Dermatology Practical & Conceptual

Congenital Langerhans Cell Histiocytosis Masquerading as Neonatal Herpes Simplex Virus Infection: A Diagnostic Challenge

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Introduction

Langerhans cell histiocytosis (LCH) is a rare inflammatory neoplasm characterized by the accumulation of myeloid precursor cells in different organs, affecting 4–5 per million children annually [1]. We describe a case of a neonate affected by congenital LCH, presenting with skin lesions resembling herpes simplex virus (HSV) congenital infection.

Case Presentation

The patient was delivered naturally after an uneventful pregnancy, at 39 weeks. At birth, he displayed widespread, non-confluent, erosive lesions affecting his entire body, including the face, scalp, palms, soles, genitalia, and mucous membranes (Figure 1). Blood tests, including a complete blood count, renal and liver function, electrolytes, and C-reactive protein, were all within normal ranges. Additionally, a lumbar puncture was performed, yielding normal results. Suspecting HSV congenital infection, acyclovir 60 mg/kg/daily was started, without improvement. Blood cultures, extensive viral polymerase chain reaction tests, and serologic studies were performed to evaluate the presence of infections caused by various pathogens such as HSV, cytomegalovirus, Epstein-Barr, parvovirus B19, coxsackievirus, varicella-zoster virus, human herpesvirus 6, human herpesvirus 8, *Streptococcus pyogenes*, *S. agalactiae*, *Escherichia coli*, *Lysteria monocytogenes*, *Haemophilus influenzae*, and *Neisseria meningitidis*. However, the results showed no evidence of any ongoing infection. Histological examination displayed a thin epidermis with spongiosis and microvesiculation, confluent parakeratosis with intracorneal micropustules, and exoserosis. Furthermore, a diffuse dermal infiltration of immature cells with irregularly indented nuclei and

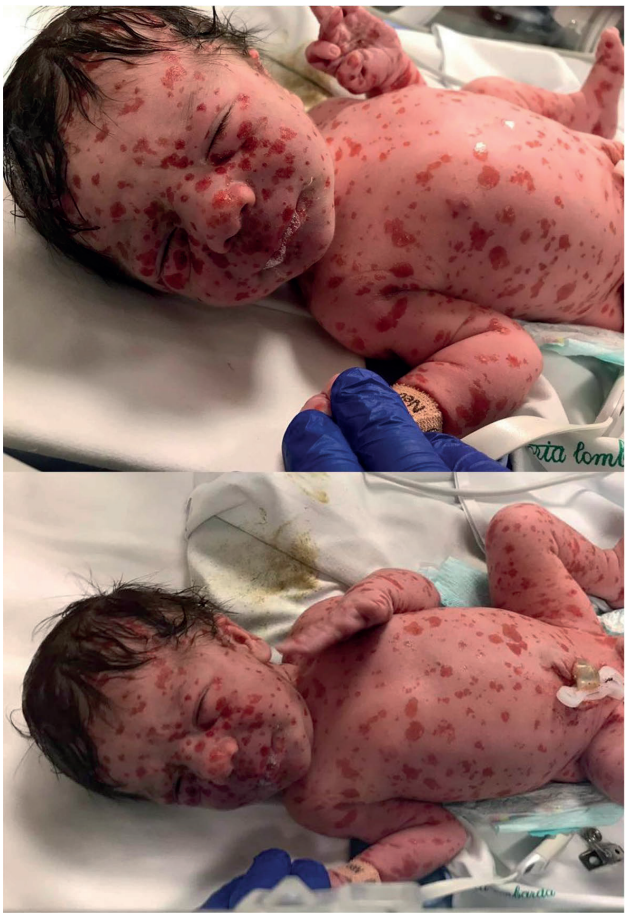

Figure 1. Diffuse skin erosions over the head, trunk, extremities, and genitals.

inconspicuous nucleoli was observed. Within an inflammatory background, the immunophenotypic and immunohistochemical profile, including positivity for Langerin, CD1a, S100, CD14, and BRAF, supported the diagnosis of LCH (Figure 2). Extensive assessments, including peripheral blood smear, cardiac and abdominal ultrasounds, full-body X-ray scans, and brain MRI, ruled out multisystemic involvement. One month after birth, the dermatological condition worsened, accompanied by elevated liver function. A hepatic biopsy revealed diffuse biliary changes, potentially associated with LCH. Treatment was initiated with a combination of vinblastine and dexamethasone. Additionally, vemurafenib, a selective BRAF inhibitor, was introduced, which resulted in partial disease control. Cutaneous congenital LCH typically occurs in newborns and presents as diffuse red-brown papules and nodules that often resolve spontaneously [2], but in some cases, it can progress to multisystemic LCH. In our patient, clinical presentation was suggestive of HSV congenital infection. Although the prepartum serological assessment for neonatal HSV did not match with acute infection, it is important to note that the risk of HSV transmission to the newborn is highest in women who acquire the infection for the first time during pregnancy while having undetectable antibodies [3]. In most cases, women do not report any prior history of HSV infection, nor do they report having genital HSV lesions either before or during delivery. In these cases, histologic examination is critical for the diagnosis.

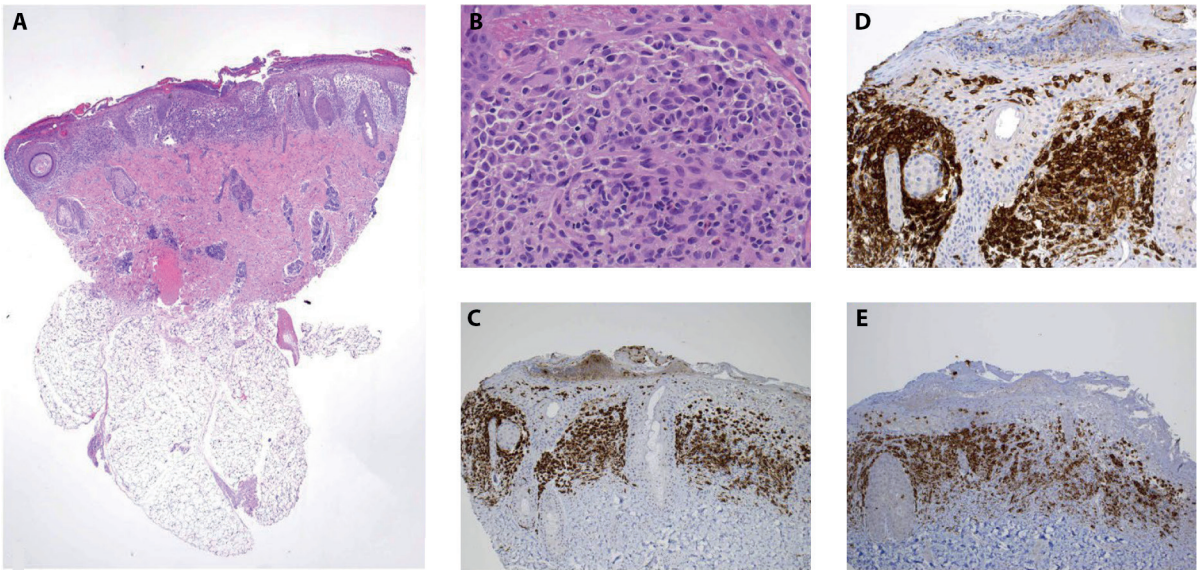

Figure 2. (A, B) The histological analysis revealed a thin epidermis characterized by spongiosis and microvesiculation. Additionally, there was confluent parakeratosis with intracorneal micropustules and exocytosis present. The dermis displayed a diffuse infiltration of immature cells, which possessed irregularly shaped, indented nuclei and subtle nucleoli (H&E, original magnification x2 and x20, respectively). (C) Immunohistochemistry showing positivity to Langerin (original magnification x4), (D) CD1a (original magnification x10), and (E) BRAF (original magnification x4).

Conclusion

LCH can present with a wide range of lesions with no typical presentation site [4]. As observed in our case, it may mimic infectious diseases, highlighting the need for prompt diagnosis and treatment. Long-term follow-up remains crucial to detect and manage multisystem involvement [5], which can result in unfavorable outcomes.

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