Zinc Deficiency Dermatitis in Premature Infants with Necrotising Enterocolitis

CH Wang, XL Ma, LP Shi

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. Of these, acrodermatitis enteropathica (AE), either inherited or acquired (AE-like), is a rare condition associated with poor absorption of zinc.

Because of the nonspecific symptoms in early zinc deficiency, there are some difficulties in diagnosis. Kienast et al 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 preterm. 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).
Zinc Deficiency Dermatitis

(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. Fetal zinc accumulation via placental trans-port is maximal at 24-34 weeks of gestation. 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). 

Acquired zinc deficiency has been described in a breast-fed preterm infant (Aggett 1980) 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). Harper et al 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 have no zinc, we suspected that the zinc deficiency dermatitis in these cases was due to zinc deficiency.

<table>
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<tr>
<th>Case No.</th>
<th>Gender</th>
<th>Gestational age (weeks)</th>
<th>Birth weight (grams)</th>
<th>Chronological age at onset of skin symptoms (days)</th>
<th>Duration of total parenteral nutrition (days)</th>
<th>Zinc serum before treatment (µg/dl)</th>
<th>Skin lesions localisation</th>
<th>Zinc serum after treatment (µg/dl)</th>
<th>Complete resolution of skin lesions (days)</th>
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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, 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. 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. The American Society for Clinical Nutrition recommends that premature newborns should be supplemented with 400 ug/kg/day of zinc during total parenteral nutrition. But Barbarot et al 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