Acrodermatitis Enteropathica – a Zinc Deficiency State

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SUMMARY
Successful therapy with zinc sulphate is reported in 3 children suffering from acrodermatitis enteropathica.


Acrodermatitis enteropathica is a rare autosomal recessive disorder. It is characterized by skin lesions, diarrhoea and alopecia. The skin lesions are typically vesicobullous and pustular during exacerbations and eczematosioid or psoriasiform during quiescent phases of the disease. They are found at mucocutaneous junctions and on the extremities.

Onset of symptoms usually occurs within the first few months of life, frequently in association with the change in diet from breast milk to cow's milk. Management of this condition in the past has consisted of complete abstinence from cow's milk, the use of human milk where necessary and the daily administration of di-iodohydroxyquinoline. Relapses on this form of treatment are frequent and complete control is often not possible. Furthermore, cases of optic atrophy caused by di-iodohydroxyquinoline have been consistently reported since 1966.

Recently Moynahan and Barnes described a girl with acrodermatitis enteropathica who failed to respond to any of the known forms of therapy. The trace elements in the serum were studied and she was found to be deficient in zinc. Oral zinc supplementation resulted in dramatic improvement of the clinical condition, with tolerance of a normal diet. Subsequently Moynahan reported the successful treatment of 9 further patients with oral zinc sulphate. This finding has been confirmed by others. We should like to report the successful management of 3 further cases.

CASE REPORTS

Case 1
A 1-month-old boy presented with an extensive eruption around the mouth and anus. This occurred after his mother stopped breast feeding and began feeding him on cow's milk. The cow's milk was stopped and breast feeding restarted, with a resultant improvement in his condition. He remained well while on breast milk, but at 6 months of age he was again weaned on to cow's milk. There was exacerbation of his symptoms and management with di-iodohydroxyquinoline and strict dietary control became necessary. He remained reasonably well on this regimen until he was 4 years old. At this stage, for no obvious reason, he developed severe diarrhoea, extensive skin lesions and alopecia. It took 9 months to regain control over his condition. He remained well for only 9 months. He then, at the age of 6 years, developed photophobia. This was thought to be caused by the di-iodohydroxyquinoline, which was discontinued. He relapsed immediately with severe manifestations of the disease and was admitted to hospital. A full blood count, urea and electrolytes, serum proteins and immunoglobulins were all normal. Serum zinc was low: 360 µg/l (normal 1 200 ± 190 µg/l). He was given oral zinc sulphate (50 mg 3 times a day) and there was a dramatic overall improvement of his condition within a week. The serum zinc level 2 weeks later was 2 240 µg/l. His condition has remained well controlled and he has been on a normal diet for 10 months.

Case 2
The 13-year-old sister of patient 1 had presented with similar symptoms and had had similar problems in childhood. At the time of her brother's admission to hospital she had been fairly well controlled on di-iodohydroxyquinoline with dietary restriction. She did, however, have seborrhoeic dermatitis on her scalp, eczematosioid lesions on her limbs and some dystrophy of her nails. The serum zinc level was 670 µg/l. Di-iodohydroxyquinoline was stopped and she was observed for 2 weeks on a normal diet. During this time her skin lesions became progressively more marked. Treatment with zinc sulphate (50 mg 3 times a day) was then started. Within 2 weeks her skin lesions had cleared completely.

Case 3
This boy presented at 2½ years of age with eczematosioid lesions at mucocutaneous junctions, bullous and pustular lesions on the extremities (Figs 1 - 3), and alopecia. He had never had diarrhoea. He had a history of recurrent severe napkin dermatitis from 1 week of age and although he had had no definitive treatment, he had enjoyed spontaneous remissions of several months' duration. The serum zinc level was 900 µg/l. As with the other patients, the response to zinc sulphate (25 mg 3 times a day) was dramatic and the lesions cleared within a week. The serum zinc level was then 840 µg/l.
DISCUSSION

Zinc is an essential element whose deficiency retards growth and maturation in animals and plants. Numerous zinc metallo-enzymes are concerned in the regulation of cellular growth, and zinc ions are needed for efficient nucleic acid and protein synthesis. Zinc deficiency in animals produces abnormalities of skin and appendages such as hair, horns, nails and hooves.

Although low levels of zinc are described in association with conditions such as kwashiorkor, tissue injury and with phytate-rich diets, no true zinc deficiency state has been described in man. Acrodermatitis enteropathica seems to fulfill the criteria in that low levels of zinc are found and administration of zinc completely reverses the condition. The addition of very small amounts of zinc to the diet will reverse the clinical picture even if the serum zinc level is not appreciably altered (as is demonstrated in case 3).

The nature of the defect in acrodermatitis enteropathica is at present unknown, despite the thorough investigation of recently reported cases. The lack of an appropriate gastrointestinal transport factor, which is corrected by additional oral zinc, is one of several possibilities. It is still not understood why breast milk is beneficial whereas cow’s milk, which contains the same amount of zinc, is definitely harmful. Nor is the therapeutic action of diiodohydroxyquinoline understood. The therapeutic role of zinc in acrodermatitis enteropathica has opened horizons for the further study of zinc metabolism in animals and man.

We know that zinc metabolism is disturbed in acrodermatitis enteropathica as well as in other conditions. However, the clinical and biochemical association in these conditions is by no means constant. This was well demonstrated in the patients described here. Whereas patients I and 2 presented with florid classic acrodermatitis enteropathica, with regard to both clinical features and low serum zinc levels, patient 3 had a purely dermatological problem. In addition, he had spontaneous remissions and on successful therapy serum zinc levels had in fact remained relatively unchanged — just below the lower limit of normal.

The possible role of zinc in the management of persistent dermatological and even gastro-intestinal problems remains to be investigated. At present we can only strongly recommend the use of oral zinc sulphate for the management of acrodermatitis enteropathica, and it seems that continuous maintenance therapy will be necessary.

REFERENCES