An Indistinguishable Case of Zinc Deficiency: Acquired Zinc Deficiency or Acrodermatitis Enteropathica?

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Abstract: Zinc (Zn) is an essential micronutrient in growth and development in children. In some condition, zinc deficiency occurred due to genetic or non-genetic caused. Skin disorders due to Zn deficiency are differentiated into acrodermatitis enteropathica (AE) and acquired zinc deficiency (AZD). These conditions are often indistinguished, since they have same skin disorders. However, AE is caused by genetic disorder that need long-life Zn supplementation, and the other hand, AZD occurred by imbalance intake of Zn, especially from breast milk. Therefore, further examination for baby and mother are required. Here, we describe a case report of a 3-month old boy with zinc deficiency. Skin disorders evolved since the patient was 2-month old as symmetrical dermatitis in perioral, acral, and skin folds area, accompanied with diarrhea. Patient was born prematurely at 34-week of gestation and was a breast-fed infant. The diagnosis of AZD was established based on typical skin lesion, diarrhea, and low serum Zn level. This decreased of serum Zn also found in his mother. Patient was treated with 10 mg Zn sulphate supplement once daily and clinical improvement was obtained after five days supplementation. Zinc level in patient remained high after one month discontinuation of Zn supplement. Clinically, AZD is difficult to distinguish with AE, thus zinc level examination in baby and mother are required, as well as observation during and after discontinued of zinc supplementation, to support the diagnosis, both for AE or AZD.

1 INTRODUCTION

Zinc (Zn) is an essential micronutrient in proteins and nucleic acids. Zn also plays role in cell growth and division, wound healing, and immune cell activity (Plum et al., 2010). Zn deficiency in children results in growth retardation, emotional disturbance, irritability, depression, gastrointestinal disorders, hypogonadism, anemia, skin disorders, and immune system disorders (Ackland et al., 2008). Skin disorders due to Zn deficiency can manifest as erythematous macules, vesicles, pustules, crusts, erosion, and scales in the periorifisium, extremities, and diaper area with symmetrical distribution (Yang et al., 2012). These lesions could resemble atopic dermatitis, seborrheic dermatitis, diaper dermatitis, candidiasis, and skin disorders from vitamin and other micronutrient deficiency (Kury et al., 2012; Kharfi et al., 2010). Theredore, this skin disease often misdiagnosis.

Zinc deficiency is classified into primary and secondary (Ackland et al., 2008).Primary deficiency results from low Zn intake or low bioavailability of Zn. Secondary deficiency is caused by genetic disorder or disease that interfere Zn absorption as well as increased Zn excretion in intestinal. Acquired zinc deficiency (AZD) and acrodermatitis enteropathica (AE) are disease that occurs due to Zn deficiency with very similar clinical manifestation (Ackland et al., 2008). AE is caused by a genetic disorder resulting in impaired absorption of Zn in the intestinal with classic triad of periorifisium dermatitis, diarrhea and alopecia, while AZD is due to imbalanced intake and Zn requirement without intestinal disturbance (Yang et al., 2012; Ruiz-Maldonado& Orozco, 2008).

Here is one case of AZD that initially undisguisable to AE because of same skin rashes. However, serum Zn level examination from patient and mother showed lower level that indicated to AZD due to imbalance intake, thus Zn supplementation was given. The purpose of this case report is to report a Zn deficiency case that clinically indistinguishable, but after discontinued of Zn supplementation, the serum Zn level examination remained normal, that indicated to AZD.

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2 CASE

A 3-month-old baby boy presented with 1-month history of skin eruption, arising initially on his inguinal area. These lesions spread bilaterally over his back, hands and feet, then onto his face. The skin lesion accompanied with diarrhea up to 6 times a day. He was treated with topical corticosteroids for skin lesion and antibiotic with other physician and improvement was not achieved. He was premature, delivered at 34 weeks, and full breast-fed infant. Physical examination revealed bright red, eroded plaques in perioral and extremities, especially folded ares, as well as vesiculobullous lesions on his hands and feet (Figure 1). Bacteria was found on Gram stain and pseudohyphae and blastospore from skin scrapings with 10% potassium hydroxide (KOH) solution. Patient had underweight and stunted, and from laboratory examination, there was hyponatremia.

From history taking and physical examination, led to Zn deficiency, which could be AZD and AE. Therefore, serum Zn examination was needed. The result were Zn level at patiet was 9 µg/l (reference range 26–141 µg /l) and Zn level of his mother at 49 µg /l (reference range 60–130 µg /l). This result confirmed AZD since usually in AE, Zn level of mother is in normal limit, however, there is genetically malfunction of Zn absorption in baby, that lead to Zn deficiency.

The patient was given oral zinc sulphate supplementation in 10 mg/day dose, and dramatic improvement of skin lesion had achieved within a few days. The lesions resolved completely over following 2 weeks. Zn supplementation still continued for 3 months, and the normal level of Zn was achieved as 101 µg /l. After a months of Zn supementation was stopped, Zn level remain normal (96 µg /l) and there was no new skin lesion at all (Figure 1). Based on this condition, the diagnosis of this patient was AZD, that could be differentiated with AE from thorough examination and follow up.

3 DISCUSSION

Zinc is an essential micronutrient for growth and development (Plum et al., 2010). It is required for the activity of more than 300 enzymes and 1,000 transcription factors, as well as controlling genetic expression, and plays an important role in protein and amino acids synthesis, cell replication and regeneration (Krebs, 2013). Zn sources in infants are mainly obtained from breast milk. Zn in breast milk is better absorbed than cow's milk or soy milk, because it contains zinc-binding ligand (Jen & Yan, 2012). Zn from food will be absorbed in the form of Zn^{+2} ions that bind to ZIP4 transporters to be absorbed in duodenum and jejunum (Deshpande et al., 2013).

Zinc deficiency characterized by abnormalities in the skin, gastrointestinal tract, and alopecia (Ruiz-Maldonado& Orozco, 2008). Skin disorders initially presented as erythematous macules with scale and may turn into vesicles, bullae, pustules, and erosion with symmetrical distribution in periorifisial, and extremities (Kharfi et al., 2010). Skin lesions may be accompanied by secondary infections caused by Candida or bacteria (Kaur et al., 2016). This disorder is accompanied by diarrhea three to six times per day which can leads to dehydration and electrolyte imbalance. In mild cases there is dry and coarse hair, which become alopecia in severe cases. Other abnormalities that can be found are anorexia, growth retardation, irritability, eye abnormalities and photophobia (Jensen et al., 2008).

Diagnosis of Zn deficiency in this patient established based on typical clinical features and laboratory tests (Kury et al., 2012). Zn serum concentrations was less than 50 µg / l are the gold standard for the diagnosis of Zn deficiency (Jen & Yan, 2012).

The skin lesions in this patient are erythematous macule with scale in symmetrically distributed between the thighs, buttocks, back and hands and around the mouth and nose, accompanied by vesicles and bullae in the legs. Complaints also accompanied with diarrhea and hair loss. We found bacteria on Gram stain and pseudohyphae and blastospore from skin scrapings with 10% KOH solution. On physical examination, the nutritional status was underweight and stunted, alopecia, and from laboratory examination, the patient was hyponatremia.

Zinc deficiency can be differentiated into congenital and acquired (Yanagisawa, 2004). AE is a congenital Zn deficiency arising from a gene mutation encoding the Zip4 protein, which is a Zn transporter in the pancreas, so there is no Zn transport from the duodenum and jejunal lumen to the epithelium (Azevedo et al., 2008). Protein Zip4 is also produced by the mother's milk glands secreted into breast milk. Therefore, in AE there is no Zn deficiency in exclusively breast-fed infants (Jen & Yan, 2012). In infants with AZD there is an imbalance between the Zn requirement and the Zn intake, one of which is due to the low Zn levels in

the mother. AZD occured due to low levels of Zn in breast milk. Low levels of Zn in breast milk can be caused by uptake Zn uptake in serum by mammary glands, due to mutations of Zn SLC30A2 (ZnT-2) transporter (Krebs, 2013). Other studies suggest that low levels of Zn in breast milk may be due to low maternal serum Zn levels (Scheplyagina, 2005). Symptoms of Zn deficiency in AZD usually occur in first six months of life. At that time there was a rapid growth in infants so the requirement for Zn also increased. AZD occurs mostly in premature infants given breast milk. This is because early in life of premature infants, Zn absorption in the intestine is inadequate (Mashhood, 2007), and Zn transfer from mother to fetus via the placenta occurs mostly in the last ten weeks of pregnancy (Ackland & Michalczyk, 2006). In breast-fed infants with AE, the symptoms of Zn deficiency occur after weaning, while infants fed formula, symptoms arise more quickly (Jen & Yan, 2012).

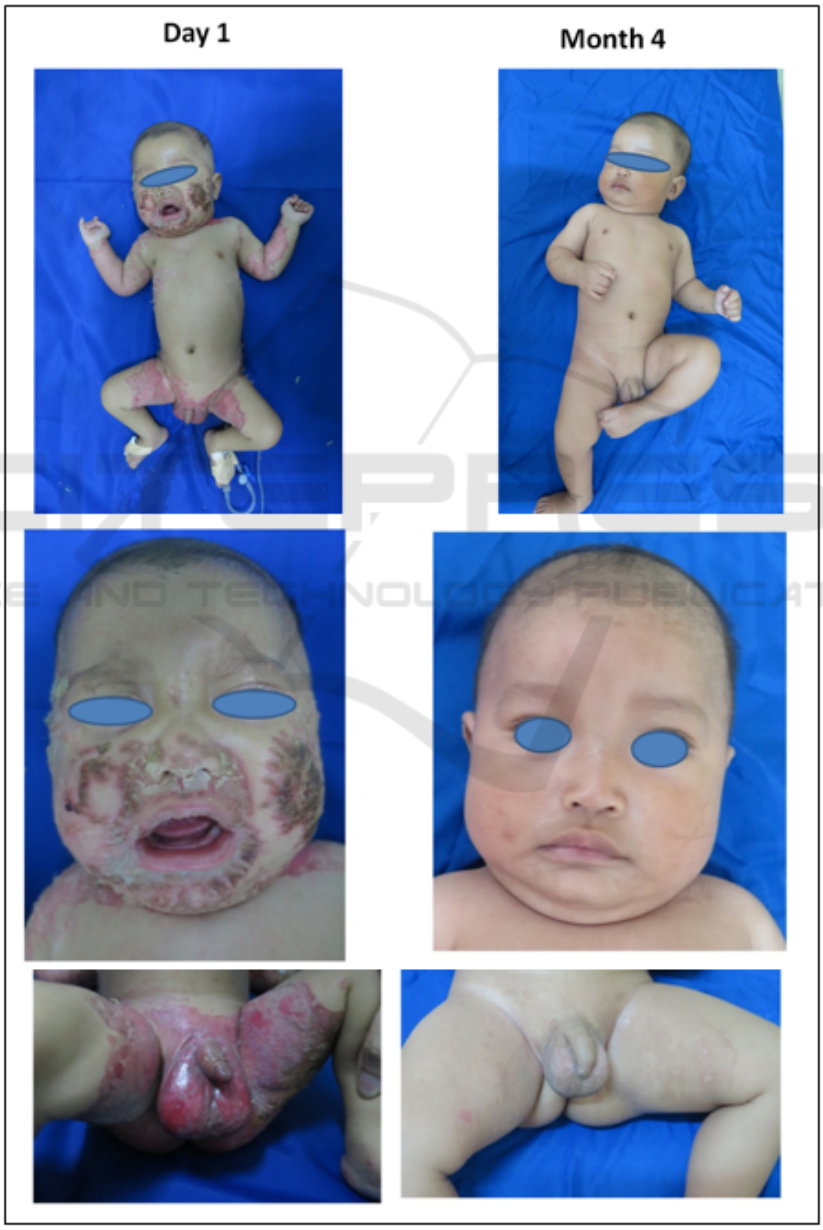

Figure 1: Skin lesion

This patient was born prematurely at eight months of gestation. From birth, the patient received exclusive breastfeeding from her mother. Clinical manifestations of typical skin disorders and diarrhea begin to develop since the patient two months old. On laboratory examination, patient had low Zn levels, as well as in her mother. Patient was given by oral Zn supplementation and the Zn level remain normal limit after discontinued Zn supplement. Therefore, diagnose of AZD was established based on low level of Zn in patient and mother, as well as the remain of Zn level of patient after discontinued therapy.

The main therapy for Zn deficiency is supplementation of Zn sulphate 10-20 mg per day for up to three to four months. Skin disorders and diarrhea usually start improving after two to three days, and skin infections show improvement after one week (Mashhood, 2007). In AZD, after discontinuation of Zn supplementation, skin disorders do not reoccured. However, in AE, discontinuation of Zn supplementation results in a decrease in serum Zn levels, and skin disorders will reappear (Kharfi et al., 2010).

In this case, patient was given by 10 mg/day Zn sulphate supplements and after one week there were clinical improvement as skin lesions healed and no diarrhea. After three months of Zn supplementation, serum Zn level was 101 µg/l, and after one month discontinuation of supplement, obtained Zn level was normal, as 96 µg/l.

4 CONCLUSIONS

It may be concluded from this case report that Zn deficiency can cause acrodermatitis, perioral dermatitis, alopecia, and diarrhea, that both found in AE and AZD. Clinically, AZD is difficult to distinguish with AE, thus in order to differentiated them, zinc level examination in mother and baby are required.

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