

Portal vein thrombosis: A case report and literature review

James Gauci, Sarah Cuschieri, Mario Vassallo

Introduction

A case report of Portal Vein Thrombosis (PVT) as a complication of protein S deficiency. PVT has been increasingly diagnosed over the years, particularly through the use of ultrasound-Doppler equipment. The lifetime risk of getting PVT in the general population has recently reported to be 1%.¹ While this condition has traditionally been associated with cirrhosis or liver malignancy, it may also occur without any liver disease.

The case report is followed by a discussion of the aetiology and clinical presentations of PVT, as well as a review of the investigations and management proposed in the literature.

Keywords

Hypertension, portal; Portasystemic Shunt, Surgical; Esophageal and Gastric Varices; Splenomegaly.

James Gauci MD, *
Foundation Trainee,
Department of Medicine,
Mater Dei Hospital
james.a.gauci@gov.mt

Sarah Cuschieri MD,
Foundation Trainee,
Department of Medicine,
Mater Dei Hospital

Mario Vassallo, MD, FRCP (Lon),
Consultant Department of Medicine,
Mater Dei Hospital

**corresponding author*

Case Report

A 36 year old lady was referred with non-specific abdominal pain, elevated liver enzymes and a prolonged INR. Abdominal examination revealed hepatosplenomegaly, which was confirmed on ultrasound. She was investigated through several blood tests; namely a full blood count, inflammatory markers, INR, haematinics, serum copper as well as caeruloplamin and alpha-antitrypsin levels. An autoimmune screen, viral screen, leishmaniasis screen and serum protein electrophoresis were also negative, as was a trephine biopsy. No abnormalities were detected.

As the cause of the hepatomegaly was obscure, a liver biopsy was arranged; this showed sinusoidal dilatation suggestive of portal vein thrombosis or Budd-Chiari syndrome. CT scan confirmed portal and splenic vein thrombosis but the superior mesenteric vein was patent. The patient was started on anticoagulants, with a target INR of 2-2.5. A thrombophilic screen was done; this confirmed protein S deficiency.

An oesophagogastroduodenoscopy (OGD) was performed, which showed Grade B oesophageal varices, gastric varices and portal hypertensive changes. In view of this, the patient was started on propranolol. She remained clinically stable for four years and was followed up by repeat OGDs.

Four years after presentation, a follow-up OGD showed progression of the oesophageal varices to Grade C, red wale signs, and small gastric ulcers. The varices were banded and the patient was started on a proton pump inhibitor (PPI).

The patient experienced her first upper GI bleed five years after her initial presentation. An emergency OGD showed Grade C varices with red wale signs, requiring banding 5 times. Warfarin was omitted despite an INR which was almost within the target range, and maximal PPI doses were administered: omeprazole 40mg bd IV. She was started on piperacillin-tazobactam 4.5mg tds IV and an octreotide pump, set at a rate of 2.5mcg/hr for a total of five days.

The patient scored 6 on the Rockall score, and was in fact managed at the Intensive Care Unit. She required several transfusions of packed red cells and

fresh frozen plasma in view of anaemia and persistently elevated INR.

During the same admission, she had further episodes of fresh bleeding; a second emergency OGD showed oesophageal ulcers, prominent gastric varices and signs of recent bleeding. She was kept on maximal PPI doses and started on sucralfate 1g qds po, as well as terlipressin 1mg tds IV.

The patient was referred for emergency surgery, and a mesentero-right-common-iliac shunt was performed. She did considerably well in the post-operative period, and her ascites was controlled with diuretics. A haematological consultation advised testing for Janus kinase (JAK)-2

gene mutation; this was positive, suggesting the presence of a myeloproliferative disorder.

She was discharged on subcutaneous enoxaparin, with regular follow-up from the gastrointestinal and haematological point of view.

Discussion

Aetiology

Portal vein thrombosis as a complication of cirrhosis and hepatocellular carcinoma has long been recognized.²⁻³ Over the years, it has been shown that PVT can also occur as a cause of several thrombophilic states and local abdominal conditions. Some studies have shown the involvement of multiple factors in the development of PVT.⁴

As shown in Table 1, prothrombotic states can be inherited or acquired. Inherited thrombophilias include genetic disorders such as factor V Leiden mutation, factor II gene mutation, protein C deficiency, protein S deficiency, antithrombin III deficiency and methylene-tetrahydrofolate-reductase (MTHFR) gene mutation.⁵⁻⁷

Acquired thrombophilias include primary myeloproliferative disorders such as polycythaemia rubra vera; PVT may actually be the first manifestation of this disease.⁸ Other acquired prothrombotic states include paroxysmal nocturnal haemoglobinuria, hyperhomocysteinaemia, antiphospholipid syndrome, increased factor III levels and thrombin activatable fibrinolysis inhibitor (TAFI) gene mutation.⁹⁻¹²

A variety of intra-abdominal inflammatory conditions may lead to PVT. These include pancreatitis and local injury to the portal vein, for example after abdominal trauma or surgery.¹³⁻¹⁴ Uncommonly, portal vein thrombosis may occur as a complication of liver transplantation.¹⁵

Pregnancy, use of oral contraceptives, chronic inflammatory diseases and malignancies represent an increased risk in patients with prothrombotic states.¹⁶ Other aetiological agents include infection with cytomegalovirus and *Bacteroides fragilis*,¹⁷⁻¹⁸ while approximately 10-30% of cases are idiopathic.¹⁶

Table 1: Aetiology of PVT

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|---|
| Inherited Prothrombotic state |
| - Protein C deficiency |
| - Protein S deficiency |
| - Antithrombin III deficiency |
| - Factor V Leiden mutation |
| - Factor II gene mutation |
| - Methylene-tetrahydrofolate-reductase (MTHFR) gene mutation |
| Acquired Prothrombotic state |
| - Primary myeloproliferative disorder (e.g. polycythaemia rubra vera) |
| - Paroxysmal nocturnal haemoglobinuria |
| - Hyperhomocysteinemia |
| - Antiphospholipid syndrome |
| - Increased factor VIII levels |
| - Thrombin activatable fibrinolysis inhibitor (TAFI) gene mutation |
| Intra-abdominal inflammation |
| - Pancreatitis, appendicitis, diverticulitis |
| - Portal vein injury e.g. abdominal trauma, surgical procedures |
| Portal hypertension |
| - Liver cirrhosis |
| - Budd-Chiari syndrome |
| Malignancy |
| - Hepatocellular carcinoma |
| - Pancreatic carcinoma |
| Infections |
| - Cytomegalovirus |
| - <i>Bacteroides fragilis</i> |
| Pregnancy |
| Drugs (e.g. oral contraceptives) |
| Idiopathic |

Presentation

The clinical presentation of PVT may be acute or chronic. This classification is not so clear-cut, as there is no definitive time frame which distinguishes the two. Studies have generally considered the presentation to be acute if symptoms develop less than 60 days prior to hospital assessment.¹⁹ PVT is also regarded as acute if imaging has ruled out the presence of significant collaterals and there is no evidence of portal hypertension.

Acute PVT is characterised by abdominal pain and nausea, though it may also be asymptomatic. Symptom severity depends on the rapidity and extent of the thrombosis. Involvement of the superior mesenteric vein may lead to bowel infarction; patients may then present with haematochezia, fever, rebound tenderness, and ascites. Such a complication is associated with a poor prognosis.²⁰ Acute PVT may then undergo spontaneous resolution, or progress to chronic thrombosis.

Chronic PVT presents with the complications of portal hypertension, including variceal bleeding (which is usually well-tolerated), splenomegaly or hypersplenism.¹⁶ Patients may complain of abdominal discomfort as a cause of the splenomegaly. Chronic PVT may also be asymptomatic and discovered incidentally on imaging.

The presence of cirrhosis, cancer and mesenteric vein thrombosis are negative prognostic factors. In fact, studies have shown that mortality is influenced more by associated disease rather than variceal bleeding *per se*.⁴

Investigations

The investigation of choice is abdominal ultrasound. Sonographic findings include the presence of solid echoes within the portal vein and demonstration of a portal cavernoma.²¹ Additional information can then be obtained through other non-invasive imaging modalities, including doppler ultrasound, CT scan, magnetic resonance angiography and endoscopic ultrasound.²²⁻²³

In our patient, while abdominal ultrasound revealed splenomegaly, it was the CT scan which clinched the diagnosis of PVT. CT scan can also be used to differentiate between recent and old thrombosis; the presence of portosystemic collaterals and cavernoma formation are both suggestive of old thrombosis.²⁴

The next step is a thorough investigation of the cause of the thrombosis. Local abdominal factors can be identified through imaging; investigation for a systemic cause, including myeloproliferative disorders and prothrombotic tendencies, is carried out through blood tests.⁽²⁴⁾ Identification of the aetiological agent is vital, as the underlying condition may require

specific treatment, and will influence the use and duration of anticoagulation.²⁵

In our patient, investigations for the presence of cirrhosis and for local abdominal causes of thrombosis were negative. A thrombophilic screen then confirmed protein S deficiency, and a positive test for JAK-2 gene mutation suggested the presence of a myeloproliferative disorder.

Treatment

The aim of the treatment is two-fold: to prevent or reverse thrombus advancement in the portal venous system, and to treat any complications that may arise.²⁵

Recommendations on the use of anticoagulation differ in acute and chronic PVT. While several studies have supported the role of anticoagulation in patients with acute PVT,²⁶ little information exists on the duration and extent of anticoagulation. It has been suggested that patients with a self-limiting course of PVT, such as acute pancreatitis, should be given a course of 3-6 months.²⁵ On the other hand, anticoagulation can be continued in patients with prothrombotic tendencies, a family history of venous thrombosis or confirmed extensive thrombosis.

Thrombolytic therapy has also been shown to lead to the resolution of acute PVT.²⁷ Studies have reported the use of thrombolytics such as recombinant tissue plasminogen activator, both systemically and through a catheter-directed infusion.¹⁶ These techniques have been very promising with regard to resolution of thrombus, resulting in improved symptomatology and avoidance of bowel resection.²⁸ However, they have had a very high rate of major complications, including bleeding. It was thus recommended that thrombolysis is reserved for patients with severe disease, while a more conservative approach should be taken for others.

The use of anticoagulation in chronic PVT is more controversial, due to the presence of varices as a complication of portal hypertension. Nevertheless, it has been shown that the benefit-risk ratio in such a scenario favours the use of anticoagulant therapy.²⁹ In the case presented above, the patient was in fact kept on life-long anticoagulation.

Management of the complications of PVT is mostly concerned with prophylaxis and treatment of gastro-oesophageal variceal bleeds. This has mostly been studied in patients with portal hypertension and cirrhosis, rather than isolated PVT. The use of beta-blockers as prophylaxis in patients with varices, has successfully reduced the rate of the first variceal bleed, and recent studies have shown that variceal band ligation (VBL) is just as effective.³⁰ Both medical therapy and VBL are also equally effective in secondary prevention of variceal bleeds.³¹

There remains a lack of information on whether one can extrapolate such data to patients with PVT. It

has been suggested that beta blockers will theoretically decrease splanchnic blood flow which may lead to progression of thrombosis,²⁵ however there is no evidence for this, as yet. In the case presented above, the patient was kept on beta-blockers, and VBL was performed as primary prophylaxis. Her first episode of variceal bleeding occurred five years as presentation, and this was once again treated with banding.

The role of decompressive shunt surgery in PVT is also not clear. Indications include failed endoscopic therapy, and symptomatic hypersplenism.²⁴ Techniques include a selective distal splenorenal shunt (Warren Zeppa) or a mesenteric left portal bypass (Rex shunt). Liver transplantation is indicated rarely in patients with complications of PVT that cannot be controlled through conservative measures or shunt surgery.

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