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Case Report

Congenital Langerhans Cell Histiocytosis Presenting with a Hemorrhagic Papulovesicular Eruption: A Case Report

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Abstract

Congenital Langerhans Cell histiocytosis (LCH) is a rare disorder defined as LCH presenting in the first 4 weeks of life. It can have different morphological presentations, posing a diagnosting challenge to clinicians. High index of suspicion and early performance of skin biopsy are mandatory for timely diagnosis. Prognosis is variable, with some self-limited cases, while other cases progress to disseminated LCH. Hereby we report on a self-limited congenital LCH that was detected at birth and regressed spontaneously with no treatment over a period of few days.

Keywords: *Congenital Langerhans Cell Histiocytosis; Hemorrhagic Papulovesicular Eruption*

Introduction

Congenital Langerhans Cell histiocytosis (LCH) is a rare disorder defined as LCH presenting in the first 4 weeks of life.

Case Summary

H T is currently a 12 months- old boy, who was evaluated for skin lesions that were noted on the first day of life. His parents are non-consanguineous, with no family history of malignancy. The mother was 29-year-old, gravida 2 para 1, had no maternal illness, and her GBS status was unknown. He was born through spontaneous vaginal delivery, at 39 weeks of gestation, with a normal Apgar score of 9/10.

Physical Examination revealed an active well looking newborn, weight and head circumference were at the 50th centile (weight of 3.12 kg, head circumference of 34 cm) and his length was at the 90th centile (53 cm). His vital signs were stable (O_2 sat= 96%, HR= 109/min, RR= 43/min, Temp= 36.8). Chest and heart examination were unremarkable, and there was no organomegaly or lymphadenopathy. The skin was marked for scattered hemorrhagic papulovesicular lesions all over the body (Photo 1a-1d).

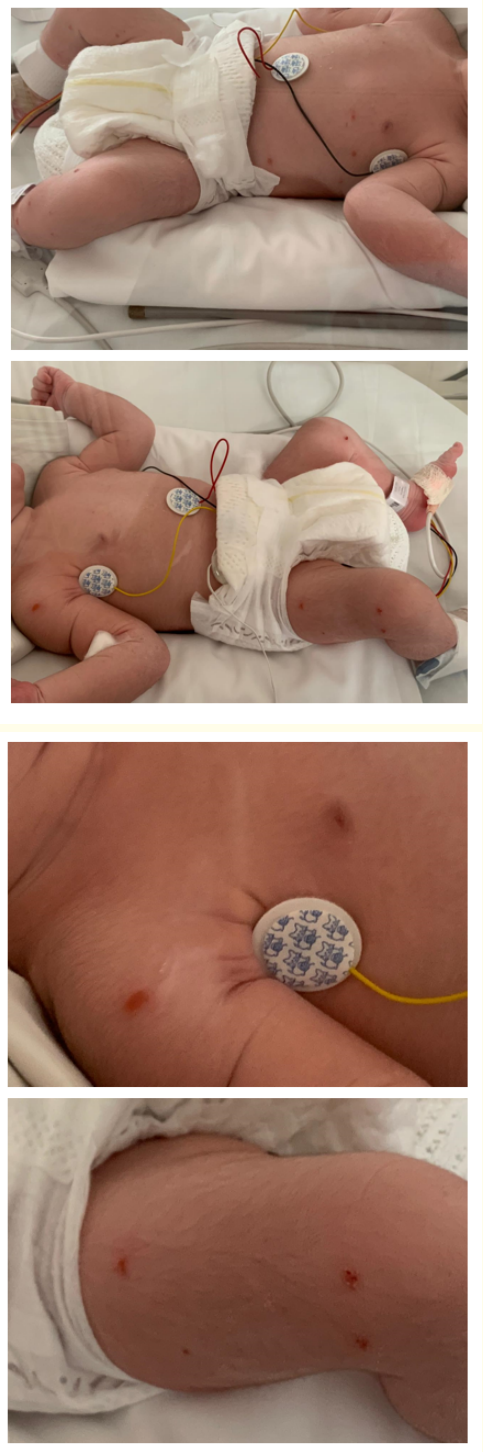


Photo 1a-1d: *Scattered crusted hemorrhagic papulovesicular rash on day 1 of life.*

Differential diagnosis included infectious and neoplastic causes. In view of the morphology of the rash, he was started on acyclovir empirically to cover for the possibility of herpes simplex infection. Later, TORCH screening was reported as negative, as well as HSV PCR from the skin lesions. Skin Biopsy was done and confirmed the diagnosis of Langerhans Cell Histiocytosis (LCH) (Figure 1-3). As recommended by the Histiocyte Society, multisystem involvement needed to be ruled out, so complete blood count, liver function tests, skeletal survey, chest radiographs, urine osmolality, and coagulation studies were performed for a complete workup. The skeletal survey ruled out the presence of any lytic lesions, and chest x-ray showed streaky lung fields with no definitive infiltrates. Laboratory results are summarized in table 1.

CBC	Hb 14 g/dl, plat 254*10^3/cmm, WBC 10.7*10^3/cmm, ANC 4.8*10^3/cmm, ALC 4.1*10^3/cmm, AMC 1.3 *10^3/cmm
Blood group	A+, DAT -ve
Hb variant analysis	HbA2 0%, HbF 81.3%, HbA 13.7%, HbS 5% (Probable sickle cell trait)
G6PD assay	Deficient
TSH	5.14
Osmolality	Serum: 278 mOsmol/kg
LFT	ALT: 11 U/L, ALP: 152 U/L, AST: 33 U/L, Bilirubin:35 umol/L, direct bilirubin: 13, total protein: 62 g/L, Albumin: 41 g/L
Electrolytes	Na: 137 meq/L, Cl: 104, K: 4.7, Urea: 3, Cr 29, HCO_3: 22, Mg 0.76
Bone profile	Ca: 2.54, P: 1.91 mmol/L
LDH	295 U/L
Microbiology	Blood culture, HSV PCR, CMV PCR, CMV IgM, Rubella IgM, HSV IgM,Toxoplasma serology: -ve CMV IgG+ve, Rubella IgG +ve, HSV IgG +ve MRSA screening: -ve
BMA	Trilineage hematopoiesis, no dysplasia, lymphoplasmocytic component unremarkable, Blasts < 1% BM trephine biopsy: No atypical cells present Chromosomal analysis of metaphases from unstimulated bone marrow cultures showed normal male karyotype 46, XY
Skeletal survey	Normal, no lytic or sclerotic lesions
Chest x-ray	Bilateral streaky lung shadows, no consolidation or collapse
US abdomen	Unremarkable study
US brain	Unremarkable study
Skin biopsy Lesion on the Rt knee	The epidermis shows focal crust formation, with neutrophil collection in the corneal layer. The papillary and superficial dermis is infiltrated by atypical cells having medium-sized and folded nuclei with occasional grooves and abundant eosinophilic cytoplasm. Scattered binucleated and multinucleated cells and scattered eosinophils (Figure 1a and 1b). The atypical cells are strongly positive for S100 (Figure 2), CD1a (Figure 3), and CD4. They are negative for CD3, CD8, CD30, ALK, and CD20. Morphology and immunohistochemistry are consistent with LCH

Table 1: *Laboratory and radiological workup of congenital LCH.*

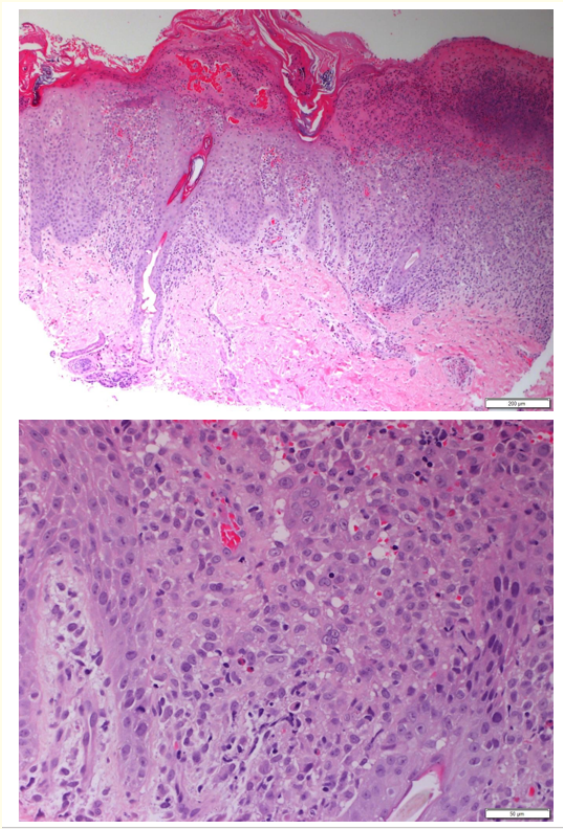


Figure 1a and 1b: *(High power) Histopathology of skin lesions of congenital LCH.*

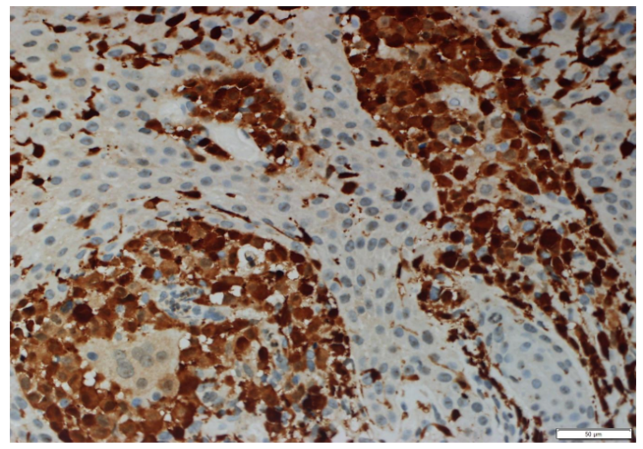


Figure 2: *Congenital LCH skin lesion: S100 stain.*

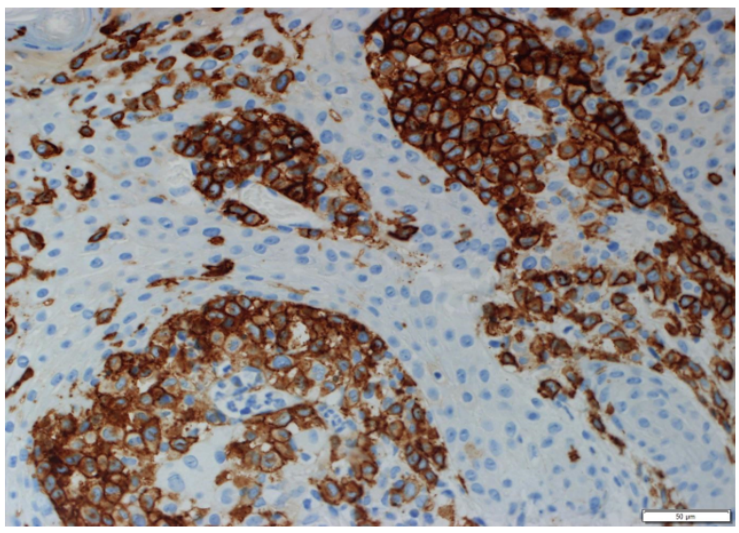
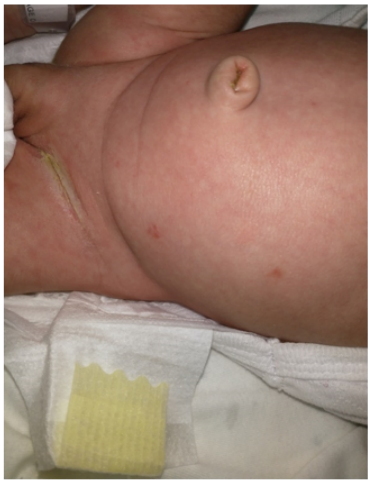
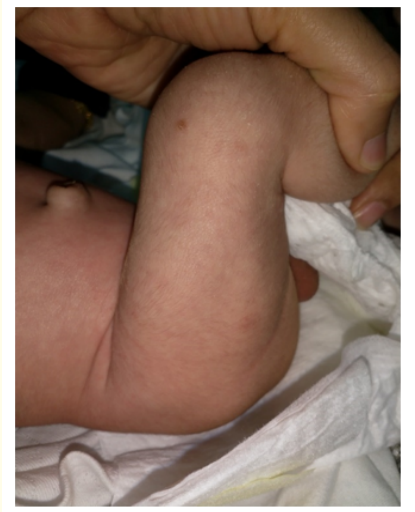


Figure 3: *Congenital LCH skin lesion: CD1a stain.*

On follow up, skin lesions spontaneously resolved within one week, and no treatment was required. The patient was discharged home, and the family was strongly advised for regular follow up. In a subsequent follow-up visit at the age of 4 weeks, he was doing well, with no complaints, no new skin lesions. He was advised to receive his regular vaccination.

Two weeks later, the patient presented to the outpatient clinic with recurrence of faint pale rosy skin lesions involving the trunk and thigh (Photo 2a and 2b). Workup was repeated and showed no other system involvement. Skin lesions were very transient and disappeared spontaneously within 3 days. The patient remained well, with no other recurrences so far. Parents were advised for regular follow up.





Photos 2a and 2b: *Recurrence of faint rosy skin rash at 6 weeks of age.*

Discussion

The current report describes a self-limited form of congenital LCH that was detected at birth in an otherwise healthy full-term Omani newborn.

LCH is a rare disease characterized by the proliferation and accumulation of pathological Langerhans cells in different locations. The clinical features of LCH range from localized, single-organ lesions to multifocal, multiorgan lesions. These lesions can either regress spontaneously or progress aggressively; thus, LCH outcome can vary in severity from benign to fatal [1].

Congenital/neonatal LCH is defined as LCH presenting in the first 4 weeks of life. It is a very rare disease that can have different morphological presentations, thus, it poses a diagnostic challenge to the pediatrician, and is usually confused with other infectious or neoplastic cutaneous lesions. Similar to our patient, some patients reported to have lesions at birth, while other patients developed manifestations later during the first month of life. In general, two forms of congenital/ neonatal LCH are identified: LCH confined to the skin, and LCH with multisystem involvement. In both forms, skin lesions in neonates are often described as being brownish to reddish maculopapular lesion/s and less commonly, hemorrhagic vesiculopustular. Frequently, before confirming a pathologic diagnosis, an infective etiology is suspected. TORCH screening, septic workup, aerobic, and anaerobic cultures, followed by broad-spectrum antibiotic coverage is the usual practice until an infective cause is ruled out. In some patients, multiple hemorrhagic papules of congenital LCH involving the skin and lungs were confused for multifocal infantile hemangiomas, for which a short course of propranolol was proved ineffective [2].

The course and prognosis of congenital LCH are variable. In the current case, LCH was self-limited, and despite recurrence, it was confined to the skin and resolved spontaneously without treatment. Similarly, most cases of congenital LCH diagnosed at birth and presented with isolated cutaneous lesions regressed spontaneously. Longaker., *et al*. reported on 4 children who presented with widespread cutaneous self-healing LCH [3].

However, several case reports documented disseminated congenital LCH, which proved fatal in a few cases. Pan JR reported on one case and reviewed 3 other cases who had multisystem involvement including the skin, digestive system, respiratory system, and hemato-

logical system. Two of these cases died within the first few weeks of diagnosis despite antibiotics and supportive care, while the other two showed evidence of progressive disease, and lost follow up after denying treatment. Of note that newborn with congenital LCH presenting initially with isolated skin lesions can gradually develop multisystem involvement, or they can have late systemic involvement after months of initial presentation highlighting the importance of following those cases closely [4,5].

As the cutaneous manifestation in isolated self-limited congenital LCH and those in disseminated disease are virtually indistinguishable, workup of high-risk organs including the lungs, liver, spleen, lymph nodes, and hematological involvement should be performed in all patients with congenital LCH. Management of cases of congenital LCH depends on the extent of organ involvement. Isolated skin lesions might require no treatment. On the other hand, with multisystem involvement, management would include chemotherapy. Guo reported complete resolution of the skin and lung lesions after 7 months of chemotherapy, followed by long term remission [2].

Conclusion

The current case highlights the importance of a high index of suspicion leading to an early performance of skin biopsy in patients who present with multiple skin lesions at birth. Early diagnosis and optimization of treatment according to the extent of pathological involvement is mandatory. Regular long term follow up for monitoring of possible relapse and/or progression to organ involvement is crucial.

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