ORIGINAL CONTRIBUTIONS

HYPOZINCEMIA IN INFANCY

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An infant had hypozincemia and features of acrodermatitis with onset of the disease before weaning and its disappearance after weaning off. Low zinc level in the mother's milk was responsible for hypozincemia in this exclusively breast-fed infant which is in contrast to the classical acrodermatitis enteropathica where jejunal absorption is defective. There were seven more children in the family affected in a similar manner.

Key words : Hypozincemia, Acrodermatitis enteropathica, Zinc.

The role of zinc as a micronutrient for promoting infant growth and development is becoming increasingly evident. In 1942, Danbolt and Closs[1] named a group of symptoms as acrodermatitis enteropathica (AE). In 1974, Moyanahan[2] pointed out that this is a zinc deficiency disorder, and hypothesised that the absence of an enzyme oligopeptidase from the intestine is responsible for hypozincemia in these cases and proves lethal in majority of them. Other findings like failure to thrive;[3] low serum zinc levels,[4] B-lipoproteinemia,[5] low levels of low density lipoproteins,[6] agammaglobulinemia,[7] fibrocystic disease,[8,9] IgM-IgA deficiency,[10] and IgG-IgA deficiency[11] have been reported in association with AE. A variant of AE with lactose and fructose intolerance[12] and another with decreased succinic dehydrogenase and leucine aminopeptidase levels in the intestinal mucosa[13] have been described. Abnormalities of fat metabolism have also been documented.[7]

Evans et al[14] studied the mechanism of zinc absorption in rats. Their findings suggest, that a zinc-binding ligand from pancreas, receptor sites on the basolateral membranes of intestinal epithelial cells, and metal-free albumen; interact with each other and help in the absorption of zinc from the intestine. Hurley et al[15] reported the presence of a zinc-binding ligand in human milk also. Although the exact mechanism of action of these zinc-binding ligands has not so far been defined, they almost certainly facilitate zinc absorption from the intestinal lumen. Atherton et al[16] have demonstrated a pronounced defect in the in vitro uptake of zinc in the jejunal biopsies from patients having AE. In classical AE, the symptoms first appear at the time of weaning. Aggett et al[17] in 1980, reported AE-like symptoms in a preterm infant who was exclusively breast fed. However, jejunal zinc accumulation in this case was normal in contrast to the classical AE. Since then a number of other similar cases[18-20] have been reported. It was later on found that unlike AE, the mothers of these children have defective mammary zinc secretion[21] leading to zinc deficiency in their babies. None of these reported cases had any significant family history to suggest the mode of inheritance of this defect.

We are reporting a breast fed baby with AE-like symptoms who had low serum zinc levels.

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His mother's milk was deficient in zinc and the level did not rise even after oral zinc supplementation, though her serum zinc level rose to higher than normal. Interestingly, there are seven other living children in the same family who also suffered from AE-like symptoms during infancy, but recovered completely after they were weaned off their mother's milk.

Case Report

A 5-month-old male child, born at 34-week gestation to healthy unrelated parents, was brought to us with skin eruptions of two months duration. He was being fed exclusively on breast milk. His first three months of life were uneventful, but in the 4th month, he developed an eruption on the peri-anal area. After about a month, similar lesions appeared on the face and then over the hands and feet a few days later. There was no diarrhoea or hair loss. He was irritable. The lesions were symmetrical, well defined and dermatitic, over the face, ears and the back of scalp. The lesions around nostrils were crusted and those below the mouth were wet and macerated (Fig. 1). Similar lesions were seen over the buttocks, peri-anal area, some fingers, toes and the back of heels (Fig. 2). Hair, nails and mucous membranes were normal. Systemic examination did not reveal any abnormality.

Haemoglobin was 10 gm/dl. TLC was 9,800/cmm. DLC was normal. Blood ESR was 2 mm. Smear from the skin lesions was negative for candida. A provisional diagnosis of acrodermatitis enteropathica was made. Serum zinc level estimated by the atomic absorption spectroscopy (Pye Unicam SP 1900 Spectrophotometer) was 39 μg/dl (Normal value 60-120 μg/dl).

One living brother, aged 5 years, and one sister who died at the age of 7 months had suffered from similar symptoms around the same age. Patient's mother has three sisters,

Fig. 1. Dermatitis on the face and ears.

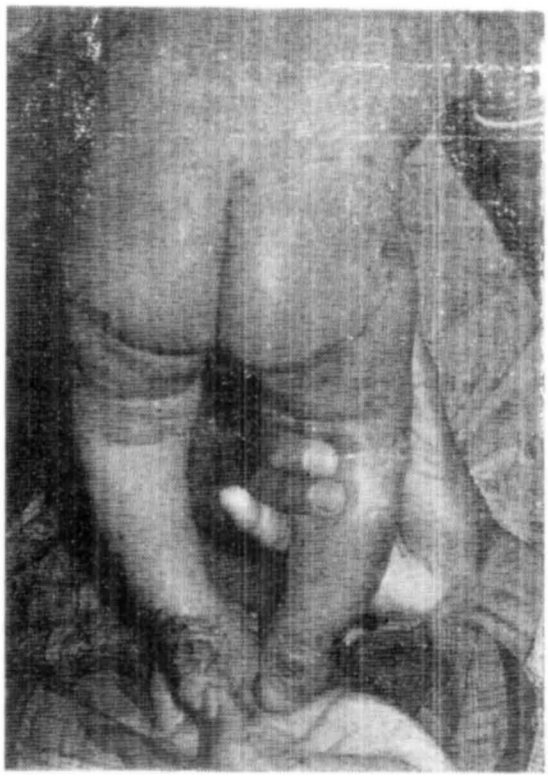

Fig. 2. Dermatitic lesions on the buttocks and heels.

twoof them are also married in the same family; one to her husband's brother and the other to the husband's uncle. Except for one female child, all the six children of both these sisters had also suffered from similar disease in their infancy (Fig. 3). The symptoms would appear around three months of age and last till the age of 12-14 months. Weaning in this family is started around eighth month and by the age of 12-14 months, the child is completely weaned off.

The patient was put on oral zinc therapy in a dosage of 50 mg zinc sulphate (11.3 mg of elemental zinc) per day. His irritability reduced within 24 hours and the skin lesions healed completely after 7 days of treatment. However, on the 10th day he developed diarrhoea with blood. Zinc therapy was stopped and he was put on antidiarrhoeal medication. With this, the diarrhoea was controlled in 4-5 days time. Zinc therapy was reintroduced but in a reduced daily dosage 25 mg of zinc sulphate (5.6 mg elemental zinc) divided into two doses. This dose was also not tolerated and he again developed diarrhoea. The dose was further reduced to 15 mg of zinc sulphate (3.4 mg of elemental zinc) per day divided into two doses which was tolerated well and the child was discharged from the hospital on this dosage. His serum zinc estimation after a period of 2 months of therapy was 90 μg/dl. In a follow up period of 4 months, the child was progressing well without any symptoms except for an attack of diarrhoeal treatment.

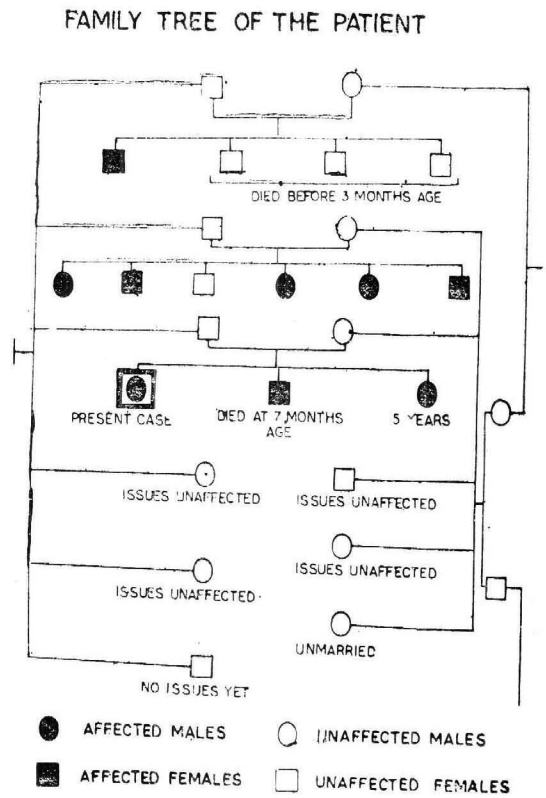

Fig. 3. Family tree of the patient.

Zinc level in the mother's serum was 88 μg/dl and 20 μg/dl in the breast milk (Normal value for the 5th month of lactation is 60-90 μg/dl. She was put on oral zinc supplement (220 mg of zinc sulphate daily) for a period of 5 days after which her serum and milk zinc levels were 600 μg/dl and 20 μg/dl respectively.

Comments

There were some unusual features in this family having acrodermatitis enteropathica, such as, early onset of the disease while the babies were still exclusively on breast feed and complete clearance of the symptoms after weaning off. A few cases of a similar nature have been reported earlier. [18-22] Zinc levels in the milk and serum of the mother were similar to those reported by Zimmermann et al,[21] i.e. serum zinc level was normal but the breast milk level was low. After oral zinc supplementation also, her milk zinc level failed to rise though her serum zinc rose to more than normal, suggesting thereby poor zinc secretion in the mother's milk leading to deficiency symptoms in her baby.

Thus, it seems reasonable to divide hypozincemia in infancy into three categories : (1) An inherent defect in the absorption of zinc from the gut i.e. classical AE (Type-I). (2) Defective secretion of zinc in mother's milk (Type-II) (3) Preterm infants who are put on prolonged parenteral alimentation (Tye-III). The proposed differentiation is useful in predicting the course and prognosis of hypozincemia in infancy. Symptomatology in all the three types is identical and is due mainly to low zinc levels. The first two types are definitely due to an inherent defect. The classical AE i.e. type-I is already known to be inherited as autosomal recessive. The genetic nature of the now proposed type-II defect was suspected by Zimmermann et al[21] but there was no family study available to substantiate it. Our report of the present case and his family is suggestive of either an autosomal recessive or sex linked inheritance. Type-III defect is essentially an acquired, temporary phenomenon in which the zinc deficiency symptoms are due to low body zinc reserves owing to prematurity and prolonged intravenous alimentation. Additional factors like excessive urinary or faecal losses may also contribute in producing or aggravating hypozincemia in such cases.

The most important point to differentiate between the first two types is the time of onset of symptoms. In type-I, the mother's milk plays a protective role against hypozincemia, whereas the same is responsible for it in type-II defect. Further more, in the latter, the mothers do not suffer from any deficiency symptoms as their serum zinc levels are normal, though they carry the trait for poor zinc secretion in breast milk. Only the optimal transport of zinc into the milk is defective. Zimmermann et al[21] hypothesised that it is due to the abnormality of a zinc-binding ligand in the breast milk. An exactly similar defect of mammary zinc secretion has been reported by Piletz and Ganschow[22] for a lethal milk mouse mutant where the pups develop acute dermatitis and die within 5-10 days of birth because of zinc deficient milk of the mothers.

From the family history, it will be noticed that one female child escaped from the disease. Detailed questioning revealed that her mother suffered from severe burns when the baby was three month old. Due to her mother's illness, this baby was weaned off early and probably this was the reason that she escaped from hypozincemia and its associated symptoms.

The prognosis in type-II defect is far better than in type-I and that is another important reason for differentiating the two. In the former, the disease disappears completely when the child is weaned off. Afterwards, these children thrive well without any zinc supple-

ment. For such cases, Leigh et al[23] preferred the term 'hypozincemia in infancy' to AE in view of the fact that the onset was earlier and the jejunal zinc accumulation was normal. Their reasoning is justified as in these cases there is no enteric pathology.

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