Extensive Thrombosis of the Portal Venous System Postsplenectomy for a Patient with Thalassemia Intermedia

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Abstract

Portal vein thrombosis is a life threatening complication after splenectomy especially for thalassemia and myelofibrosis and require a high index of suspicion to establish an early diagnosis. Prompt anticoagulation should be initiated once the diagnosis is established to prevent potentially fatal complications such as bowel infarction or later portal hypertension.

In this case report, we describe a patient with thalassemia intermedia who undergo splenectomy for massive splenomegaly and developed acute portal vein thrombosis .Anticoagulation started but another CT abdomen done 2 months later showed no change in thrombosis in addition , the patient escaped follow up.

CASE PRESENTATION

A 35-year-old male was diagnosed as a case of thalassemia intermedia since childhood on occasional packed red transfusion and iron chelation therapy admitted to the Haematology Department of Baghdad Teaching Hospital with insidious onset of progressive severe abdominal pain. Past history was significant for hepatitis C (probably transfusion-transmitted) and splenectomy 2 weeks ago for massive splenomegaly causing mechanical discomfort. His current medication include folic acid 5 mg/day.On examination, the patient was pale, Jaundiced, not tachypneic, No LAP, no raised JVP. Vital signs include BP 120/80, temp 37.5 $^{\circ}$C, and PR 100/min. cardiorespiratory examination was unremarkable. Abdominal examination revealed midline scar, no ascites, no tenderness, no mass, and hepatomegaly 2 cm below costal margin.

Immediately after admission, the patient put on nil by mouth, IV fluids, triple antibiotics (cefotaxime , gentamicin and metronidazole) , acid suppressants and narcotic analgesia and the surgical team responsible for the splenectomy was called for help. Results of laboratory investigations are shown in tables 1 and 2.

Table 1- Results of Laboratory investigations

CBP	
Haematocrit (%)	26
White cell count($\times 10^9$/L)	19.5
Differential count (%)	
Neutrophils	87
Lymphocytes	10
Blood Film	Hypochromic with few normochromic cells , anisopoikilocytosis , many nucleated RBCs are seen
Platelet count ($\times 10^9$/L)	2350
Biochemistry	
Urea (mg/dL)	40
Creatinine (mg/dL)	1.5
Uric acid (mg/dL)	9.0
Protein (g/dL)	
Total	7.6
Albumin	3.5
Globulin	4.1
Calcium (mg/dL)	8.0
Bilirubin (mg/dL)	3.5
ALT (unit/L)	12
AST (unit/L)	6

AST : Aspartate aminotransferase , ALT : Alanine aminotransferase

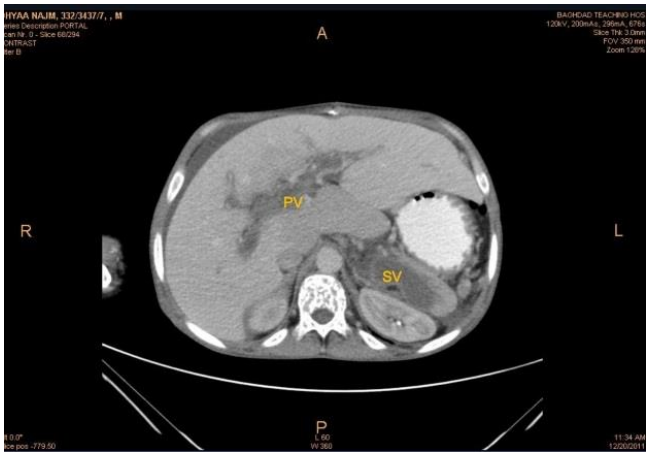
Table 2 – Characteristics of the removed spleen

Splenic Weight
>3 Kg
Splenic Histology
• Dilated splenic cords and sinuses
• Prominent endothelial lining
• Hemosiderin-laden macrophages
• Scattered lymphoid follicles

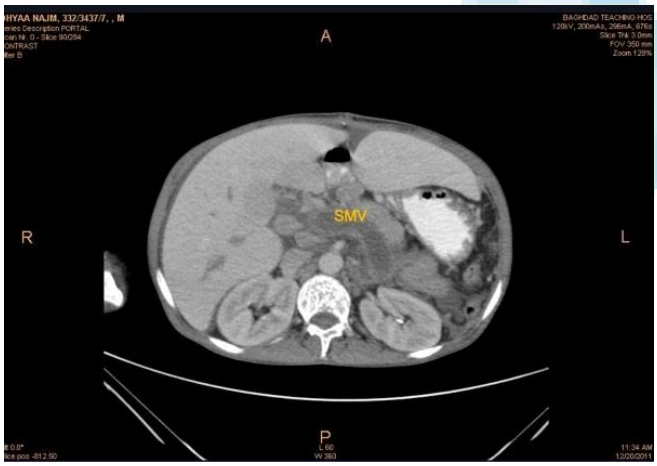
Abdominal imaging (Urgent plain abdomen, U/S and Doppler study, CT abdomen) .Hepatomegaly, spleen not seen; enlarged portal vein contain thrombus extending to the superior mesenteric vein and splenic vein, mild ascites. Pancreas and other intra-abdominal structures are normal.

Figure 1: Contrast computed tomography of the abdomen on admission showed severe thrombosis of : (A) portal vein (PV) and splenic vein (SV) (B) superior mesenteric vein (SMV)

A: portal vein



B: superior vena cava



Other Investigations:

•S. Ferritin > 1000 ng/mL

•Echo study –Normal

•Baseline PT/PTT/INR –Normal

•CXR PA view –Normal

Evaluation done by gastroenterologis :

Upper GI Endoscopy showed no oesophageal varices Normal. Non-cirrhotic portal vein thrombosis

Treatment:

A provisional diagnosis of portal/mesenteric/splenic vein thrombosis had been established and the patient started on immediate anticoagulation by low molecular weight heparin (LMWH) 150

U/Kg/day, aspirin and warfarin with monitoring by INR.

Follow up:

CT abdomen with contrast done 2 months after first admission showed the same findings on the previous film and the patient escaped follow up.

Discussion

The current indications of splenectomy for haematologic disorders are shown in Table 3. However, Splenectomy should be performed for clinical indications rather than for specific diagnoses.

Table 3:Current indications for splenectomy in hematological disorders

Current Indications for Splenectomy for Haematologic Diseases
Hereditary spherocytosis
Other hereditary hemolytic anemias (eg, stomatocytosis, pyropoikilocytosis pyruvate kinase deficiency)
Sickle cell disease
Thalassemia major or intermedia
Immune thrombocytopenia
Myeloproliferative disorders
Autoimmune hemolytic anemia
Hypersplenism
Lymphoproliferative disorders
Thrombotic thrombocytopenic purpura

Adapted from Crary SE , Buchanan GR. *Blood* 2009 ; 114: 2861-2868

In many instances, removal of the spleen will improve the condition of patients with hemolytic anemia due to intrinsic disorders of erythrocyte membranes and enzyme disorders and of those with chronic conditions, such as storage diseases and portal hypertension.The clinical benefit to be obtained from splenectomy should at least balance, and preferably outweigh, the potential long term risks of postsplenectomy septicemia, an increased risk for thrombosis, and the shift of storage cells from the spleen to other organs, such as the bone marrow, where they may do more harm in the absence of the spleen[1]

Thrombosis of the portal venous system is a unique, and potentially life-threatening, complication after splenectomy. However, as radiographic imaging has improved in quality and increased in frequency, it is becoming clear that portal vein thrombosis occurs more often than previously reported[2]

The reported incidence of portal venous thrombosis varies greatly within the literature 1 and is not clearly determined[3,4]

Incidence was greatly unappreciated, with 0.2-55% of patients developing PVT 2,5 All episodes occurred within

2 months, and the majority within 2 weeks of the surgery. 6 Asymptomatic thrombosis was observed in 33 to 66% of postsplenectomy patients[2]

Risk Factors for portal vein thrombosis are shown in Table 4 and the risk factors for portal vein thrombosis postsplenectomy according to presence or absence of hemolysis and splenic function are shown in table 5.

Table 4- Risk Factors for Portal Vein Thrombosis Postsplenecomy

Risk Factors for Portal Vein Thrombosis Postsplenecomy
Preoperative general clinical or laboratory risk factors, such as age, obesity and previous thrombosis
Local surgical factors
Splenic vein remnant is attached to the portal vein
Laparoscopic than with open splenectomy
Greater splenic weight
Impact of the underlying disease process on the incidence of Portal Vein Thrombosis after splenectomy
Myeloproliferative disorders
Haemolytic anaemias whether congenital or acquired
Thromocytosis
Higher platelet count shortly after splenectomy does not consistently correlate with the risk of thrombosis

Adapted from Crary SE , Buchanan GR.. Blood 2009 ; 114: 2861-2868

Table 5- Risk of Portal Vein Thrombosis Based on the Presence or Absence of Hemolysis and Splenic Function

Pathophysiologic State	Example	Risk for PVT
Neither Haemolysis nor Splenectomy	Normal person	person's unique genetic and environmental risk factors.
Haemolysis with Intact Spleen	Hereditary spherocytosis Glucose-6-phosphate dehydrogenase deficiency β-Thalassmia minor	Decreased or depend on the person's unique genetic and environmental risk factors.
Splenectomy without Haemolysis	Hereditary spherocytosis Ideopathic Throbocytopenic Purpura Trauma	Increased or depend on the person's unique genetic and environmental risk factors.
Splenectomy and Ongoing Haemolysis	Thalassemia intermedia Hgb E/ β -thalassemia Sickle cell anemia Hereditary stomatocytosis	Greatly increased

Modified from Crary SE , Buchanan GR.. Blood 2009 ; 114: 2861-2868

Evidence in thalassemia supports the presence of a hypercoagulable state greatly exacerbated by splenectomy, which is the result of [3,7,8]

*Platelet activation

*Enhanced red blood cell adherence to the endothelium

*Reduced levels of the natural anticoagulants protein C and protein S

*Increased thrombin generation.

*Procoagulant cell-derived microparticles

*Persistence of abnormal erythrocytes in the circulation which have been rendered "procoagulant" resulting from increased exposure of phosphatidylserine on the outer membrane surface

Thalassemia Intermedia (TI) is characterized by chronic intravascular hemolysis and marked ineffective erythropoiesis. Thromboembolic complications have been most frequently reported after splenectomy in thalassemia intermedia (TI).[9,10]

In a recent large survey of 8860 patients with thalassemia, the prevalence of thromboembolic events among those with TI was 4% . Remarkably, 94% of these complications occurred after splenectomy.[11]

SCREENING FOR THROMOPHILIA

This include testing for the following:

1. Factors XII , VIII , fibrinogen

2. Activated protein C resistance

3. Protein C and S deficiency

4. Antithrombin III deficiency

5. Prothrombin 20210 mutation

6. Hyperhomocystinaemia

7. Antiphospholipid syndrome (lupus anticoagulant , anti-β glycoprotein -1 and anticardiolipin antibodies IgG and IgM) [5,6]

Several studies have reported testing for these thrombophilia risk factors at the time of the thrombotic insult but it is not cost effective and the contribution of thrombophilia is yet to be determined .[3]

Treatment

Unfractionated Heparin (UFH) and Low Molecular Weight Heparin (LMWH). Patients with documented asymptomatic or symptomatic portal vein thrombosis usually received intravenous standard heparin or therapeutic doses of LMWH followed by oral anticoagulant therapy with warfarin for 3-6 months.[12] Anticoagulation can also be given as an extension of previous preoperative prophylaxis with LMWH. [6]

Thrombolytic therapy. Thrombolytic therapy has been tried in a small number of cases with encouraging results; use of thrombolytic therapy is most attractive when thrombosis is fairly acute.[13]

Thrombolytic therapy is either catheter-based thrombolysis with alteplase (tissue plasminogen activator, tPA) directly into the thrombus via a transhepatic catheter placed percutaneously [14,15] or systemic thrombolysis (using streptokinase) . [14]

Prevention

This can be summarized as follows:

1. Optimal preoperative evaluation
2. History (prior thrombotic episodes , use of prothrombotic drugs (e.g OCPs)
3. Investigations (CBP , PT/PTT/INR , fibrinogen , D-dimer) [5]
4. Anti-thrombotic prophylaxis with LMWH and with aspirin (if platelet count > 1000 × 109 [6,14]
5. Routine doppler U/S of the splenectomised patients during the first postoperative week 5
6. Ligation of the splenic vein as close as possible to the junction with the superior or inferior mesenteric vein may prevent stasis in the stump of splenic vein and prevent thrombosis [14]

Conclusion

Portal vein thrombosis is a life threatening complication after splenectomy that requires a high index of suspicion to establish an early diagnosis.. Routine postoperative surveillance may be warranted in individuals at risk An aggressive approach to thrombotic prophylaxis should also be considered in high-risk patients with hemolytic anemias and massive splenomegaly.

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