Acrodermatitis enteropathica during parenteral nutrition: a pediatric case report

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Abstract. **Background:** Acrodermatitis enteropathica is a rare disorder characterized by dermatitis, alopecia and diarrhoea. Its acquired form can be caused by inadequate zinc intake, malabsorptive processes, excessive renal or intestinal loss. A rare cause of acquired zinc deficiency is iatrogenic nutritional deficiency due to parenteral nutrition. The diagnosis can be difficult because of non-specific signs and symptoms. **Case presentation:** A 5-years-old child affected by several comorbidities was admitted to Pediatric ward for acute pancreatitis and started total parenteral nutrition. Diarrhoea, alopecia and erythematous bullous skin lesions appeared 15 days after the start of a standardized parenteral nutrition mixture. Zinc serum dosage was very low. A fast clinical improvement was obtained after oral zinc supplementation. **Conclusion:** Even few days of zinc shortage, especially in frail patients, may cause acrodermatitis enteropathica. Despite its rarity, acrodermatitis enteropathica should be strongly considered in the differential diagnosis of skin lesions for these patients. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** Acrodermatitis enteropathica, pediatric parenteral nutrition, zinc deficiency

Background

Acrodermatitis enteropathica (AE) is a rare disorder caused by zinc deficiency characterized by the triad: dermatitis, alopecia and diarrhea (1). AE can be congenital, showing in infants during the first period of life, or acquired. The congenital form is due to an autosomal recessive mutation of the SLC39A4 gene (1), which is located in chromosome 8q24.3, and codes the zinc-ligand binding protein (Zip4). This protein is expressed in the duodenum and jejunum and its mutation reduces the intestinal absorption of zinc (2). Over 30 mutations of this gene have currently been reported (3).

Acquired AE recognizes a lot of different causes: inadequate zinc intake, excessive renal or intestinal loss, malignancy, drugs, ethanol, pregnancy, malnutrition, high-fiber diet or malabsorption syndromes, such as cystic fibrosis (4-5).

A rare cause of acquired zinc deficiency is an iatrogenic nutritional deficiency caused by total parenteral nutrition (TPN).

AE early clinical signs are nonspecific and they can also mimic common dermatoses, particularly atop dermatitis, and, therefore, often lead to a delay in diagnosis and treatment (5).

Here we describe the challenging AE diagnosis in a pediatric patient with several comorbidities and
report a complete diagnostic workflow for pediatric patients with chronic complex conditions.

Case presentation

A 5-years-old child, with a chronic complex condition and several comorbidities, consequent to C. Koseri meningoencephalitis occurred in the neonatal period, including spastic tetraparesis, focal epilepsy, tetraventricular hydrocephalus, severe blindness, and intellectual disability was admitted to Pediatric ward for acute pancreatitis. On admission patient’s clinical condition was fair and enteral nutrition via nasal feeding tube was started. Due to the worsening of general conditions and to the increased respiratory requirements, on hospital day 5, total PN was started. A standardized PN mixture (Numeta G13%) was infused via a central venous catheter (6). Numeta G13% is formulated in order to supply the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and The European Society of Clinical Nutrition and Metabolism (ESPEN) guidelines for pediatric nutritional needs with a balanced formulation of amino acids (protein), glucose (carbohydrates), lipids (fats) and electrolytes (7). Presuming that the patient would be on TPN for a short period of time, the trace elements (TE) package was not added to the standardized TPN bag. Otherwise, due to the increased risk of aspiration, and to elevated lipase (600–1000 μ/L), concerning pancreatitis, TPN was continued for approximately 4 weeks as the only source of nutrition.

After 15 days on TPN, he developed diarrhea and skin lesions (figure 1).

The lesions first were macules involving cheeks, hands and foot fingers, and ears. Within a few days,
the eruption involved perianal and perineal regions and evolved into large tense bullae and then into scaly plaques and ulcerations, surrounded by healthy skin. In addition, the child presented with diffuse alopecia, pain and irritability.

An infectious cause was initially suspected, so cutaneous swabs were done and treatment with topical antibiotics agents (Gentamicin) and steroids (Betamethasone) was started. Conversely, though, all cutaneous swabs resulted negative for bacterial or mycotic infections and no improvement was obtained.

The patient underwent two dermatological evaluations that suggested additional laboratory studies, comprehensive of zinc dosage, which was found very low (10 μg/dl with normal values 68-107 μg/dl). Thus, suspecting acquired AE, oral zinc supplementation was started in the amount of 5 mg daily, i.e. the highest dosage according to ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Iron and trace minerals (8).

After just 4 days of oral zinc supplementation, a clinical improvement was obtained, with the recovery of normal intestinal transit and reepithelialization of the skin lesions. The patient was discharged after 42 days of hospitalization in good clinical condition and during an outpatient follow-up visit after 32 days of zinc supplementation he shows a complete resolution of the lesions, with total restitutio ad integrum of the skin.

**Discussion and conclusions**

Zinc is an essential micronutrient obtained from diet. About 17% of the world’s human population suffers from zinc deficiency (9), with prevalence in areas of high cereal and low animal-protein diets. In the human body, zinc is stably maintained in a weight of 2–3 g (10).

The roles of zinc in biology can be grouped into three categories: catalytic, structural and regulatory functions (11). Skin is the third most zinc-abundant tissue (skeletal muscle 60%, bones 30%, liver 5%, and skin 5%) (12). It is involved in wound healing (13) and is crucial for epidermal stem cells (14).

Zinc deficiency can be inherited or acquired. An underrecognized risk group for the acquired one is represented by TPN fed patients, without adequate zinc supplementation (15).

AE’s classic clinical manifestations, i.e. skin lesions, diarrhea and alopecia, are flanked by other symptoms, such as paronychia, onicodistrophy, angular stomatitis, cheilitis, conjunctivitis and photophobia (2). Skin manifestations predominate and are characterized by asymptomatic, sharply demarcated eczematous plaques with peripheral scaling and crust. These lesions are localized in the acral, periorificial (sparing the upper lip), and anogenital regions. Fingers and toes may also be involved, along with symmetrical involvement of the extensor surfaces of elbows, knees, hands, and feet.

In clinical practice, it is not infrequent to face patients who have an incomplete diet or are already defied when hospitalization happens.

When these patients need TPN, the most frequent choice is to use a standard, commercial, formulation (7). These are safely prepared to meet the need of patients of similar age and clinical conditions but do not necessarily meet all their nutritional requirements, even more in the case of long-term parenteral nutrition (i.e. > 3 months long) (16).

Alternatively, an individually tailored TPN formulation, adapted to the patient’s nutritional needs, can be prescribed. As for standard TPN, it may be lacking in TE. Moreover, the role of TE is not often known or takes a back seat during hospitalization for acute severe illnesses, even if they are essential to support normal physiological processes. Their lack can lead to the so-called “hidden hunger”, which is the presence of multiple micronutrient deficiencies (particularly iron, zinc, iodine, and vitamin A), that can occur without a deficit in energy intake (17). In current practice there is no consensus on TE prescription, and, for pediatric patients, it requires age-related dosing (18). Focusing on zinc, children with hypercatabolism have high zinc requirements due to elevated losses. Current recommendations suggest supplying 400-500 mg/kg/d in preterm infants, 250 mg/kg/d in infants from term to 3 months, 100 mg/kg per day for infants from 3 to 12 months, and 50 mg/kg/d in children >12 months of age (up to a maximum of 5 mg/d for routine supplementation) (8). Zinc status (serum Zn, alkaline phosphatase) should be periodically
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References


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