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Copper-deficiency anemia after esophagectomy: A pitfall of postoperative enteral nutrition through jejunostomy

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ABSTRACT

INTRODUCTION: Copper deficiency leads to functional disorders of hematopoiesis and neurological system. There have been some reports of copper deficiency occurring to the patients on enteral nutrition through a jejunostomy in long-term-care hospitals. However, it is extremely rare to find patients with copper deficiency several months after esophagectomy, regardless of enteral nutrition through the jejunostomy. To the best of our knowledge, this is the first case report of a patient who experienced copper-deficiency anemia after esophagectomy and subsequent enteral nutrition through the jejunostomy.
PRESENTATION OF CASE: A 73-year-old man presented with pulmonary failure after esophagectomy for esophageal cancer with video-assisted thoracoscopic surgery, and needed long-term artificial ventilator support. Nutritional management included enteral nutrition through a jejunostomy from the early postoperative period. Copper-deficiency anemia was detected 3 months postoperatively; therefore, copper supplementation with cocoa powder was performed, and both serum copper and hemoglobin levels subsequently recovered.
DISCUSSION: Copper-deficiency anemia has already been reported to occur in patients receiving enteral nutrition in long-term care hospitals. However, this is the first case report of copper deficiency after esophagectomy despite administration of standard enteral nutrition through the jejunostomy for several months.
CONCLUSION: It is extremely rare to find copper-deficiency anemia several months after esophagectomy followed by enteral nutrition through the jejunostomy. However, if anemia of unknown origin occurs in such patients, copper-deficiency anemia must be considered among the differential diagnoses.

1. Introduction

Copper plays a role as a cofactor for various enzymes in the human body, and is indispensable for myeloid and neurological structure and function.[1,2] Copper deficiency leads to functional disorders of hematopoiesis such as anemia and neutropenia, as well as neurological disorders such as myelopathy.[3–5] Copper is absorbed mainly from the duodenum and proximal jejunum, and partly from the stomach.[6,7] Some recent reports have noted that patients on enteral nutrition through a jejunostomy in long-term-care hospitals sometimes experience copper deficiency.[8] However, it is extremely rare to find patients with copper deficiency several months postoperatively, regardless of enteral nutrition through the jejunostomy. We report herein the case of a patient who experienced copper-deficiency anemia after esophagectomy and subsequent enteral nutrition through the jejunostomy. This patient recovered with copper supplementation.

2. Presentation of case

A 73-year-old man with a chief complaint of dysphagia was diagnosed with thoracic esophageal cancer at a local hospital. He was then referred to our hospital for further examination and treatment. He had no medical history of copper metabolic disorders such as Menkes disease or occipital horn syndrome, and family history

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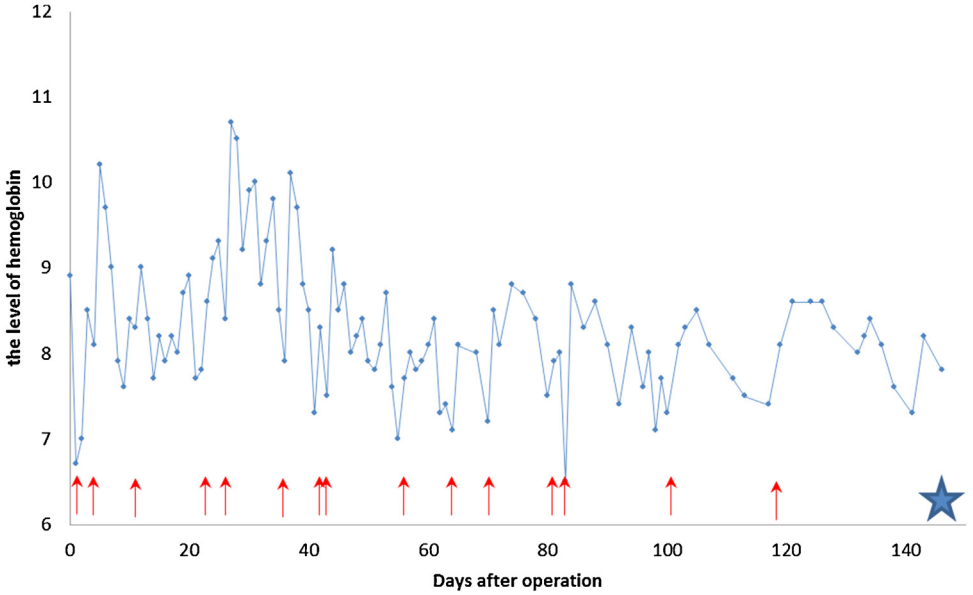

Fig. 1. Postoperative hemoglobin levels. Arrows, transfusions; star, first day of copper supplementation.

was not contributory. He had been smoking 20 cigarettes a day for 30 years and drinking 200 ml of red wine a day for 50 years. His preoperative laboratory tests and pulmonary function tests were within normal limits.

Preoperative diagnosis was cT1bN0M0 cStage IA (UICC TNM classification, 7th edition), and the patient underwent esophagectomy with two-field lymphadenectomy followed by reconstruction with a gastric tube via retrosternal route and jejunostomy. The jejunostomy tube (9 Fr) was inserted through the antrum of gastric tube, and the end of it was located at the ligament of Treitz through pylorus. Operation time was 9 h 52 min, and blood loss was 2420 ml, which was highly invasive to him. Moreover, the upper lobe of the right lung was twisted during the operation. It was fixed through emergent reoperation on the same day, but the patient developed subsequent severe pulmonary failure and required long-term artificial ventilatory support.

Oral intake was impossible due to his deteriorated deglutition ability; therefore, nutritional management started from postoperative day 3 as enteral nutrition with a small amount of standard nutrient solution through the jejunostomy. His general condition improved, and thus the amount of nutrient solution was gradually increased to 1210 kcal of energy and 1.6 mg of copper by 1 month postoperatively. By 3 months postoperatively, inflammatory response had completely disappeared, and no signs of bleeding or deficiency of serum iron, ferritin, folic acid or vitamin 12 were noted. However, the patient was suffering continuous anemia, and required intermittent transfusions (Fig. 1). Serum levels of copper and ceruloplasmin were 7 μg/dl (normal range, 68–128 μg/dl) and 8 mg/dl (normal range, 21–37 mg/dl), respectively. It was considered that copper deficiency was attributable to problems with the nutrition pathway, leading to copper malabsorption despite the seemingly ample copper administration. Copper supplementation using cocoa was then started. Ten grams of commercially available cocoa powder (0.4 mg of copper) was mixed with 100 ml of warm water, and then administered through the jejunostomy once daily in the morning (Fig. 2). No side effects arose from cocoa supplementation, and the 9-Fr nutritional tube did not become clogged by the cocoa/water mixture.

Serum levels of copper and hemoglobin gradually increased, reaching 76 μg/dl and 9.8 g/dl, respectively, by 61 days after starting cocoa supplementation. During the supplementation period, no transfusions were administered. As copper levels increased, zinc

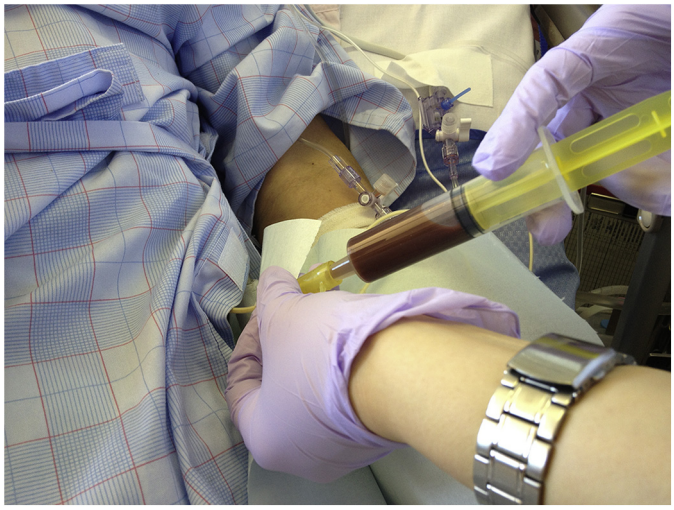

Fig. 2. Copper supplementation with cocoa powder through the jejunostomy.

levels decreased; however, none of the symptoms were attributable to zinc deficiency (Fig. 3). Since anemia was alleviated and the general condition of the patient improved, he was referred to another hospital to continue long-term rehabilitation.

3. Discussion

Copper-deficiency anemia has already been reported to occur in patients receiving enteral nutrition in long-term care hospitals.[9] However, to the best of our knowledge, this represents the first case to be reported of copper deficiency after esophagectomy despite administration of standard enteral nutrition through the jejunostomy for several months. The standard nutrient solution has been noted to lack the requisite amount of copper,[9] so most of the formulae for current nutrient solutions have been improved to meet this requirements. The recommended daily allowance of copper by the US National Academy of Sciences is 900 μg per day for adult men and women.[10] Japanese government recommends a dietary allowance of 700 μg per day in woman and 800 μg per day in men aged 18 years old and older.[11] The patient in the present case

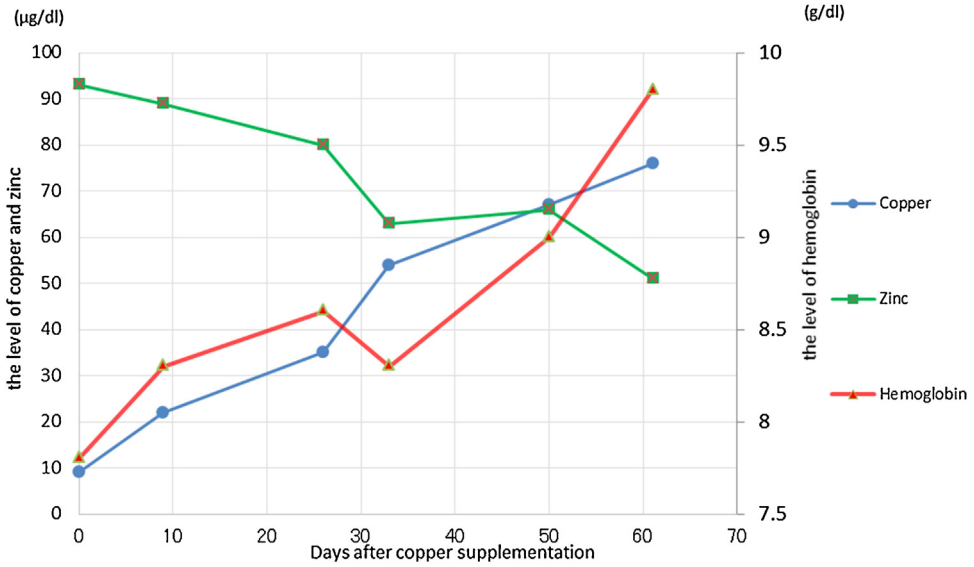

Fig. 3. Simultaneous increases in serum copper and hemoglobin levels after copper supplementation, and concomitant decrease in serum zinc levels.

suffered from copper deficiency despite administration of copper at 1.6 mg/day.

The main reason for copper deficiency in the present case was the nutritional pathway through the jejunostomy. Since nutrition bypassed the duodenum, which is the main site of copper absorption, copper deficiency must have occurred regardless of the seemingly ample administration. Nishiwaki et al.[8] reported that the mean serum copper level in patients with enteral nutrition through the jejunostomy declined from 93.6 μg/dl to 43.9 μg/dl in 6 months. Furthermore, copper deficiency resolved after changing the nutritional pathway from jejunostomy to gastrostomy. This result implies the importance of a nutritional pathway passing through the duodenum.

Copper deficiency after bariatric surgery has been reported in recent years.[12] Theoretically, copper deficiency can occur after other types of surgeries such as gastrectomy with Roux-en-Y reconstruction and pancreaticoduodenectomy because food does not pass through the duodenum in those cases. However, to the best of our knowledge, no such cases have been reported. Copper deficiency in those cases may not have been fully investigated, so this issue remains to be assessed in the future.

We acquired commercially available cocoa powder for copper supplementation in the present study. This source was selected based on the ease of obtainment and administration compared with other copper-rich foods such as crustaceans, organ meats, and beans. If this method had not worked well, we would have considered the following three methods: (1) increasing the level of copper supplementation up to 40 g/day, as described by Tokuda et al.[9]; (2) extracting the jejunostomy tube slightly so that the end of the tube could be placed in the stomach; or (3) intravenous administration of copper.

Copper and zinc are known to compete for absorption.[13] We also confirmed a decline in serum zinc levels as copper supplementation continued. No symptoms of zinc deficiency were encountered in this patient; however, we recognized that monitoring of serum zinc levels is necessary when copper supplementation is performed.

Some reports have described advantages of postoperative enteral nutrition after major surgical operations such as esophagectomy and pancreaticoduodenectomy,[14,15] and the nutritional pathway in those cases typically involves jejunostomy. We also routinely place a jejunostomy in patients after esophagectomy in our hospital. The present experience highlighted the possibility of copper deficiency, even if a seemingly ample amount of copper is being administered to the patient, when enteral nutrition through the jejunostomy is continuously performed for several months postoperatively. When treating such cases, regular monitoring of serum copper levels is warranted, and copper deficiency should be considered among the differential diagnoses for anemia of unknown origin.

4. Conclusion

It is extremely rare to find copper-deficiency anemia several months after esophagectomy followed by enteral nutrition through the jejunostomy. However, if anemia of unknown origin occurs in such patients, copper-deficiency anemia must be considered among the differential diagnoses.

Conflict of interest

Authors Masatoshi Nakagawa, Kagami Nagai, Isao Minami, Mai Wakabayashi, Junko Torigoe and Tatsuyuki Kawano have no conflict of interest or financial ties to disclose.

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There is no involvement of any sponsors in this study.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author contributions

Masatoshi Nakagawa involved in writing the manuscript and data collections.

Kagami Nagai and Tatsuyuki Kawano involved in revising the manuscript.

Isao Minami, Mai Wakabayashi and Junko Torigoe involved in data collection.

Key learning points

- It is very rare to find patients with copper-deficiency anemia regardless of postoperative enteral nutrition. However, when enteral nutrition is given through jejunostomy, it can occur because nutrition bypass duodenum and proximal jejunum which are the main parts for copper absorption.
- Copper-deficiency anemia is very rare after surgery. However, if patients suffer anemia of unknown origin after surgery, we should consider copper-deficiency anemia as one of differential diagnoses.

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