A Case of Acrodermatitis Enteropathica Misdiagnosed as Staphylococcal Scalded Skin Syndrome

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Abstract

Acrodermatitis enteropathica (AE) is a rare genetic autosomal recessive disorder, characterized by periorificial dermatitis, alopecia, and diarrhea due to zinc deficiency. We report a case of a 9-month-old baby boy with hair loss for 2 months, diarrhea for 1.5 months, skin peeling starting around mouth, nose, anus, gradually spreading all over body over 1 month, and fever for 10 days. Due to superadded bacterial infections and altered clinical picture, he was diagnosed as a case of staphylococcal scalded skin syndrome. With low serum zinc levels and improvement of skin lesions and diarrhea within 8 days of starting oral zinc therapy, it was confirmed to be a case of acrodermatitis enteropathica. It is important to consider AE as one of the differential diagnoses in pediatric chronic diarrhea cases with acral and/or periorificial skin lesions to prevent delay in the zinc supplementation treatment and mortality.

Keywords: Acrodermatitis, periorificial dermatitis, zinc deficiency

Introduction

Acrodermatitis enteropathica (AE) is a recessively inherited defect of intestinal zinc absorption, caused by mutation in zinc transporter protein, zinc-ligand binding protein 4 (ZIP4), encoded by the gene solute carrier family 39 member 4 (SLC39A4).[1,2] Zinc is an essential co-enzyme for metal enzymes such as alkaline phosphatase, and it is also an important structural component of gene regulatory proteins required for the intracellular binding of tyrosine kinase to T-cell receptors. AE usually appears during infancy after weaning of breastfeeding. Signs and symptoms in infancy include diarrhea, mood changes, anorexia, and neurological disturbance. Eczematous/desquamative/bullous/vesicular skin lesions evolve predominantly on the extremities and periorificially. In toddlers and school-going children, zinc deficiency is characterized by growth retardation, alopecia, hypogonadism, neuropsychiatric abnormalities, and recurrent infections.[3] Spontaneous remission or death due to multiple organ failure are known to occur.[3,4] For diagnosis, zinc levels in the serum, urine, or hair are considered, but they are neither specific nor sensitive. In individuals with the typical clinical picture, decreased zinc plasma levels (<70 mg/dL) corroborate the diagnosis of AE.[4] Zinc absorption tests are cumbersome and genetic testing which are confirmatory (defect in 8q24, gene SLC39A4), are not easily available, or are not affordable to the patients. Most dermatologists/pediatricians therefore rely on immediate results of a therapeutic zinc supplementation (1–3 mg/kg body weight/day) as a confirmation of the diagnosis.[3,4]

Case Report

A 9-month-old male infant, product of a nonconsanguinous marriage, full-term normal delivery, exclusively breast fed till the age of 6 months and weaned off over the next 2 months, achieved milestones for age, and 7.5 kg body weight, presented with loss of hair for 2 months, diarrhea for 1.5 months, and peeling of skin all over body ×1 month. Mother noticed gradual

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loss of scalp hair over the last 2 months. The baby started having watery, yellowish-greenish stools, 10–12 times/day for 1.5 months. After a few days, the baby started developing erythematous scaly lesions over the feet and hands and later around mouth and perianal area. The baby was given some topical applications by the village quack. He developed pustules over the existing lesions and also in the groin and axillae. In a few days, the baby developed skin peeling almost all over the body and fever [Figure 1]. He was diagnosed as staphylococcal scalded skin syndrome (SSSS) in a pediatric hospital and was given intravenous antibiotics and hydrocortisone. The baby's condition improved, fever subsided, and pustules regressed. However, by day 5, baby developed fever again and continued to have skin peeling and diarrhea. When the baby was brought to our institute, he was lethargic, irritable, febrile and had tachycardia, anasarca, and pallor. Other systemic examination did not reveal any abnormalities.

Dermatological examination revealed extensive exfoliation of skin and erythema over the entire body in sheets with denuded areas over the perioral region, flexures, flanks, and perianal region. Perioral tightening of the skin was noticed. There was no skin tenderness. Nikolsky's sign was negative. No mucosal lesions were seen. Although the clinical picture had altered, depending on the onset of lesions postweaning, their first appearance being periorificially, and on feet, alopecia, and chronic diarrhea, provisional diagnosis of sepsis with underlying nutritional deficiency of Zinc was established. Other diagnoses such as congenital bullous ichthyosiform erythroderma, SSSS, and Steven–Johnson's syndrome were also considered [Figure 2 shows a patient of SSSS for comparison, treated at our institute, few months before this case].

The baby was shifted to the pediatric intensive care unit and was given barrier nursing. The baby was started on broad-spectrum Intravenous (IV) antibiotics, oral zinc sulfate syrup was given in the dose of 2 mg/kg body weight/day (15 mg)[3] along with multivitamin and oral protein supplements. He was given topical therapy with potassium permanganate compresses over oozy areas, topical antibiotic and antifungal creams for raw areas, and emollients over dry scaly areas.

The investigations revealed anemia (Hb: 4.2 g/dl), leukocytosis (18,700 cells/cumm – neutrophil predominance), hypoproteinemia (4.4 g/dl), hypoalbuminemia (2.4 mg/dl), and low serum alkaline phosphatase: 46U/L. C-reactive protein was positive. Pus culture and sensitivity revealed *Escherichia coli* and *Pseudomonas aeruginosa* growth. Serum zinc levels were low – 45 μg/dl (normal range 70–120 μg/dl).[5] Ultrasonography of the abdomen showed fatty liver. Skin biopsy showed parakeratosis, extensive vacuolization of the upper epidermal cells, acanthosis and spongiosis in the epidermis, and perivascular lymphocytic infiltration in the papillary dermis [Figure 3].

Chest X-ray, remaining liver function and renal function tests, urine and stool examination, blood culture, and urine and stool culture did not reveal any abnormality. ELISA for HIV, venereal disease research laboratory test, and antibodies for hepatitis B and C were negative. Genetic mutation testing was not performed due to unaffordability of the parents.

IV albumin and packed red blood cell transfusion were given in view of anasarca and anemia. Antibiotics were changed as per culture and sensitivity report. The baby was afebrile by day 5 of admission. Diarrhea improved by day 8. Erosions started healing by day 10. Erythema and scaling regressed by day 14. By day 20, the child was afebrile, playful, and smiling, his vitals were stable, and skin lesions had completely regressed [Figure 4]. The child was discharged with the counseling to

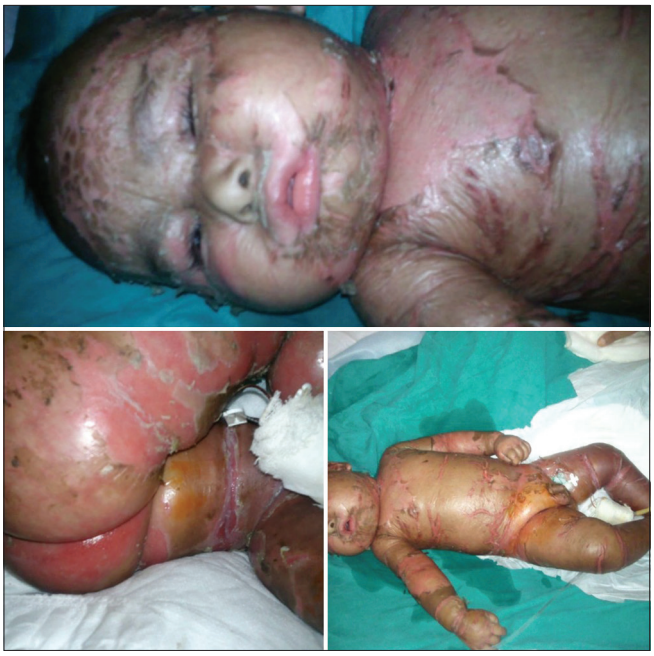

Figure 1: Periorificial dermatitis with skin peeling all over the body

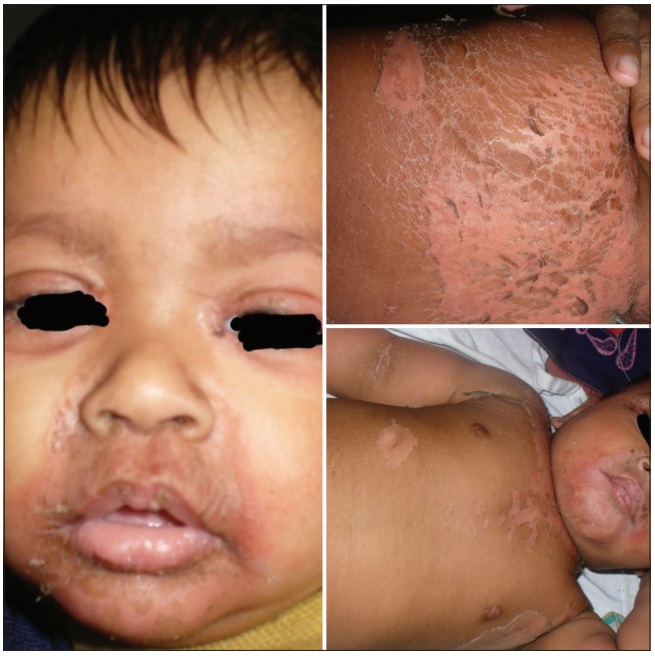

Figure 2: A case of staphylococcal scalded skin syndrome

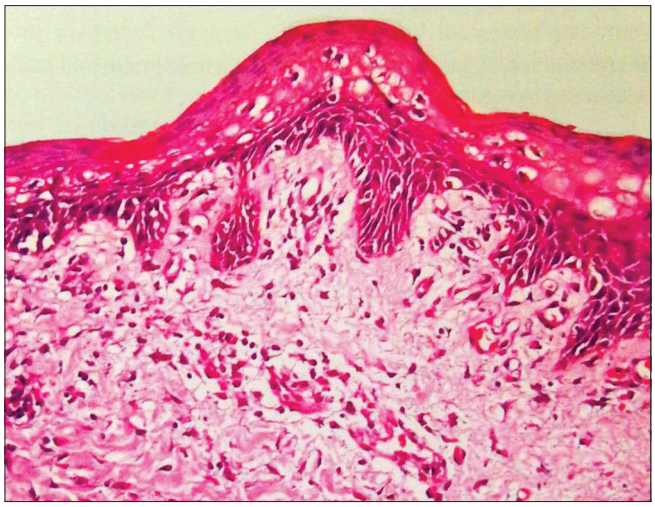

Figure 3: Histopathological image showing parakeratosis, extensive vacuolization of the upper epidermis, acanthosis and spongiosis in the epidermis and perivascular lymphocytic infiltration in the papillary dermis

the parents regarding continuation of syrup zinc lifelong. They were also advised to include seafood, liver, eggs, meat, legumes, nuts, whole grains, and leafy vegetables in the child's diet, which are good sources of zinc.

The oatient was brought to follow-up after 2 months, and he was perfectly fine, growing well. The parents were following the advice of zinc supplementation diligently.

Discussion

Zinc is an essential trace element required for the adequate functioning of the cells and plays an important role in the metabolism of proteins, carbohydrates, and Vitamin A.[1] It is a cofactor of various enzymes such as alkaline phosphatases, alcohol dehydrogenase, and RNA polymerase.[2] Zinc deficiency can be acquired or inherited. The causes of acquired zinc deficiency include premature infants, low birth weight, zinc deficiency in maternal milk, exclusive parenteral nutrition, malabsorption syndromes such as Crohn's disease and celiac disease, alcoholism, low calcium and phytate diet, and kwashiorkor.[3]

The inherited deficiency of zinc is classically known as "AE." It is caused by an autosomal recessive mutation of SLC39A4) gene on chromosome 8q24.3, which leads to a congenital partial or total deficiency of the zinc transporter protein ZIP 4.[4]

The clinical manifestations of acquired zinc deficiency and AE are similar and consist of three main symptoms: periorificial dermatitis, alopecia, and diarrhea. This clinical triad is observed in only 20% of patients with AE.[5] The lesions that usually start as erythematous, eczematous lesions are rarely vesiculobullous or pustular lesions, located around perioral, anogenital, and acral areas. Without treatment, skin lesions become erosive and spread to other periorificial areas of the face (eyes, nose, and ears), neck, lower abdomen, back, inguinal area, and thighs. Diffuse alopecia, loss of eyelashes and eyebrows, glossitis,

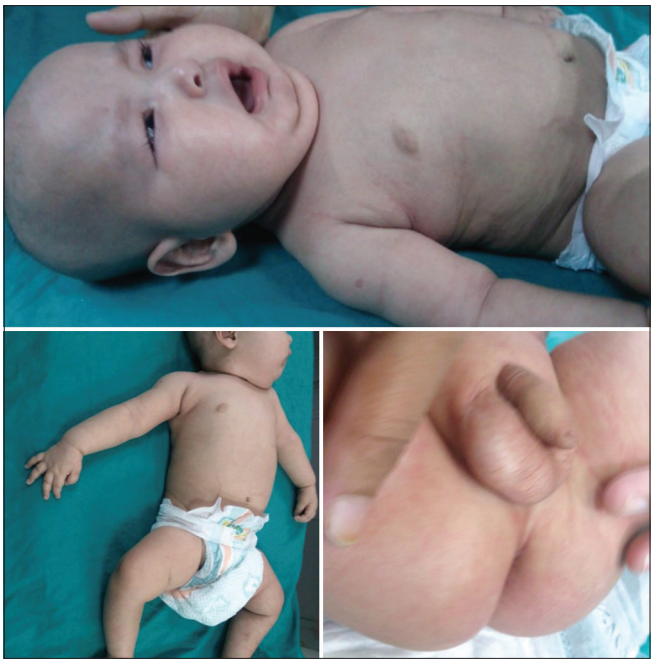

Figure 4: A case of staphylococcal scalded skin syndrome

gingivitis, stomatitis, onychodystrophy, onycholysis, and pachyonychia are observed in long-standing untreated cases.[6] In our case, the classical triad was observed in the form of alopecia, diarrhea, and skin lesions starting periorificially.

Diarrhea can be intermittent or totally absent. Children with prolonged watery diarrhea in AE usually manifest neuropsychological symptoms, such as irritability, lethargy, depression, and anorexia. Growth retardation, anemia, and ophthalmic symptoms of photophobia, blepharitis, and conjunctivitis are commonly seen.[7] Secondary bacterial infections and candidiasis (*Candida albicans*) can modify the clinical picture. In our case also, the child was only being treated for skin infections and not the underlying condition before presenting at our institute. The clinical findings of AE present with a broad spectrum and make the diagnosis challenging. The diagnosis is established by clinical symptoms, with or without low plasma zinc levels and rapid clinical response to zinc supplementation.[8]

Low hemoglobin, serum alkaline phosphatase and serum zinc levels, hypoproteinemia, skin lesions starting periorificially, alopecia, and diarrhea led us to the diagnosis of AE, which was further confirmed by dramatic clinical response to oral zinc supplementation within a few days.

The differential diagnoses to consider are superficial bacterial and fungal skin infections, napkin psoriasis, atopic dermatitis, seborrheic dermatitis, contact dermatitis, Langerhans cell histiocytosis, and cystic fibrosis.[9] Once the diagnosis is established, the treatment consists of daily oral zinc supplementation in the dose of 1–3 mg/kg, which leads to a rapid disappearance of the symptoms within a few days. With treatment, the survival rate is 100% and children show

normal growth physically and neurologically.[10] Parents need to be counseled regarding life-long treatment and monitoring of this condition.

Conclusion

AE mimics many dermatological diagnoses in pediatric patients such as SSSS, congenital bullous ichthyosiform erythroderma, Steven–Johnson's syndrome, and other dietary deficiencies. Hence, pediatric patients of chronic diarrhea, skin lesions, and growth retardation should be evaluated for serum zinc levels and given a trial of zinc supplementation therapy to prevent mortality.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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