

Surgical Complications in Myeloproliferative Neoplasm Patient with Essential Thrombocythemia: A Case Report

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Introduction: Essential thrombocythemia (ET) is a myeloproliferative neoplasm (MPN) which could complicate surgical procedures due to thrombosis and spontaneous bleeding. However, currently, there is neither concrete guideline nor prerequisite for ET patients who underwent operations.

Case Report: A 48 year-old-female was admitted to the emergency unit on 21 February 2020 due to vomiting and inability to pass gas/stool. The patient previously had an operation for uterine myoma two weeks before which showed thrombocyte count of 688,000/mm³. The patient was previously diagnosed with essential thrombocythemia with positive JAK2V617 point mutation on 24 June 2019. Laboratory examination showed thrombocyte 1,134,000/mm³ and leukocyte 22,700/mm³ suggestive of neutrophilia. CT scan showed fluid collection with blood density in the abdomen and pelvis. She was then diagnosed with obstructive ileus due to abdominal abscess and intestine adhesion. Adhesiolysis by laparoscopy was performed on 29 February 2020 with thrombocyte count of 727,000/mm³. Patient was able to pass flatus and defecate three days post-surgery. However, a decrease of hemoglobin to 8.2 g/dL on 3 March 2020 with thrombocyte count of 700,000/mm³ was suggestive of internal bleeding. She was discharged three weeks post-surgery after improvement of clinical condition with thrombocyte count of 850,000/mm³. She was given hydroxyurea 1000 mg once every two days, aspirin 80 mg OD, anagrelide 1 mg OD, and amlodipine 10 mg OD.

Conclusion: Myeloproliferative disease patients with high thrombocyte count are subjected to increased risk of thrombotic complications in perioperative settings, thus perioperative management and risk assessment are important to improve quality of life and prevent complications. Surgery in MPN patients with elevated thrombocytes may be considered if the benefits outweigh the risks. More studies in this field should be conducted in-order to provide more data for a guideline or systematic review/meta-analyses.

Keywords: myeloproliferative neoplasms, essential thrombocythemia, surgery, thrombosis

Introduction

Myeloproliferative neoplasms (MPN) are disorders of clonal haematopoiesis involving myeloid cell line.¹⁻³ Essential thrombocythemia (ET) is a type of MPN characterized by elevated thrombocytes. However, diagnosing ET is difficult due to non-specific symptoms and the need of bone marrow examination to find hyperproliferation of megakaryocyte lineage.¹⁻³ ET can also transform to other MPN phenotypes such as polycythemia vera (PV).³ Therefore, both ET and PV are difficult to be diagnosed, especially in developing countries.

ET carries an increased risk of thrombosis and bleeding.⁴ There are currently several clinical guidelines which stratify the risk of ET patients and determine the type of treatment given.^{5,6} However, there are no up to date recommendations related to surgery in ET patients and there are wide beliefs that ET patients with high thrombocyte can not undergo

surgical procedure safely.⁷ Thus, we present a case of a patient with ET-type MPN who successfully underwent hysterectomy surgery complicated by postoperative obstructive ileus due to adhesions.

Case Report

A 48-year-old woman was admitted to hospital on 21 February 2020, 2 weeks after hysterectomy with a complaint of excessive vomiting (Figure 1). The patient was diagnosed with ET with confirmation of JAK2V617F mutation in June 2019. She had myoma, but operations were rescheduled several times due to high count of thrombocytes and low count of red blood cells which could lead to complications. After medications and transfusions, she was approved to be operated by the doctors earlier in February 2020.

The patient returned because of vomiting. She was then hospitalized and the nasogastric tube was inserted. Patient was given hydrea 1000 mg BID and anagrelide 0.5 mg BID. On 24 February 2020, patient was unable to pass neither gas nor stool. Therefore, laboratory examinations were conducted, and the results showed elevation of platelets (Table 1). Meanwhile, whole abdomen CT scan showed fluid collection in pelvic pouch, partial obstruction due to small intestine adhesions, right lobe hepatomegaly, and atherosclerosis of the abdominal aorta, bilateral common iliac artery, right internal iliac artery, and left femoral artery (Figure 2).

Based on the presentations above, the patient was diagnosed with obstructive ileus due to intra-abdominal abscess and intestinal adhesion. The patient also experienced bleeding post hysterectomy operation. She was still unable to pass gas or stool until 26 February 2020. Thus, consultation with a surgeon was made on 27 February 2020 which resulted in a suggestion to conduct a laparoscopic operation despite the high level of thrombocytes. Therapies given were anagrelide 0.5 mg BID, vitamin K, and transamin. Before the operation, she was also given one unit thrombocyte concentrate (TC) and another unit if needed during the operation. Two bags of Packed Red Blood Cell (PRC) and 3 units of Fresh Frozen Plasma (FFP) were given before operation. The operation was conducted on 29 February 2020 through supraumbilical approach with 11 mm and 5 mm incision on the right abdomen and left abdomen, respectively. The small intestines were inflated and adhered to omentum with several adhesive bands. In addition, the small intestines were adhered to the lateral abdomen which had the hematoma. Removal of adhesion and adhesive bands was made, followed by cleaning of abdominal fibrin and blood and drainage.

Post-operation, on 1 March 2020, laboratory tests showed hemoglobin 14.1 g/dL, hematocrit 43%, leukocyte 18,000/mm³, and thrombocytes 675,000/mm³. Flatulence was regained on 2 March 2020 and defecation was regained on 3 March 2020. Patient was given antibiotic. Post-operative pain was felt up to 3 March 2020. On 4 March 2020, the patient complained about diarrhea, 4 to 7 times at night, with black brownish stool and pain in the abdomen and no fever. The patient's stool examination found erythrocytes. Fecal Occult Blood Test (FOBT) was also found positive. Esomeprazole, vitamin K, and transamin were given. On 5 March 2020, the patient's stool was dark red and her hemoglobin was 8.6 g/dL, hematocrit 25%, leukocyte 9700/mm³, thrombocyte 707,000/mm³. Twelve hours later hemoglobin decreased to 8.2 g/dL, hematocrit 25%, erythrocyte 2,920,000/mm³, ESR 66 mm/hour, and thrombocytes 700,000/mm³. Follow up on 6 March 2020 showed hemoglobin 8.1 g/dL, hematocrit 25%, leukocyte 8300/mm³, thrombocyte 643,000/mm³, aPTT 59 seconds with control 37.3 seconds, PT 10.8 seconds with control 10.8 seconds, and normal thrombocyte aggregation. Patient was then given PRC for 600 ml and TC for 1 unit. Haemoglobin increased to 8.9 g/dL, haematocrit 27%, erythrocyte 1,300,000/mm³, ESR 99 mm/hour, and thrombocytes 689,000/mm³ twelve hours after PRC administration. In addition, one bag of PRC and 500 cc of FFP were given. The patient then had gastroscopy on 7 March 2020. The result was iatrogenic erosive gastritis. Biopsy sample was also taken for pathological anatomy diagnosis. Pathology anatomy diagnosis showed chronic gastritis with no *Helicobacter pylori*. Therapies given were PRC, TP, and Fresh Frozen Plasma (FFP). On 10 March 2020, patient's stool was yellow. She was given anagrelide 1 mg OD, transamin 250 mg TID, and was instructed to stop consuming aspirin.

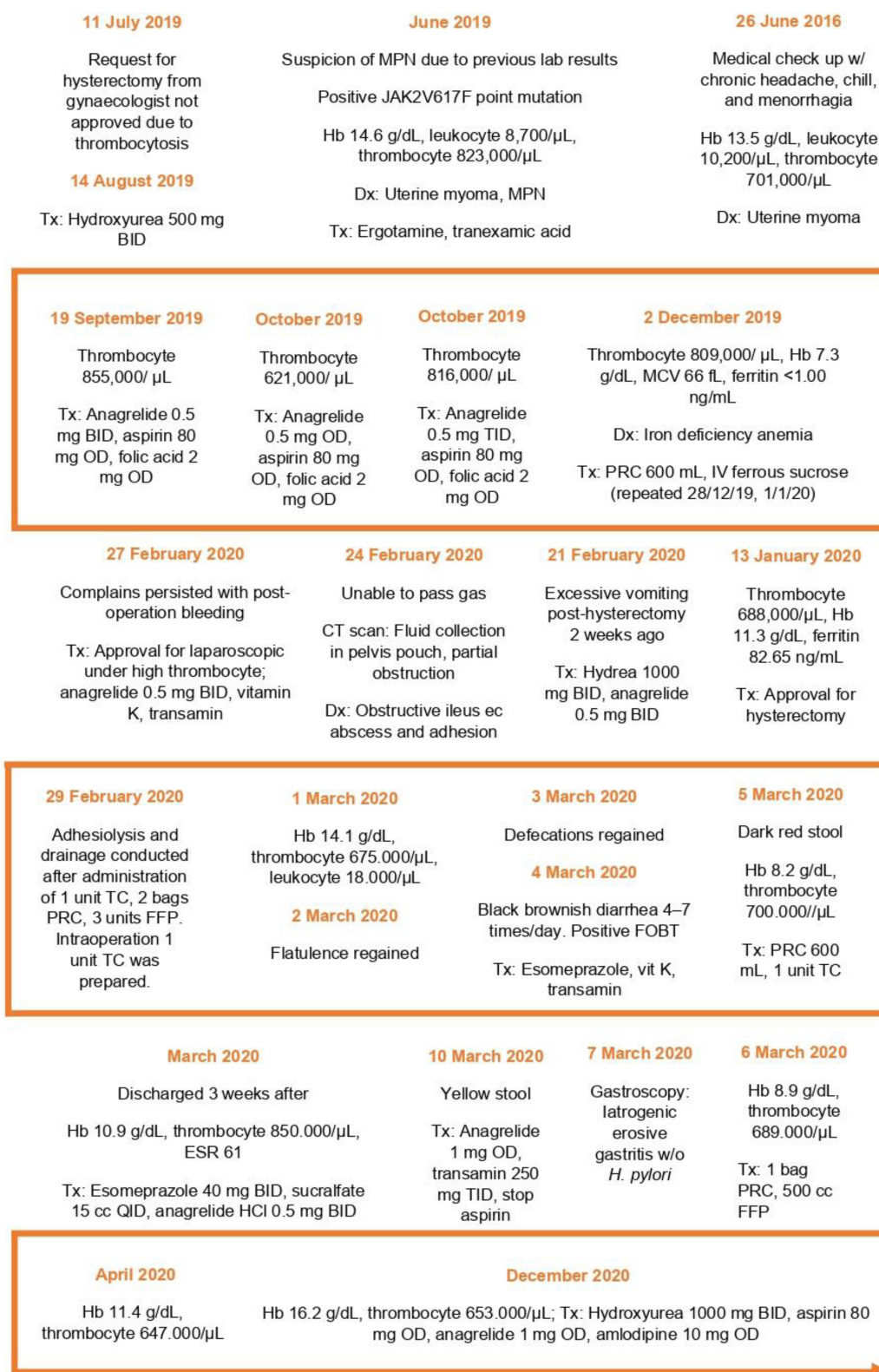


Figure 1 Patient's clinical presentations flowchart.

Table I Laboratory Examination Result of the Patient on 21 February 2020

Parameter (Units)	Result	Reference Range, Adults
Hemoglobin (g/dL)	13.7	11.7–15.5
Hematocrit (%)	42	35–47
Leukocyte (/mm ³)	22,700	4500–11,000
Platelet (/mm ³)	1,134,000	150,000–440,000
Total protein (g/dL)	7.7	6.6–8.8
Albumin (g/dL)	4.1	3.5–5.2
Globulin (g/dL)	3.6	2.3–3.5
Total bilirubin (mg/dL)	0.44	0.1–1.2
Direct bilirubin (mg/dL)	0.3	≤0.2
Indirect bilirubin (mg/dL)	0.14	0.1–1.0
AST (U/L)	24	<31
ALT (U/L)	43	<31
Gamma GT (U/L)	111	>32
Alkaline Phosphatase (IU/L)	379	42–98
CK-MB (U/L)	563	<480
Ureum (mg/dL)	21	7–18
Creatinine (mg/dL)	0.8	0.7–1.4
Uric acid (mg/dL)	3.1	2.6–6.0
Fasting glucose (mg/dL)	120	<100
Sodium (mEq/L)	137	136–146
Potassium (mEq/L)	4.6	3.5–5.1
Hepatitis B antigen	Non-reactive	Non-reactive
Anti HCV	Non-reactive	Non-reactive
CEA (ng/mL)	1.09	0–5.0

The patient was discharged after 3 weeks with hemoglobin 10.9 g/dL, hematocrit 34%, reticulocyte 3.4%, ESR 61 mm/hour, and thrombocyte 850,000/mm³. Therapies given were esomeprazole 40 mg BID, sucralfate 15 cc QID and anagrelide 0.5 mg BID. Four days after, the patient showed haemoglobin 11.4 g/dL, haematocrit 34%, reticulocyte 1.6%, ESR 69 mm/hour, thrombocyte 647,000/mm³. Eight months later, laboratory examinations showed hemoglobin 16.2 g/dL, hematocrit 52%, erythrocyte 7,000,000/mm³, thrombocyte 653,000/mm³. Therapies given were hydroxyurea 1000 mg taken once every two days, aspirin 80 mg OD, anagrelide 1 mg OD, and amlodipine 10 mg OD.

**Figure 2** Whole abdomen CT scan result of patient on 24 February 2020 showing fluid collection with blood density in abdomen and pelvis.

Discussion

Patients with high platelet counts are at high risk of hemostasis complication such as bleeding, thrombotic events, and thromboembolic events.^{1,8} The complications could be exaggerated by surgery as it was known that patients with ET have higher risk of bleeding and arteriovenous thrombosis by 10.5% and 500%, respectively.⁹ A study by Wada et al reported a patient with ET receiving cholecystectomy and choledochotomy at thrombocyte level of 1,302,000/mm³.¹⁰ The patient experienced 40 mg intraoperative bleeding, which was then given low molecular weight heparin (LMWH) on postoperative care. However, the patient experienced a bloody discharge from intra-abdominal drainage and was then re-operated for hemostasis.¹⁰

Even though patients with high platelet counts are at high risk of thrombosis, platelet count and thrombosis may not be linearly related in patients with MPN. Surgery and recent COVID infection could increase platelet count, but reactive conditions were associated with risk of venous thrombosis in both non-MPN and MPN patients.^{11,12} Our patient in this case report has JAK2-V617F mutation, which should be noted as one of the factors contributing to the increase of hemostasis and thrombosis complication. A study by Castelli et al mentioned that V617F mutation in ET caused higher risk of heparin induced thrombocytopenia with thrombosis (HITT).¹³ Another very important result from the study conducted by Castelli et al was that V617F homozygous mutation had higher risk of HITT compared to ET patients with heterozygous V617F mutation.¹³ Previous study by Castelli et al showed that HITT is more prevalent in ET patients with V617F mutation compared to ET patients without V617F.¹⁴

Meanwhile, a study by Varela et al reported a 41-year-old female undergoing laparoscopic resection for colon carcinoma. The patient was given hydroxyurea 0.5 mg, agrylin 1 mg BID, and aspirin 100 mg OD, who was further admitted for operation on thrombocyte level of 920,000/mm³.¹⁵ Laparoscopic was conducted without complications, but there was tachycardia with bleeding of the anterior branch of the right internal iliac artery in CT scan; hence, reoperation for embolization was performed. The patient was hospitalized for 16 days and did not show any new sign of bleeding or thrombosis.¹⁵ These findings were similar with a finding from a case series by Gurrieri et al which suggested thrombocyte count above 800,000/mm³ was associated with an increased risk of thrombotic complications.¹⁶ The same study suggested that operations were considered safer in patients with thrombocyte count below 450,000/mm³, within which 12% of patients receiving plateletpheresis had complications.¹⁶

Operations could be conducted safely in a not-too-high thrombocyte level. A study by Cai et al and Amarapurkar et al reported operations conducted on ET patients, which were on a 36-year-old female and a 38-year-old female with thrombocyte counts of 313,000/mm³ and 280,000/mm³, and without hemostasis complication.^{17,18} Another newer case was presented by Zhu et al which involved a 61-year-old female with ET and a thrombocyte count of 915,000/mm³.¹⁹ Patient was not given thrombotic prophylaxis but only experienced anastomotic bleeding. However, the study by Cai et al reported elevation of thrombocyte to 1,137,000/mm³ after operation, which means low thrombocyte count did not guarantee the development of hemostasis complication.¹⁷ Therefore, adequate perioperative care was important for prognosis of ET patients who underwent surgery.

Preoperative management of surgical procedures in ET patients consists of individual risk assessment of venous thromboembolism, appropriate use of compression stockings or pharmacological treatment, controlling platelet count, as well as correcting coexisting cardiovascular risk factors.²⁰ It is recommended to postpone elective surgery in high risk and symptomatic ET patients until the platelet count is reduced to 400,000/mm³ and coexisting cardiovascular risk factors are corrected.^{8,20} Platelet count can be lowered using cytoreductive therapy, whereas if active ischemia is present, plateletpheresis can be considered. In cases of emergency when lowering platelet count is not possible, perioperative thromboprophylaxis may be used.⁸

Risk stratification can be done using IPSET-t. Two points are accounted for any positive thrombotic history and evidence of JAK2-V617F mutation and 1 point is added for any cardiovascular risk factors such as smoking, hypertension, obesity, dyslipidemia, and diabetes. High risk is considered with a score greater than 2, low risk is considered when the score is lower than 2, and intermediate risk has a score equal to 2. Another instrument that could be used is the rIPSET-t (revised IPSET-t), which is under development.²¹

Conclusion

Myeloproliferative disease patients with high thrombocyte count are subjected to increased risk of thrombotic complications in perioperative settings, thus perioperative management and risk assessment are important to improve quality of life and prevent complication. Surgery in MPN patients with elevated thrombocytes may be considered if the benefits outweigh the risks. More studies in this field should be conducted in-order to provide more data for a guideline or systematic review/meta-analyses.

Informed Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy. Institutional approval was deemed not necessary by our institution for this case report. No funding was received for this case report.

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Disclosure

The authors declare that they have no conflict of interest to disclose.

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