Digestive Tract Symptoms in Congenital Langerhans Cell Histiocytosis: A Fatal Condition in an Illness Usually Considered Benign

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Introduction: Congenital Langerhans cell histiocytosis is usually limited to cutaneous lesions and has a good prognosis. In rare cases of gut involvement, mortality is high and early and aggressive treatment essential.

Materials and Methods: We report a case of histiocytosis in a newborn with bowel involvement, and performed a literature review of 13 similar cases worldwide documented between 1973 and 2008.

Results: Skin eruptions are usually the initial symptoms at birth. Bloody stools or protein-losing enteropathy are the first signs of bowel involvement that appear mostly in the first 4 weeks of life. Risk organs (hematopoietic system, liver, spleen) are often affected in the newborns with intestinal Langerhans cell histiocytosis. Prognosis is usually poor, with 78.5% mortality.

Conclusions: Even if histiocytosis in a neonate appears limited to autoinvoluting skin lesions, it is important to exclude all other organ involvement, including the bowel and stomach, as early treatment is vital.

Key Words: newborn, congenital Langerhans cell histiocytosis, gastrointestinal tract, skin disease, spontaneous remission

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Langerhans cell histiocytosis (LCH) can involve many organs. The neonatal form of LCH usually presents as a cutaneous eruption. The morphologic characteristics of the skin lesions, even their spontaneous regression, do not indicate the extent and prognosis of the disease. We report a neonate with multiple congenital autoinvoluting purpuric skin lesions and involvement of the bowel. The gastrointestinal tract (GIT) is not considered a risk organ in LCH by The Histiocyte Society. To assess the impact of neonatal LCH gastrointestinal (GI) involvement, a literature review of gut LCH in this age period was made.

**CASE REPORT**

A term female baby was born after an uneventful pregnancy. Maternal serologies including hepatitis C and B, HIV, and gonorrhea were negative, and immunity to rubella virus was demonstrated.

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The authors declare no conflict of interest.

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**DISCUSSION**

Proliferation and dysfunction of Langerhans cells leads to the clinical spectrum of LCH. Although multiple organ systems can be affected, cutaneous manifestation is often the first sign of the disease in neonates. It has been described as erythematous vesiculopustulous skin rash, as red-brown nodules, as a Blueberry Muffin Baby phenotype or as eczematous scaling lesions. Only about 20% present petequias or mucosal lesions.

LCH presenting with a congenital skin rash has been termed congenital self-healing reticulohistiocytosis to
<table>
<thead>
<tr>
<th>Case Number</th>
<th>Source</th>
<th>Age at Onset, Sex</th>
<th>Presenting Symptoms</th>
<th>Digestive Symptoms and GI Involvement</th>
<th>Other Organs Involved</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Current case</td>
<td>Birth, F</td>
<td>Skin lesions, diffuse violaceous macules, and papules</td>
<td>Bloody diarrhea at 2 wk of age, rectal and colon biopsies LCH +</td>
<td>Skin biopsy LCH + hematologic, pulmonary and bone involvement</td>
<td>Steroids, Vinblastine, Mercaptopurine</td>
<td>No active disease at 2 y</td>
</tr>
<tr>
<td>2</td>
<td>Aviner et al^4</td>
<td>Birth, F</td>
<td>Skin lesions, vesiculopapulomacular lesions, discrete mucosa lesions</td>
<td>Bloody stools at 5 d of age, rectal biopsy LCH +</td>
<td>Skin biopsy LCH + cystic pulmonary lesions</td>
<td>Steroids, Vinblastine</td>
<td>Died at 26 d</td>
</tr>
<tr>
<td>3</td>
<td>Hait et al^3</td>
<td>2 d of life, F</td>
<td>Skin lesions, white pustules on an erythematous base</td>
<td>Bloody stools in the first month of life, rectosigmoid, stomach biopsies LCH +</td>
<td>Skin biopsy LCH +, hematologic, liver and spleen involvement</td>
<td>Steroids, Vinblastine, low-dose Methotrexate, Mercaptopurine</td>
<td>Remission at 6 mo, relapsed at 13 mo and died</td>
</tr>
<tr>
<td>4</td>
<td>Stein et al^1</td>
<td>&lt; 1 mo, M</td>
<td>Skin lesions, eczematosus (seborrhoea-like) dermatitis bloody stools</td>
<td>Bloody diarrhea &lt;1 mo of life</td>
<td>Skin LCH +, GI, bone, and liver</td>
<td>Prednisone, Vinblastine, Etoposide Steroids, Vinblastine, Etoposide, Vincristine, Cyarabine, Ciclosporine</td>
<td>No active disease at 4 y Died at 32 mo</td>
</tr>
<tr>
<td>5</td>
<td>Couderc et al^5</td>
<td>Birth, F</td>
<td>Skin lesions, disseminated purpuric, nodulic, and maculopapulous elements at birth. Associated vomiting and diarrhea</td>
<td>Vomiting and diarrhea, EEP at 8 d, rectal biopsy LCH +</td>
<td>Skin LCH +, Bone marrow, liver, spleen</td>
<td>Steroids, Vinblastine, Etoposide Steroids, Vinblastine, Etoposide, Vincristine, Ciclosporine</td>
<td>Died at 3.5 mo</td>
</tr>
<tr>
<td>6</td>
<td>Geissmann et al^6</td>
<td>Birth, F</td>
<td>Skin lesions</td>
<td>Diarrhea and bloody stools, EEP &lt;1 mo, colon and rectum biopsies LCH + Vomiting, EEP &lt;1 mo, duodenum biopsies LCH +</td>
<td>Skin LCH +, palatate, hematologic dysfunction, hepatomegaly, and cholestasis</td>
<td>Steroids, Vinblastine, anti-CD1 antibodies</td>
<td>Died at 4 mo</td>
</tr>
<tr>
<td>7</td>
<td>Geissmann et al^6</td>
<td>Birth, M</td>
<td>Skin lesions</td>
<td>Diarrhea and bloody stools, EEP &lt;1 mo, colon and rectum biopsies LCH + Vomiting, EEP &lt;1 mo, duodenum biopsies LCH +</td>
<td>Skin LCH +, liver, hematologic dysfunction</td>
<td>Steroids, Vinblastine, Etoposide interferon-α</td>
<td>Died at 4 mo</td>
</tr>
</tbody>
</table>
emphasize the good prognosis. This term can cause confusion as multiple organs may be severely affected at the moment of diagnosing LCH or during follow up.¹–³ It seems that the morphologic characteristics of the skin lesions, even their spontaneous regression, do not indicate the extent and prognosis of the disease.

In the case series reported by Stein et al,¹ neonates with multisystem disease had a mortality rate of 16% but only 1 child had GI involvement. To find cases of LCH in neonates with GIT involvement, Google and Pubmed literature searches were performed using the key words “Langerhans cell histiocytosis,” “neonatal,” and “gastrointestinal involvement.” We found 13 similar cases. Presenting symptoms, GI symptoms, other organs affected, and outcomes are summarized in Table 1.

We reviewed 14 documented cases in the last 40 years including the present patient. From these, 8 cases were female and 6 male. The presenting symptom was in almost all neonates, a skin eruption at birth (13 of 14 cases), described as purpuric papules and macules, papulovesicular lesions, or as an eczematous rash. Only in 1 case skin eruptions appeared after GI symptoms at 6 weeks of age. GI symptoms occurred in 8 cases in the first 2 weeks of life, in 5 in the first month, and in 1 case at 6 weeks. Most of the neonates (8) presented bloody stools, 5 were diagnosed with exudative enteropathy and 1 with malabsorption. It seems that in cases of bowel involvement, other organs are often affected: the liver (9 cases), spleen (3), hematopoetic system (6), bones (4), and the lung (9).

Although the described case presently has a full remission at 2 years of age, prognosis in other similar cases has been poor, with 78.5% mortality. A total of 50% of these children (7) died in the first 4 months.

**CONCLUSIONS**

Literature shows that GIT involvement in LCH in the neonatal period is rare. Although the GIT is not considered a risk organ in LCH by The Histiocyte Society, prognosis was not good in most of neonatal cases reviewed. Skin lesions almost always preceded GIT disease, therefore, cutaneous LCH in the neonatal period requires aggressive evaluation and early treatment.

**REFERENCES**


