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Case Report

Extreme Reactive Thrombocytosis Post-Splenectomy in 16 Years Old Boy

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Abstract: Thrombocytosis is a common occurrence in childhood. The most common causes of thrombocytosis are infection, trauma, surgery, and malignancy. Splenectomy may cause reactive thrombocytosis, which affects approximately 75-80% of patients and is associated with an increased risk of thrombotic and hemorrhagic complications. The appearance of thrombocytosis must be diagnosed in order to determine the treatment and prognosis. Antiplatelet agents, cytoreductive therapy, and/or therapeutic apheresis can be used to accomplish this. We reported a 16-year-old male who developed extreme reactive thrombocytosis following splenectomy. He was admitted to the hospital with a grade IV spleen rupture as a result of blunt abdominal trauma and underwent total splenectomy. After splenectomy, his platelet count was $229x10^9$/L and increased to $1154x10^9$/L on the ninth postoperative day. He stated that he was suffering from a fever, headache, fatigue, and abdominal pain. Therefore, he was referred to a consultant pediatric haemato-oncology specialist for thrombocytosis management and was diagnosed with extreme reactive thrombocytosis. Cytoreductive agents such as hydroxyurea were used to treat him. His platelet count decreased to less than $400x10^9$/L after 37 days of treatment. At 1-year follow-up, his complete blood count remains normal. He has been asymptomatic. We concluded that splenectomy may lead to extreme thrombocytosis, resulting in thrombotic and hemorrhagic complications. Thus, physicians should clinically monitor patients to ensure prompt diagnosis and appropriate treatment, as well as to prevent thrombosis and hemorrhage complications.

Keywords: Extreme Thrombocytosis, Post-splenectomy, Cytoreductive, Hydroxyurea

1. Introduction

The spleen and liver are the most frequently injured intra-abdominal organs in traffic accidents, followed by falls from elevated heights, bicycle accidents, and child abuse. Intra-abdominal injury contributes to approximately 80% of all visceral injuries caused by blunt trauma and occurs in approximately 5-10% of children who sustain blunt torso trauma [1, 2].

Patients with suspected splenic injury typically present with pain in the left upper quadrant, abdominal ecchymosis or abrasions, abdominal wall rigidity and tenderness, and decreased bowel sound [3]. As a delayed manifestation of splenic injuries, left subcostal pain, left shoulder pain, abdominal distension, rigidity, rebound tenderness, left upper quadrant fullness, or anemia can happen [4].

Splenic injuries can be treated non-operatively or surgically via angioembolization, splenorrhaphy, or partial splenectomy. Surgery is indicated in patients who do not improve with nonoperative management and in those who have sustained severe injuries [5]. Postoperative bleeding, thrombocytosis, vascular thrombosis, pancreatitis, intra-abdominal abscess, and post-splenectomy sepsis (also known as overwhelming post-splenectomy infection) are all possible complications of splenectomy [6]. Splenectomy can lead in reactive thrombocytosis, which occurs in approximately 75-80% of patients. Platelet count typically increases by 30-100% following splenectomy, usually peaking between 7-20 days postoperatively [7].

Thrombosis and hemorrhage are two common

complications of thrombocytosis. Post-splenectomy venous thrombosis is typically associated with platelet counts between 600 and 800x10^9/L and affects approximately 5% of patients [7]. Serial blood counts should be obtained following splenectomy for monitoring.

Extreme thrombocytosis increases the risk of developing a variety of complications, including neurological (vasomotor), thrombotic, and hemorrhagic complication. Headaches, vertigo, visual symptoms, lightheadedness, chest pain, nausea, acral dysesthesia, erythromelalgia, aphasia, and dysarthria are mostly clinical manifestations of vasomotor symptoms [8].

The management of reactive thrombocytosis should focus on reducing morbidity and preventing vascular thrombosis complications. When the platelet count is greater than 500 x10^9/L, prophylactic anticoagulants are indicated to prevent thrombosis and hemorrhage in reactive thrombocytosis. There are several treatment options, including anti-platelet medication, cytoreductive therapy, and apheresis techniques. Patients with extreme thrombocytosis and evidence of arterial or venous thrombosis may require cytoreductive agents such as hydroxyurea or anagrelide, and also with regular platelet count monitoring [7, 8].

2. Case Report

A sixteen-year-old boy presented to Sanglah Hospital's emergency department with the chief complaint of abdominal pain. The patient was referred from Sanjiwani Hospital with an intra-abdominal bleeding suspicion. He has a nine-day history of being involved in a motorcycle accident. He sustained a blunt abdominal injury. Since the day before admission, he had complained of abdominal pain in the left upper quadrant. The pain was described as constant, severe, tenderness, and non-radiating Additionally, he had complained of nausea, vomiting, and a fever.

On physical examination, he looked fatigue and pale. His consciousness level was normal (15 on the glass glow coma scale), and his blood pressure was 100/60 mmHg. His pulse rate remained consistent at 100 beats per minute. The respiratory rate was 20 times per minute, and the temperature in the axilla was 36,7°C. His body weight was 57 kilograms and his height was 165 centimeters. The abdominal cavity was distended with fullness, tenderness, and rebound tenderness, most prominent in the left upper quadrant, along with a decreased bowel sound. The cardiovascular and respiratory systems were examined and found to be normal.

Laboratory values were significant for a hemoglobin (Hb) level of 8.77 g/dL, hematocrit (Hct) of 25.10%, white blood cell count (WBC) of 21.85×10^9/L (neutrophil 86.93%, lymphocyte 7.31%), and a platelet count of 254.4×10^9/L. Coagulation of the blood and electrolyte balance result are normal. In the previous hospital, radiology examinations revealed no evidence of free air beneath the diaphragm. As a result, the patient was diagnosed with generalized peritonitis caused by suspected hollow-organ perforation, blunt abdominal trauma, mild anemia due to intra-abdominal bleeding. The trauma surgery division planned the patient for emergency laparotomy.

Due to the fact that the integrity of the splenic capsule was disrupted on the renal surface and a 3 to 5 cm splenic laceration with subcapsular hematoma was observed, he underwent total splenectomy (Figure 1). He was diagnosed as ruptured spleen grade IV, generalized peritonitis caused by blunt abdominal trauma, intra-abdominal bleeding.

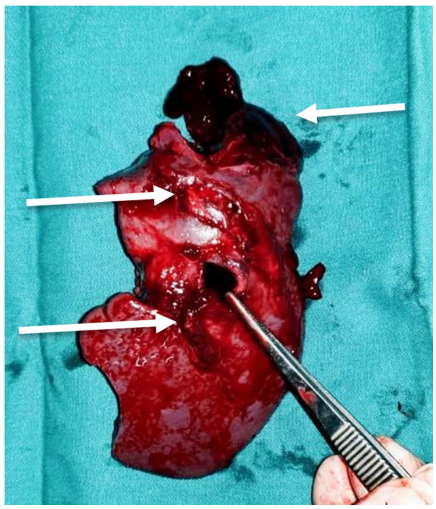

Figure 1. *Spleen rupture. White arrow showing splenic laceration and subcapsular hematoma.*

A routine complete blood count was performed post-operatively. His platelet count was 229x10^9/L immediately following the splenectomy but increased abnormally to 1154x10^9/L nine days later. Other laboratory results revealed a hemoglobin level of 10.66 g/dL, a Hct of 32.3%, and leucocyte count of 15.76x10^9/L. He complained of a fever, headache, fatigue, and abdominal pain, with the upper left quadrant being the most tender. There was no vomiting, loss of consciousness, blurred vision, chest pain, dysesthesia, or aphasia. He was referred to consultant pediatric haemato-Oncology for thrombocytosis management. He was diagnosed with severe thrombocytosis caused by splenectomy and was treated with cytoreductive agents such as hydroxyurea 500 mg every 8 hours. He will perform serial complete blood count evaluation. His platelet count remained elevated at 1232x10^9/L, and his hemoglobin level was 10.85 g/dL. He remained no complained, planned to discharge from the hospital and took 500 mg of hydroxyurea orally every eight hours.

One month after the splenectomy, he had no complaints and his platelet count became decreased to 537x10^9/L. The dosage of hydroxyurea has been decreased to 125 mg every 8 hours. His platelet count reaches normal (356x10^9/L) two months after splenectomy, with normal hemoglobin of 13.3 g/dL. Thus, the hydroxyurea treatment was discontinued. After 12 months of splenectomy, he has no complaints and can activities normally, even though the number of platelets is still above 400x10^9/L. The characteristics of blood count in relation to hospital course showed in Table 1.

Table 1. *Characteristics of blood count in relation to hospital course.*

Variable	Postoperative Duration						
	Day 0	Day 8	Day 12	Day 26	Day 35	9th month	12th month
Platelet (10^9/L)	229.3	1084	1232	537	356	471	445
WBC (10^9/L)	33.16	17.62	14.78	12.23	8.5	10.69	12.35
Hb (g/dL)	9.36	10.32	10.85	12.1	13.3	16.1	16.0
Hct (%)	27.01	31.53	34.49	34.1	34.1	44.9	44.8

Abbreviations: PLT, platelet; WBC, white blood cell; Hb, hemoglobin; Hct, hematocrit.

The characteristics of hemoglobin, leukocyte, and platelet during treatment hydroxyurea showed in Figures 2, 3 and 4.

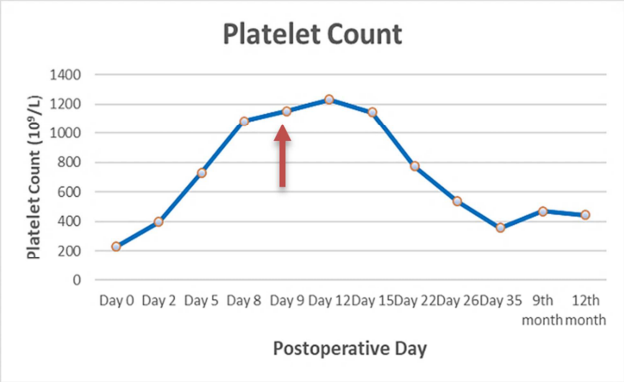

Figure 2. *Platelet count. Red arrow showing time beginning hydroxyurea treatment.*

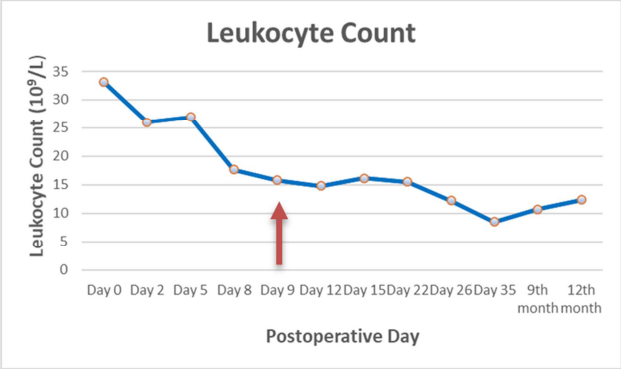

Figure 3. *Leukocyte count. Red arrow showing time beginning hydroxyurea treatment.*

3. Discussion

Thrombocytosis is a frequent condition in clinical practice and is defined as an elevated platelet count of more than 450x109/L, which usually happens in between 3-13% of children. Males appear to be more affected than females, at a 2.5:1 ratio [9, 10]. Mild thrombocytosis (450 to 700 x109/L), moderate thrombocytosis (700 to 900x109/L), and severe thrombocytosis (greater than 900x109/L) are all classified as thrombocytosis. Extreme thrombocytosis is defined as a platelet count of 1000 x109/L or greater and is more frequently associated with reactive thrombocytosis (66–82%) than primary thrombocytosis [10, 11].

Reactive thrombocytosis is frequently caused by infection, trauma, surgery, or occult malignancy. Spleen removal can result in reactive thrombocytosis, which occurs in approximately 75-80% of cases [7, 9]. Thrombocytosis after splenectomy occurs as a result of decreased platelet storage and removal in the reticuloendothelial system [7] Platelet count typically increases by 30% to 100% following splenectomy, peaks between 7 and 20 days postoperatively, and returns to normal within weeks, months, or, in rare cases, years. The increase in platelet count may be indicative of the severity of inflammation [12, 13].

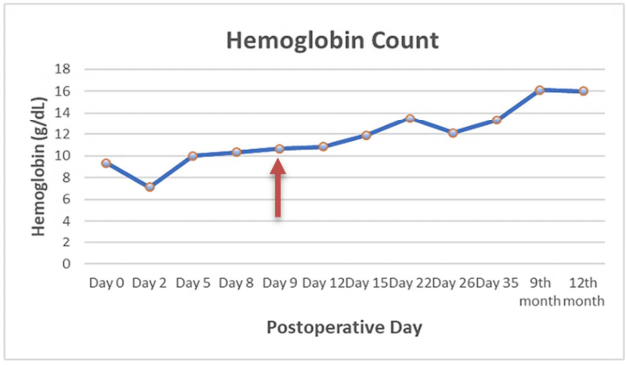

Figure 4. *Hemoglobin count. Red arrow showing time beginning hydroxyurea treatment.*

Although reactive thrombocytosis is not typically associated with thromboembolic or hemorrhagic events, complications following splenectomy have been associated with additional thrombotic risk factors [8]. Splenectomy can significantly increase the risk of vascular complications by 1.35 fold when compared to no splenectomy and typically occurs two days after splenectomy. Thrombocytosis can cause platelet hyper aggregation, which may lead venous or arterial thrombosis. Vascular thrombosis can result in various complications, including stroke, coronary artery ischemia, pulmonary embolism, ischemia, deep vein thrombosis, and visceral/splanchnic vein thrombosis [14]. Extreme thrombocytosis may increase the risk of hemorrhage and thromboembolism. The manifestation of vasomotor disturbance includes headache, dizziness, visual disturbance, chest pain, nausea, acral dysesthesia, erythromelalgia, aphasia, and dysarthria. Serial blood counts should be performed following splenectomy [12, 14].

The management of reactive thrombocytosis should focus on the underlying cause of the thrombocytosis with the goal of reducing morbidity and preventing venous thromboembolism complications. Platelet reduction is not necessary in

asymptomatic patients with reactive thrombocytosis. On the other hand, patients with thrombocytosis, who have additional cardiovascular and/or thrombotic risk factors or who are experiencing active ongoing complications, should be treated. Anticoagulant prophylaxis is indicated to prevent thrombosis and hemorrhage in patients with reactive thrombocytosis following splenectomy [13-15]

The first line of therapy is platelet antiaggregating medication such as acetylsalicylic acid or aspirin; however, anticoagulant therapy following splenectomy may increase the risk of hemorrhage. Aspirin is given to reduce the risk of thromboembolic events and vasomotor symptoms in patients with severe thrombocytosis, Lower doses of 40–100 mg once or twice daily are preferred over higher doses. In extreme thrombocytosis patients with a high risk of arterial or venous thrombosis, cytoreductive therapy such as hydroxyurea or anagrelide has been mostly initiated [15].

Anagrelide is a newer platelet-lowering agent that is non-leukemogenic and inhibits megakaryocyte proliferation and differentiation. Anagrelide is an oral imidazoquinazoline derivative that decreases platelet counts and inhibits platelet aggregation via platelet anti-cyclic AMP phosphodiesterase activity. The initial dose is 0.5 mg twice daily, titrated to achieve the desired platelet count. The platelet count typically responds within 7-14 days, with a complete response taking approximately 4-12 weeks. Fluid retention, palpitations, arrhythmias, heart failure, headaches, and anemia are indeed common side effects. There is a dearth of long-term data on anagrelide's side effects and complications, with mild to moderate anemia being a frequent occurrence [16, 17]. In this patient, anagrelide could not be administered due to the drug's scarcity in Bali.

Hydroxyurea is an antimetabolite that inhibits ribonucleoside diphosphate reductase enzymes in a highly selective manner. By and large, hydroxyurea is well tolerated, readily available, and relatively inexpensive. The initial dose of hydroxyurea is recommended to be 20-30 mg/kg daily. Doses are adjusted to maintain platelet counts between $100x10^9$/L and $400x10^9$/L and to avoid hematological toxicity. If the platelet count continues to increase until mild myelosuppression is achieved, the hydroxyurea dose may be increased by 5 mg/kg/day, but not to exceed 35 mg/kg/day [17, 18].

The other approach is platelet pharesis. These are techniques for decreasing platelet count in patients with extreme thrombocytosis, which may be associated with a variety of thrombotic or hemorrhagic complications. Specifically, the platelet count temporarily decreases. Thus, it should be followed by the administration of a myelosuppressive agent to ensure that the platelet count remains within the recommended range (400 $x10^9$/L) [19].

In our case, the patient was treated with a cytoreductive drug, hydroxyurea 10 milligrams twice daily. Complete blood count monitoring reveals a decrease in platelet count 37 days after therapy. He has been asymptomatic and has been acting normally.

The risks of infection, sepsis, and sepsis-related mortality appear to be approximately two to three times greater in asplenic patients, when compared to the general population. However, patients who have previously undergone splenectomy for trauma have a decreased risk of infection. Regular monitoring of the risk of infection following splenectomy is recommended [20].

4. Conclusion

Patients undergoing splenectomy must be closely monitored for postoperative complications. Thrombocytosis following splenectomy must be managed carefully to avoid thrombosis and bleeding complications. One of the treatment options for thrombocytosis is cytoreductive therapy, particularly hydroxyurea, which is quite affordable and generally well tolerated. This management strategy has been shown to reduce post-splenectomy complications and hospital stay.

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