literature search was performed using the key words "Langerhans cell histiocytosis," and "neonate" for articles published between 1999 and 2012. Three cases of neonatal LCH were identified.

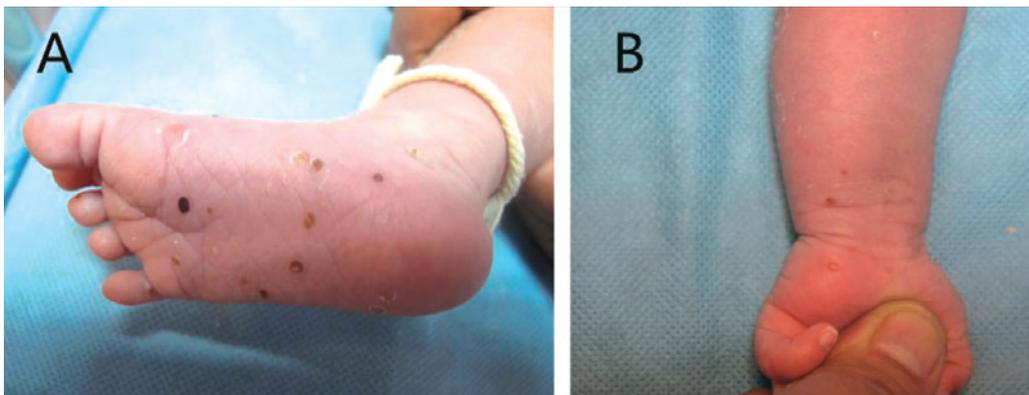


Figure 1 Haemorrhagic vesicopustules on the plantar surface and pustules on the palm of a newborn.

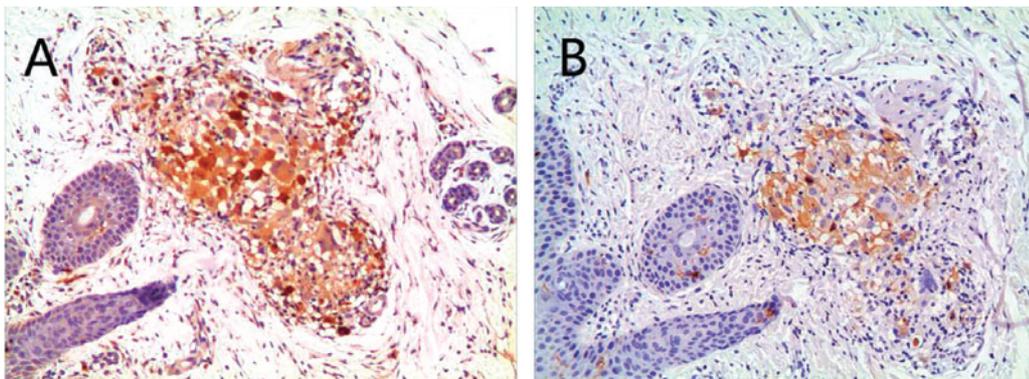


Figure 2 Expression of S100 (A) and CD1a antigen (B) in skin biopsies showing Langerhans cells with typical dendritic projections, infiltrating epithelial layers. (Immunohistochemical reaction, counterstained with haematoxylin x100 original magnification).

One neonate was born at gestational age of 33 weeks, and the other two were term neonates. Clinical manifestation was shown at birth in 2 cases, and three days after birth in one case. The age at diagnosis ranged from 17 days to 28 days.

There was multi-systemic involvement which included dermal system, digestive system, respiratory system, haematological system in all three patients. The cutaneous lesions were characterised by maculopapular rash, haemorrhagic vesicopustule involving the face, chest, back, and extremities in all three cases. Intermittent passage of stool with streaks of blood was encountered in one case, and passage of fecal occult blood test positive stool was witnessed by their pediatricians in two cases. The clinical manifestations of respiratory distress were encountered in all cases. Fever, hepatomegaly and splenomegaly were observed in all three neonates.

One of the three newborns had a high white blood cell count, while the other two had a high level of C-reactive protein. The prothrombin time and activated partial thromboplastin time were longer than control with bleeding tendency in one case. Among the three patients, no one exhibited bone involvement by radiological examination.

Test results of scrapings from the lesions were positive for LCH in all cases. One of the patients had a skin biopsy that demonstrated a few nodules infiltrated into superficial layer. The bone marrow aspirations revealed typical pathological changes of histiocytes in two cases.

The neonate reported by Cai et al demised at the age of sixteen days after about sixteen days of treatment with antibiotics and supportive therapy.² The patient reported by Sun et al discharged at the age of one month after 8 days of treatment before the diagnosis was established and the outcome was unclear because the parents refused to continue the therapy.³ The patient reported by Huang et al demised at the age of seventeen days after one week of treatment with antibiotics and supportive therapy.⁴

Discussion

LCH is a clonal proliferative disease that occurs predominantly in childhood and involves the main antigen presenting cell of the epidermis.^{5,6} Typical cutaneous lesions of LCH manifest as scaly, erythematous, seborrhoea-like eruptions of brown to red papules, especially in the intertriginous zones.⁷ In fact, as we and others have shown,

neonates commonly show maculopapular rash, haemorrhagic vesicopustule involving the face, chest, back, and extremities that are easily mistaken for an infectious process, and incrustation and overlying pustules may be observed later in the course.⁸

The differential diagnosis of a neonate with haemorrhagic vesicopustule includes many infections and neoplastic disorders. Infectious disorders to consider include toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, varicella, syphilis, congenital candidiasis, and listeriosis. Neoplastic disorders include congenital leukemia, LCH, and generalised eruptive histiocytoma. If the newborn does not manifest toxicity symptoms and the initial test results do not suggest infection, LCH should be considered. So we suggest that careful observation should be applied to newborns with cutaneous disease and skin biopsies be considered in neonates with complicated cutaneous lesions as early as possible.

It is likely that neonatal LCH should be treated as a multisystemic disease irrespective of the patient's initial presentation. Although she was a thriving neonate except for haemorrhagic vesicopustules and had no other evidence of disseminated disease at her admission, our patient developed into multisystemic disease. All of the other three reported neonates with LCH had multisystemic involvement besides skin lesions at the time of presentation.

It is obvious that the prognosis of neonatal LCH is relatively poor. Two of the patients died within about half a month of diagnosis and the current case showed evidence of progression in the clinical follow-up, except that the other neonate did refuse to continue the therapy and was lost to follow up. Neonates with multisystem LCH have less favorable prognosis compared with infants and older children, and therefore follow-up is needed as well as systemic therapy.⁹ It remains unclear if gender, age of onset, clinical manifestation, histopathologic findings or procedure of treatment contributes to the outcome of neonatal LCH.¹⁰

Because of small number of patients and deficiency in data on this disease, further review in neonatal LCH is necessary.

Declaration of Interest

We declare that we have no conflict of interests.

References

1. Stålemark H, Laurencikas E, Karis J, Gavhed D, Fadeel B, Henter JI. Incidence of Langerhans cell histiocytosis in children: a population-based study. *Pediatr Blood Cancer* 2008;51:76-81.
2. Cai Q, Xue XD, Liu CL, Fu JH, Zhang JH. Langerhans cell histiocytosis in a neonate: a case report [in Chinese]. *Chin J Practical Pediatr* 2009;24:888-90.
3. Sun ZY, Li YT, Wei ZX. A case report of Letterer-Siwe disease in a neonate [in Chinese]. *Chin J Pediatr* 2003;41:380.
4. Huang M, Zhang JH, Yang YJ. A case report of Langerhans cell histiocytosis in a neonate [in Chinese]. *Chin J Pediatr* 1999;37:382.
5. Hait E, Liang M, Degar B, Glickman J, Fox VL. Gastrointestinal tract involvement in Langerhans cell histiocytosis: case report and literature review. *Pediatrics* 2006;118:1593-9.
6. Wang J, Wu X, Xi ZJ. Langerhans cell histiocytosis of bone in children: a clinicopathologic study of 108 cases. *World J Pediatr* 2010;6:255-9.
7. Stein SL, Paller AS, Haut PR, Mancini AJ. Langerhans cell histiocytosis presenting in the neonatal period. *Arch Pediatr Adolesc Med* 2001;155:778-83.
8. Avram MM, Gobel V, Sepehr A. Case records of the Massachusetts General Hospital. Case 30-2007. A newborn girl with skin lesions. *N Engl J Med* 2007;357:1327-35.
9. Minkov M, Prosch H, Steiner M, et al. Langerhans cell histiocytosis in neonates. *Pediatr Blood Cancer* 2005;45:802-7.
10. Mohr MR, Sholtzow M, Bevan HE, Fisher RG, Williams JV. Exploring the differential diagnosis of hemorrhagic vesicopustules in a newborn. *Pediatrics* 2011;127:e226-30.