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Selenium Deficiency during Long-Term Management of Crohn's Disease with Full Elemental Diet: A Case Report

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Abstract

Elemental diet (ED) is an efficacious treatment for patients with Crohn's disease (CD). A full ED, Elental® (Ajinomoto Pharmaceutical, Tokyo, Japan), is often used for induction and maintenance therapy in CD patients, particularly in those with abdominal pain due to active CD with expansive ulcers and multiple strictures. Selenium deficiency is rare, but occurred in patients under long-term management with full ED, because elental does not include selenium. A 35-year-old man had received long-term full ED treatment since the diagnosis of CD. Symptoms of curly, ulotrichous hair, recurved nails, dysarthria, visual disturbances and sensory disturbances of the limbs were exaggerated. Serum concentration of selenium was below the detection limit of 2.0 μg/dL. He was diagnosed with systemic disorder caused by selenium deficiency. With continuous administration of sodium selenite, hair and nail changes and dysarthria resolved, but visual and limb sensory disturbances remained unchanged. The present case suggests that selenium supplementation should be started when distinctive symptoms associated with selenium deficiency appear in a patient receiving long-term ED.

Keywords: Selenium deficiency; Full elemental diet; Crohn's disease

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Introduction

Crohn's disease (CD) is a chronic and progressive inflammatory disorder involving the entire gastrointestinal tract and is a disabling disease characterized by accumulated intestinal damage and loss of body weight [1]. Significant body weight loss also leads to loss of the mesenteric fat pad, resulting in superior mesenteric artery (SMA) syndrome [2]. This causes chronic, intermittent, or acute complete or partial obstruction of the duodenum [2].

The therapeutic strategies for CD comprise pharmacotherapies such as immunomodulators and anti-tumor necrosis factor (TNF)-α antibodies [3,4] and elemental diet (ED) such as Elental® (Ajinomoto pharmaceutical, Tokyo, Japan) [5]. Because ED offers a safe and effective therapy, full ED is often used for induction and maintenance therapy in patients, particularly those with abdominal pain due to active CD [5]. However, long-term full ED with Elental® can sometimes cause trace mineral deficiencies that are difficult to cover using commercially available oral materials [5]. Among various trace mineral deficiencies, selenium deficiency can damage multiple organs, and can even cause lethal heart failure because of the rarity of this clinical entity and the difficulty of diagnosis [6].

We report herein a rare case of selenium deficiency showing distinctive physical and neurological disorders under long-term management of full ED due to repeated abdominal pain from SMA syndrome associated with CD.

Case Report and Discussion

A 35-year-old man was referred to our hospital because of slow progression of visual disturbance and dysarthria in March 2016. He had been diagnosed with colitis-type CD at 22 years old. Since then, the patient has been taking mesalazine and a total of 1800 mL to 2000 mL (1 Kcal/mL) of ED in a day per orally, for the treatment of CD. In 2009, a small bowel series and colonoscopy showed normal results. The patient was in clinical remission. However, because repeated and continuous abdominal pain persisted, full ED (Elental®) was continued. In 2011, dysarthria emerged along with abnormalities of the hair and nails. On referral, physical examination revealed curly, ulotrichous hair, recurved and flat nails (Figure 1A and 1B), visual disturbance and sensory disturbance of the

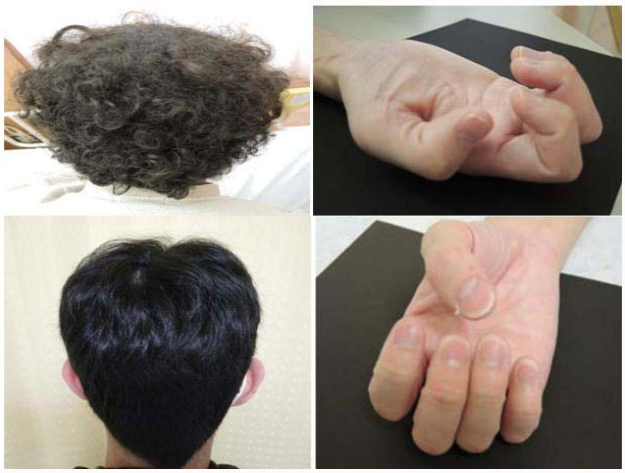

Figure 1: Appearance of the hair and nails. Curly, ulotrichous hair (A) and recurved, flat nails on the second, third and fourth fingers of the right hand (B) before administration of sodium selenite. Recuperated hair (C) and nails (D) six months after administered.

Table 1: Laboratory data for CBC, biochemistry, vitamins and trace mineral elements on admission.

CBC		ChE	408 U/L	Vitamin A	203 IU/mL
WBC	4100 /μL	T-Bil	0.6 mg/dL	B1	70 ng/mL
RBC	402 ×10⁴ /μL	BUN	16.8 mg/dL	B12	1660 pg/mL
Hb	15.6 g/dL	Cre	0.9 mg/dL	C	4.2 μg/mL
Ht	45.50%	UA	1.1 mg/dL	E	0.84 μg/mL
MCV	113.2 fL	Glu	68 mg/dL		
MCH	38.8 pg	TC	130 mg/dL	Fe	99 μg/dL
MCHC	34.30%	TG	50 mg/dL	Cu	91 μg/dL
PLT	23.3 ×10⁴ /μL	Na	140 mEq/L	Zn	82 μg/dL
		K	4.3 mEq/L	Mn	1.3 μg/dL
Biochemistry		Cl	104 mEq/L	Se	≤ 2.0 μg/dL
TP	7.1 g/dL	Ca	9.6 mEq/L		
Alb	4.5 g/dL	CRP	0.03 mg/dL		
AST	23 U/L				
ALT	33 U/L				
LDH	180 U/L				
ALP	176 U/L				
γ-GTP	21 U/L				

limbs and low body weight (height: 179 cm; weight: 58 kg; BMI: 18.1). Laboratory investigations demonstrated macrocytosis with (mean corpuscular volume (MCV), 113.2 fL), and, high concentration of vitamins B1 and B12. Trace mineral elements (Fe, Cu, Zn and Mn) were within normal ranges (Table 1). Brain magnetic resonance imaging and angiography showed normal results. Ophthalmological examination showed that appearance of the optic discs and flicker sensitivity was normal. Visual evoked potential (VEP) testing showed that amplitude of the P100 wave was decreased during pattern stimulation. Abdominal computed tomography (CT) showed partial compression of the third portion of the duodenum, which passes between the superior mesenteric artery and aorta, and dilatation of the oral side, resulting in SMA syndrome (Figure 2). Clinical history, hair abnormality and macrocytosis were suggestive of selenium deficiency. Serum selenium concentration was below the detection limit of 2.0 μg/dL. Based on these findings, a systemic disorder caused by selenium deficiency was diagnosed. Sodium selenite has not been approved for the treatment of selenium deficiency in Japan.

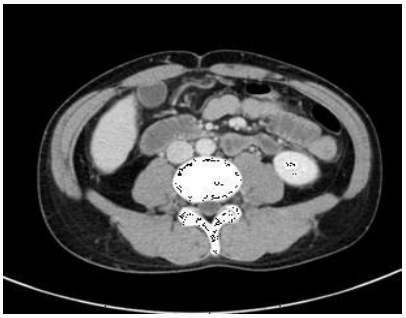

Figure 2: Abdominal CT with contrast media on admission shows partial compression of the third portion of the duodenum and the dilatation on the oral side. Superior mesenteric artery (SMA) syndrome was diagnosed.

Written consent was therefore obtained from the patient after a study protocol for sodium selenite administration was approved by Nagoya City University Ethics Committees. Intravenous administration of sodium selenite at 100 μg/day at day 1 and at 200 μg/day at day 2-7, was performed, and administration at 200 μg/day twice a week thereafter was continued. Six months after starting administration, curly and ulotrichous hair, nail changes and dysarthria gradually resolved (Figure 1C and 1D), and MCV rapidly normalized to 88.7 fL. Serum selenium concentrations gradually increased to 10.9 μg/dL (within normal limits) by December 2016. However, visual abnormalities and sensory abnormalities of the limbs remained unchanged, and persisted.

Selenium deficiency causes distinct physical manifestations like hair and nails changes, and visual and limb sensory disturbances, but definitive diagnosis is difficult due to the rarity. We have reported here a rare case of selenium deficiency in a patient receiving long-term management with full ED due to repeated abdominal pain from SMA syndrome associated with CD. Continuous administration of sodium selenite resulted in partial improvement.

Elental® comprises amino acids, very little fat, vitamins, trace elements, and a major energy source, dextrin, but, does not include selenium [5]. The therapeutic effects of ED such as Elental® reportedly result from reductions in not only immune stimulation in the gut [7] and intestinal permeability [8,9], but also the concentrations of cytokines associated with mucosal inflammation [10]. Thus, based on the usefulness of ED in CD patients, continuous full and/or half ED is frequently used for inducing and maintaining remission [5,11,12]. On the other hand, one report described the risk of decreased concentrations of serum selenium under long-term management with full ED [13]. In general, selenium deficiency is known to arise among 1 month to 6 years after starting total parenteral nutrition (TPN) [14-16]. Long-term full ED administration is also supposed to cause selenium deficiency. Clinical knowledge regarding increased risks for selenium deficiency during full ED, and signs and symptoms of selenium deficiency are generally lacking for physicians and gastroenterologists. In addition, sodium selenite has not been approved for the treatment of selenium deficiency in Japan. Therefore, a long time may pass before a definitive diagnosis of selenium deficiency is reached and treatment is started. In the present case, 13 years elapsed before treatment with sodium selenite was started.

Selenium is incorporated in glutathione peroxidase (GPx) and selenoprotein P as a key element, and plays an important role in the stability of the plasma membranes of neurons, erythrocytes, muscle and liver cells. GPxs act as reductases eliminating the oxidants and lipid peroxides constitutively produced in cells [17,18]. Attenuation of GPxs by selenium deficiency cause cardiac and skeletal myopathy [19,20], liver damage, erythrocyte macrocytosis [21,22], encephalopathy [21], neuropathy [21] and nail and hair abnormalities [6,22-24]. In particular, whitened nail beds in the hands and/or feet represent a well-known sign. In the present case, curly, ulotrichous hair was observed in addition to recurved and flat nails on the hands, but nail beds were not whitened. Based on the fact that nail changes gradually resolved soon after sodium selenite was administered, recurved and flat nails may also represent a symptom associated with selenium deficiency. Moreover, this suggested that changes to nails and hair might support definitive diagnosis of selenium deficiency and monitoring of the effects of therapeutic treatment, as the turnover of nails and hair is rapid.

Visual disturbance is another key symptom observed in selenium deficiency, and other neurological symptoms included dysarthria, spasticity of the extremities, ataxia and sensory disturbance. These manifestations occurred 1-12 years after starting TPN or elemental enteral nutrition [6,21,25]. In the present case, visual disturbances and sensory disturbances of the limbs remained unchanged, and persisted. Most cases with neurological disorders receiving sodium selenite have shown no or only slight improvement [21]. These unfavourable outcomes may mainly result from irreversible oxidative damage to the brain related to the low levels of GPxs and other selenoproteins due to selenium deficiency [25].

In conclusion, clinical history and manifestations including hair and nail changes, visual disturbances and sensory disturbances of the limbs, and macrocytosis may be useful to make a diagnosis. Since the prognoses of visual and sensory disturbances don't seem so good, selenium should be administered rapidly before those disturbances emerge if deficiency is suspected.

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