

Acute onset of blisters in an infant with acrodermatitis enteropathica: A case report

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Abstract

We represent a pediatric case of the congenital disorder caused by zinc malabsorption, acrodermatitis enteropathica, presenting with acute onset of blisters. Although blisters can be seen in this condition, it is not always a key feature and can therefore be overlooked when considering a differential diagnosis of acute blistering in infancy. We therefore review the common and less common features of this cutaneous eruption as well as provide an extensive differential diagnosis for acute blistering in infancy. We also emphasize the importance of lifelong treatment with zinc supplementation in these children.

Keywords

Pediatric dermatology, nutritional deficiency, zinc

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Introduction

Zinc is one of the ten trace elements essential for health. It is found in many foods and is particularly concentrated in animal-sourced foods. Dietary zinc is absorbed in the duodenum and jejunum of the small intestine through a specific zinc transporter, ZIP4.^{1,2} It is then released into the bloodstream via other zinc transporters. In the human body, skin is the third most zinc abundant tissue following skeletal muscle and bone.³ Zinc is a cofactor for over 1000 enzyme reactions and over 2000 transcription factors and is therefore associated with multiple cellular functions including regulating lipid, protein and nucleic acid synthesis and degradation. In skin, zinc is concentrated in the epithelium. It is involved in epidermal keratinocyte differentiation and growth as well as in anti-inflammatory processes and wound healing.²⁻⁴

There are four types of zinc deficiency: insufficient intake, increased loss, malabsorption and increased requirement. Acrodermatitis enteropathica falls into the malabsorption category. Acrodermatitis enteropathica is a rare and severe disorder affecting 1–5 of 500,000 births.^{1,5} It is inherited as an autosomal recessive disorder resulting from the loss of function mutation of the SLC39A4 gene located on the long arm of chromosome 8 coding the ZIP4 transporter.^{2,4} The typical onset is in early childhood following weaning of breast milk which has an abundance of bioavailable zinc compared to other milk substitutes which may even be deficient in their zinc quantities.¹ The clinical features are diverse. Cutaneous manifestations predominate and are usually asymptomatic,

sharply demarcated eczematous or psoriasiform plaques with peripheral scaling and crust. These lesions are usually found in an acral, periorificial (sparing the upper lip) and anogenital distribution pattern.

Case report

A 10-month-old healthy boy presented to the dermatology clinic with a 2-week history of an eruption consisting of well demarcated red-to-brown plaques with overlying scale on his knees, cheeks and chin as well as blistering and crust on the hands and feet (Figure 1). All lesions were asymptomatic. The anogenital area, oral mucosa and scalp were unaffected and there were no nail changes. He did not have a fever and had been eating and drinking well with regular wet diapers. He did not have vomiting, diarrhea or weight loss. His energy levels were normal with no lethargy or behavioral changes. He was otherwise healthy, never had problems with his skin prior to this eruption and there are no known skin diseases in his family. He had been strictly formula fed until 6 months of age when he was introduced to a variety of solid foods. Three weeks prior to the eruption, he was switched from formula to

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Figure 1. Initial presentation of an asymptomatic cutaneous eruption consisting of well demarcated red-to-brown plaques with scale on the knees and cheeks and crusted and blistering plaques on the hands and feet in a 10-month-old boy.

homogenized milk. The parents suspected that the homogenized milk was responsible and he was switched to coconut milk.

When considering an acute blistering eruption in an infant, the differential diagnosis is broad, including categories such as infectious, inherited, autoimmune and reactive (Table 1).⁶ The history, psoriasiform morphology and distribution of this eruption was suspicious for acrodermatitis enteropathica; however, blistering is not one of the key features of this disease. Blood work for further diagnostic clarity was ordered including serum zinc and alkaline phosphatase (a zinc-dependent enzyme) levels. Serum zinc was found to be low at 2.6 $\mu\text{mol/L}$ (normal levels 9.9–19.9 $\mu\text{mol/L}$) and alkaline phosphatase was also low at 58 U/L (normal levels 145–320 U/L) confirming the clinical suspicion of a zinc deficiency. Genetic testing showed a pathogenic variant, c.599C>T, p.(Pro200Leu), of the SLC39A4 gene further confirming the diagnosis of acrodermatitis enteropathica. Zinc supplementation (zinc gluconate, 3 mg/kg) was initiated and after only 1 week the skin lesions had improved and at the 7-week follow-up visit, there was almost complete resolution of the eruption (Figure 2).⁶

Discussion

The classic triad of acrodermatitis enteropathica includes perioral, intertriginous and acral dermatitis, alopecia and diarrhea; however, this only occurs in 20% of cases (Table 2). Other less common manifestations include paronychia,

Table 1. Blistering diseases of infancy.

Inherited causes
Epidermolysis bullosa: simplex, junctional, dystrophic
Kindler syndrome
Bullous ichthyosis
Hailey–Hailey
Porphyrias
Vesicular/bullous phase of incontinentia pigmenti
Autoimmune causes
Chronic bullous disease of childhood
Bullous pemphigoid
Cicatricial pemphigoid
Epidermolysis bullosa acquisita
Bullous systemic lupus erythematosus
Pemphigus
Dermatitis herpetiformis
Infectious causes
Herpes simplex virus
Varicella
Hand, foot and mouth
Cellulitis
Blistering dactylitis
Scabies
Staphylococcal scalded skin syndrome
Bullous impetigo
Reactive causes
Erythema multiforme
Stevens–Johnsons syndrome/toxic epidermal necrolysis
Bullous insect bites
Miscellaneous causes
Blistering photodermatoses
Nutritional deficiencies
Bullous mastocytosis
Unusual presentation of common condition

onychodystrophy, angular stomatitis, cheilitis, conjunctivitis and photophobia.¹ The diagnosis of acrodermatitis enteropathica is based on clinical and laboratory findings such as low serum zinc and alkaline phosphatase (a zinc dependent enzyme) levels; however, molecular genetic analysis confirms acrodermatitis enteropathica, as in the above-mentioned case.⁵ Without proper treatment, potential complications of zinc deficiency include extensive erosions and secondary infections due to zinc's important role in wound healing and cellular immunity.¹

Treatment involves lifelong zinc supplementation with oral zinc sulfate, gluconate or acetate, although zinc sulfate has been described as the most tolerable compound.¹ There is no clear consensus on the exact dose for zinc supplementation. The more common approach is 3 mg/kg/day although



Figure 2. Seven-week follow-up after high-dose zinc sulfate treatment. Near complete resolution of lesions is noted.

Table 2. Acrodermatitis enteropathica: triad of clinical features.

Perioral, intertriginous and acral dermatitis
Alopecia
Diarrhea

some will treat with 1-2mg/kg/day with higher doses of 5–10mg/kg/day to treat exacerbations.⁵ Skin lesions will usually improve within 24–48h of treatment. Zinc side effects include diarrhea, nausea, vomiting, mild headaches and fatigue. Regular monitoring of zinc levels and increasing the dose with growth is recommended to maintain adequate treatment. Monitoring copper and iron levels is also recommended due to the possible interaction of zinc supplements with these elements. It is important to note that flares can occur in patients with normal serum zinc levels and that

supplementation at the recommended 3 mg/kg/day dose will significantly improve any lesions.⁴⁻⁶ It has also been reported that severe and/or chronic effects of zinc deficiency such as mental status changes or depression treated with zinc supplementation showed significant efficacy.² Reports indicate that even inconsistent zinc supplementation can lead to recurrent skin manifestations potentially resulting in severe skin erosions. The importance of high-dose lifelong supplementation is therefore important to discuss with parents when infants are first diagnosed with acrodermatitis enteropathica to prevent flares or further complications.

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