Autoimmune Haemolysis After Operation of Gastric Cancer Complicated With Drug-refractory Idiopathic Thrombocytopenic Purpura: a Case Report and Review of the Literature

Xiao Pang

Central Hospital: Hopital Central

Wei-Kang Guan

Central Hospital: Hopital Central

Yu-Lin Pan

Central Hospital: Hopital Central

Yi-Chao Zhang

Central Hospital: Hopital Central

Li-Ya Xu

Central Hospital: Hopital Central

Jun Zhang (✉ 1024782475@qq.com)

Central Hospital: Hopital Central <https://orcid.org/0000-0001-7907-7235>

Research Article

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Abstract

Background: To the best of our knowledge, few reports are available at home and abroad on autoimmune haemolysis occurring after operation of gastric cancer complicated with drug-refractory idiopathic thrombocytopenic purpura (ITP)(Table 1). The treatment process in this case is usually risky, and multidisciplinary collaboration is often required. Therefore, the case report aims to improve the awareness of the perioperative management of this type of patients.

Case presentation: A 69-year-old male admitted to the hospital for "anaemia" was diagnosed with gastric adenocarcinoma after gastroscopy and biopsy. This diagnosis was confirmed to be an early stage by abdominal CT imaging. However, the patient had an extremely low platelet level and a history of hormone therapy. Moreover, administration of thrombopoietin and immunoglobulin was ineffective for treatment. After transfusion of aphaeretic platelets, laparoscopic total gastrectomy with D2 lymphadenectomy and splenectomy were performed. Anastomotic bleeding and autoimmune haemolysis occurred after the operation. Haemolytic symptoms were spontaneously relieved after a period of hospitalisation.

Conclusion: This case involved many disciplines, and revealed the interaction and mutual promotion of gastric cancer, ITP and autoimmune haemolysis, but further relationships need to be further investigated.

Background

Tumours rarely combined with two types of blood diseases resulting from the failure of immune mechanism regulation. Blood diseases may combine arbitrarily and interact with each other. Here, we present a patient with drug-resistant idiopathic thrombocytopenic purpura(ITP) who experienced gastric cancer and autoimmune haemolysis.

Case Presentation

A 69-year-old male patient was admitted to the Department of Haematology because of fatigue and dizziness lasting 1 month. The patient had fatigue for 1 month, and the symptom was gradually aggravated 1 week prior to his visit. The patient was unable to carry out physical activity and had dizziness. Five years ago, the patient was hospitalised at the Department of Haematology of our hospital for treatment of thrombocytopenia and diagnosed with ITP with a platelet count of $7 \times 10^9/L$ on admission. After treatment with 30mg qd of prednisone for 3 days, the patient was voluntarily discharged from the hospital. The patient took platelet-elevating drugs irregularly after discharge and did not return to re-examination. No family history of cancer or haematological diseases. On admission, the patient's temperature was 36.6°C, heart rate was 77 bpm, respiratory rate was 16 breaths per minute, blood pressure was 138/97 mmHg, and the physical examination revealed no positive sign. But the patient's routine blood test showed a haemoglobin level of 63 g/L, platelet count of $34 \times 10^9/L$, bone marrow smear indicated hypochromic microcytic anaemia, enhanced abdominal CT examination revealed stage T1–2N0 cancer (Fig. 1), gastroscopy revealed 1.5×1cm² necrotic foci at the posterior wall of the lesser curvature of the gastric body, and a pathological test confirmed adenocarcinoma (Fig. 2). The patient was finally diagnosed with gastric cancer.

The patient was transferred from the Department of Haematology to the Department of General Surgery and double-checked routine blood examination (haemoglobin level, 71g/L; platelet count, $36 \times 10^9/L$). After a multidisciplinary discussion, we decided to continuously subcutaneous inject 15000 IU of thrombopoietin (TPO) into the patient for 2 weeks. However, no satisfactory therapeutic effect was found after re-examination. Accordingly, on the sixth day, we combined intravenous immunoglobulin (IVIG; 400mg/kg) for 5 days. Last, laparoscopic total gastrectomy with D2 lymphadenectomy (LTG-D2) + splenectomy + Braun's anastomosis was performed after platelet transfusion. Serious abdominal adhesion was observed during the operation, and the operation time lasted 7 hours. On the first day after operation, the patient was re-examined with routine blood test and revealed a haemoglobin level of 80 g/L and platelet count of $62 \times 10^9/L$. On the fifth day after operation, 200–400mL of a dark red blood-like fluid was founded from the patient's nasogastric tube. We considered gastrointestinal anastomotic stoma bleeding and decided to use somatostatin, a proton pump inhibitor, thrombin and suspended red blood cells for treatment. Bleeding of the anastomotic stoma gradually decreased, but dark-brown urine was noted on the 13th day after operation. The patient was re-examined with routine blood test and revealed a white blood cell (WBC) count, haemoglobin level, and platelet count of $21.93 \times 10^9/L$, 52g/L and $116 \times 10^9/L$, respectively. The patient's liver function was generally normal. Routine urine test showed 4 + bilinogen and 11.9% reticulocytes. Indirect and indirect anti-human-globulin (Coomb's test) tests were negative. After remote consultation in the Department of Haematology of the West China Hospital of Sichuan University, blood transfusion-related haemolysis was excluded, considering possibilities of Coomb's test-negative autoimmune haemolysis, infection, tumour and other factors. We considered the effects of hormones and immunosuppressants on the anastomotic stoma and infection control, decided to temporary observation and adjust cefoperazone/sulbactam to imipenem/cisastatin (1g q8h). Thereafter, the patients was regularly examined through routine blood and urine tests, and the relevant indices gradually improved. The patient was discharged on the 26th day after operation with a WBC of $8.56 \times 10^9/L$, haemoglobin level of 62g/L and platelet count of $57 \times 10^9/L$ (Fig. 3).

The patient's postoperative pathological test: stomach and lymph nodes: moderately and highly differentiated tubular adeno carcinoma invading the muscularis mucosa without lymph node metastasis (Fig. 4); spleen: congestive splenomegaly (Fig. 4). Pathological stage: T1aN0M0, stage IA. The patient was followed up 3 months and 6 months after operation and re-examined with routine blood test. A WBC count, haemoglobin level and platelet count of 5.72/ 6.35×10⁹/L, 92/114g/L and 44/41×10⁹/L, respectively.

Discussion

ITP is an autoimmune disease, and its cause has yet to be identified. The pathogenesis of ITP is generally recognised to involve stimulation of the immune system by the antigenicity produced by platelet membrane proteins, thus causing destruction or reduction of platelets[1]. Drug-refractory ITP refers to PLT count $\geq$ 30000/ μ L or increase by less than twice the baseline count after drug treatment[2]. Earlier studies suggested that splenectomy as a second-line treatment regimen may cause short-term platelet responses in approximately 87% of ITP patients[3–5]. However, because chemotherapeutic drugs could produce myelosuppression, drug-refractory ITP is an absolute contra-indication of chemotherapy. Whilst we considered endoscopic submucosal dissection(ESD)for early gastric cancer, especially well-differentiated gastric cancer of the non-ulcerative type (< 2cm), the problem of long-term thrombocytopenia could not be resolved. Therefore, radical gastrectomy + splenectomy is the only choice for the treatment of gastric cancer complicated with drug-refractory ITP.

Gastric cancer surgery belongs to a kind of operation within a time limit. Considering the influence of hormones and immunosuppressants on operation outcomes, IVIG combined with platelet treatment is effective in case of failure of conventional TPO treatment before operation[6]. If the need to increase the platelet count within a short period of time arises, the conventional treatment plan is administration of IVIG (0.4g/kg) for 4–6 hours a day for up to 5 days. If the patient's poor response to the conventional treatment and tolerance to IVIG, the infusion time of IVIG is increased. For example, an IVIG dose of 1g/kg with continuous infusion for 24 hours and 1U platelets every 8 hours[7]. Previous studies suggested that the effect of IVIG on platelets depends on the specificity of autoantibodies to platelet receptors. IVIG could increase the platelet count of GPIIa–IIb receptor-specific antibodies but not that of the GPIB receptor[8, 9].

Compared with the average person, ITP patients are at greater risk of developing post-operative anastomotic stoma bleeding because of their abnormal coagulation mechanism. Thus, post-operative observation of blood pressure, heart rate, haemoglobin level and drainage and nasogastric tubes is very important. Although most cases of bleeding could be improved by conservative treatment with internal medicine[10], uncontrollable bleeding may be fatal to patients who are unable to address the issue in time. Re-operation, endoscopic haemostasis and interventional surgery are all available options for bleeding[11]. A growing number of reports have revealed that, compared with other methods, therapeutic endoscopy has more advantages in terms of reducing trauma, identifying bleeding sites and assessing rebleeding and could achieve more satisfactory results[12–15]. In addition, therapeutic endoscopy can be easily combined with other treatment methods. Umano Y et al. reported that microwave therapy under endoscopy could help bleeding sites coagulate[16]. Tanizawa Y and Tang SJ et al. reported the use of titanium clips for haemostasis under endoscopy[13, 17]. Granata A et al. reported the use of styptic powder for haemostasis under endoscopy[18]. Several other studies on the use of adrenaline injection and heating probes to achieve haemostasis under endoscopy have also been published[14, 15].

ITP and autoimmune haemolysis are diseases caused by the failure of the autoimmune mechanism and related to tumourigenesis to a certain extent; indeed, the probability of tumourigenesis in patients with ITP and autoimmune haemolysis is 12–13 times higher than that of the normal population[19]. However, the specific mechanisms of these relations are not clear. A previous study revealed that the higher probability of tumourigenesis due to ITP and autoimmune haemolysis may be related to the production of carcinogenic substances by red blood cells, platelets or anti-red blood cells and anti-platelet autoantibodies [20]. Tumour cells could also produce antibodies that cross-react with the antigens of red blood cells, resulting in haemolysis [21]. Haemolytic anaemia due to tumour-related immune haemolysis could be improved by beginning chemotherapy[22]. In the present case report, we opted to observe the patient without using targeted treatments. Interestingly, the patient's immune haemolysis disappeared spontaneously, probably because the corresponding antigens disappeared after the elimination of tumour factors.

Conclusions

We reported that one patient with gastric cancer complicated with ITP had an extremely low platelets count on admission. Finally, we chose LTG-D2 and splenectomy for gastric cancer, but anastomotic stoma bleeding and autoimmune haemolysis occurred after operation. The patient recovered and was discharged from the hospital after receiving active treatment. No complications were noted at the patient's 6-month follow-up. This combination of gastric cancer with drug-resistant ITP has rarely been reported at home and abroad. The relationship between cancer and haematological system diseases requires further study.

Abbreviations

CT=Computed Tomography

ITP=Idiopathic Thrombocytopenic Purpura

TPO=Thrombopoietin

IVIg=Intravenous Injection

LTG-D2=Laparoscopic Total Gastrectomy with D2 lymphadenectomy

WBC=White Blood Cell

ESD=Endoscopic Submucosal Dissection

Declarations

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Author contributions

Writing—original draft: Xiao Pang, Wei-Kang Guan.

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Availability of data and materials

All data and material are fully available without restriction.

Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of Dazhou Central Hospital. Informed consent was obtained from the patient for the publication of the report.

Consent for publication

Written informed consent for publication was obtained from the participant.

Competing interests

The authors declare that they have no conflict of interest.

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Table

Table 1
Cases of gastric tumor patients suffer with ITP or autoimmune hemolysis.

Ref.	Lowest number of platelets(/ul)	Therapy for ITP	Type of gastric tumor	Treatmengt for gastric tumor	Therapy for hemolysis	Prognosis of gastric tumor
Bachmeyer,etal,2000[23]	40000	Splenectomy and iv immunoglobulin	Gastric MALT lymphoma	Chemotherapy (CHOP regimens)	/	/
Noda M,etal,2004[24]	27000	/	Gastric MALT lymphoma	EMR	/	Without recurrence in 2 years
Wakata Nobuo,etal,2006[20]	1000	Iv immunoglobulin, methylprednisolone, platelet transfusion and splenectomy	Gastric adenocarcinoma(Contains signet ring cells)	Subtotal gastrectomy	High doses of immunoglobulin	Without recurrence in 2 years
Villias Constantionos,etal,2008[25]	76000	Splenectomy	GIST	Subtotal gastrectomy and Roux-en-Y anastomosis	/	/
Hamabe A,etal,2011[26]	52000	Eradicate helicobacter pylori,iv immunoglobulin and splenectomy	Gastric MALT lymphoma	Total gastrectomy and Roux-en-Y anastomosis	/	Without recurrence in 2 years
Monica Tang,etal,2017[27]	20000	Platelet transfusion	/	chemotherapy	Plasma exchange and prednisone	/
Seo HS,etal,2018[28]	32000	Oral steroid	Gastric cancer	Subtotal gastrectomy	/	Stomach wall IgG4-related disease nine years later
Zhao zhewei,etal,2018[29]	1000	Platelet transfusion and splenectomy	Gastric adenocarcinoma	Subtotal gastrectomy and Roux-en-Y anastomosis	/	/

Figures

Figure 1

CT images show gastric tumors.

Figure 2

Pathological findings of endoscopic biopsy at high and low magnification: adenocarcinoma.

Figure 3

Platelet count fluctuation of the patient during hospitalization.

Figure 4

A showed that the tumor invaded the mucosa. B shows that at high magnification, a well differentiated glandular structure was seen. C shows the congestive splenomegaly.