

Disseminated Papules and Nodules on the Skin and Oral Mucosa in an Infant

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A 38-week-old infant boy presented at birth with disseminated, nonblanching, purple to dark red papules and nodules on the skin and oral mucosa. He was born spontaneously after an uncomplicated pregnancy. The mother experienced an episode of oral herpes simplex virus during pregnancy. The infant was otherwise healthy. Laboratory tests including a complete blood cell count and routine serum biochemical analyses were within reference range; however, an infectious workup was positive for herpes simplex virus type 1 and cytomegalovirus antibodies. Ophthalmologic and auditory screenings were normal.

WHAT'S YOUR DIAGNOSIS?

- congenital cutaneous Langerhans cell histiocytosis
- congenital syphilis
- disseminated neonatal hemangiomas
- leukemia cutis
- rubella

PLEASE TURN TO **PAGE 135** FOR THE DIAGNOSIS

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THE DIAGNOSIS:

Congenital Cutaneous Langerhans Cell Histiocytosis

Although the infectious workup was positive for herpes simplex virus type 1 and cytomegalovirus antibodies, serologies for the rest of the TORCH (toxoplasmosis, other agents [syphilis, hepatitis B virus], rubella, cytomegalovirus) group of infections, as well as other bacterial, fungal, and viral infections, were negative. A skin biopsy from the right fifth toe showed a dense infiltrate of CD1a⁺ histiocytic cells with folded or kidney-shaped nuclei mixed with eosinophils, which was consistent with Langerhans cell histiocytosis (LCH) (Figure 1). Skin lesions were treated with hydrocortisone cream 2.5% and progressively faded over a few weeks.

Langerhans cell histiocytosis is a rare disorder with a variable clinical presentation depending on the sites affected and the extent of involvement. It can involve multiple organ systems, most commonly the skeletal system and the skin. Organ involvement is characterized by histiocyte infiltration. Acute disseminated multisystem disease most commonly is seen in children younger than 3 years.¹

Congenital cutaneous LCH presents with variable skin lesions ranging from papules to vesicles, pustules, and ulcers, with onset at birth or in the neonatal period. Various morphologic traits of skin lesions have been described; the most common presentation is multiple red to yellow-brown, crusted papules with accompanying hemorrhage or erosion.¹ Other cases have described an eczematous, seborrheic, diffuse eruption or erosive intertrigo. One case of a child with a solitary necrotic nodule on the scalp has been reported.²

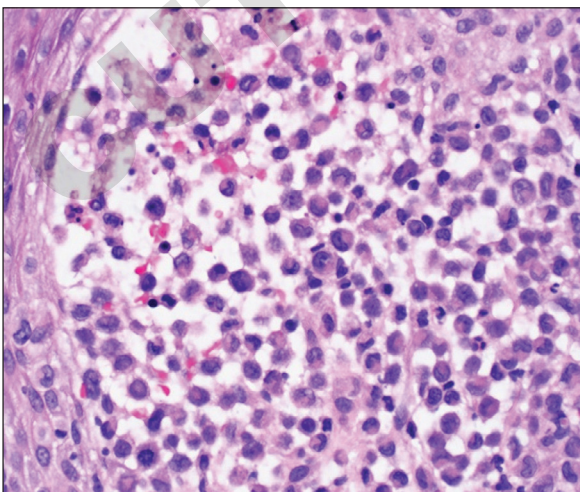


FIGURE 1. A dense infiltrate of histiocytic cells with folded or kidney-shaped nuclei mixed with eosinophils (H&E, original magnification $\times 40$).

Our patient presented with disseminated, nonblanching, purple to dark red papules and nodules of the skin and oral mucosa, as well as nail dystrophy (Figure 2). However, LCH in a neonate can mimic other causes of congenital papulonodular eruptions. Red-brown papules and nodules with or without crusting in a newborn can be mistaken for erythema toxicum neonatorum, transient neonatal pustular melanosis, congenital leukemia cutis, neonatal erythroipoiesis, disseminated neonatal hemangiomas, infantile acropustulosis, or congenital TORCH infections such as rubella or syphilis. When LCH presents as vesicles or eroded papules or nodules in a newborn, the differential diagnosis includes incontinentia pigmenti and hereditary epidermolysis bullosa. Langerhans cell histiocytosis may even present with a classic blueberry



FIGURE 2. The clinical presentation of Langerhans cell histiocytosis in an infant. A, Disseminated, nonblanching, purple to dark red papules and nodules were present on the oral mucosa. B, Nail dystrophy also was present.

muffin rash that can lead clinicians to consider cutaneous metastasis from various hematologic malignancies or the more common TORCH infections. Several diagnostic tests can be performed to clarify the diagnosis, including bacterial and viral cultures and stains, serology, immunohistochemistry, flow cytometry, bone marrow aspiration, or skin biopsy.³

Langerhans cell histiocytosis is diagnosed with a combination of histology, immunohistochemistry, and clinical presentation; however, a skin biopsy is crucial. Tissue should be taken from the most easily accessible yet representative lesion. The characteristic appearance of LCH lesions is described as a dense infiltrate of histiocytic cells mixed with numerous eosinophils in the dermis.¹ Histiocytes usually have folded nuclei and eosinophilic cytoplasm or kidney-shaped nuclei with prominent nucleoli. Positive CD1a and/or CD207 (Langerin) staining of the cells is required for definitive diagnosis.⁴ After diagnosis, it is important to obtain baseline laboratory and radiographic studies to determine the extent of systemic involvement.

Treatment of congenital LCH is tailored to the extent of organ involvement. The dermatologic manifestations resolve without medications in many cases. However, true self-resolving LCH can only be diagnosed retrospectively after a full evaluation for other sites of disease. Disseminated disease can be life-threatening and requires more active management. In cases of skin-limited disease, therapies include topical steroids, nitrogen mustard, or imiquimod; surgical resection of isolated lesions; phototherapy; or systemic therapies such as methotrexate, 6-mercaptopurine, vinblastine/vincristine, cladribine, and/or cytarabine. Symptomatic patients initially are treated with methotrexate and

6-mercaptopurine.⁵ Asymptomatic infants with skin-limited involvement can be managed with topical treatments.

Our patient had skin-limited disease. Abdominal ultrasonography, skeletal survey, and magnetic resonance imaging of the brain revealed no abnormalities. The patient's family was advised to monitor him for reoccurrence of the skin lesions and to continue close follow-up with hematology and dermatology. Although congenital LCH often is self-resolving, extensive skin involvement increases the risk for internal organ involvement for several years.⁶ These patients require long-term follow-up for potential musculoskeletal, ophthalmologic, endocrine, hepatic, and/or pulmonary disease.

REFERENCES

1. Pan Y, Zeng X, Ge J, et al. Congenital self-healing Langerhans cell histiocytosis: clinical and pathological characteristics. *Int J Clin Exp Pathol.* 2019;12:2275-2278.
2. Morren MA, Vanden Broecke K, Vangeebergen L, et al. Diverse cutaneous presentations of Langerhans cell histiocytosis in children: a retrospective cohort study. *Pediatr Blood Cancer.* 2016;63:486-492. doi:10.1002/pbc.25834
3. Krooks J, Minkov M, Weatherall AG. Langerhans cell histiocytosis in children: diagnosis, differential diagnosis, treatment, sequelae, and standardized follow-up. *J Am Acad Dermatol.* 2018;78:1047-1056. doi:10.1016/j.jaad.2017.05.060
4. Haupt R, Minkov M, Astigarraga I, et al. Langerhans cell histiocytosis (LCH): guidelines for diagnosis, clinical work-up, and treatment for patients till the age of 18 years. *Pediatr Blood Cancer.* 2013;60:175-184. doi:10.1002/pbc.24367
5. Allen CE, Ladisch S, McClain KL. How I treat Langerhans cell histiocytosis. *Blood.* 2015;126:26-35. doi:10.1182/blood-2014-12-569301
6. Jezierska M, Stefanowicz J, Romanowicz G, et al. Langerhans cell histiocytosis in children—a disease with many faces. recent advances in pathogenesis, diagnostic examinations and treatment. *Postepy Dermatol Alergol.* 2018;35:6-17. doi:10.5114/pdia.2017.67095