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# A neonatal pustule: Langerhans cell histiocytosis

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## Abstract

Langerhans cell histiocytosis (LCH) is a rare, clinically heterogeneous disease that most commonly occurs in pediatric populations. Congenital self-limited LCH is a benign variant of LCH. It most commonly presents as a diffuse eruption and reports of single lesion cases are infrequent in the literature. Even in the case of congenital self-limited LCH, there is potential for future multisystem relapse, making long-term follow-up important. We present a case of single lesion self-limited LCH in a full-term male infant with interesting morphology. Physical examination revealed a painless, 6 millimeter, well-demarcated, papule encircled by erythema with central hemorrhage. An infectious workup was negative and a punch biopsy was obtained, which showed a dermal infiltrate of histiocytes consistent with a diagnosis of LCH. The lesion healed without intervention within three weeks. Our case highlights the need for dermatologists to consider LCH in the differential diagnosis for lesions of varying morphology in children, as proper identification is necessary to monitor for multisystem recurrence.

*Keywords: Langerhans cell histiocytosis, pediatric*

## Introduction

Langerhans cell histiocytosis (LCH) is a group of rare, clonal proliferative disorders with a broad spectrum of clinical manifestations, ranging from benign cutaneous lesions to malignant multisystem disease. Langerhans cell histiocytosis is the most common histiocytic disorder in the pediatric population, with

an incidence of three to five cases per million [1]. It is believed to be underdiagnosed owing to the self-healing nature of certain variants and lack of proper clinical identification.

Congenital self-limited LCH was first described by Hashimoto and Pritzker in 1973 [2]. It typically manifests at birth or in the post-natal period and cutaneous findings vary, but it most often presents as a widespread eruption of red-to-brown papulonodules [3]. To date, only 40 single lesion cases have been documented in the literature. We present a case of single lesion LCH in a full-term male infant with interesting morphology.

## Case Synopsis

A full-term male infant presented with an asymptomatic lesion of the posterior left thigh that was noted within the first 24 hours of life. Physical examination revealed a painless, 6 millimeter, well-demarcated, papule encircled by erythema with central hemorrhage (**Figure 1**). The papule was heterogeneous in color with black to grey in the center and yellow to green along the periphery. The newborn was well appearing and there was no family history of dermatologic or autoimmune conditions. The differential diagnosis was broad and included ecthyma, candidiasis, herpes simplex virus, congenital varicella, lymphoma, aplasia cutis, LCH, mastocytosis, and juvenile xanthogranuloma. Prenatal screening was negative for group B streptococcus. Swabs for bacterial cultures and

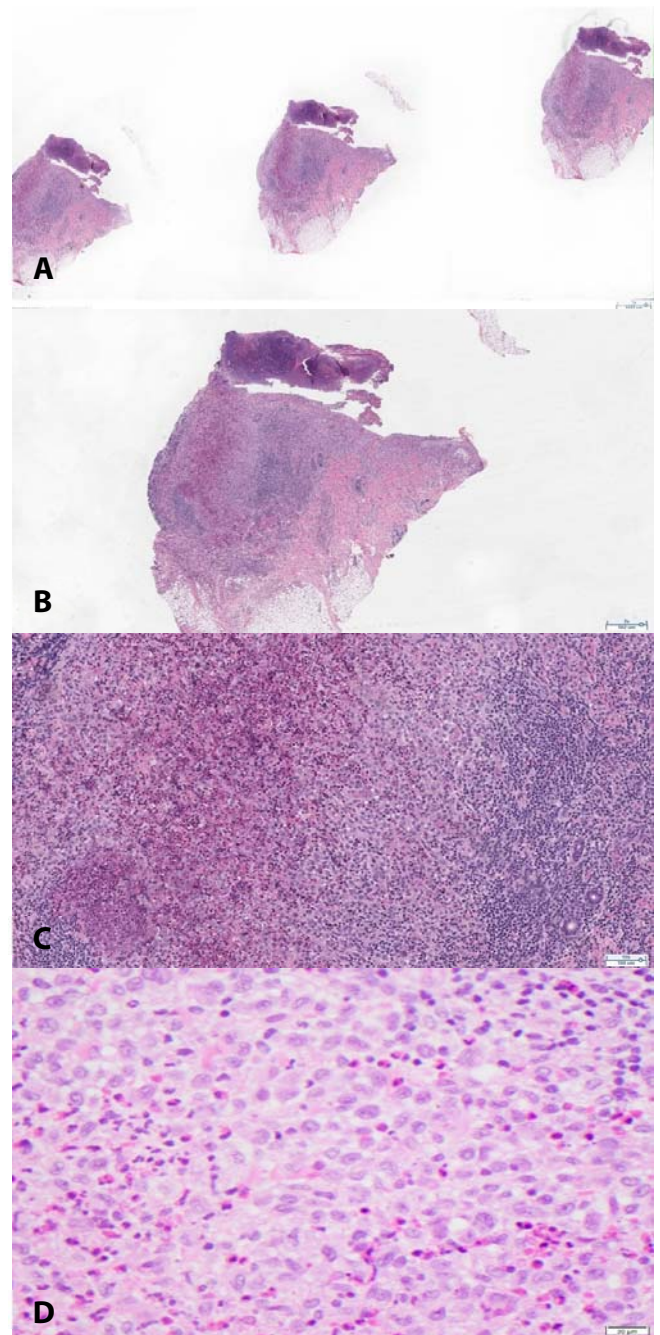


**Figure 1.** Well demarcated papule encircled by erythema with central hemorrhage on the patient's posterior thigh.

fungal cultures, and viral polymerase chain reactions for HSV were negative. A punch biopsy specimen was obtained and sent for histopathological analysis.

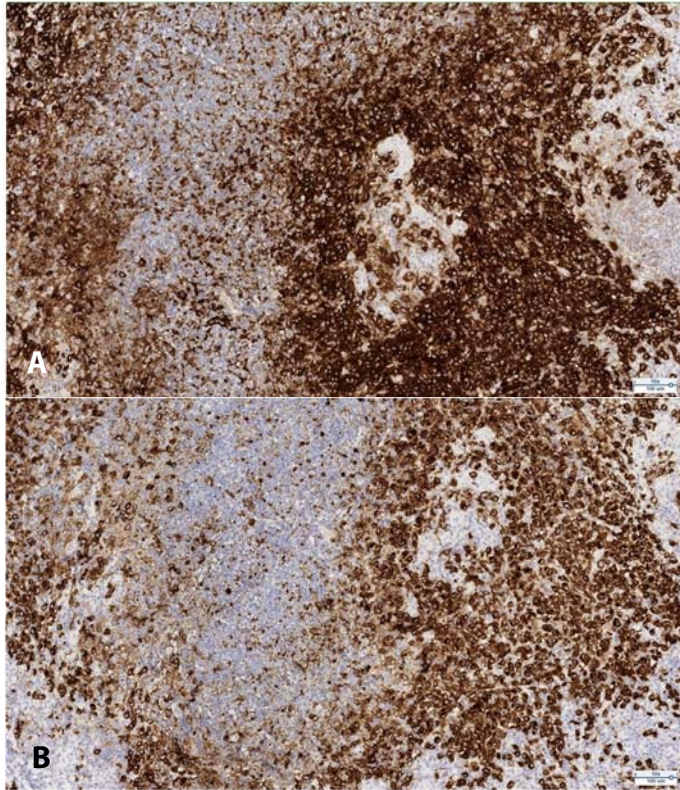
The histopathological evaluation of the skin biopsy specimen revealed epidermal ulceration (**Figure 2A**) in association with a subjacent dense dermal infiltrate of histiocytoid appearing cells manifesting indistinct cell borders and lightly eosinophilic cytoplasm (**Figure 2B**). These cells exhibited irregular, eccentrically disposed nuclei with focal 'bean-shaped' contours and a finely dispersed chromatin (**Figures 2C, D**); mitoses were rare. Although the epidermis was mostly denuded, in a small area of intact epidermis the dermal infiltrate was focally epidermotropic. In addition, there was a polymorphous inflammatory background comprising small mature lymphocytes and numerous eosinophils. Utilizing immunohistochemistry, lesional cells stained strongly positive for CD1a (**Figure 3A**) and Langerin (**Figure 3B**). These findings were consistent with a diagnosis of LCH.

The patient was referred to the oncology department for a more extensive workup, including hematologic and coagulation studies, liver function tests, musculoskeletal exam, chest X-ray, and BRAF



**Figure 2. A)** The biopsy shows an area of epidermal denudement in association with a subjacent nodular infiltrate extending into the deeper reticular dermis. H&E, 10x. **B)** Higher power magnification shows a striking dense histiocytoid infiltrate accompanied by numerous lymphocytes and eosinophils. H&E, 20x. **C)** Higher power magnification demonstrates the classic cytology that is encountered in LCH. In particular there are nodular aggregates of histiocytoid appearing cells that are remarkable for their oval to bean shaped nuclei showing a, finely dispersed chromatin and eccentric disposition within the cell. They have a morphology clearly disparate to the background inflammatory cell populace which is predominated by lymphocytes and as well there are scattered eosinophils. H&E, 100x. **D)** H&E, 400x.





**Figure 3.** The lesional cells were positive for **A) CD1a** and **B) Langerin** by immunohistochemistry, 100 $\times$ .

genetic testing. The workup was negative for any signs of systemic disease and the papule healed without intervention in three weeks. No new lesions have developed.

### Case Discussion

Congenital self-limited LCH is a rare, benign variant of LCH. In typical unilesional cases, it presents as a painless papule or nodule with ulceration or an overlying scale crust [3]. In our case, the lesion was infectious-appearing as there was an oozing, pustular component. Patients presenting with a solitary lesion are uniquely challenging for the differential diagnosis is broad. However, distinguishing between self-limited disease and systemic LCH is crucial as systemic LCH can become aggressive and require chemotherapy [4].

The overall prognosis for single lesion skin limited LCH is excellent and most lesions spontaneously

resolve within 4-18 weeks [3]. However, skin findings cannot predict systemic disease and obtaining an oncology consultation is recommended for further evaluation [5]. Patients should undergo general evaluation, which includes a thorough physical examination, blood count and differential, coagulation studies, and liver function testing [5]. Radiographic skeletal survey and chest X-ray are additionally indicated to assess for bone and pulmonary involvement [5]. Testing for BRAF mutations is newly included in of the work-up of LCH since the literature suggests that oncogenic BRAF V600E mutations may play a role in its pathogenesis with implications for targeted treatment [6]. More recently, it has been suggested that circulating cell-free DNA with detectable BRAF V600E mutations may be a useful biomarker for predicting high risk disease and monitoring response to therapy [7].

Multisystem LCH involving the bone marrow, spleen, or liver portends a poor prognosis and as many as 8-13% congenital LCH cases may later result in multisystem relapse [4, 5]. Although our patient's work up was negative for underlying systemic disease, he continues to be followed for recurrence or dissemination. It is important for clinicians to know that regression of cutaneous disease cannot rule out future dissemination and close long-term follow-up with a multidisciplinary team is necessary.

### Conclusion

Dermatologists should consider LCH in the differential diagnosis for lesions of varying morphology in children. Given the inconsistent and unpredictable nature of LCH and large variety in clinical presentation, heightened vigilance is required even when limited disease is suspected. This case highlights the need for long-term follow-up to monitor for disease recurrence or dissemination, which carries a poor prognosis.

### Potential conflicts of interest

The authors declare no conflicts of interests.

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