HK J Paediatr (new series) 2014;**19**:240-243

Zinc Deficiency Dermatitis in Premature Infants with Necrotising Enterocolitis

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Abstract Zinc deficiency dermatitis in preterm which has been described in infants with enteropathy or exclusively breastfed is a rare condition of severe zinc deficiency which may increase mortality of preterm. Here we report 9 cases of preterm with necrotizing enterocolitis who developed zinc deficiency dermatitis after long time of total parenteral nutrition and lack of zinc supplementation. At a postnatal age of 41-74 days, all the infants developed skin lesions, including early erythema, progressing to vesiculobullous lesions, and later escharosis. Zinc deficiency was confirmed by the finding of lower plasma zinc concentration (28.9-48.5 μg/dl). All infants recovered with a near normal skin appearance after 9-21 days' treatment with zinc supplementation. Premature infants with enteropathy on long time of total parenteral nutrition are at risk of developing zinc deficiency. Zinc should be routinely supplemented for those infants and plasma zinc concentration should be checked for the prompt diagnosis when these patients develop onset of skin lesions.

Key words Necrotising enterocolitis; Preterm; Total parenteral nutrition; Zinc deficiency dermatitis

Introduction

Zinc is an essential trace element which plays an important role in growth, reproduction, tissue repair and cellular immunity. Zinc deficiency can induce a great number of disorders, including growth retardation, alopecia, diarrhea, dermatitis, and an increase of infections.[1] Of these, acrodermatitis enteropathica (AE), either inherited or acquired (AE-like), is a rare condition associated with poor absorption of zinc.[2]

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Received November 5, 2013

Because of the nonspecific symptoms in early zinc deficiency, there are some difficulties in diagnosis. Kienast et al[3] had reported ten cases of zinc deficiency dermatitis in exclusively breast-fed infants who were initially misdiagnosed and mistreated as impetigo or eczema. Here we summarise 9 cases of premature infants with necrotising enterocolitis who developed zinc deficiency dermatitis after long time of total parenteral nutrition and lack of zinc supplementation.

Case Presentation

A total of 9 premature infants, born at 26~35 weeks of gestation with birth-weight of 870~1720 g, were admitted to our neonatal intensive care unite during a period of 4 years (2009.1-2013.1).

All of them developed severe necrotising enterocolitis. Eight of them got surgery therapy and one was treated with conservative therapy. They received total parenteral nutrition for a duration of 19~40 days. During the total parenteral nutrition, a standard protocol of amino acid solution, dextrose and intravenous lipids, with multiple

vitamins was used, but zinc was not added because of the nationwide shortage of injectable zinc and the inappropriateness of trace element mixture for perterm. All the infants developed cholestasis because of long-term fasting and parenteral nutrition.

At a postnatal age of 41~74 days, all the infants developed skin lesions, including early erythema, progressing to vesiculobullous lesions, and later escharosis (Figures 1 & 2). These lesions mainly located in face, perioral area, neck folds, extremities, and genital area. According to the clinical characteristics and the known risk factors including prematurity and prolonged total parenteral nutrition without zinc supplementation, zinc deficiency dermatitis was suspected and confirmed by the finding of lower plasma zinc concentration (28.9~48.5 μg/dl) than normal (>60 μg/dl). Other causes of skin lesions were searched for and excluded, particularly essential fatty acid deficiency, amino acid deficiency and bacterial infection associated skin lesions.

All the infants were started partial enteral nutrition by the time the skin lesions occurred. Oral Zinc Gluconate (2 mg/kg/day of zinc) was initiated. All infants recovered with a near normal skin appearance after 9~21 days' treatment and repeated plasma zinc concentration

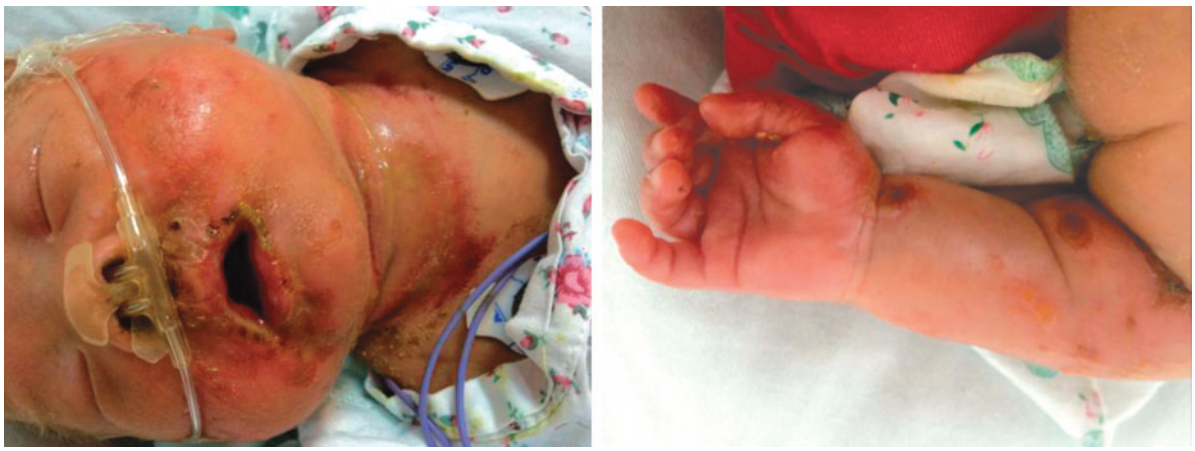

Figure 1 Erosive and vesiculobullous lesions around mouth, face and neck (left). Erythema, bullae and escharosis around forearm and hand (right).

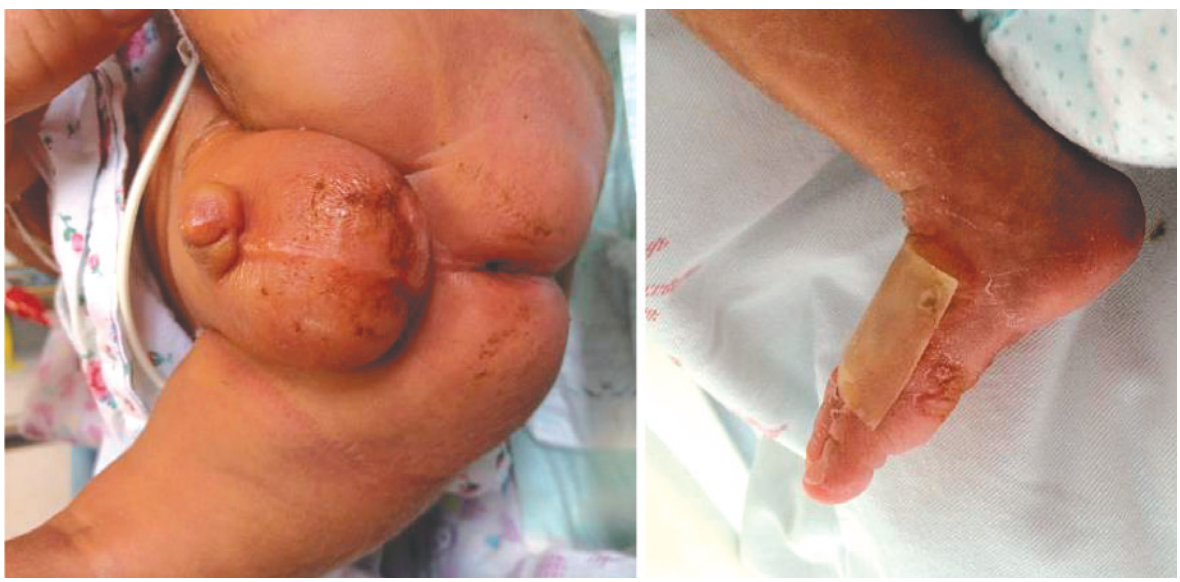

Figure 2 Erosive lesions and escharosis around genital area (left). Bullae and erosive lesions around foot (right).

(108.7~177.7 μg/dl) increased to normal. Zinc supplementation was discontinued after complete resolution of the skin lesions and total enteral feeding with preterm formula, and no further recurrence of skin lesions were detected. Cases 1-9 are summarised in Table 1.

Discussion

Zinc is an essential cofactor in approximately 300 enzyme-dependent processes.[4] Fetal zinc accumulation via placental trans-port is maximal at 24-34 weeks of gestation.[5] Premature infants are especially susceptible to development of zinc deficiency because of a combination of a low zinc store and an increased zinc requirement. Several zinc metalloenzymes are related to specific disorders and problems of preterm infants: carboanhydrase (metabolic acidosis), DNA- and RNA-polymerases (impaired growth), alkaline phosphatase (osteopenia praematurorum), superoxide dismutase (bronchopulmonary dysplasia), pancreatic protease (impaired digestion).[6]

Acquired zinc deficiency has been described in a breast-fed preterm infant (Aggett 1980)[7] and when total parenteral nutrition is administered without zinc supplementation. It can also result from reduced zinc absorption or increased losses due to gastrointestinal pathology or surgery (Arlette 1983).[8] Harper et al[9] once reported a preterm neonate with necrotising enterocolitis developed zinc deficiency dermatitis because of lower zinc supplementation during total parenteral nutrition.

In the cases reported here, the gestational age was very small with an average of 28.4 weeks, which accounted for the low zinc storage. All the infants had developed necrotising enterocolitis and were treated with long-term fasting and total parenteral nutrition, leading to the increased trace element loss from the inflamed gut mucosa and incapable intestinal absorption of zinc. With multiple factors, all the infants developed cholestasis. Because there was no injectable zinc for preterm in our country and other preparations of multiple parenteral trace elements might

Table 1 The characteristics, nutritional status and clinical aspects of our cases

Case No.	Gender	Gestational age (weeks)	Birth-weight (grams)	Chronological age at onset of skin symptoms (days)	Duration of total parenteral nutrition (days)	Zinc serum before treatment (μg/dl)	Skin lesions localisation	Zinc serum after treatment (μg/dl)	Complete resolution of skin lesions (days)
1	M	26	870	62	20	32.3	Face, perioral, neck folds, extremities, genital, perianal	108.7	17
2	M	27	950	41	19	36.8	Face, perioral, neck folds, extremities	115.3	21
3	M	27	1100	51	24	32.5	Perioral, neck folds, extremities	121.2	12
4	M	28	1100	67	40	36.3	Perioral, neck folds, extremities, genital	177.7	12
5	F	26	960	65	36	28.9	Perioral, extremities	113.8	20
6	M	27	950	74	25	35.7	Perioral, genital	120.8	19
7	M	35	1720	60	33	38.9	Perioral, extremities	130.3	9
8	F	31	1350	50	18	48.5	Perioral, extremities	129.3	16
9	M	29	1300	48	20	46.9	Perioral	142.9	9
Mean	–	28.4	1144	57.6	26.1	37.4	–	128.9	15

cause trace element toxicity in cholestatic infants, no alternatives to the injectable zinc supplements were available, which accounted for the main reasons of zinc deficiency.

Skin lesions of acquired zinc deficiency dermatitis is similar to AE, classically located in periorificial, intertriginous, and acral areas,[10,11] which were also observed in our cases and shown in the Figures. Skin lesions usually appear as early small moist and erythema, progressing to vesiculobullous lesions, and finally escharosis.[6] These lesions may be the seat of bacterial or fungal infection because of the impaired immune function induced by zinc deficiency.

The management of a patient with zinc deficiency dermatitis is by zinc supplementation at daily oral dosage of 1-2 mg/kg/day.[12,13] The American Society for Clinical Nutrition recommends that premature newborns should be supplemented with 400 ug/kg/day of zinc during total parenteral nutrition[14,15] But Barbarot et al[16] recommended the zinc dosage should be doubled or tripled in premature infants at high risk of zinc deficiency because the infants still developed skin lesions with the common zinc supplementation as recommendations. Response to treatment may take days to weeks, depending on the degree of zinc depletion. All the cases responded well to zinc supplementation which showed an excellent prognosis.

In summary, Premature infants with necrotising enterocolitis on long time of total parenteral nutrition are at very high risk of zinc deficiency. Most of these infants may also have cholestasis which limits the use of multiple parenteral trace elements. Injectable zinc should be manufactured and supplemented in total parenteral nutrition of preterm infants. Plasma zinc level should be checked for the prompt diagnosis when these patients develop onset of skin lesions and zinc supplementation should be initiated with increased dosage until resolution of the lesions.

Declaration of Interest

We declare that we have no conflict of interests.

References

1. Yanagisawa H. Zinc deficiency and clinical practice. JMAJ 2004; 47:359-64.
2. Maverakis E, Fung MA, Lynch PJ, et al. Acrodermatitis enteropathica and an overview of zinc metabolism. J Am Acad Dermatol 2007;56:116-24.
3. Kienast A, Roth B, Bossier C, Hojabri C, Hoeger PH. Zinc-deficiency dermatitis in breast-fed infants. Eur J Pediatr 2007; 166:189-94.
4. Tapiero H, Tew KD. Trace elements in human physiology and pathology: zinc and metallothioneins. Biomed Pharmacother 2003;57:399-411.
5. Hambidge KM, Krebs NF, Jacobs MA, Favier A, Guyette L, Ikle DN. Zinc nutritional status during pregnancy: a longitudinal study. Am J Clin Nutr 1983;37:429-42.
6. Obladen M, Loui A, Kampmann W, Renz H. Zinc dificiency in rapidly growing preterm infants. Acta Paediatr 1998;87:685-91.
7. Aggett PJ, Atherton DJ, More J, Davey J, Delves HT, Harries JT. Symptomatic zinc deficiency in a breast-fed preterm infant. Arch Dis Child 1980;55:547-50.
8. Arlette JP. Zinc and the skin. Pediatr Clin North Am 1983;30: 583-96.
9. Harper JI, Thompson D, Kovar IZ, Copeman PW, Barltrop D. Zinc deficiency in a preterm neonate with necrotizing enterocolitis. J R Soc Med 1984;77(Suppl 4):40-1.
10. Perafan-Riveros C, Franca LF, Alves AC, Sanches JA Jr. Acrodermatitis enteropathica: case report and review of the literature. Pediatr Dermatol 2002;19:426-31.
11. Jensen SL, McCuaig C, Zembowicz A, Hurt MA. Bullous lesions in acrodermatitis enteropathica delaying diagnosis of zinc deficiency: a report of two cases and review of the literature. J Cutan Pathol 2008;35(Suppl 1):1-13.
12. Suchithra N, Sreejith P, Pappachan JM, George J, Rajakumari PK, Cheriyan G. Acrodermatitis enteropathica-like skin eruption in a case of short bowel syndrome following jejuno-transverse colon anastomosis. Dermatol Online J 2007;13:20.
13. Kodama H. Trace Element Deficiency in Infants and Children. JMAJ 2004;47:376-81.
14. Greene HL, Hambidge KM, Schanler R, Tsang RC. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. Am J Clin Nutr 1988;48:1324-42.
15. Friel JK, Andrews WL. Zinc requirement of premature infants. Nutrition 1994;10:63-5.
16. Barbarot S, Chantier E, Kuster A, et al. Symptomatic acquired zinc deficiency in at-risk premature infants: high dose preventive supplementation is necessary. Pediatr Dermatol 2010;27:380-3.