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Acrodermatitis enteropathica by zinc deficiency: case report

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Abstract: *Zinc is an important mineral for regulation and development of the tissues of the human body, especially the epithelium. The lack of this element causes skin lesions, alopecia, difficulty of healing and diarrhea – which is very severe in the pediatric age. Although most causes of zinc deficiency are because of the diet, sometimes the lack of the nutrient can be related to genetic cause, like in Acrodermatitis enteropathica (AE), which is a recessive autosomal disease that can be fatal in children if not managed correctly. The objective of this study was to describe a case report of a child with AE that was mismanaged for several years in different services of the country before being properly diagnosed and adequately treated.*

Keywords: *zinc deficiency, acrodermatitis enterophatica, child.*

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I. Introduction

Zinc is an important chemical element for the homeostasis of the human body, once it is essential to the development and regulation of the tissues. Among these tissues, the epithelium, especially the skin, depend on the presence of zinc to keep its integrity. Despite the diversity of symptoms caused by the deficiency of this component, the periorificial dermatitis, the alopecia, difficulty of wound healing and diarrhea are striking consequences on the lack of zinc[1]. Thereby, zinc deficiency (ZD) is particularly worrying at childhood, once the element is needed for tissue development. Besides that, ZD is an important cause of morbidity and mortality on pediatric age group[2] and it can come from poor diet supplies or diseases that interfere on zinc metabolism[3]. Uncommonly ZD can occur due to genetic mutations, such as the acrodermatitis enteropathica (AE) – a recessive autosomal condition that leads to triad: periorificial and intertriginous dermatitis, alopecia and diarrhea[1]. Without the adequate treatment, this genetic disease can be fatal, especially in children bellow five years old[4].

This case report was approved by the UNIOESTE's Research Ethics Committee in 2021, December, 6th, under the number 5.148.873/2021 and its objective was to report a case of AE managed at a university hospital of Western Paraná State, Brazil, along with literature review.

II. Case description

E.N.A., female, 3 years 9 months, from Maranhão (North East from Brazil), first child of non-consanguineous parents. Pregnancy without complications, cesarean section delivery due to oligohydramnios, full-term, weight at birth: 2960g, hospital discharge along with the mother, neonatal blood screening test without abnormalities.

At the age of two and a half years, presents a circinate erythematous-scaly lesion on knee, non-prickly and not painful, without further complications. Continues with the appearing of new erythematous wounds of rough aspect and well-defined limits, mainly on knees, elbows, perioral and perineal regions. Associated to it, the patient had frequent abdominal pain, abdominal distention and episodes of diarrhea. She had previous hospitalizations due to the skin lesions, acute diarrhea and gingivostomatitis.

Since the beginning of the symptoms, the preschooler was investigated by several medical specialties in different cities, that diagnosed and treated diseases such as cow milk protein allergy, other food allergies and hypovitaminosis D. They used corticosteroids, topic antibiotics, topic antifungals, oral methotrexate during 3 months and many oral corticosteroid cycles for variable time, being that at the moment she attended to our service, in 2021, August, 8th, she was using corticosteroids for one year.

To the physical examination, she presented cushingoid facies, diffuse thinning of hair. Papules and plaques with well-defined limits on perioral region, elbows, fists, hands, popliteal fold and insteps (figures 1.a and 1.b). There was a large erythematous-scaly plaque on gluteal region (figure 1.a), with well-defined edges and hematic crusts on the periphery. The laboratorial exams of the child are displayed at table 1. Beyond those, it was also requested a Genetic Test for Next-Generation Sequencing customized panel that resulted on "Variant: SLC39A4: NM_130849.4: c.692T>C – a mutation on the gene that codifies the zinc binding protein, leading to the disease of the patient".

The preschooler was diagnosed with AE and ACTH-independent Cushing's Syndrome, secondary to the long-drawn use of corticosteroids and hypervitaminosis D. She was treated with zinc supplementation, gradual withdraw of corticosteroids and monitorization of vitamin D levels.

After less than a month of zinc restitution, in 2021, September,17th, the dermatological lesions were already healing, and the patient presented only hyperchromic plaques on the previously wounded areas, in re-epithelization. The hair improvement was visible, with better growth and normal color recovery.

Table 1: The laboratorial exams of the child.

Test	Result	Reference value
Anti-SCL	Non-reactive	-
Anti-endomysium IgG	Non-reactive	-
Anti-transglutaminase IgA and IgG	Non-reactive	-
Anti-gliadin IgA and IgG	Non-reactive	-
Anti-RNP	Non-reactive	-
Anti-DNA	Non-reactive	-
Anti-nuclear factor	Non-reactive	-
Basal cortisol between 06 and 10h	0.4 µg/dL	6.2-18 µg/dL
Vitamin D	> 150 ng/dL	20-100 ng/dL
Zinc	40.15 µg/dL	70-115 /dL

III. Discussion

Zinc deficiency (ZD) is common on pediatric age group and goes unnoticed due to subclinical cases – therefore, it is not valued neither diagnosed[5]. It may happen secondary to diseases such as dengue fever and diarrhea[3], surgeries that modify the morphology of the gastrointestinal tract, such as bariatrics[6] or genetic mutations[1].

The AE is a recessive autosomal genetic condition that affects 1 in 500,000 live births, regardless of race and sex, that leads to intestinal zinc absorption deficit due to the absence of an essential transmembrane protein to the element capture (Zip4)[1,7,8]. Zinc is fundamental to more than 100 enzymes, in addition to being important to the metabolism of nucleic acids[7]. The deficit is led by a mutation on the *SLC39A4* gene, that codifies the carrier of the element, leading to its malfunction[9]. Zinc acts as a cofactor to alkaline phosphatase, RNA polymerase and alcohol-dehydrogenase[10].

Common clinical manifestations occur on the skin and digestive tract, causing the triad: acral and intertriginous dermatitis, alopecia and diarrhea[1,7]. Paronychia, onychodystrophy, angular cheilitis, conjunctivitis and photophobia can also be present[7,11]. The lack of treatment on the progression of the disease can lead to inadequate weight gain due to hyporexia, short stature, puberal delay, male hypogonadism, hypogeusia and wound healing deficit [7,12]. Furthermore, it can increase likelihood to fungal and bacterial infections, whereas children with ZD have eight times more likely to develop urinary tract infection than the healthy ones[7,13]. The lack of zinc can be associated to attention deficit hyperactivity disorder[14].

The gold standard complementary exam to AE diagnosis is the dosage of plasmatic zinc levels, that can, although, be normal, even with low tissue levels, due to the exit of the element from the tissues to the blood. Alkaline phosphatase levels can help, once it is an enzyme that depends on zinc to its correct function[7].

Owing to its dermatological clinical manifestations AE, which is unusual, can lead to diagnostic difficulty, such as in the case report, where upon the child was submitted to diverse immune tests and laboratorial tests that did not contribute to the diagnosis, but, otherwise, led to incorrect treatments which resulted in other harmful conditions to the health of the child, that went through several doctors until she was correctly diagnosed and treated. Moreover, the diagnose delay is onerous to the health system and to the patients, besides causing risks to their lives, being a genetic disease that is potentially fatal at childhood.

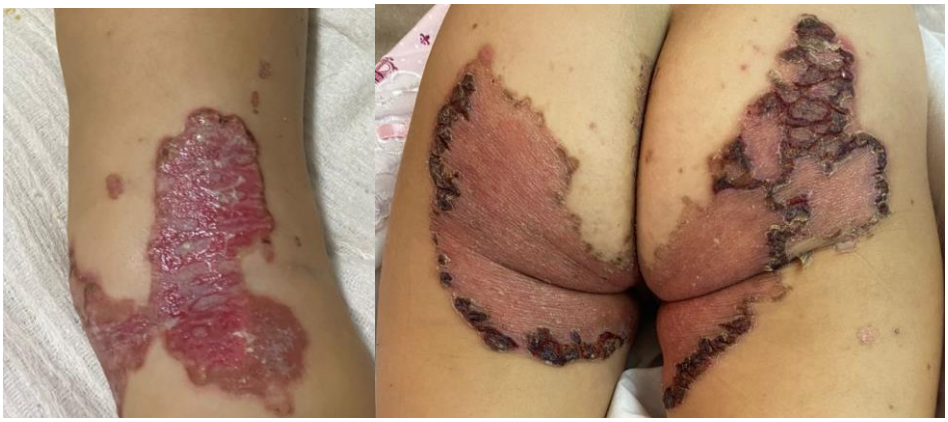
IV. Conclusion

It was reported a classic case of ZD and its dermatological complication, the AE. Zinc supplementation resulted on complete resolution of the case. In addition to that, the Cushing's Syndrome secondary to the long-term corticosteroid use had to be managed with gradual withdraw. A better understanding about AE is essential to avoid diagnose and treatment delay. Descriptions like this are important so that medical community come to

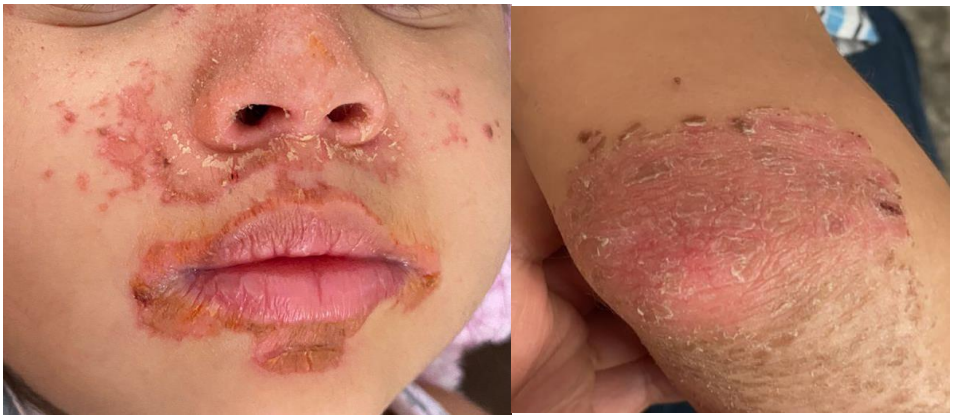
know the disease and its consequences, besides the correct management of the cases, favoring the precocious diagnose and treatment.

Figure 1: lesions on skin of patient.

a. Knee and butocks



b. Mouth and elbow



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