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Anorexia nervosa responding to zinc supplementation: A case report

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Summary:
An emaciated 16-year-old female with anorexia nervosa was hospitalized for treatment of vomiting, epigastralgia and diarrhea. The finding of a taste disorder, low serum alkaline phosphatase activity and relatively low serum zinc level strongly suggested a zinc deficiency. Zinc was initially administered intravenously (40 μmol/day) for 7 days, then orally (15 mg elemental zinc/day) for about 60 days. Her digestive symptoms disappeared after the second day of intravenous treatment and she began to gain weight. She rapidly regained her normal weight after one month of receiving the oral zinc supplementation. Both exocrine pancreatic function and intestinal absorption were improved by the prolonged oral administration of zinc. In such cases zinc supplementation may be a therapeutic option in addition to psychologic and other approaches to management. *Gastroenterol Jpn 1992;27:554-558.*

Key words: *anorexia nervosa; exocrine pancreas; intestinal absorption; zinc deficiency.*

Introduction

Anorexia nervosa is considered to be induced by psychophysiological factors. Severe weight loss due to self-starvation can lead to life-threatening emaciation, the mortality of which is as high as 21.5%[1,2]. An elemental diet or intravenous hyperalimentation is often administered to rapidly improve the patient's nutritional status.

This report describes a patient with anorexia nervosa whose symptoms responded to the intravenous administration of zinc with continued oral zinc supplementation, and considers the relationship between anorexia nervosa and zinc deficiency.

Case Report

A 16-year-old girl was admitted to Kyushu Rosai Hospital with severe weight loss, vomiting and diarrhea. Three months before admission she had become concerned about her thick ankles and began to restrict her food intake, especially of meat. Her body weight fell from 43 kg to 31 kg, and she became amenorrheic. Although she then tried to eat normally, the development of vomiting, epigastralgia and diarrhea prevented any weight gain.

On admission she was 156 cm tall and weighed 31 kg (58% of ideal body weight). Except for dry skin and yellowish palms and soles, no skin lesions were noted. While there was mild epigastric tenderness, no other abnormalities were detected on the physical examination.

As shown in **Figure 1**, the patient's serum alkaline phosphatase was significantly low, 38 IU/l (normal; 75-200 IU/l). Her serum levels of protein, cholesterol, electrolytes, and blood urea nitrogen were all within the normal range. Serum level of trace metals were: zinc; 66 μg/dl (normal; 65-110 μg/dl), iron; 56 μg/dl (normal; 60-120 μg/dl), and copper; 120 μg/dl (normal; 89-147 μg/

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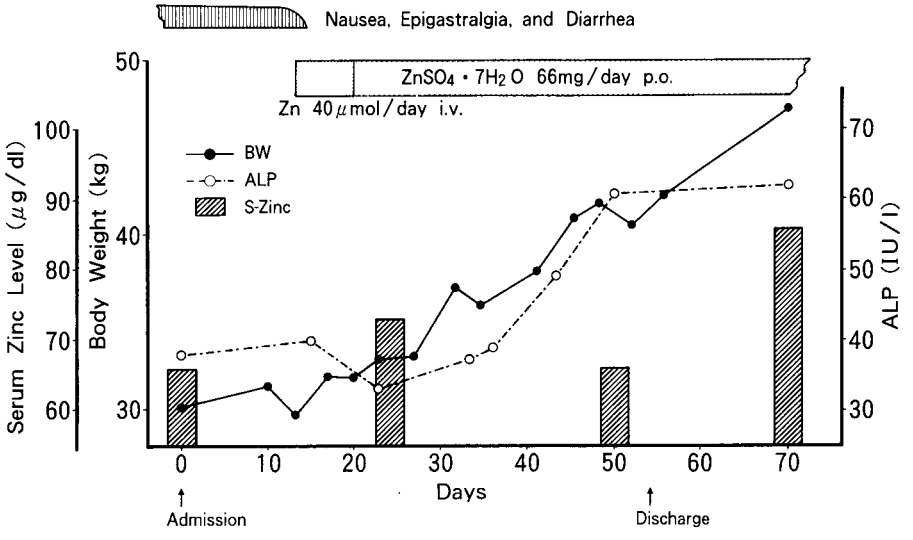

Figure 1. Clinical course of anorexia nervosa during zinc supplementation. BW: body weight, S-ALP: serum alkaline phosphatase, S-Zinc: serum zinc level.

dl). The serum carotene level was increased to 484 μg/dl (normal; 80–400 μg/dl), but the serum level of vitamin A was normal at 865 ng/ml (normal; 410–1200 ng/ml). The serum level of growth hormone was slightly increased (5.4 ng/ml). The levels of triiodotyronine (34 ng/dl) and thyroxine (4.2 μg/dl) were both decreased, suggesting low T_3 syndrome. No lesions were observed on endoscopic examination of the upper gastrointestinal tract.

The patient's symptoms persisted during hospitalization, despite the administration of anticholinergics and a minor tranquilizer, so that her weight decreased to 29.5 kg. Since she complained of not enjoying her meals as before, a taste disorder was suspected. Performance of a test of taste acuity using zinc sulfate[3] confirmed the presence of hypogeusia. In this test, she could not distinguish a solution of 0.1% $ZnSO_4$-$7H_2O$ from water. The findings of a taste disorder, low serum alkaline phosphatase, and a relatively low serum level of zinc strongly suggested a zinc deficiency.

Zinc supplementation was begun with the administration of 40 μmol of zinc given daily for 7 days, followed by the oral administration of zinc sulfate ($ZnSO_4$-$7H_2O$), 66 mg/day, containing 15 mg of elemental zinc. On the second day of intravenous zinc administration the patient's vomiting, epigastralgia and diarrhea disappeared. She gradually became active and began to enjoy her meals without any psychiatric care. After only one month of receiving the zinc supplement, she regained her normal weight (43 kg) without the administration of an elemental diet or the need for intravenous hyperalimentation. Tests of exocrine pancreatic function and intestinal absorption were performed before the start of zinc supplementation and after she had regained body weight, and these tests proved both improvement of exocrine pancreatic function and intestinal absorption. Secretions of pancreatic enzyme and bicarbonate were determined by gastrointestinal intubation following stimulation by caerulein (0.05 μg/kg BW) and secretin (1 U/kg BW). Results of these tests were as follows: caerulein-secretin test: maximum bicarbonate concentration; 87.1 mEq/l to 122.5 mEq/l (normal; >70.9 mEq/l), amylase output; 1621 Somogyi U/kg to 2961 Somogyi U/kg (normal; >1370 Somogyi U/kg), D-xylose urinary excretion after 5 g of D-xylose ingestion; 1.4 g to 2.9 g (normal; >1.5 g). The patient was discharged after 41 days of zinc replacement therapy. Although alopecia and pitting edema of the lower legs developed during observation, these symptoms disappeared with a return to normal weight. Zinc administration was continued until one month after discharge. Six months after discharge, the patient's weight remains stable at

47 kg and she is asymptomatic.

Discussion

The existence of a zinc deficiency was initially suspected in this case of anorexia nervosa from the low serum level of alkaline phosphatase. While the serum alkaline phosphatase level is often higher than normal in teenagers because of their rapid bone metabolism, its value was quite low in this 16-year-old patient. Since alkaline phosphatase is one of the many metalloenzymes of zinc, its serum level would depend on the patient's zinc status[4], except for the increase in the leakage of this enzyme from organ tissue into blood, as seen, for example, in case of liver dysfunction. The taste disorder observed in this patient provided additional evidence for a zinc deficiency. It was previously reported that a patient with zinc deficiency showed hypogeusia[5]. Bryce-Smith and Simpson developed a test to evaluate the existence of hypogeusia caused by zinc deficiency[3]. Patients with this disorder cannot distinguish a solution of 0.1% $ZnSO_4$-$7H_2O$ from water. Hypogeusia in our patient was confirmed by this taste test, and following the administration of zinc supplementation her taste sensation returned to normal. Casper et al. reported that in anorexia nervosa the ability to taste for bitter and sour substances was severely affected, while that for salty and sweet substances was unaffected[6]. Katz et al. reported that anorexic patients had a significantly lower sensitivity to sweet substances[7]. As not every taste sensitivity is affected, anorexic patients may not be conscious of their taste disorder, but instead complain of a loss of appetite. The serum level of zinc in this case was low but within the normal range. This serum zinc level may not reflect the real value because of the hemoconcentration caused by rapid emaciation. There was, however, no evidence of hemoconcentration in this case according to the normal values for hematocrit, serum protein, and blood urea nitrogen. If the serum zinc level is below normal, a zinc deficiency would surely be recognized. However, a normal serum zinc level does not necessarily exclude the existence of a zinc deficiency, as the level of zinc may be affected by diurnal rhythm, the ingestion of food, accidental hemolysis, or contamination during blood sampling. There also remains the question as to whether the normal range for serum zinc is the same in teenagers as in adults, because of the much greater demand for zinc in the former. There is currently no reliable means of determining the status of body zinc that is practical for routine clinical use[8]. Accordingly, zinc status should be evaluated comprehensively, considering the serum level of alkaline phosphatase and of serum zinc, and the existence of a taste disorder, among other relevant findings.

We suspected that this patient may have developed zinc deficiency because she strictly limited her intake of meat, a major source of zinc[8]. The demand for zinc is increased during growth, so that some teenagers may perhaps have a latent zinc deficiency[8]. A decreased intake of zinc in teenagers would induce an overt zinc deficiency, and this would develop hypogeusia. Besides the loss of appetite caused by this hypogeusia, such digestive symptoms as vomiting, epigastralgia and diarrhea may also decrease her intake and absorption of zinc, and develop an overt zinc deficiency.

Bakan was the first to speculate that zinc deficiency may play a role in the etiology of anorexia nervosa[9], considering the similarity of the symptoms of anorexia nervosa and those of zinc deficiency; weight loss, appetite loss, disorders of sexual development, skin lesions and nausea. He cited three factors as possibly responsible for a zinc deficiency. The first is stress. Females whose zinc status is marginally dificient may be adversely affected by unusually severe stress[10]. The second is estrogen. Young females experience increased levels of estrogen naturally, and oral contraceptives have been reported to decrease plasma levels of zinc[11]. The third is dietary habits. Teenagers in the United States frequently consume soya products which contain phytic acid and phosphorous, substances which inhibits the absorption of zinc. These factors would explain the frequent finding of anorexia nervosa in young females during such stressful situations as puberty, college entrance examinations or marriage. Casper et al. reported that plasma levels of

zinc were significantly lower in patients with anorexia nervosa than in a control group[6], thus supporting Bakan's hypothesis.

Although it is understandable that a deficiency of zinc may be induced in a patient with anorexia nervosa as described above, it is interesting that the anorexia nervosa in our patient seemed to respond solely to the administration of zinc supplements. The patient's increased appetite with the recovery of her sense of taste may have been one contributory factor to the increased intake of food. However, in this case, the disappearance of the digestive symptoms and the improvement of exocrine pancreatic function and of intestinal absorption may have been more important regarding the weight gain. Digestive symptoms such as vomiting and epigastralgia may be attributed to psychogenic factors, or to the so-called SMA syndrome, in which the third portion of the duodenum is squeezed between the abnorminal aorta and the superior mesenteric artery because of emaciation[12]. It is reported that patients with anorexia nervosa can develop acute pancreatitis[12,13]. The digestive symptoms in our patient, which had failed to respond to the administration of a minor tranquilizer and anticholinergic agents, disappeared on the second day of intravenous zinc replacement therapy, preceding any weight gain, and her serum amylase level was within the normal range. Therefore, her symptoms may have resulted from a zinc deficiency. More than 100 metalloenzymes that contain zinc as a co-factor have been discovered, for example, DNA polymerase and RNA polymerase, suggesting that zinc metalloenzymes may be closely related to the synthesis and metabolism of protein[14,15]. The pancreatic acinar cell is a major source of digestive enzymes, and there is active protein synthesis in the pancreas. The intestine is a site of continuous renewal of absorptive cells and transport proteins. Therefore, the pancreatic acinar cells and the intestinal absorptive epithelium may be particularly sensitive to zinc deficiency[16,17] Sandstead et al reported that the impaired synthesis of DNA induced by a dietary zinc deficiency in the rat returned to normal only 24 hours after a single injection of zinc[14]. The improvement of exocrine pancreatic function and intestinal absorption may be due to a rapid normalization of protein synthesis in the pancreas and intestinal epithelium.

Obviously, psychosomatic factors play an important role in the development of anorexia nervosa. If the patient persistently refuses to eat, zinc administration may of course be ineffective. It is essential to convince the patient that she has a distorted body image; thus, psychological treatment may be required. In addition, zinc replacement may relieve the taste disorder and the impaired digestive and absorptive functions, leading to an increased intake of food and weight gain. Katz et al reported that the depression and anxiety observed in anorexia nervosa also responded to the administration of zinc supplements[7]. There are only a few reports of patients with anorexia nervosa who responded to oral zinc replacement therapy[7,18-20]. One reason may be that there is no reliable parameter for confirming a zinc deficiency, so that the response to zinc is considered the most reliable measure[8]. Since zinc supplements are inexpensive and of low toxicity, zinc supplementation is a practical choice of therapy. The initiation of dosage by the intravenous route is recommended, because of the impaired intestinal absorption of zinc in anorexia nervosa[21].

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