Journal of Pediatric Gastroenterology and Nutrition
41:483–484 © October 2005 Lippincott Williams & Wilkins, Philadelphia

Clinical Quiz

*A. C. Prior, †M. Selores, ‡R. Pina, §J. Amil Dias, *F. M. Costa, *L. Vale, and *L. Gomes

*Departments of *Pediatrics, †Dermatology, and ‡Pathology, Hospital Geral de Santo António, and §Department of Pediatrics, Hospital de São João, Porto, Portugal*

An 8.5-month infant was admitted as a result of generalized edema hypoproteinemia and hypoalbuminemia. His pregnancy and delivery were uneventful. Several days after birth a papulosquamous cutaneous eruption was noticed in the trunk; this was treated with emollients, with partial improvement. At the age of 6 months he began having diarrhea without blood or mucous (tid) and occasional vomiting. He was on solid food, which was gradually being removed in an attempt to control symptoms. Ten days before admission, edema of the lower limb was noticed, with progressive extension. The skin lesions became erythematous and desquamative, still papular, without apparent pruritus (Fig. 1). Weight and growth were normal (50th percentile). Clinical examination was otherwise irrelevant.

Laboratory investigations revealed normal liver enzymes and the absence of proteinuria. There was no anemia, leukopenia or thrombocytopenia.

1. What is the most likely etiology of this edematous state?
   a. Liver failure
   b. Nephrotic syndrome
   c. Protein-losing enteropathy
   d. Starvation
2. What differential diagnosis should one consider concerning cutaneous disease?
   a. Seborrheic dermatitis versus atopic dermatitis
   b. Miliaria versus atopic dermatitis
   c. Seborrheic dermatitis versus Langerhans-cell histiocytosis
   d. Seborrheic dermatitis versus Miliaria

Endoscopic evaluation showed numerous duodenal erosions and marked abnormal mucosa (Fig. 2).

Skin and jejunal biopsies were performed. The histopathologic examination of both specimens showed the presence of aggregates of pathologic Langerhans cells, intermediate cells, interdigitating cells, macrophages, T cells and giant histiocytes.

Immunohistochemical study for S100 protein and for CD1a antibody demonstrated strong immunoreactivity in the histiocytic cells.

3. What is the diagnosis?
   a. Hodgkin disease
   b. Xanthogranuloma juvenile
   c. Langerhans' cell histiocytosis
   d. Acrodermatitis enteropathica

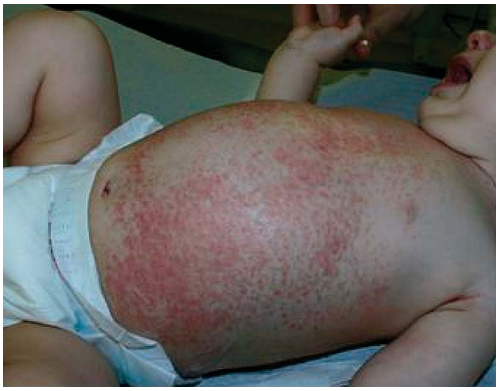

FIG. 1. Infant's erythematous and descamative rash.

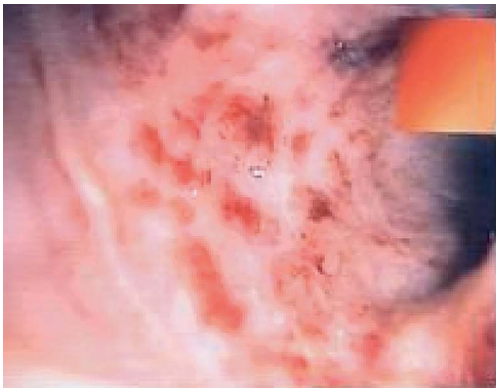

FIG. 2. Duodenal erosions on endoscopy.

ANSWER: See page 484.

ANSWER/DISCUSSION

1. c) Protein-losing enteropathy
2. c) Seborrheic dermatitis versus Langerhans cell histiocytosis
3. c) Langerhans cell histiocytosis

The occurrence of digestive involvement and protein-losing enteropathy in Langerhans cell histiocytosis has rarely been described (1–3). It is probably underdiagnosed, as gastrointestinal tract disease can be clinically silent. Digestive involvement seems to confer a worse prognosis to the disease, probably because of refractory hypoalbuminemia (3,4).

Although the exact mechanism of diarrhea and malabsorption is unclear, it seems that histiocytic infiltrates promote inflammatory bowel changes involving the lamina propria and may be responsible for vomiting, anorexia, malabsorption and exudative enteropathy, even before the occurrence of major alterations on the surface epithelium (3).

Preliminary data suggest that the ability of Langerhans cell histiocytosis cells to invade the digestive tract is likely to depend on overexpression of certain integrins, namely $\alpha 4\beta 7$ (which is not expressed by normal skin-resident Langerhans cells), and on the underexpression of other adhesion molecules, such as E-cadherin (2,3).

Prognosis in Langerhans cell histiocytosis is highly variable; it is clearly worse in cases of multisystemic involvement, organ dysfunction and young age (1–3).

In the present case, further studies unveiled bone marrow involvement, besides skin and digestive tract, conferring the patient a poor prognosis. Chemotherapy was initiated, according to the LCH-III Protocol of the Langerhans Cell Society, with poor response. Thereafter, the infant developed several complications and died 7 months after his initial admission to the hospital.

The presented case reminds us that Langerhans cell histiocytosis, although rare, should be considered in the differential diagnosis of protein-losing enteropathies (1–4).

REFERENCES

1. Arico M, Egeler RM. Clinical aspects of Langerhans cell histiocytosis. *Hematol Oncol Clin North Am* 1998;12:247–58.
2. Geissmann F, Emile JF, Andry P, et al. Lack of expression of E-cadherin is associated with dissemination of Langerhans' cell histiocytosis and poor outcome. *J Pathol* 1997;181:301–4.
3. Geissmann F, Thomas C, Emile JF, et al. Digestive tract involvement in Langerhans cell histiocytosis. The French Langerhans Cell Histiocytosis Study Group. *J Pediatr* 1996;129:836–45.
4. Santos-Machado TM, Cristofani LM, Almeida MT, et al. Disseminated Langerhans' cell histiocytosis and massive protein-losing enteropathy. *Braz J Med Biol Res* 1999;32:1095–9.