Malnutrition and micronutrient deficiency following gastrointestinal cancer surgery: A case report and mini-review of the literature

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Abstract. Malnutrition is a common issue following gastrointestinal cancer surgery, negatively affecting the quality of life and clinical outcomes of patients following surgery. However, this issue is often overlooked, and limited data are available on the long-term effectiveness of nutritional intervention. The present study describes the case of a female patient developing severe malnutrition and micronutrient deficiencies following a gastrectomy for stomach cancer and a pancreaticoduodenectomy due to tumor recurrence. The patient received comprehensive nutrition intervention, combining both oral feeding and supplemental parenteral nutrition, oral and intravenous multi micronutrients supplements and personalized pancreatic enzyme replacement therapy. Her clinical condition markedly improved, as well as the edema caused by malnutrition and cutaneous lesions caused by micronutrient deficiency. Gastrectomy and pancreaticoduodenectomy are both major surgeries that severely affect the nutritional status of patients, as these are the main digestive organs of the body, particularly in the background of cancer and more adverse events from chemotherapy treatment. Progressive protein-energy malnutrition and micronutrient deficiencies are the results of decreased dietary intake, anatomical changes and malabsorption following gastrointestinal surgery. Thus, surgeons/clinicians should consider the comprehensive treatment of patients, including comprehensive nutritional care before, during and following surgery in order to prevent malnutrition and its complications. This would also enhance the effectiveness of surgery and the long-term clinical results following surgery for patients with cancer.

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Introduction

According to clinical data, malnutrition is observed in 50-80% of patients with gastrointestinal cancer, and it is associated with poor clinical outcomes and longer periods of hospitalization (1,2). In particular, patients with pancreatic or gastric cancer have been shown to have the highest frequency of weight loss (3). However, the clinical manifestations of malnutrition, particularly micronutrient deficiency, which is not apparent immediately, can exist for a long period of time before the clinical signs of severe malnutrition and its complications appear (4,5).

The present study describes the case of a female patient who had previously undergone a gastrectomy, as well as a subsequent pancreaticoduodenectomy with cholecystectomy, bile-jejunostomy, pancreatojejunostomy and gastrojejunostomy. For this reason, the distal gastric resection, duodenum and partial pancreatic resection, gallbladder resection and intestinal anastomoses in the post-operative reconstruction of the digestive tract, caused poor digestive function, ultimately resulting in malnutrition and micronutrient deficiencies. The aim of the present case report was to share the clinical experience of the authors with the clinical manifestations of malnutrition and micronutrient deficiency following gastrointestinal surgery.

Case report

A 70-year-old female patient presented in the outpatient cancer clinic for a follow-up appointment and was admitted to Viet Duc University Hospital (Hanoi, Vietnam) for treatment in the Oncology Department on February 1, 2023.

According to her medical history, the patient had undergone a partial gastrectomy with gastroduodenostomy (Billroth I) in January, 2009 for stomach cancer and

pancreaticoduodenectomy due to tumor recurrence with lymph node metastases of the head of the pancreatic region in March, 2020. She had undergone seven cycles of adjuvant chemotherapy and this was then discontinued due to significant toxicities and intolerance.

Upon a physical examination at the time of admission, the patient was alert, fatigued and hemodynamically stable. She had mildly pale skin and mucous membranes. The peripheral lymph nodes were not palpable. The abdomen was soft, non-tender, with deep palpation, and no masses were present.

The notable physical findings in the patient were generalized edema with mild facial edema, moderate bilateral pitting edema of the lower extremities and no ascites. Accompanied by dry cutaneous lesions, red stretch marks were observed on her extremities; these were more evident in the lower limbs. Her legs were red and swollen, with small ulcers, and the patient had refused to walk for 2 days due to pain (Fig. 1). There were no oral mucosal lesions. There were no other notable findings from the physical examination.

The patient had a nutrition consultation on February 2, 2023. The assessment of her nutritional status was PG-SGA C, her height was 160 cm, her current weight was 42 kg and her body mass index was 16.4 kg/m^2 (with edema). She had lost weight unintentionally; her normal healthy weight had been 53 kg and she had reached 38 kg 1 month prior. The nutrition-focused physical examination revealed moderate to severe loss of muscle and subcutaneous fat. There were signs of micronutrient deficiency, such as the partial loss of lingual papillae on the surface of the tongue edges, dry and pale skin combined with ulcers, and perifollicular petechiae hemorrhage on her anterior shins bilaterally.

The patient stated that she had not been eating well due to anorexia, and had a poor appetite from the second surgery in 2020. The 24-h food recall revealed that her meals consisted of rice, porridge and milk with 5-6 meals/day, with a total energy count of 900-1,000 kcal/day, a protein intake of 35-40 g/day, and a poor vegetable and fruit intake. Her daily intake was noted to average 50-60% of the nutritional demand. She had normal bowel movements once per day. Currently, she was being treated with Creon® at 25.000 UI orally, three times daily. She did not receive any vitamins or mineral supplementation.

Laboratory tests revealed hypoproteinemia with an albumin level of 24.1 g/l, prealbumin level of 3.6 mg/dl and lack of a certain micronutrients, indicated as follows: Zinc, 6.5 μmol/l; iron, 7.8 μmol/l; ferritin, 18.5 μg/l; corrected calcium, 2.1 mmol/l; and 25-OHD, 10.8 ng/ml. A complete blood count revealed megaloblastic anemia, with a red blood cell count of 2.85 T/l, a hemoglobin count of 93 g/l and a hematocrit of 0.29%. Her mean corpuscular volume/mean corpuscular hemoglobin/mean corpuscular hemoglobin concentration ratio was 102.6/32.8/320.

Other biochemical indicators of glucose (3.64 mmol/l), electrolytes (sodium, 140.5 mmol/l; potassium, 3.6 mmol/l; chloride, 107.5 mmol/l), magnesium (0.85 mmol/l), phosphorus (1.15 mmol/l), urea (7.54 mmol/l) and creatinine (54.23 μmol/l) were within the normal range, and the levels of liver enzymes and bilirubin were slightly elevated as follows: aspartate aminotransferase, 67.7 U/l; alanine aminotransferase, 61.98 U/l; total bilirubin, 31.4 μmol/l; direct bilirubin, 13.4 μmol/l.

Figure 1. Clinical appearance of the lower legs of the patients upon admission (February 2, 2023).

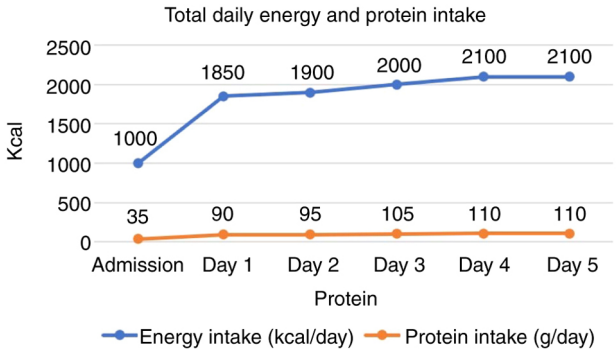

Figure 2. Total daily energy intake from 1,000 to 2,100 kcal/day; protein intake by case from 35 to 110 g/day.

The patient's serum levels of carcinoembryonic antigen (10.94 ng/ml) and cancer antigen 19-9 (87.69 U/ml) were slightly elevated. A contrast-enhanced computed tomography was performed and this ruled out recurrent cancer. No thrombus in the veins and arteries was observed on the Doppler ultrasound of the lower extremities on both sides. A clinical immunology-allergy specialist consultation was requested and immunology testing was performed to rule out vasculitis. Accordingly, the patient was diagnosed with macrocytic anemia, micronutrient deficiency and severe malnutrition.

The patient had a risk of refeeding syndrome; however, her phosphorus (1.15 mmol/l), potassium (3.6 mmol/l) and magnesium (0.85 mmol/l) levels were normal; thus, it was decided to provide intensive nutrition from oral feeding combined with supplemental parenteral nutrition. The patient received dietary advice and was encouraged to take the medical formula (Peptamen®) as an oral nutritional supplement with short peptide enteral nutrition preparationsto potentially improve absorption and optimal micronutrient intake. The total daily energy and protein intake of the patient is presented in Fig. 2.

As partial parenteral nutrition, the patient received 500 ml of 10% Aminoplasmal (acid amin)® and 250 ml of 20% SMOFlipid®(Lipid). She was also administered daily infusions of 20% human albumin solution. Parenteral micronutrients, including multivitamins, trace elements and electrolytes, were provided daily. She also received daily an intramuscular injection of vitamin B12 (1,000 mcg), as well as via oral route

Figure 3. Clinical appearance of the lower legs of the patient on the 5th day of treatment (February 7, 2023).

daily, 20 mg zinc, 3,000 UI vitamin D3 and B complex C® (vitamin B1 15 mg, vitamin B2 10 mg, vitamin B6 5 mg, Vitamin PP 50 mg and vitamin C 100 mg) twice a day, Energy Pharmaton® (multivitamins) once a day, Tardyferon B9® (50 mg of elemental iron as ferrous sulfate with 0.35 mg folic acid) twice a day and 500 mg of calcium as calcium citrate twice a day. Creon® was also administered to the patient for use at home to better correct pancreatic exocrine insufficiency (PEI) with doses of 50,000 units of lipase with meals and 25,000 units with each snack, with a total of nine capsules of Creon® at 25.000 UI per day.

The symptoms of the patient markedly improved following 5 days of treatment with rapid cutaneous improvement, and the resolution of her edema. Her weight increased from 38 to 42 kg. Her lower legs on both sides were no longer red and swollen, the small ulcers were dry, and healing and red stretch marks gradually developed scabs (Fig. 3). The appetite of the patient had increased, with an improvement in the quality of her dietary intake. She was able to mobilize both lower extremities without pain and was discharged in a good clinical condition from the hospital on the 6th day of admission. Nutrition counseling was provided to the caregiver prior to discharge.

Discussion

Following gastrointestinal surgeries, the rapid and uncontrolled passage of food into the intestine leads to a decreased digestibility and absorption of macronutrients and micronutrients due to the absence of the jejunum and duodenum, and the damage to the extrinsic parasympathetic innervation, combined with a lack of coordination of the gallbladder bile and pancreatic secretion into the duodenum. Malabsorption may result from the incomplete digestion of proteins and lipids due to the absence of pepsin and hydrochloric acid, combined with late contact of the ingested food with the pancreatic juice. In addition, the more important cause, malabsorption, is a consequence of exocrine pancreatic insufficiency following pancreaticoduodenectomy (6). The obvious symptoms that can be seen are the progressive worsening of malnutrition with weight loss, and a decrease in the muscle mass fat mass of the patient. This is also accompanied by anemia, edema and malnourishment due to malnutrition and micronutrient deficiencies. In such cases, the amount of malabsorption leads to clinical malnutrition that necessitates nutritional support, including parenteral nutrition.

PEI is defined as a deficiency of exocrine pancreatic enzymes resulting in an inability to maintain normal digestion (7). The factors that contribute to PEI following pancreatic surgery are the loss of pancreatic tissue volume, extensive denervation following lymph node dissection, the asynchronous mixing of pancreatic-biliary secretions with the meal, and a surgically altered anatomy (6,8). In addition, an increased incidence of pancreatic insufficiency following upper gastrointestinal surgery has also been observed, where extra-pancreatic factors impair the final activity of pancreatic enzymes (9). These consequences lead to the reduced absorption of protein, fat and fat-soluble vitamins, leading to weight loss and malnutrition. Fat malabsorption is the predominant cause of the symptoms of pancreatic steatorrhea, resulting in weight loss, as well as deficiencies in the fat-soluble vitamins A, D, E and K (10). In addition, fat absorption may decrease following partial or total gastrectomy, due to the lack or decrease in the levels of digestive enzymes and less contact between ingested food, digestive enzymes and biliary salts (6).

Pancreatic enzyme replacement therapy is indicated for the conditions described above presenting with clinically clear steatorrhea, weight loss, or symptoms related to maldigestion and malabsorption. For adults, therapy should commence with doses of 50,000 units of lipase with main meals, and half the dose to be taken with a snack (6,7,11). In the patient in the present study, manifestations of pancreatic insufficiency were not apparent, possibly as the patient had previously been supplemented with pancreatic enzymes, but still had symptoms of anorexia, bloating and progressive weight loss without steatorrhea. There was no accurate test available to diagnose this, such as the measurement of fecal elastase-1 or 3-day fecal fat quantification. Thus, based on clinical experience, the dose of pancreatic enzymes was increased to optimize treatment after determining the method of drug administration and the patient's compliance and need to monitor her response.

Dermatitis resembling flaky paint-hyperpigmented areas on arms, thighs and calves, is possibly due to deficiencies in protein. In addition, there can also be skin damage due to a lack of essential fatty acids and/or a combination of multiple micronutrient deficiencies such as zinc, vitamin C, niacin and riboflavin (12).

A closer look at vitamins, as well as trace elements, should be considered to assess for a decreased intake of foods and post-operative malabsorption and the need for supplementation. Over time, virtually all gastric surgical procedures potentially lead to micronutrient deficiencies due to the resection or exclusion of functionally active gastric mucosa necessary for gastric acid and intrinsic factor secretion, which in turn, is essential for correct micronutrient absorption. The acid environment of the stomach facilitates protein degradation, allowing for the release and dissolution of calcium, magnesium, iron and other trace elements for eventual absorption, and is also essential for the absorption, secretion and activation of ascorbic acid (13). Additionally, the resection of the duodenum during the pancreaticoduodenectomy may place patients at risk of developing iron and mineral deficiencies. Zinc deficiency has been reported in up to 68% of patients undergoing pancreas

resection, predominately following pancreaticoduodenectomy, and is associated with PEI (14).

The majority of water-soluble vitamins are easily absorbed from the proximal gastrointestinal tract. The rapid transit of food through the intestine allows for the decreased time absorption for these vitamins. Fat-soluble vitamins and essential fatty acids are considered to be absorbed in the mid- and distal ileum, due to the necessity of bile acid and pancreatic lipase to facilitate absorption; therefore, these are affected by conditions with fat malabsorption, as in the case of the patient described herein. Calcium absorption begins due to the intragastric acid pH favoring the dissolution of calcium salts to form soluble calcium chloride, a step facilitating the proper absorption of this ion through vitamin D-dependent transcellular transport in the duodenum and proximal jejunum (13). Following the removal of the duodenum during a pancreaticoduodenectomy, patients exhibit markedly diminished calcium absorption.

Another notable finding in this patient is megaloblastic anemia, which may be due to vitamin B12, and/or folic acid (vitamin B9) deficiencies. In addition, anemia is caused by a combination of iron deficiency.

Nutritional anemias resulting from a vitamin B12, folate, or iron deficiency are common in individuals who have had a gastrectomy, both total or subtotal gastrectomy. A previous retrospective cohort study on long-term gastric cancer survivors without recurrence or metastasis following gastrectomy revealed that the cumulative incidence rate of anemia following surgery exhibited a linear increase, presenting as in 18.7% in the 1st year, and increasing to 39.5% in the 5th year (15). Iron deficiency anemia is found in ~30% of patients who have undergone a gastrectomy, due to a reduced iron intake and defects in iron absorption in the bypass of the duodenum and upper jejunum, or chronic bleeding in the gastric mucosa. The prevalence of vitamin B12 deficiency anemia is ~50% in gastrectomy cases caused by a lack of intrinsic factor secretion following surgery (15). A key role is played by the corpus oxyntic mucosa composed of parietal cell mass depletion, whose main function is gastric acid secretion and intrinsic factor production, mostly located in the body, and to a lesser extent in the antrum and fundus (13).

Vitamin deficiencies are typically subclinical and require testing for diagnosis. However, due to the lack of these laboratory tests at the Viet Duc University Hospital, the authors were only able to perform a few micronutrient tests and mainly administer empiric treatment in the case that symptoms of deficiency were suspected. Note that ferrous iron is the preferred form due to its high bioavailability. Vitamin C has been shown to enhance iron absorption and increase the proliferation of dermal fibroblasts, a function critical for wound healing (16).

In conclusion, by describing the present clinical case, the present study hopes to highlight the impacts of nutrition on the clinical outcomes of patients following gastrointestinal cancer surgery. Post-discharge individualized dietary counseling and regular nutrition assessment are effective interventions to reduce post-operative weight loss and malnutrition. Deficiencies in several micronutrients, such as iron, vitamin B12, calcium and ascorbic acid may lead to potentially severe consequences when not promptly diagnosed and treated. Thus, it is critical to routinely monitor patients who have undergone any previous gastric surgery for micronutrient deficiency. Therefore, the success of surgery not only helps the patient to remove cancerous tumors, but also helps the body to recover and function following surgery, the pivotal role of nutritional interventions.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

All authors (TTD, PLTP, PTN, AGP and HNV) contributed to the conception and design of the study. Material preparation was performed by TTD and HNV. Data collection and analysis were performed by PLTP, PTN and AGP. Analysis was performed by PTN and AGP. The first draft of the manuscript was written by TTD, PTN and HNV, and all authors commented on previous versions of the manuscript. TTD and PTN confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for her participation in the present study.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of the present case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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