

Series Editor: Camila K. Janniger, MD

# Acquired Zinc Deficiency in Full-term Newborns From Decreased Zinc Content in Breast Milk

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*Zinc deficiency occurs in children when the demand for zinc exceeds its supply. Malnutrition, prematurity, total parenteral nutrition dependence, and burns increase the demand for zinc, whereas congenital malabsorption syndromes represent clinical situations where less zinc is supplied to the growing child. Clinical recognition of acral eczematous lesions, alopecia, and gastrointestinal tract symptoms in settings of the aforementioned medical history often lead to the diagnosis. Zinc deficiency in healthy, full-term, breast-fed infants can occur. The cause of these deficiencies has been attributed to decreased zinc levels in maternal breast milk. We present a case of acquired zinc deficiency in a healthy breast-fed infant, with a review of the English language literature of reported cases.*

*Cutis.* 2007;79:425-428.

**Z**inc deficiency occurs in children when the demand for zinc exceeds its supply. Malnutrition, prematurity, total parenteral nutrition dependence, and burns create an increased demand for zinc, whereas congenital malabsorption syndromes supply less zinc to the growing child.<sup>1,2</sup> Interestingly, several reports have identified zinc deficiency in healthy, full-term, breast-fed infants.<sup>3-9</sup> These deficiencies have been attributed to low zinc

levels in maternal breast milk. The exact nature of the mammary defect remains unknown. We describe a case of zinc deficiency in a full-term breast-fed infant and review the English language literature of reported cases.

## Case Report

A 14-week-old white infant presented to the pediatric dermatology clinic with a chief complaint of rash on the left upper eyelid, left chin, and left ear. His mother stated that the lesions had been present since approximately 12 weeks of age. One week prior to consultation, the infant received a 5-day course of cefixime and mupirocin for his skin lesions, as well as tobramycin ophthalmic drops. The infant was otherwise healthy and did not exhibit any unusual behavior. He breast-fed well and had normal stools. His weight, however, had dropped from the 10th percentile at birth to below the third percentile at 14 weeks of age.

**Past Medical History**—The mother was gravida 1, para 0, aborta 0. The patient was delivered by cesarean birth for late decelerations due to placental separation. No other complications were observed during pregnancy.

**Physical Examination**—The patient was a thin-appearing, active, 14-week-old infant. Results of cutaneous examination revealed erythematous patches with scaling and crusting over the left eyelid, bilateral auricular helices, and buttocks. The left chin exhibited a linear, light tan, rough plaque with cracking and erythema at the lip angles (Figure). Both thumbs exhibited paronychia yellow crusting.

**Laboratory Examinations**—Laboratory investigations were conducted for both the patient and his mother. Laboratory studies of the infant detected the following values: low serum zinc, 23  $\mu\text{g}/\text{dL}$  (reference range, 70–150  $\mu\text{g}/\text{dL}$ ); and low alkaline

Accepted for publication February 1, 2007.

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The authors report no conflict of interest.

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Fourteen-week-old infant with cutaneous signs of zinc deficiency.

phosphatase, 99 IU/L (reference range, 150–420 IU/L),<sup>10</sup> a zinc-dependent enzyme. A pediatric gastroenterology consult was obtained to identify any gastrointestinal causes for zinc malabsorption.

**Clinical Course**—On presentation to pediatric gastroenterology, the patient was small and thin but active and well-appearing. His weight was below the third percentile and his height was at the 25th percentile. His abdomen appeared distended and his liver was 1.5 to 2 cm below the costal margin. There was no splenomegaly. He was otherwise healthy. The infant exclusively breast-fed and refused formula supplementation.

Maternal diet history revealed a complete and varied diet. The patient's mother had continued her prenatal vitamins. Although maternal serum zinc level at that time was normal, 116  $\mu\text{g}/\text{dL}$  (reference range, 70–150  $\mu\text{g}/\text{dL}$ ),<sup>10</sup> zinc was absent in her breast milk. Because the mother was of short stature and of Mediterranean ancestry, she was screened for celiac disease as a possible etiology of zinc deficiency. Results of the maternal celiac screen were negative and therefore nonrevealing as a cause of decreased zinc levels present in the breast milk.

Zinc supplementation in the form of zinc sulfate was instituted in the patient at a dosage of 1 mg/kg daily (6 mg per 2.5 cc of oral solution daily). The infant continued to grow slowly, remaining below the third percentile in weight on subsequent visits. The introduction of solid foods at 4 months of age did not improve his growth parameters. However, after one week of zinc sulfate therapy, clinical improvement of skin lesions was noted. At 6 months of age, the infant had a normal zinc level, 108  $\mu\text{g}/\text{dL}$ . Results of a repeat testing of the infant at 6 months were negative for celiac disease and metabolic disorders; additionally, results of a sweat test were negative.

We were unable to link the zinc deficiency to a more global picture causing an organic etiology of the patient's failure to thrive. Despite normal serum zinc levels and improvement of his skin manifestations,

he continued to have suboptimal weight gain. To date, the infant remains small but is maintaining a steady weight curve with caloric supplementation. He is developmentally appropriate.

### Comment

Zinc is a trace element found in all tissues of the human body.<sup>11</sup> Fish and meat provide the best dietary sources of zinc.<sup>12</sup> At a molecular level, zinc plays an essential role in cell proliferation, healing, and tissue repair, as well as in protein, carbohydrate, and vitamin A metabolism. Zinc is present in numerous metalloenzymes, most notably in alkaline phosphatase and in RNA and DNA polymerase.<sup>1</sup> Thus, zinc is an important mineral for the proper functioning and maintenance of hair, skin, nails, and the immune system.

Clinical findings in zinc deficiency encompass a broad spectrum, making diagnosis challenging. Nevertheless, zinc deficiency should be suspected in patients exhibiting any combination of an acral distributed eczematous patch, blepharitis, alopecia, perleche, intractable vomiting, diarrhea, loss of appetite, apathy, and irritability.<sup>1,13,14</sup> The prototypical cutaneous sign is a vesiculobullous lesion on an erythematous base that quickly crusts over, creating a sharply marginated, lichenified, or psoriasiform plaque.<sup>14</sup> These eroded surfaces alter immune function and permit the growth of yeast and bacteria, creating impetigo, perleche, and paronychia infections.

The triad of acral and periorificial skin lesions, alopecia, and diarrhea characterizes the genetic form of zinc deficiency, acrodermatitis enteropathica.<sup>14</sup> The genetic and acquired forms of zinc deficiency often overlap clinical features; however, they differ in their time of presentation. The genetic form of the disease is due to an autosomal-recessive mutation in the *SLC39A* (solute carrier family 39 member 4) gene, an intestinal zinc transporter.<sup>14,15</sup> Because breast milk is thought to facilitate zinc absorption, the genetic form of zinc deficiency usually commences when the child is weaned off the breast. The acquired form of the disease is caused by an imbalance between zinc supply and demand outside this particular defect, and often develops at a later time. Acquired zinc deficiency may develop despite the child staying on breast milk, as in our case.

Zinc status in early infancy primarily is determined by liver stores accumulated during the last trimester of pregnancy. Infants and adults share similar values of serum zinc concentrations.<sup>16</sup> Most premature newborns are in negative zinc balance the first few weeks of life due to both a decreased ability to store zinc

## Cases of Full-term Infants Developing Zinc Deficiency From Breast Milk

Year	Reference	Age of Onset, wk	Sex	Predominant Features
Presented in 2006	Haliasos et al (present case)	12	Male	Rash
1998	Mancini and Tunnessen <sup>3</sup>	10	Male	Rash, decreased weight gain
1998	Glover and Atherton* <sup>5</sup>	32	Female	Rash, irritable
1990	Lee et al <sup>4</sup>	12	Female	Rash, alopecia, diarrhea
1987	Roberts et al <sup>6</sup>	14	Male	Rash
1987	Roberts et al <sup>6</sup>	16	Female	Rash, diarrhea, irritable
1986	Kuramoto et al <sup>†7</sup>	7	Female	Rash
1986	Kuramoto et al <sup>†7</sup>	10	Female	Rash
1985	Bye et al* <sup>8</sup>	8	Male	Rash, failure to thrive

\*Siblings.

†Siblings.

and an increased requirement.<sup>17,18</sup> Despite the high bioavailability of zinc in milk, premature newborns who are exclusively breast-fed often develop symptoms of zinc deficiency because of the normal decline in human milk zinc content that is associated with the length of lactation.<sup>19,20</sup> By 20 weeks of lactation, maternal breast milk zinc levels may be too low to meet the needs of a rapidly growing infant.<sup>18,19</sup> Total parenteral nutrition with inadequate zinc supplementation or with increased zinc requirements due to prematurity, burns, infection, and surgical procedures also may elicit a deficiency.<sup>9,11,21</sup>

In our patient, neither an increased demand for zinc nor a decreased ability to store it could account for this infant's dermatologic findings. Rather, the problem centered on the supply of zinc through maternal breast milk. To date, a search of the English language literature revealed 9 published cases of full-term infants exhibiting zinc deficiency because of low zinc in maternal breast milk (Table). Two sets of the 9 cases represent siblings.<sup>5,7,8</sup> In all 9 cases, the infants presented with the rash between 7 and 32 weeks of age.

Because clinical findings are not pathognomonic, laboratory evaluation is indispensable to forming the diagnosis of this disorder. Levels of serum zinc and alkaline phosphatase, a zinc-dependent enzyme, should

be measured in a child with suspected zinc deficiency. After the diagnosis is made, the source of deficiency can be determined by measuring maternal serum and breast milk zinc levels in breast-fed infants. Resolution of signs and symptoms on discontinuation of breastfeeding often helps distinguish genetic versus acquired zinc deficiency due to low zinc content in breast milk.<sup>11</sup> In the absence of other predisposing factors, such as prematurity, burn, sickle cell disease, malignancy, or drugs, consultation with a pediatric gastroenterologist may aid in the search for other causes of zinc deficiency. Intestinal malabsorption syndromes, Crohn disease, sprue, pancreatic insufficiency, blind loop syndrome, diets high in phytates and calcium, total parenteral nutrition, and anorexia nervosa all have been reported to cause zinc deficiency.<sup>1,22</sup>

Treatment consists of zinc supplementation, most often with zinc sulfate for oral replacement and zinc chloride for intravenous replacement.<sup>11</sup> Cutaneous healing is noted within 48 hours, with complete resolution within 4 weeks.<sup>1</sup> Systemic symptoms also return to normal shortly after induction of therapy.<sup>3</sup>

## REFERENCES

1. Perafan-Riveros C, Frana LF, Alves AN, et al. Acrodermatitis enteropathica: case report and review of the literature. *Pediatr Dermatol.* 2002;19:426-431.

2. Piela Z, Szuber M, Mach B, et al. Zinc deficiency in exclusively breast-fed infants. *Cutis*. 1998;61:197-200.
3. Mancini AJ, Tunnessen WW Jr. Picture of the month. acrodermatitis enteropathic-like rash in a breast-fed, full-term infant with zinc deficiency. *Arch Pediatr Adolesc Med*. 1998;152:1239-1240.
4. Lee MG, Hong KT, Kim JJ. Transient symptomatic zinc deficiency in a full-term breast-fed infant. *J Am Acad Dermatol*. 1990;23:375-379.
5. Glover MT, Atherton DJ. Transient zinc deficiency in two full-term breast-fed siblings associated with low maternal breast milk zinc concentration. *Pediatr Dermatol*. 1998;5:10-13.
6. Roberts LJ, Shadwick CF, Bergstresser PR. Zinc deficiency in two full-term breast-fed infants. *J Am Acad Dermatol*. 1987;16:301-304.
7. Kuramoto Y, Igarashi Y, Kato S, et al. Acquired zinc deficiency in two breast-fed mature infants. *Acta Derm Venereol*. 1986;66:359-361.
8. Bye AM, Goodfellow A, Atherton DJ. Transient zinc deficiency in a full-term breast-fed infant of normal birth weight. *Pediatr Dermatol*. 1985;2:308-311.
9. Stevens J, Lubitz L. Symptomatic zinc deficiency in breast-fed term and premature infants. *J Paediatr Child Health*. 1998;34:97-100.
10. Robertson J, Shilkofski N. *The Harriet Lane Handbook*. Philadelphia, Pa: Elsevier Mosby; 2005.
11. Nelder K. Acrodermatitis enteropathica and other zinc deficiency disorders. In: Freedberg IM, Eisen AZ, Wolf K, et al, eds. *Fitzpatrick's Dermatology in General Medicine*. 5th ed. New York, NY: McGraw-Hill; 1999: 1738-1744.
12. Aggett PJ, Harries JT. Current status of zinc in health and disease states. *Arch Dis Child*. 1979;54:909-917.
13. Nadruz W Jr, Bellinazzi VR, Carvalheira JB. Zinc deficiency leading to intractable vomiting. *Arch Intern Med*. 2002;162:2376-2377.
14. Paller AS, Mancini AJ. *Hurwitz Clinical Pediatric Dermatology*. 3rd ed. Philadelphia, Pa: Elsevier Saunders; 2006.
15. Kury S, Dreno B, Bezieau S, et al. Identification of SLC39A4, a gene involved in acrodermatitis enteropathica. *Nat Gene*. 2002;31:239-240.
16. Picciano MF. Nutrient composition of human milk. *Pediatr Clin North Am*. 2001;48:53-67.
17. Dauncey MJ, Shaw JC, Urman J. The absorption and retention of magnesium, zinc, and copper by low birth weight infants fed pasteurized human breast milk. *Pediatr Res*. 1977;11:1033-1039.
18. Moore ME, Moran JR, Greene HL. Zinc supplementation in lactating women: evidence for mammary control of zinc secretion. *J Pediatr*. 1984;105: 600-602.
19. Vuori E, Kuitunen P. The concentrations of copper and zinc in human milk. a longitudinal study. *Acta Paediatr Scand*. 1979;68:33-37.
20. Moran JR, Vaughan R, Stroop S, et al. Concentrations and total daily output of micronutrients in breast milk of mothers delivering preterm: a longitudinal study. *J Pediatr Gastroenterol Nutr*. 1983;2:629-634.
21. Odom RB, James WD, Berger TG. Nutritional diseases. In: Odom RB, James WD, Berger TG, eds. *Andrews' Diseases of the Skin: Clinical Dermatology*. 10th ed. New York, NY: Saunders-Elsevier; 2006: 611-614.
22. Quirk C, Seykora J, Wingate B, et al. Acrodermatitis enteropathica associated with anorexia nervosa. *JAMA*. 2002;288:2655-2656.