JPDS Journal of the Philippine Dermatological Society

CASE REPORT

Treatment response as a diagnostic feature in zinc deficiency-associated dermatitis in a three-month-old Filipino male: A case report

Sher Claranza O. Liquido, MD, DPDS,[1] Jamaine Melisse L. Cruz-Regalado, MD, FPDS[1]

ABSTRACT

INTRODUCTION Zinc deficiency is of high magnitude in developing countries such as the Philippines. Zinc deficiency dermatitis is recognized through characteristic cutaneous presentation supported by diagnostic workups which may not be feasible or practical in low-resource settings.

CASE REPORT A three-month-old Filipino male was brought in for erosions of three (3) weeks duration that were unresponsive to topical and systemic antimicrobial treatment. On examination, he had multiple erythematous erosions with yellowish to brownish, crusted borders with predilection on the face, inguinal and gluteal areas, flexures of the extremities, and digits. Workup revealed normal zinc levels, decreased alkaline phosphatase, and bacterial growth in cultures. Histopathology revealed intraepidermal vesiculobullous dermatitis. Given the clinicopathologic presentation, a diagnosis of zinc deficiency-associated dermatitis was made. Along with antimicrobials and topical care, oral zinc sulfate with elemental zinc at 3 mg/kg/day was started, with remarkable improvement within three (3) days and near-resolution after eight (8) days of zinc therapy. Zinc supplementation was administered for three (3) months with gradual tapering. The skin remained clear despite the withdrawal of zinc supplementation. Response to treatment supported the impression of zinc deficiency, while sustained skin clearance upon withdrawal verified an acquired etiology.

CONCLUSION Zinc deficiency-associated dermatitis is more common in areas where costly diagnostic modalities are not readily available. In clinically suspected zinc deficiency, response to treatment can serve as a retrospective diagnostic feature, and sustained clearance upon withdrawal may aid in identifying etiology. Trial of therapy may then be considered in optimizing the cost-effective management of zinc deficiency-associated dermatitis.

KEYWORDS zinc deficiency, nutrition, pediatric dermatology

INTRODUCTION

Zinc deficiency is estimated to be at 20% of the world population and is more common in developing countries.[1] In the Philippines, the national estimate is high at 30% of the country's population.[2]

Skin is the third most zinc-abundant tissue. Deficiency can manifest through characteristic cutaneous involvement.[3] Diagnostic tests are only supportive to the clinical picture and there is no consensus as to which modality is most appropriate in establishing deficiency.[4] Moreover, zinc deficiency-associated dermatitis is commonly encountered wherein cost-effective management is needed and diagnostic modalities may not be feasible. In this case report, we describe zinc deficiency-associated dermatitis in a pre-term infant whose therapeutic response aided in the diagnosis.

CASE REPORT

A three-month-old Filipino male presented with erosions of three weeks duration. The lesions started as erythematous patches on the testicular and gluteal area which eroded and enlarged. Benzalkonium chloride with cetrimide cream was applied without improvement. Brownish plaques then developed on the cheeks, spreading to the neck, ears, and occipital area. Several flaccid bullae also formed on the medial thighs. Upon consultation, unrecalled dosage of cefalexin oral drops and fluticasone propionate cream were prescribed for a week. However, as febrile episodes developed and lesions continued to progress, medications were revised to oral clindamycin (9 mg/kg/day), cefixime (8 mg/kg/day), oral fluconazole (12 mg/kg/day), and topical miconazole cream. The fever lysed, but minimal improvement prompted admission.

[1]Department of Dermatology, St. Luke's Medical Center, Quezon City, Philippines

Corresponding author
Sher Claranza O. Liquido, MD, DPDS

Conflict of interest
None

Source of funding
None

JPDS
Journal of the Philippine Dermatological Society

The patient was born preterm to a primigravid at 33 weeks via normal spontaneous delivery, with a low birth weight of 1,790g. He had been exclusively breastfed without latching problems. The mother had unrestricted and adequate food intake. The family history was unremarkable.

Upon examination, the patient was irritable with low-grade fever at 37.9oC, wasted (z-score below -2), and severely underweight (z-score below -3) at 3.42kg and 54cm in length. There were erythematous erosions with yellowish to brownish peripheral crusts on the face extending to the ears and neck. The lips were dry, but other parts of the oral mucosa were unremarkable. There were dusky red papules coalescing to plaques with crusted erosions on the trunk, inguinal, gluteal area, flexures of extremities, and digits (Figure 1a and 1b). There were no lymphadenopathies palpated.

Pertinent workup revealed decreased alkaline phosphatase at 127 U/L (Reference Interval (RI): 134-518 U/L), and serum zinc level within range at 10.1 µmol/L (RI: 8.6-19.1 µmol/L). Blood culture revealed *Staphylococcus epidermidis*. Wound culture and sensitivity had growth of *Pseudomonas aeruginosa* and *Klebsiella pneumonia*. Tissue bacterial culture revealed *Staphylococcus haemolyticus*, while fungal culture was negative for growth. Skin biopsy from a bulla on the thigh revealed psoriasiform spongiosis with intraepidermal vesiculobullous dermatitis. There was pallor and ballooning degeneration on the upper epidermis. Immunohistochemical staining CD1a revealed a relative paucity of Langerhans cells in the epidermis (Figure 2). Given the clinicopathologic features, the diagnosis of zinc deficiency-associated dermatitis with concomitant bacterial infection was made.

The patient was started on elemental zinc at 3 mg/kg/day as oral zinc sulfate. Antimicrobials consisted of intravenous vancomycin (60 mg/kg/day), cefepime (50 mg/kg/dose every 12 hours), and oral metronidazole (26 mg/kg/day), with fungal coverage from fluconazole (12 mg/kg/day). Topical care consisted of mupirocin ointment over the erosions twice daily after normal saline solution compress.

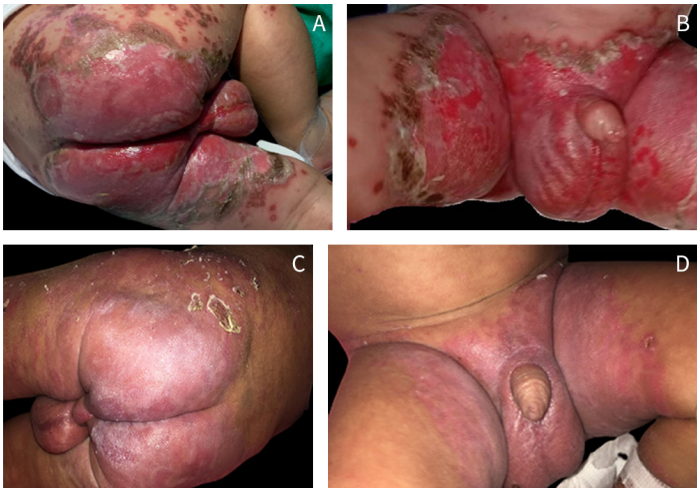

Figure 1. Baseline photos - erosions with yellowish to brownish crusted borders (A, B); After eight days of zinc supplementation (C, D).

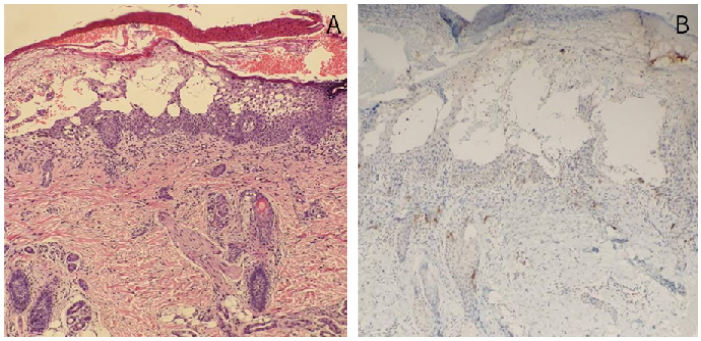

Figure 2. Hematoxylin and eosin (x100) Intraepidermal vesiculobullous dermatitis with pallor and ballooning degeneration on the upper epidermis (A); CD1a (x100) – relative paucity of Langerhans cells in the epidermis (B).

There was remarkable improvement after three (3) days of zinc supplementation with drying of the erosions. On the eighth day of zinc therapy, minimal crusts remained, and re-epithelialization was complete with dusky red erythema over affected areas (Figure 1c and 1d). Upon discharge, medications were continued as oral zinc sulfate (3 mg/kg/day elemental zinc), copper (2.5 mg/day), folic acid (2.5 mg/day), and multivitamins. Complete resolution was reported after two weeks of supplementation. After a month, repeat alkaline phosphatase was elevated at 667 U/L (RI: 134-518 U/L). To identify the cause of deficiency, breastmilk zinc level was determined, found to be 11.2 µmol/L at four months post-partum.

Zinc was administered for three (3) months with gradual tapering. After three months of discontinuation, zinc level determination was repeated and found low at 7.95 µmol/L (RI: 8.6-19.1 µmol/L). However, as the skin remained clear even upon the introduction of mixed feeding, with the weight and length of the patient normalized, no further supplementation was pursued.

DISCUSSION

Zinc is involved in metabolism as a cofactor of enzymatic reactions and transcription processes.[3] The etiology of the deficiency is classified as either inborn or acquired.[1] Our case was considered acquired because the patient was a three-month-old purely breastfed preterm who had unremarkable family history. Inborn autosomal recessive acrodermatitis enteropathica would have presented upon weaning or in infants who are fed formula wherein zinc has a lower bioavailability as compared to breastmilk.[1] As a preterm infant, he is susceptible to deficiency as relevant intrauterine zinc transfer occurs during the last 10 weeks of gestation.[5] They are born with lower baseline zinc levels which are challenged over the first few years of life. When

preterm infants undergo growth spurts, there is increased zinc demand with concomitant losses from an immature gut.[5,6] Zinc in breastmilk also rapidly declines during the postpartum period.[4] Cutaneous infection may increase zinc demand as well.[4] These baseline deficits of zinc in a preterm infant and increased demand compounded with a cutaneous infection may have led to an overt zinc deficiency-associated dermatitis.

The patient had characteristic cutaneous presentation of symmetric eczematous plaques that progressed to vesiculobullous lesions and erosions with peripheral crusted borders on the mouth, perineal, and acral areas.[1] This distribution supported the proposal that zinc deficiency-associated dermatitis is a contact dermatitis involving areas exposed to irritants. This is due to the decrease in the Langerhans cells in the epidermis tasked to rectify the irritant dermatitis.[7] As in the patient, there was relative paucity of Langerhans cells in the CD1a staining.

Currently, there is no consensus on the specific workup to establish zinc deficiency. Zinc level determination is prone to inaccuracies as it can be affected by acute inflammation, hemolyzed samples, or when blood is drawn after meals.[4] With this, zinc levels were of minimal value in the case of analyzing deficiency. For the breastmilk zinc level, there is no definite normal range interval, though supportive to the diagnosis if below 10.7 µmol/L[8]. In this case, the breastmilk zinc level at four (4) months postpartum was at 11.2 µmol/L, which was also noncontributory to establishing etiology. Nonetheless, alkaline phosphatase, which is a zinc-dependent enzyme, was useful in establishing the diagnosis. Alkaline phosphatase level is low in zinc deficiency with a corresponding increase with supplementation as was observed in our case.[8] Histopathology was also supportive of the diagnosis showing pallor of the upper epidermis and intracellular edema, albeit nonspecific in presentation.[9] With the clinical presentation supported by workup findings, the case was still deemed dermatitis from zinc deficiency even with initial serum zinc level within range. Supplementation for mild to moderate acquired zinc deficiency ranges from 0.5-1.0 mg/kg/day elemental zinc, but this may vary depending on the disease.[8] Our patient was started at 3 mg/kg/day given the extent of cutaneous affectation. Response to treatment has been proposed as a useful diagnostic feature in a case report by Dev and Sethuraman (2017), wherein total resolution was observed after a week.[10] In the case presented, near-resolution was observed after eight (8) days of zinc supplementation (Figure 1). The patient was able to catch up in anthropometric measurements and improvement was sustained upon discontinuation of zinc supplementation. Aside from being the primary form of treatment, zinc supplementation aided in establishing the diagnosis of the patient wherein the dramatic response served as a retrospective diagnostic modality for deficiency. Sustained clearance of the skin upon withdrawal of the supplement also supported an acquired etiology, as inborn forms would have recurred, needing lifelong treatment.[10]

As such, in patients suspected of zinc deficiency-associated dermatitis clinically, a trial of zinc therapy to observe response may be considered as means of confirming deficiency and supporting considered etiology. This may be of value in maximizing cost-effective management, especially in resource-limited settings wherein prevalence of zinc deficiency is high.

REFERENCES

1. Lekwuttikarn R, Teng JMC. Cutaneous manifestations of nutritional deficiency. Curr Opin Pediatr [Internet]. 2018;30(4):505–13. Available from: http://dx.doi.org/10.1097/mop.0000000000000652
2. Capanzana M, Marcos J, Perlas L, Trio P, Ulanday J, Cheong R, et al. Zinc status of Filipinos By Serum Zinc LEVEL: 7th national Nutrition Survey, Philippine 2008. European Journal of Nutrition & Food Safety. 2015;5(5):565–6
3. Ogawa Y, Kinoshita M, Shimada S, Kawamura T. Zinc and skin disorders. Nutrients [Internet]. 2018;10(2):199. Available from: http://dx.doi.org/10.3390/nu10020199
4. Maverakis E, Fung MA, Lynch PJ, Draznin M, Michael DJ, Ruben B, et al. Acrodermatitis enteropathica and an overview of zinc metabolism. J Am Acad Dermatol [Internet]. 2007;56(1):116–24. Available from: http://dx.doi.org/10.1016/j.jaad.2006.08.015
5. Lakdawala N, Grant-Kels JM. Acrodermatitis enteropathica and other nutritional diseases of the folds (intertriginous areas). Clin Dermatol [Internet]. 2015;33(4):414–9. Available from: http://dx.doi.org/10.1016/j.clindermatol.2015.04.002
6. Jahnke I, Vogt A, Stieler KM, Hennermann J, Blume-Peytavi U. Symmetrical inflammatory erosive plaques and blisters in an infant. J Dtsch Dermatol Ges [Internet]. 2017;15(9):956–9. Available from: http://dx.doi.org/10.1111/ddg.12985
7. Ogawa Y, Kawamura T, Shimada S. Zinc and skin biology. Arch Biochem Biophys [Internet]. 2016;611:113–9. Available from: http://dx.doi.org/10.1016/j.abb.2016.06.003
8. Yan AC. Cutaneous Changes in Nutritional Disease. In: Kang S, Orringer JS, McMichael AJ, Margolis DJ, Enk AH, Bruckner AL, et al., editors. Fitzpatrick's Dermatology. 9th ed. New York:McGraw-Hill; 2019. p. 2199–233.
9. Patterson JW, Hosler GA, Prenshaw KL, Weedon D. Metabolic and storage diseases. In: Weedon's skin pathology. 5th ed. China: Elsevier; 2021. p. 593–616.
10. Dev T, Sethuraman G. Diagnosis of acrodermatitis enteropathica in resource limited settings. BMJ Case Rep [Internet]. 2017;2017. Available from: http://dx.doi.org/10.1136/bcr-2017-220928