Denouement and Discussion

Severe Zinc Deficiency in Infancy (Acrodermatitis Enteropathica–like Picture)

Based on the history, clinical picture, and low alkaline phosphatase level, we considered zinc deficiency with an acrodermatitis enteropathica–like picture. This was confirmed (serum zinc level, 30.7 µg/dL [to convert to micromoles per liter, multiply by 0.153]; all measurements by atomic absorption). We started zinc supplementation with an initial bolus of zinc gluconate (10 mg/kg/d) over 3 days and subsequent maintenance therapy of 2 mg/kg/d. The bacterial superinfection was treated intravenously with amoxicillin and clavulanate potassium (skin swab positive for *Staphylococcus aureus*) for 10 days. The skin lesions and child's irritability improved rapidly (**Figure 3**) and the stools normalized within 3 days. Follow-up blood work 2 weeks later showed that the level of alkaline phosphatase, a zinc-dependent metalloenzyme, had also normalized. Further analyses revealed a very low zinc level in his mother's breast milk (17.0 µg/dL) and a normal maternal blood zinc level of 76.5 µg/dL. After discharge, the boy was weaned off breast milk. Three months later zinc supplementation was stopped after levels of zinc (84.3 µg/dL) and alkaline phosphatase (763 U/L) had been reevaluated, and another 3 months later the child was still symptom-free. The child's condition was most likely attributable to acquired zinc deficiency due to defective secretion of zinc into the maternal breast milk.

Zinc is an essential component of more than 300 enzymes and is indispensable for vital processes such as cell division, tissue healing, and immunological and reproductive functions.[1] Zinc acts as an antioxidant and in zinc-containing enzymes is needed as a catalytic agent or for the structural stability of the enzyme.[1] Low zinc levels impair the immune response especially by compromising T-cell maturation and function and by inhibiting phagocytosis, natural killer cell activity, and antibody production.[1,2] Clinical manifestations include skin lesions, alopecia, diarrhea, impaired wound healing, photophobia, growth inhibition, neurological and hematological disturbances, and impaired gonad function.

Zinc deficiency in infancy can be either acquired or the consequence of a genetic defect. Acrodermatitis enteropathica is a rare autosomal recessive disorder with an estimated incidence of 1 in 500 000 children.[2] Owing to a defect of the gene *SLC39A4* localized on chromosome 8 (8q24.3), the transmembranous protein Zip4, acting as a zinc transporter in the intestine, is defectively produced. This results in intestinal zinc absorption of about only 3% of the administered amount.[3] Because breast milk seems to contain a factor (most likely citrulline) that enhances intestinal zinc absorption, first clinical symptoms (typically severe dermatitis, predominantly of the anogenital area, the acres, and periorally, as well as diarrhea) usually occur in term infants shortly after breastfeeding is stopped. In those cases, lifelong zinc supplementation is required and effective, most likely because of increased paracellular zinc absorption occurring with high intestinal zinc concentrations.

If zinc deficiency manifests in a fully breastfed infant, acquired zinc deficiency is the most likely explanation. While preterm infants are more prone to develop zinc deficiency due to diminished prenatal zinc storage, postnatal intestinal zinc absorption, and a higher zinc demand, the most frequent reason for acquired zinc deficiency in fully breastfed term infants is a zinc secretion defect of the maternal breast gland.[4] Zinc supplementation usually resolves the symptoms very quickly, but attempts to increase zinc levels in breast milk through maternal zinc supplementation have not been successful.

It is not uncommon to initially mistake the disorder for diaper rash, staphylococcal scalded skin syndrome, psoriasis, atopic eczema, or other skin conditions and delay appropriate treatment. In the presence of the typical skin lesions, the clinician should always consider zinc deficiency as the underlying cause, especially when the lesions are accompanied by diarrhea and/or a low alkaline phosphatase level. Owing to therapeutic consequences (acrodermatitis enteropathica requiring lifelong zinc supplementation vs acquired zinc deficiency requiring temporary zinc supplementation), the specific diagnosis should always be elaborated.

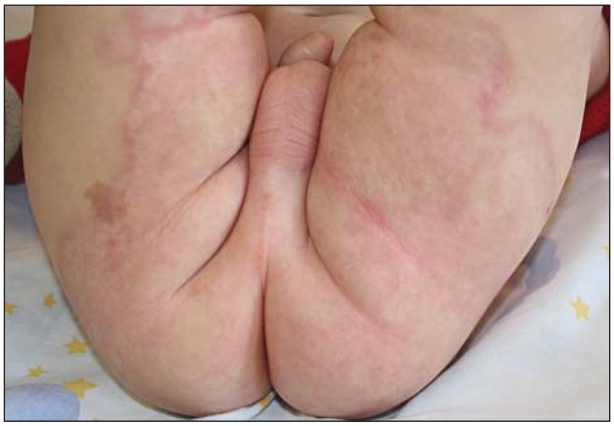

Figure 3. Skin 2 weeks after initiation of zinc supplementation.

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