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□ Case Report □

A case of acquired acrodermatitis enteropathica with a normal serum zinc level but a low level in the hair

Kyung Il Oh, M.D., Jung Hee Kim, M.D., Ji Eun Lee, M.D.
Dae Hyun Lim, M.D. and Byong Kwan Son, M.D.

Department of Pediatrics, College of Medicine Inha University, Incheon, Korea

Acrodermatitis enteropathica (AE) is a rare autosomal recessive disorder of early infancy, and is characterized by periorificial dermatitis, alopecia, and intractable diarrhea. Serum zinc levels are usually low in untreated patients and the oral administration of zinc sulfate can clear skin lesions and other symptoms. Although premature and cow's milk-fed infants are at particular risk of developing AE, there have been a few reports about AE in term and breast-fed infants. We report a case of transient AE in a 4-month-old breast-fed infant. This patient suffered from diarrhea and dermatitis for more than a month. Her skin lesions were erythematous, scaly, crusted, psoriasiform, eczematous, with an eruption at the chin, and a periorificial disposition with involvement of the flexural areas of lower extremities. Her serum zinc level was almost normal at 129 μg/dL (reference range: 60-121 μg/dL), but the zinc level in her hair was low: 8 mg percent (reference range: 10-21 mg percent). Skin biopsy findings were consistent with AE. Seven days after zinc supplementation, the skin lesions and diarrhea improved. The authors recommend that a clinical trial of zinc supplementation be considered in cases where there are suspicious of AE, even when the serum zinc level is normal. **(Korean J Pediatr 2007;50:209-212)**

Key Words : Acrodermatitis enteropathica, Zinc

Introduction

Acrodermatitis enteropathica (AE) was first described by Brandt and later named by Danbolt and Closs[1]. AE is a rare inherited disorder that is transmitted in an autosomal recessive manner, and which results from defective zinc absorption, characterized by clinical features such as dermatitis, diarrhea and alopecia[1-3]. It invariably presents in infancy, and particularly, at the time of weaning[4].

AE can be subdivided into a congenital form, which demands continuous life-long zinc supplementation, and an acquired form, which requires only transient supplementation. Transient AE is rarer in breast milk-fed infants than in cow milk-fed infants because the zinc binding ability of breast milk inhibits AE development[5]. AE can be present with normal zinc level as well as low, because tissue uptake of zinc from serum may be retarded[6].

Here, we describe a 4-month-old breast fed infant with AE and a normal serum zinc level. The patient was treated with zinc sulfate (3 mg/kg/d) and 7 days later her condition was much improved.

Case Report

A 4-month-old female infant was referred to our hospital for the evaluation of refractory diarrhea and crusted vesicular lesions. These lesions were well defined, erythematous, glazed, moist plaques with a perioral, perigenital, and perianal distribution and had been present for a month. The patient was born full term and had normal skin at birth.

She had taken exclusively breast milk since birth. Her mother had no significant medical history and there was no family history of any skin or allergic diseases.

On physical examination, the infant was chronically ill-looking. Her height and weight were 63 cm (10-25 percentile) and 7.7 kg (75-90 percentile), respectively. The cutaneous manifestations were characterized by patches,

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책임저자 : 임대현, 인하의대 부속병원 소아과학교실
Correspondence : Dae Hyun Lim, M.D.
Tel : 032(890-3780 Fax : 032)890-2844
E-mail : dhyunlim@inha.ac.kr

papules, and tiny vesicles on her cheeks, chin, abdomen and chest, and on the flexural areas of lower extremities. They were erythematous, scaly, and erosive, and interconnected, and were particular severe in the perioral and perianal regions (Fig. 1).

Laboratory tests including serum electrolyte level and complete blood cell count were normal except for the eosinophil count (6.8%). Her serum IgE level was 38.68 IU/mL. Her specific IgE antibody levels to egg white and milk were both less than 0.35 KU/L, and her serum zinc level was 129 μg/dL (reference range 60-121 μg/dL), although a tissue analysis of zinc in hair returned a low finding of 8 mg% (reference range 10-21 mg%) and a zinc to copper ratio in hair of 4 to 1. Serum albumin and protein levels were normal.

A microscopic examination of the skin lesions revealed scattered parakeratosis and marked acanthosis with keratinocyte hypogranulosis and dysmaturation, and an edematous papillary dermis (Fig. 2).

Thus, the patient was suspected as having AE clinically and histologically, and was started on an oral preparation of zinc sulfate (3 mg/kg/d), despite her normal serum zinc level. Her diarrhea and poor appetite ameliorated within 72 hours and she showed a marked improvement of the erythematous, glazed, moist plaques on perioral and perianal regions day 7s after commencing zinc sulfate administration. No recurrence occurred after withholding treatment for 5 months.

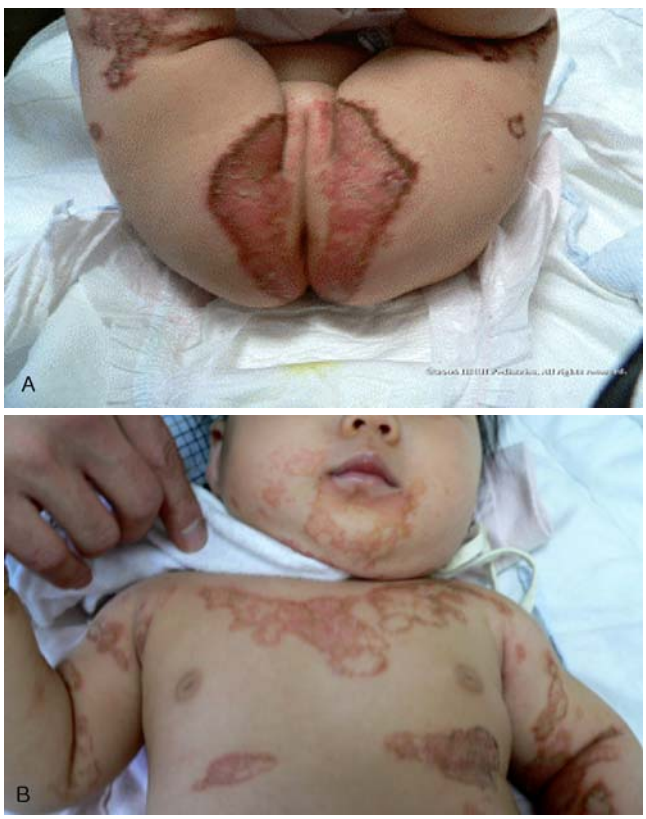

Fig. 1. Erythematous, erosive patches and psoriasiform rash with peripheral scaling on perianal areas (A) and chin and trunk (B).

Discussion

Clinical features of AE usually start after weaning, when the protective effect of zinc binding ligand in mothers milk is no longer present[4]. On the other hand, the main factors of acquired AE are almost certainly prematurity, an inadequate zinc diet, malignancy, and absorptive disorders[2]. Premature infants seem to be at increased risk of zinc deficiency and may exhibit a negative zinc balance until the third month of life, even when zinc intake is adequate[5, 7-9]. Among acquired AE patients, some experience transient symptoms with no underlying causative disorder, and can be treated with zinc supplementation for a short period without recurrence.

However, the clinical manifestations of AE are similar regardless of cause[2]. Erythematous, scaly, thin papules and coalescing plaques are distributed predominantly in acral locations, on the face and extremities, and have a symmetric predilection for perioral, periorbital, and perianal areas. Alopecia, refractory diarrhea, paronychia, stomatitis, apathy,

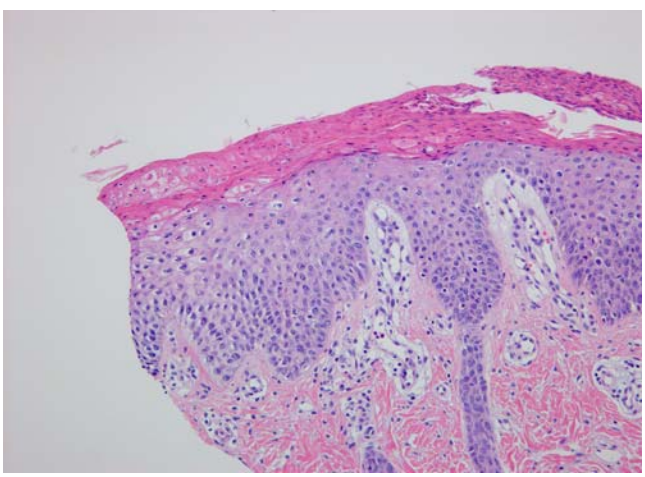

Fig. 2. The finding of skin biopsy shows that the lesion is consist of hyperkeratosis and parakeratosis, marked acanthosis with hypogranulosis and dysmaturation of keratocytes, and edematous papillary dermis (H&E stain, ×200).

irritability, and failure to thrive occur with varying frequencies. In our patient, the clinical features typical of AE developed at approximately age three months, intractable diarrhea and typically erythematous and eczematous skin lesions on periorificial areas. The characteristic microscopic findings of the skin lesions were irregular acanthosis, parakeratosis, loss of granular layer, psoriasiform hyperplasia and dermal lymphocyte perivascular infiltration[10, 11]. The histologic findings of our patient were also consistent with AE.

AE was already reported as zinc deficiency in the analysis of patients' variable diet, and it was found that patients with AE have impaired ability to absorb dietary zinc which was decreased by 2-3%, compared with absorptive rate, 27-65%[12, 13]. Zinc absorption is known to be competitively inhibited by iron and copper[14, 15] and fat malabsorption and intestinal inflammation may also impair zinc absorption[16]. As with our patient, hair zinc analysis revealed a zinc to copper ratio of 4:1, whereas the ideal ratio is 8:1[9]. Thus, we consider that this patient zinc absorption was probably perturbed by above normal levels of copper.

A diagnosis of AE is usually established by the presence of typical skin lesions and clinical symptoms, and this can be confirmed if serum zinc level is low. However, this is not necessary to confirm the diagnosis[17, 18]. Some authors have reported AE without hypozincemia, and have postulated that the accumulation of zinc bound in an immobile chemical form in tissue could make the element unavailable for metabolic processes. Moreover, even if total zinc levels in plasma are normal, the amount of usable zinc may be reduced due to an impaired secretion to peripheral tissues[6]. AE with a normal zinc level was diagnosed based on the presence of typical clinical symptoms and a dramatic response to zinc supplementation[19]. In our patient, serum zinc level was normal, but, a hair mineral analysis demonstrated low zinc levels.

In AE patients, hair zinc analysis is preferred to blood zinc analysis. Only 10% of total body zinc is present in plasma, and 75% of this zinc is bound by albumin, which facilitates its metabolization. The average plasma zinc concentration is 0.85 μg/ml, compared with 50 μg/g in muscle, liver, kidney and 100 μg/g in eye, bone, prostate, and hair[16]. Blood examinations reflect mineral status for a short period, and may be normal even though cells and tissues are deprived of mineral, or alternatively unbalanced because of changes in the homeostasis maintenance system. Since the test indicates mineral status after changes occurred in cells and tissues producing energy, it is quite often when the test may not show significant values even if the patient complains of any symptoms without an afferent disease but not in a good health[20].

Moreover, plasma zinc concentrations can be depressed without zinc depletion in such circumstances as acute infections[21]. The hair analysis, on the other hand, provides long-term intracellular information, and specimens are easily transported, stores, and obtained. However, hair zinc levels may be markedly depressed in mild zinc deficiency states and normal in cases of severe zinc deficiency when hair growth is arrested[16]. Unfortunately, analytic method and the interpretation of hair analyses have not been fully evaluated or standardized in Korea.

Pediatric case reports of AE are not common; 38 cases have been reported in the Korean medical literature to date[9, 15, 22-25]. Among these 38 cases, serum zinc levels were documented in 28, which included 22 (78.5%) with a decreased zinc level and 6 (21.4%) with a normal zinc level. Of the six patients with a normal zinc level, three had associated diseases (rhabdomyosarcoma, leukemia, and histiocytosis) and the other three had no causative disease. Two of the three AE patients with a normal zinc level and no underlying disorder and were breast-fed, and the other of three were on cows milk formulae. Zinc tissue levels were not reported. This present case may be the first with documented zinc levels in serum and hair. One patient (3%), who had moniliasis, dehydration, glomerulonephritis, and anemia reportedly died, and 12 of the 38 patients received zinc supplementation and completely improved and did not recur.

AE usually responds to zinc supplementation within a few weeks, and occurred within 7 days in the described case. Zinc sulfate is inexpensive and safe. Congenital AE demands continuous zinc supplementation for a lifetime, whereas the acquired form may only require zinc treatment for a short period. In our patient, symptoms started to improve on day 3 and had completely cleared by day 7. Moreover, after discontinuation of oral zinc sulfate skin lesions did not recur.

Here, we present a case of transient AE with a normal serum zinc level and a low hair zinc level that responded to 7 days of zinc supplementation, and which did not recur. We recommend that zinc supplementation could be considered to treat patients clinically suspected of having AE

despite a normal serum zinc level.

한 글 요 약

혈중 아연 농도는 정상이나 모발 검사에서는 감소된 아연 농도를 보인 일과성 장병성 선단 피부염 1례

인하대학교 의과대학 소아과학교실

오경일 · 김정희 · 이지은 · 임대현 · 손병관

장병성 선단 피부염은 위장관에서 아연 흡수가 제대로 되지 않아 발생하는 질환으로서 주로 이유기의 영·유아에 호발하고 상염색체 열성 유전하는 질환이다. 홍반, 인설, 가피, 건선양 피부와 습진의 특징적인 피부 병변이 개구부와 사지 말단 부위에 대칭적으로 나타나고, 만성 설사, 탈모증, 조갑 주위염, 그리고 성장 장애가 나타나는 드문 질환이다. 혈중 아연 농도가 대부분에서 떨어져 있지만 정상 혈중 농도에서도 말초 조직 내의 아연 농도가 떨어지면 증상이 나타난다. 다른 원인 질환이 없고 만삭으로 정상 분만한 모유 수유 영아에서 조직학적으로 일치하며, 혈중 아연 농도는 정상이지만 모발에서 아연 농도가 떨어진 장병성 선단 피부염 증례를 경험하였기에 문헌 고찰과 함께 보고하는 바이다.

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