Arch Argent Pediatr. 2025;e202510752

Multisystem Langerhans cell histiocytosis with gastrointestinal involvement in an infant: A case report

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ABSTRACT

Langerhans cell histiocytosis is a rare disease characterized by the accumulation of Langerhans cells, which are myeloid dendritic cells, associated with significant inflammation and varied systemic involvement. Gastrointestinal involvement is rare, preceded in more than 80% of cases by skin lesions.

We report the case of a 5-month-old girl whose clinical presentation was skin lesions and proctorrhagia. A transdisciplinary approach allowed us to reach a diagnosis and initiate timely treatment.

Keywords: *Langerhans cell histiocytosis; gastrointestinal diseases; skin manifestations.*

doi: http://dx.doi.org/10.5546/aap.2025-10752.eng

To cite: Fiestas K, Geraige W, Torres M, Roitman P, Arco K, Vaquer G. Multisystem Langerhans cell histiocytosis with gastrointestinal involvement in an infant: A case report. *Arch Argent Pediatr.* 2025;e202510752. Online ahead of print 7-AUG-2025.

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Funding*: None.*

Conflict of interest: *None.*

Received*: 5-12-2025*
Accepted*: 6-18-2025*

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare clonal disease. Recent studies suggest that it is caused by a differentiation error in myeloid precursor dendritic cells, which arises from abnormal activation of the mitogen-activated protein kinase pathway.[1,2] It has a higher incidence between the ages of 1 and 4 years, with a slight predominance in males;[3] when gastrointestinal involvement is present, it is more common in females under 1 year of age.[4] Its clinical presentation may affect a single organ (73%) or be multisystemic (23%), with the most frequent involvement being bone (80%), followed by skin (33%), lung, liver, spleen, bone marrow, lymph nodes, central nervous system, and pituitary gland.[2]

Gastrointestinal involvement is rare (1-5%), although its incidence is probably underestimated due to the nonspecific nature of its symptoms. It has been reported in isolation and the context of multisystemic LCH, preceded by skin lesions in more than 80% of cases. Its manifestations are variable, ranging from diarrhea, abdominal pain, vomiting, and proctorrhagia to the presence of polyps, severe malabsorption, and intestinal perforation.[5] Histopathology shows a mild to moderate decrease in the glands of the mucosal *lamina propria*, with Langerhans cells distributed in patches or in a diffuse pattern, which exhibit a contoured nucleus with grooves and a pale granular cytoplasm with eosinophil infiltration, depending on the stage of the disease. Immunohistochemistry with positive markers for langerin (CD207) and CD1a confirms the diagnosis.

The prognosis varies depending on the involvement of one or more organs. Children under 2 years of age with multisystem LCH are at high risk, with a mortality rate of 55.5%, which increases to 78.5% when high-risk organs (liver, spleen, and bone marrow) are affected.[6,7]

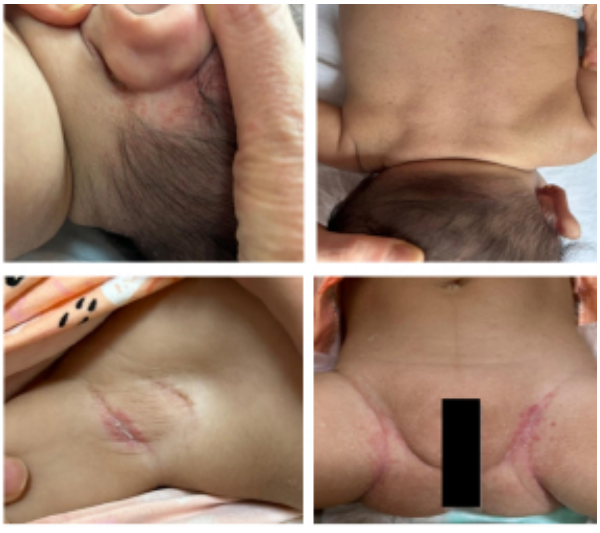
To raise awareness of this rare condition, we present the clinical case of an infant with multisystem LCH involving the gastrointestinal tract, highlighting the importance of considering its diagnosis in the presence of gastrointestinal symptoms and atypical skin lesions.

CLINICAL CASE

A 5-month-old female infant with no relevant perinatal history or family history of cancer presented at 2 months of age with proctorrhagia and skin lesions characterized by erythematous-scaly papules on the scalp, retroauricular region, trunk, and folds (*Figure 1*). Cow's milk protein allergy (CMPA) was suspected, and an exclusion diet with extensively hydrolyzed formula was initiated.

At 3 months of age, with moderate anemia, negative food allergy tests, persistent proctorrhagia, and atypical skin lesions, the

Figure 1. Atypical skin lesions at the first evaluation



Papular-erythematous-scaly lesions in the retroauricular region, scalp, trunk, and folds.

patient began feeding with an amino acid-based formula and received topical treatment with corticosteroids and antibiotics, with no response. In conjunction with the Dermatology Department, a sample of skin lesions was taken for biopsy. Two weeks later, skin biopsy confirmed LCH with immunoreactivity for CD1a, langerin, CD68, and S100.

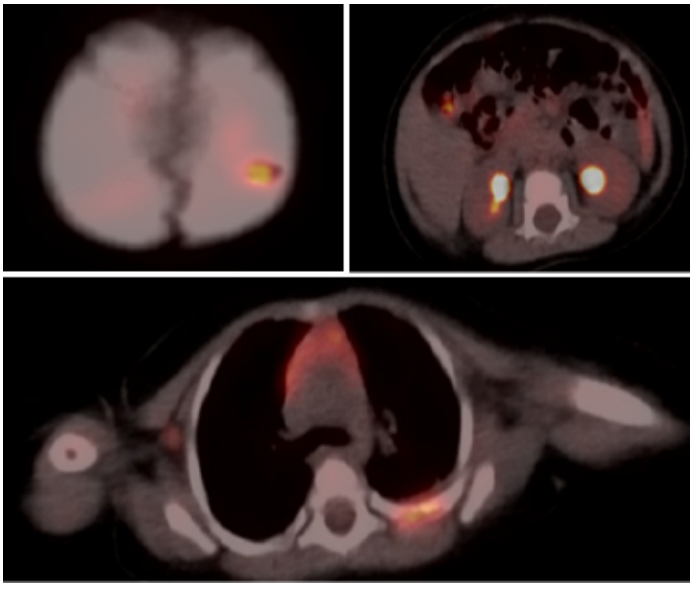
She was admitted for various diagnostic procedures due to suspected multisystem involvement. Laboratory tests revealed moderate anemia. A whole-body PET-CT (positron emission tomography) scan showed involvement of the skull, ribs, and lymph nodes (*Figure 2*). Upper gastrointestinal endoscopy revealed a stomach with some longitudinal erythematous erosions and a duodenum with multiple erythematous, infiltrative-appearing papillary lesions. Rectosigmoidoscopy revealed mucosa with loss of vascular pattern and papillary, erythematous lesions, some in clusters, as well as an infiltrative appearance (*Figure 3*). Histological examination showed Langerhans cells accompanied by eosinophil infiltration, with immunoreactivity for CD1a, langerin, CD68, and S100 (*Figure 4*), consistent with LCH.

Multisystemic LCH was confirmed, with involvement in the gastrointestinal, bone, and skin systems. Therefore, chemotherapy was initiated according to the international HISTSOC-LCH-III protocol, which consisted of vinblastine, meprednisone, and 6-mercaptopurine, without any side effects. This treatment led to gradual symptom improvement and the resolution of anemia. After 3 months of chemotherapy, upper and lower endoscopy was performed with negative immunoreactivity for CD1a and langerin, and PET-CT showed disappearance of pathological metabolic activity at the bone and lymph node levels. After 12 months of chemotherapy, the patient continues to progress well and is being monitored on an outpatient basis by an interdisciplinary team.

DISCUSSION

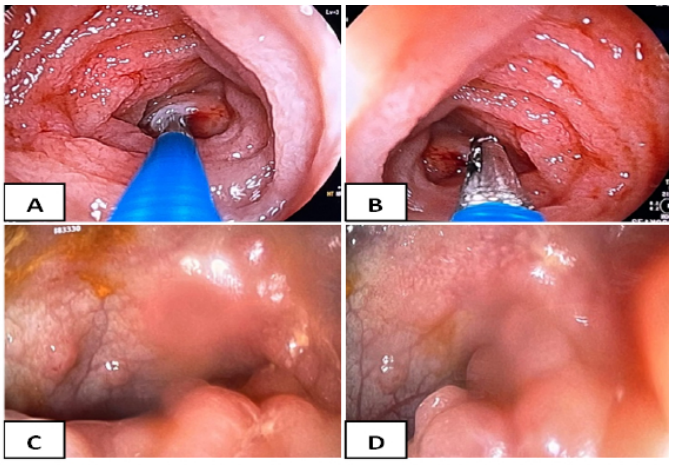
LCH encompasses a group of disorders with different clinical manifestations depending on the organ affected. The age and sex of the case presented are consistent with the most frequently reported cases of multisystem LCH with gastrointestinal involvement in the literature. Bone and skin involvement were also found, as these are commonly affected systems in this disease. Our case is a clear example of the typical presentation of multisystem LCH with gastrointestinal involvement, where the absence of malabsorption and involvement of at-risk organs could be related to the favorable outcome in this patient.[6-8] Endoscopic findings vary, and although normal mucosa may be

Figure 2. Positron emission tomography at diagnosis



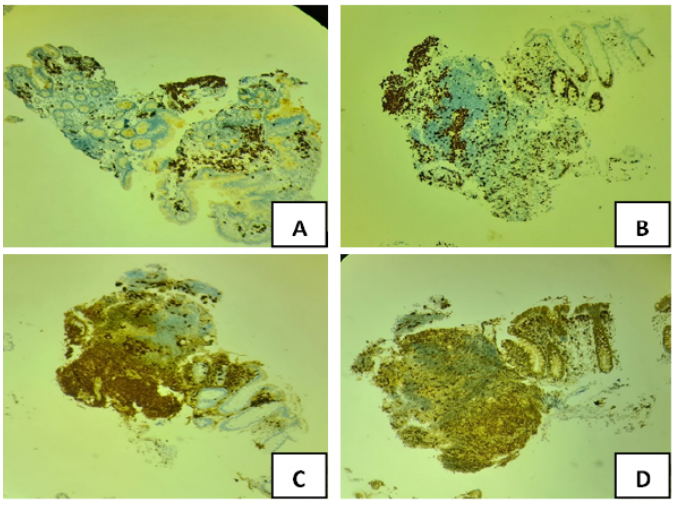
Pathological bone (cranial vault and costal) and infradiaphragmatic lymph node metabolic activity.

Figure 3. Upper and lower digestive video endoscopy at diagnosis



(A - B) Duodenum with erythematous, infiltrative-appearing papillary lesions. (C - D) Colonic mucosa with loss of vascular pattern and erythematous mamelon-like lesions, some in clusters.

Figure 4. Immunohistochemistry in duodenal and colon biopsy



Positive markers: (A) CD1A, (B) Langerin: CD207, (C) S100, and (D) CD6.

observed, the duodenum and colon are usually multifocally involved with superficial erosions, as in our case. Other findings include hemorrhagic ulcers, narrowing of the distal duodenum, isolated polyps in the stomach, and nodular lesions in the colon.[9,10] There are very few studies with endoscopic controls to confirm the non-recurrence of the disease.[2] Radiological findings are usually nonspecific, but PET-CT is necessary for follow-up once induction treatment has begun, as it is capable of detecting metabolically active foci of LCH.[11]

Other similar cases of LCH with gastrointestinal involvement have been reported: one with symptoms similar to inflammatory bowel disease;[4] others associated with panhypopituitarism;[12] another report with perianal lesions, recurrent suppurative otitis, and pulmonary involvement;[13] and a challenging case of abdominal pain in which, after appendectomy, endoscopy was performed, which revealed colonic involvement.[2] Other cases similar to the one reported, with proctorrhagia and skin lesions, were initially managed as APLV.[1]

Since clinical and radiological findings are not specific, biopsy allows us to confirm the

diagnosis through immunoreactivity for CD1a and langerin, as in our patient. Treatment modalities are determined individually, depending on the extent and affected organ, and may include observation, surgery, radiotherapy, or topical, oral, or intravenous medications.[14] In patients with multisystem involvement and high or low risk, 12 months of chemotherapy is recommended, with a reported low reactivation rate of 30%. Most disease reactivations occur in bone, skin, or other non-risk locations.[15]

It is concluded that gastrointestinal involvement in LCH is rare. Therefore, in infants with nonspecific gastrointestinal symptoms, such as the case reported, that do not resolve after treatment, biopsy is essential to obtain a differential diagnosis.

The interdisciplinary approach allowed us to reach a diagnosis, perform the necessary interventions, and initiate timely treatment. ■

Acknowledgments

Dr. Emanuel Martínez, Pathology Department; Dr. Gisela Drago and Dr. Elena Sarabia, Oncology Department; and Dr. Marina Meneses, Dr. Florencia Sánchez, and Dr. María Jimena Fernández, Dermatology Department, Dr. Humberto Notti Hospital.

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