A 13-MONTH-OLD infant with methylmalonic acidemia presented with an erythematous, desquamating rash that had begun in the diaper area and progressively spread to involve parts of the face, extremities, and trunk (Figure 1 and Figure 2). As part of his treatment for methylmalonic acidemia, dietary protein was restricted (1.2 g/kg per day). Before the rash began, he had gastroenteritis and was not able to tolerate this diet for 3 days.
Cutaneous Lesions Associated With Isoleucine Deficiency

Figure 1 and Figure 2. The rash is erythematosus, desquamating, and most prominent in the diaper area where it began. The perioral area is spared in this infant.

Methylmalonic aciduria (MMA) is a disorder of branched-chain amino acid metabolism in which methylmalonic acid accumulates in body fluids. Infants with this disorder usually present in the first few weeks of life with vomiting, acidosis, and ketonuria. Lethargy, hypotonia, and coma may ensue. Associated laboratory abnormalities may include hyperammonemia, neutropenia, and thrombocytopenia. If undiagnosed, recurrent episodes of vomiting, dehydration, and ketoacidosis may lead to mental retardation and death.

Methylmalonic aciduria is the result of a defect in the enzyme methylmalonyl CoA mutase, which requires adenosylcobalamin, a metabolite of vitamin B12, as a coenzyme. Two forms of the mutase apoenzyme deficiency have been described—mut0, referring to no detectable enzyme activity, and mut−, indicating abnormally reduced enzyme activity.1 About half of the patients with MMA have a deficiency of the mutase apoenzyme and are not responsive to vitamin B12 therapy. The other half of patients with a defect in the formation of adenosylcobalamin are responsive to vitamin B12 treatment. Treatment of the mutase-deficient patients includes a diet low in threonine, isoleucine, valine, and methionine.

A rash, in many cases similar to the rash of acrodermatitis enteropathica, has been described in several metabolic disorders, including MMA,2,3 maple syrup urine disease,4-6 propionic acidemia,3 and citrullinemia.7 The first 3 disorders are closely related inborn errors of branched-chain amino acid metabolism, and they usually require strict restriction of branched-chain amino acids as part of dietary therapy. In the patients with rash and very low serum concentrations of isoleucine, institution of isoleucine supplementation resulted in rapid clearing of the rash.3,5,6

The rash of acrodermatitis enteropathica usually begins in the periorificial areas of the body (anus, mouth, nose, and eyes) as moist, erythematous lesions that may become vesicular or bullous. As the lesions dry, the resulting plaques often resemble psoriatic lesions. The lesions spread to the extremities and may involve the trunk as well. Zinc deficiency is the cause of the rash and the associated findings. In many children the rash described in the infants with branched-chain amino acid disorders is similar to the rash of acrodermatitis enteropathica, although the rash did not have a perioral component in this infant and in some of the children with MMA described in other reports.2 The rash may be more precisely described as an exfoliative erythroderma in many infants with branched-chain amino acid disorders who have developed low isoleucine levels.

Acrodermatitis enteropathica-like rashes have been described in several other disorders including essential fatty acid deficiencies, biotin-responsive multiple carboxylase deficiency, cystic fibrosis, kwashiorkor, and necrolytic migratory erythema.3,6

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