Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 09/27/2021
Approved on: 09/03/2023

CASE REPORT

ACRODERMATITIS ENTEROPATHICA: CASE REPORT IN CHILDREN WITH CROHN'S DISEASE

Livia Caramaschi Florêncio[1], Eloana Pasqualin Lange[1], Elizandra Gomes Pereira[2], Mariana Bueno Xavier Silva[3], Gabriela Roncada Haddad[1]

Keywords:
Acrodermatitis,
Crohn disease,
Zinc deficiency.

Abstract

Objectives: Acrodermatitis Enteropathica (AE) is a rare disease that can be transmitted by autosomal recessive inheritance, it can be related to parenteral nutrition without zinc, or it can be secondary to malabsorptive syndromes. Clinically, it is characterized by the triad of acral and periorificial dermatitis, alopecia and diarrhea, accompanied by growth restriction. The condition can be fatal if left untreated. **Methods:** We describe the case of a child with AE and Crohns Disease (CD), with AE being a known complication, secondary to malabsorption caused by CD. **Results:** Treatment for CD was started with systemic steroids, Azathioprine and Mesalazine, and local care with the diaper area. Oral zinc replacement was also started. The child showed significant clinical and dermatological improvement within a few weeks. **Conclusions:** The diagnosis of AE is made with serum zinc levels lower than 70 ug/dL. Treatment involves zinc supplementation, at a dose ranging from 1 to 3 mg/kg/day. In the case described, the zinc value was 65 ug/dL. In this case, we started replacement with 2mg/kg/day, with rapid clinical improvement. Zinc deficiency AE is a well-known complication of CD, secondary to malabsorption. In the case described, the cutaneous condition came after the intestinal condition, with the deficiency in the absorption of zinc being secondary to Crohns Disease, leading to a condition with extensive lesions, but with a quick response to the treatment and with an important improvement of the condition.

[1] Universidade Estadual Paulista Júlio de Mesquita Filho, Departamento de infectologia, dermatologia, diagnóstico por imagem e radioterapia - Botucatu - São Paulo - Brasil.
[2] Universidade Estadual Paulista Júlio de Mesquita Filho, Faculdade de Medicina - Botucatu - São Paulo - Brasil.
[3] Universidade Estadual Paulista Júlio de Mesquita Filho, Departamento de Pediatria - Botucatu - São Paulo - Brasil.

Correspondence to:
Gabriela Roncada Haddad.
Universidade Estadual Paulista Julio de Mesquita Filho. Av. Prof. Mário Rubens Guimarães Montenegro, s/n - UNESP - Campus de Botucatu - Botucatu/SP - CEP 18618687
E-mail: gabriela.haddad@yahoo.com

Resid Pediatr. 2023;13(4). DOI: 10.25060/residpediatr-2023.v13n4-737

This work is licensed under a Creative Commons Attribution 4.0 International License.

INTRODUCTION:

Enteropathic acrodermatitis (EA) is a rare disease, which manifests mainly in children, and may be congenital, transmitted by autosomal recessive or acquired inheritance.[1]

When congenital, it manifests itself when the infant is weaned, when they start to receive other milks with low zinc availability. When acquired, it occurs in children on parenteral nutrition without zinc and in premature infants in whom the need for zinc is greater than the amount provided by breast milk, or secondary to malabsorptive syndromes.[2,3]

Clinically, it is characterized by the classic triad of acral and periorificial dermatitis, alopecia and diarrhea, and is also accompanied by growth restriction.[1,4]

We describe the case of a child with EA and Crohn's Disease (CD), with EA being a known complication, secondary to malabsorption caused by CD.[5]

CASE REPORT:

Female patient, aged 1 year and 6 months, admitted with suspicion of chronic enterocolitis associated with malabsorption and diarrhea. She presented a history of changes in her intestinal habit 6 months after the introduction of cow's milk, around 1 year of age, receiving diagnosis initially due to cow's milk protein allergy (CMPA), associated with episodes of rectal prolapse, with a formula with free amino acids being started, with a reduction in bleeding in the feces, but maintenance of diarrhea. For 2 months she had been drowsy and hypoactive. Thus, the hypothesis of inflammatory bowel disease, mainly Crohn's disease, was raised.

The patient had lesions in the inguinal and genital regions, of the type of extensive exulcerated plaques (figure 1), which appeared concomitantly with the diarrhea, characterized by liquid evacuations, with streaks of blood. Associated with the condition, she presented irritability and low weight gain. She had also reported facial edema and hair loss for 2 months (figure 2). She had no fever or other systemic symptoms, as well as allergies or pathological conditions in the family. At the time of admission, she was only taking ferrous sulfate, vitamin A and D, and weighed 8.4kg. She had anemia, hypoalbuminemia, elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and alkaline phosphatase. Serologies for syphilis, hepatitis, toxoplasmosis, cytomegalovirus and HIV were non-reactive. Abdominal CT scan showed edema and distention of colonic loops.

The serum zinc value was 65 ug/dL (micrograms per deciliter), below the lower limit of 70 ug/dL, confirming the hypothesis that zinc deficiency was due to an absorptive abnormality.

The findings of the histopathological examination performed from upper digestive endoscopy and colonoscopy confirmed the hypothesis of Crohn's disease, with endoscopic findings of inflammation and diffuse erosions, associated with a component of cow's milk protein allergy. The dermatological



Figure 1. Erythematous plaque exulcerated in the genital, inguinal, perianal and gluteal regions



Figure 2. Tempoparietal alopecia on the scalp.

findings were suggestive of acrodermatitis enteropathica (AE), with cytoplasmic pallor, vacuolation and keratinocytes necrosis.

Treatment for Crohn's Disease was initiated with systemic corticosteroids and Azathioprine, with subsequent addition of Mesalazine, and local care for the diaper area, such as barrier cream, more frequent diaper changes and the suggestion to leave the child for a few periods of the day without diapers. Oral zinc replacement was also started, 2mg/kg/day. The child showed significant improvement in a few weeks, with the new zinc dosage being 114.7 ug/dL.

COMMENTS:

EA occurs in patients with abnormal zinc enteral absorption, secondary to malabsorptive syndromes, or due to mutation of the zinc transporter gene SLC39A4, which encodes the transmembrane protein ZIP4.[6,7,8] This protein, present in breast milk and pancreatic secretions is responsible for the absorption of zinc by the cell, enabling it to be used for the synthesis of proteins essential for metabolism. Another mutation has been reported in mothers, in the SLC30A2 gene, which results in decreased zinc secretion in breast milk, leading to zinc deficiency in infants.[7]

Since zinc is present in breast milk, the clinical manifestations of this deficiency usually appear during the weaning of affected infants, when they start to receive other milks with low availability. In cases where the mutation is present in the mother, the condition begins early.

The incidence of this disease is estimated at 1:500,000 children, with no predilection for race or sex. It is characterized by the triad: dermatitis, diarrhea and alopecia. However, only 20% of patients present all three components simultaneously.[9] Skin lesions begin as erythematous, erosive, scaly plaques, with a characteristic crusty border on the periphery, which occur on the face, perioral area, scalp, anogenital region, extremities and extensor regions, such as elbows and knees.[7,10] Vesicles, blisters and pustules occur, which can exulcerate and present secondary infection by bacteria, mainly Staphylococcus aureus, and Candida.There can be cheilitis, stomatitis, onychodystrophy, paronychia, progressive diffuse alopecia, pigmentary changes and wound scarring. Furthermore, as zinc deficiency leads to a decrease in immunity, there is a greater predisposition to fungal and bacterial infections. Eye abnormalities are also reported, conjunctivitis, blepharitis and photophobia.[6] Systemic symptoms, such as diarrhea with frothy and bulky stools, irritability, mental depression, anemia, growth and development disorders, are described. The condition can be fatal if not treated.

Differential diagnoses include protein-energy malnutrition, contact dermatitis, psoriasis, seborrheic dermatitis, epidermolysis bullosa, candidosis, Leiner syndrome, Langerhans cell histiocytosis.

To diagnose the condition, it is necessary to measure serum zinc, which is low in these patients - levels below 70 ug/dL on an empty stomach and 65 ug/dL after a meal. Alkaline phosphatase, a zinc-dependent metalloproteinase, is reduced and may be useful for diagnosis in some cases. In cases of diagnostic doubt, histopathological analysis of the affected skin can be used, which shows psoriasiform hyperplasia with necrolysis. The gold standard test for the congenital form is genetic testing, searching for mutations in the SLC39A4 gene.

Treatment involves enteral or parenteral zinc supplementation for the patient's entire life in congenital cases and in acquired cases until control of the underlying disease and normalization of zinc levels, with an average dose of 1 to 3 mg/kg/day of elemental zinc.[6] Among the available formulations, zinc gluconate and zinc sulfate can be found, available orally, the latter being the first choice and, parenterally, zinc chloride can be used. The response to treatment is quick and with significant improvement in the condition. The most common side effects include hypocupremia, irritation and gastric bleeding. Serum zinc levels should be monitored frequently.

Inflammatory bowel disease (IBD) is an idiopathic, inflammatory disease of the intestinal tract. The two main types of IBD are Ulcerative Colitis (UC) and Crohn's disease (CD). The UC is limited to the colon and/or rectum and affects only the mucous and submucosal layers of the intestine; CD can affect any part of the intestine, from the mouth to the anus, most cases start in the terminal ileum, and affect the entire thickness (transmural) of the intestinal wall.[11]

Among patients with Inflammatory Bowel Diseases, 40% present extraintestinal manifestations, which are more common in patients with CD when compared to patients with ulcerative colitis. AE due to zinc deficiency is a well-known complication of CD,[5,12] secondary to malabsorption, and being the most common skin manifestation of nutritional deficiency in inflammatory bowel diseases.[11]

In the case described, the skin condition came after the intestinal disorder, with the deficiency in zinc absorption being secondary to Crohn's disease, leading to a condition with extensive lesions.

REFERENCES

1. Chisaki C. Alterações do metabolismo de cálcio, ferro, zinco e cobre. In: Junior WB, Chiacchio ND, Criado PR. Tratado de Dermatologia. 3 ed. Rio de Janeiro: Atheneu; 2018. 1971-1976
2. Rivitti EA. Alterações do metabolismo do cálcio, ferro, cobre, zinco e selênio. In: Rivitti EA. Dermatologia de Sampaio e Rivitti. 4 ed. São Paulo: Artes Médicas; 2018. 960-967
3. Ranugha P, Sethi P, Shastry V. Acrodermatitis enteropathica: the need for sustained high dose zinc supplementation. Dermatol Online J. 2018 Dec 15;24(12):13030/qt1w9002sr. Published 2018 Dec 15. https://escholarship.org/uc/item/1w9002sr
4. Martínez-Bustamante ME, Peña-Vélez R, Almanza-Miranda E, Aceves-Barrios CA, Vargas-Pastrana T, Morayta-Ramírez Corona

ARR. Acrodermatitis enteropática [Acrodermatitis enteropathica]. Bol Med Hosp Infant Mex. 2017 Jul-Aug;74(4):295-300. Spanish. doi: 10.1016/j.bmhimx.2017.05.002. Epub 2017 Jul 5.

5. Diaconescu S, Strat S, Balan GG, Anton C, Stefanescu G, Ioniuc I, Stanescu AMA. Dermatological Manifestations in Pediatric Inflammatory Bowel Disease. Medicina (Kaunas). 2020 Aug 23;56(9):425. doi: 10.3390/medicina56090425.
6. Ciampo IRLD, Sawamura R, Ciampo LAD, Fernandes MIM. Acrodermatitis Enteropathica: Clinical Manifestations And Pediatric Diagnosis. Rev Paul Pediatr. 2018 Apr-Jun;36(2):238-241. doi: 10.1590/1984-0462/;2018;36;2;00010. Epub 2018 Jan 15.
7. Jagadeesan S, Kaliyadan F. Acrodermatitis Enteropathica. 2020 Apr 17. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441835/
8. Nistor N, Ciontu L, Frasinariu OE, Lupu VV, Ignat A, Streanga V. Acrodermatitis Enteropathica: A Case Report. Medicine (Baltimore). 2016 May;95(20):e3553. doi: 10.1097/MD.0000000000003553.
9. Silva LLC, Sobral Filho JF, Albuquerque LMA, Cavalcanti NS, Brito PKST. Acrodermatite enteropática em uma criança com deficiência de zinco herdada. Resid Pediatr. 2014;4(3):106-108
10. Habka S, Monte L, Baião B. Acrodermatite enteropática ou síndrome de má absorção secundária à fibrose cística?. Resid Pediatr. 2021;11(3):1-3 DOI: 10.25060/residpediatr-2021.v11n3-208
11. Huang BL, Chandra S, Shih DQ. Skin manifestations of inflammatory bowel disease. *Front Physiol*. 2012;3:13. Published 2012 Feb 6. doi:10.3389/fphys.2012.00013
12. Krasovec M, Frenk E. Acrodermatitis enteropathica secondary to Crohn's disease. Dermatology. 1996;193(4):361-3. doi: 10.1159/000246296.