

Gastric cancer with severe immune thrombocytopenia: A case report

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Abstract

BACKGROUND

Primary immune thrombocytopenia (ITP) is a rare autoimmune disease associated with a high bleeding risk. For those patients with gastric cancer, surgical treatment may be the only option for therapy. Here, we present the first case of gastric cancer with severe and medically refractory ITP treated by radical resection of the gastric cancer and splenectomy.

CASE SUMMARY

A 54-year-old female patient was admitted to our surgical department with a 2 mo history of decreased appetite, nausea, vomiting, and weight loss, which progressed to difficulty in feeding 3 d prior to her visit. According to her medical history, she was diagnosed with refractory ITP [platelets (PLT), 3000-8000/ μ L] 10 years ago. After admission, the patient underwent a splenectomy and a distal subtotal gastrectomy (D2 radical resection) with Roux-en-Y reconstruction simultaneously. She had an uneventful postoperative course with a slight increase in her PLT count. This case is unique in terms of the patient's complication of severe and medically refractory ITP.

CONCLUSION

Simultaneous splenectomy, preoperative PLT transfusion, and early enteral nutrition were important treatment methods for helping this patient recover.

Key words: Gastric cancer; Immune thrombocytopenia; Surgical treatment; Case report

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Core tip: Immune thrombocytopenia (ITP) is a rare autoimmune disease with a reduced platelet count. Severe and medically refractory thrombocytopenia is an absolute contraindication to chemotherapy or radiotherapy. For those patients with a malignant tumor, surgical treatment may be the only option despite a high risk of bleeding. This case might contribute to improving our understanding of the behavior and perioperative management of severe and medically refractory ITP patients with gastric cancer.

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INTRODUCTION

Primary immune thrombocytopenia (ITP), also known as idiopathic thrombocytopenia purpura, is an autoimmune disease associated with a reduced platelet (PLT) count without any obvious initiating and/or underlying cause. Severe and medically refractory thrombocytopenia is an absolute contraindication to chemotherapy or radiotherapy. For those patients with gastric cancer, surgical treatment may be the only option for therapy despite a high risk of bleeding. This uncommon condition can be worrisome for surgeons. Here, aiming to lay a foundation for future clinical work, we report the first case of gastric cancer complicated by severe and medically refractory ITP treated by subtotal gastrectomy and splenectomy and a review of the related literature.

CASE REPORT

A 54-year-old woman was admitted to our hospital with a 2-mo history of decreased appetite, nausea, vomiting, and weight loss, which progressed to difficulty in feeding 3 d prior to her visit. A rapid urease test and serum antibody testing demonstrated that she was negative for *Helicobacter pylori* (*H. pylori*). An upper gastrointestinal endoscopy showed irregular erosion on the pylorus with pyloric stenosis. Multiple mucosal biopsies were obtained, and a histological analysis revealed gastric adenocarcinoma. Serum levels of tumor markers were significantly elevated (CA19-9 273.1 U/mL and CA242 > 150.0 U/mL). Abdominal contrast-enhanced computed tomography revealed a thickening wall of the gastric antrum with significantly enhanced, multiple small lymph nodes around the stomach but no obvious retroperitoneal

lymph nodes, and a normal spleen. She worked in a plastics factory and was exposed to chemicals and radioactive materials for several years. She was diagnosed with ITP (PLT 3000-8000/ μ L) 10 years ago. Prednisolone therapy (80 mg/d for 2 wk) was started; and her PLT increased to 50000-60000/ μ L. However, PLT decreased to 3000-7000/ μ L immediately after reduction of corticosteroids. Then, dexamethasone therapy (40 mg/d for 4 d) was started. PLT increased to 170000/ μ L temporarily but decreased to 3000-7000/ μ L 3 d after therapy. Other medications including immunoglobulins (10 g/d for 4 d), androgen derivatives (danazol 400 mg/d for 3 mo), cyclosporine A (200 mg/d for 2 wk), and thrombopoietin (50 μ g/d for 7 d) were administered respectively. However, she no longer responded to any of these medical therapies. Other previous medical history included congenital ventricular septal defect and subclinical hypothyroidism. Her family history was unremarkable. On admission, her physical examination and blood biochemistry laboratory results were within normal limits. Hematological tests revealed a decreased PLT count of 5000/ μ L and a normal hemoglobin (HGB) level of 111 g/L. Subsequently, she presented with melena and bloody drainage which was observed in the nasogastric tube; the HGB and PLT decreased to 85 g/L and 1000/ μ L, respectively. Her general condition was examined before surgery. Because of decreased appetite and difficulty in feeding, her weight dropped to 66 kg from her normal weight of 80 kg (body mass index dropped from 30.1 kg/m² to 24.8 kg/m²). Although both cardiac function and pulmonary function were at normal levels, her high nutritional risk may affect the postoperative recovery.

The patient underwent a splenectomy and a distal subtotal gastrectomy (D2 radical resection) with a Roux-en-Y reconstruction simultaneously. A needle catheter jejunostomy was performed to ensure postoperative enteral nutrition (EN). In total, four pheresis units (one pheresis unit contains approximately $2.5-4.0 \times 10^{11}$ PLTs, equal to 10-12 whole blood donor units) of PLT were transfused. The patient's PLT counts fluctuated between 30000-60000/ μ L during the surgery and PLT were administered accordingly (one pheresis unit was administered 1 h before induction of anesthesia; two pheresis units administered during surgery; and one pheresis unit 2 h after surgery).

The patient resumed EN (oligopeptide, low-fat, isocaloric, non-residue diet; Peptisorb, Nutricia, Schiphol, The Netherlands) on the morning of the 2nd postoperative day. She had an uneventful postoperative course with a slight increase in the PLT count (Figure 1) and was discharged on the 15th postoperative day. The histopathological examination after the subtotal gastrectomy revealed a poorly differentiated gastric adenocarcinoma which had reached the serosal layer. The cancer had also metastasized to 3/30 lymph nodes. The pathological stage was pT4aN2M0, IIIA. There was no evidence of recurrence, and she showed a consistent and stable increase in the PLT count around 20000/ μ L for

Table 1 Cases of immune thrombocytopenia patients suffering with gastric malignant tumors

Ref.	PLT level (/μL)	Gastric tumor	<i>H. pylori</i>	Treatment for gastric tumor	Prognosis of gastric tumor
Bachmeyer <i>et al</i> ^[6] , 2000	40000	Gastric MALT lymphoma	Positive	Chemotherapy	-
Noda <i>et al</i> ^[7] , 2004	27000	Gastric MALT lymphoma	Positive	Endoscopic mucosal resection	Without recurrence in 2 yr
Wakata <i>et al</i> ^[8] , 2006	73000-10800	Gastric cancer	-	Subtotal gastrectomy and splenectomy	Without recurrence in 2 yr
Villias <i>et al</i> ^[9] , 2008	76000	Gastric cancer and GIST	-	Subtotal gastrectomy and splenectomy	-
Hamabe <i>et al</i> ^[10] , 2011	52000	Gastric cancer and gastric MALT lymphoma	Positive	Total gastrectomy and splenectomy	Without recurrence in 2 yr

MALT: Mucosal associated lymphoid tissue; *H. pylori*: *Helicobacter pylori*; GIST: Gastrointestinal stromal tumor; PLT: Platelet.

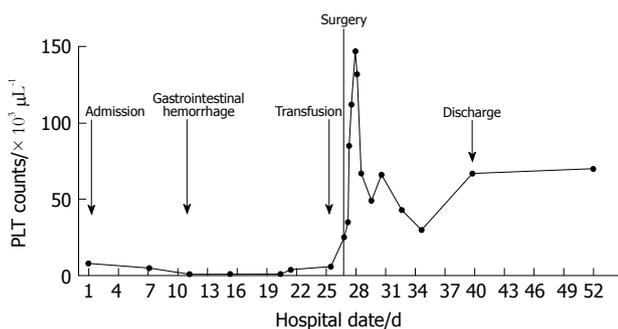


Figure 1 Platelet count fluctuation of the patient during hospitalization. PLT: Platelet.

about 2 years after the operation.

DISCUSSION

ITP is an immune-mediated disease associated with a reduced PLT count lower than 100000/μL^[1]. The mechanism of ITP includes that PLT membrane proteins become antigenic and stimulate the immune system resulting in thrombocytopenia due to immune-mediated PLT destruction and/or suppression of PLT production^[2]. Some studies defined very severe thrombocytopenia as PLT count < 10000/μL^[3]; however, some researchers suggest that the severity of the disease is based clinically on bleeding scores rather than a PLT count^[4,5]. In this case, the patient presented with gastrointestinal hemorrhage accompanied with acute anemia. According to Khellaf's bleeding score^[4], this patient had a high bleeding score (> 8), which indicated a severe ITP with a high risk of life-threatening hemorrhage. Patients are considered to have medically refractory ITP when they require treatment following failure to respond to medical treatment. Response was defined as PLT count > 30000/μL and at least a 2-fold increase in the baseline count and absence of bleeding^[1]. In this case, the patient was considered nonresponse to medication.

To the best of our knowledge, only five cases of ITP patients suffering with gastric malignant tumors have been reported in English in MEDLINE (Table 1)^[6-10]. Patients in these cases suffered mild ITP with a PLT level larger than 20000/μL. The commonest pathology is gastric cancer and gastric mucosa associated lymphoid

tissue (MALT) lymphoma. *H. pylori* may play a key role in the pathogenesis of both gastric malignant tumors and ITP. Noda *et al*^[7] reported a case of regression of ITP after resection of gastric MALT lymphoma and eradicating treatment of *H. pylori*. In terms of treatment, endoscopic resection could be performed only when the tumor is restricted to the mucosa during eradication therapy. Subtotal/total gastrectomy combined with splenectomy is the most appropriate treatment when tumors invade the submucosa. And this is the first case of gastric cancer with severe and medically refractory ITP. The extremely low PLT level led to a high risk of bleeding, especially during the perioperative period.

Corticosteroids with or without intravenous immunoglobulin (IVIg) are the standard first-line treatment for ITP patients with a PLT count < 30000/μL^[11]. For patients who have failed corticosteroid therapy, a splenectomy is recommended as a second-line treatment. According to recent research, a short-term response to a splenectomy was achieved in approximately 87% of ITP patients^[12-14]. Whereas in patients with a PLT count on admission of < 40000/μL, only 40% may achieve a long-term stable response^[14]. In our patient, the thrombocytopenia continued with PLT counts fluctuating between 3000-8000/μL and she showed a poor response to preoperative medical boosting. Considering its satisfactory and high response rates in short-term postoperative time, it is reasonable for patients to undergo a splenectomy in terms of low complication rates and low bleeding risk.

According to some studies, PLT transfusions were recommended only in a few life-threatening cases that require a rapid rise in PLT count to achieve hemostasis, such as intracranial hemorrhage or major surgery^[1,15]. Despite the short-term efficacy, PLT transfusion every 30 min to 8 h and a PLT transfusion in conjunction with IVIg or steroids have been effective for increasing PLT levels in emergency situations^[16-18]. Traditionally, for safety, most guidelines recommend a PLT count of at least 30000-50000/μL for prophylaxis during surgery^[19,20]. Recently, some researchers reported that a perioperative PLT transfusion might be unnecessary for a laparoscopic splenectomy in ITP patients^[21,22]. However, there is still a lack of evidence to guide preoperative PLT transfusions used as prophylaxis for surgery, especially for those

with a high bleeding risk. In this case, a PLT transfusion resulted in a rapid rise of PLT count ranging from 30000 to 60000/ μ L during the operation and ensured a successful surgery.

Postoperative patients with advanced gastric cancer generally suffer from various complications, such as infection and malnutrition^[23]. Early EN is important to implement as a way to accelerate rehabilitation of intestinal function and immune response in patients undergoing a gastrectomy, especially in patients with severe complications^[24]. Needle catheter jejunostomy was reported to be safe and progressive EN support could be implemented successfully^[25,26]. In this patient, the step-by-step EN feeding program was initiated on the 2nd postoperative day using the needle catheter jejunostomy.

In conclusion, we report a case of advanced gastric cancer complicated with severe and medically refractory ITP that was successfully cured by radical resection of the gastric cancer. Simultaneous splenectomy, preoperative PLT transfusion, and early EN were important assistances to the treatment of this patient.

ARTICLE HIGHLIGHTS

Case characteristics

The patient suffered from decreased appetite, nausea, vomiting, and weight loss for 2 mo with a past medical history of thrombocytopenia, which progressed to difficulty in feeding and gastrointestinal hemorrhage.

Clinical diagnosis

The patient was diagnosed with gastric cancer accompanied with severe and medically refractory immune thrombocytopenia.

Differential diagnosis

Mucosal biopsy from endoscopy was useful for differential diagnosis and histological analysis revealed a gastric adenocarcinoma.

Laboratory diagnosis

Laboratory findings revealed elevated tumor markers (CA19-9 and CA242), low platelet count, and decreased hemoglobin.

Imaging diagnosis

Abdominal contrast-enhanced computed tomography revealed a thickening wall of the gastric antrum with significantly enhanced, multiple small lymph nodes around the stomach but no obvious retroperitoneal lymph nodes and a normal spleen.

Pathological diagnosis

The histopathological examination after the subtotal gastrectomy revealed a poorly differentiated gastric adenocarcinoma which had reached the serosal layer and the cancer had also metastasized to 3/30 lymph nodes.

Treatment

The patient underwent a splenectomy and a distal subtotal gastrectomy (D2 radical resection) with a Roux-en-Y reconstruction simultaneously.

Related reports

Five cases of immune thrombocytopenia (ITP) patients suffering with gastric malignant tumors have been reported in English in MEDLINE. Patients in these cases suffered mild ITP with a platelet (PLT) level larger than 25000/ μ L. The commonest pathologies are gastric cancer and gastric mucosa associated

lymphoid tissue (MALT) lymphoma. *Helicobacter pylori* (*H. pylori*) may play a key role in the pathogenesis of both gastric malignant tumors and ITP. Noda *et al*^[7] reported a case of regression of ITP after resection of gastric MALT lymphoma and eradicating treatment of *H. pylori*. In terms of treatment, endoscopic resection could be performed only when the tumor is restricted to the mucosa during eradication therapy. Subtotal/total gastrectomy combined with splenectomy is the most appropriate treatment when tumors invade the submucosa.

Experiences and lessons

For patients with cancer and medical refractory ITP, surgical treatment may be the only option for therapy despite a high risk of bleeding. Simultaneous splenectomy, preoperative PLT transfusion, and early enteral nutrition are important treatment methods for postoperative recovery.

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