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CASE REPORT : PORTAL VEIN THROMBOSIS DUE TO PROTEIN S DEFICIENCY

Medicine

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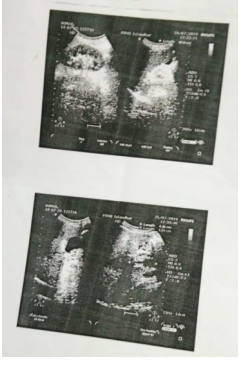
KEYWORDS

INTRODUCTION

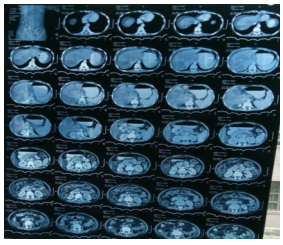
A case report of Portal Vein Thrombosis (PVT) as a complication of protein S deficiency. PVT has been increasingly diagnosed over the years, particularly through the use of ultrasound-Doppler equipment. Portal vein thrombosis (PVT) is a blood clot of the portal vein, also known as the hepatic portal vein. This vein allows blood to flow from the intestines to the liver. A PVT blocks this blood flow. Although PVT is treatable, it can be life-threatening. 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.

Case Report

A 28 year old lady was referred with non-specific abdominal pain, elevated liver enzymes and a prolonged INR. Abdominal examination revealed ascites and hepatosplenomegaly, which was confirmed on ultrasound. She was investigated through several blood tests; namely a full blood count, inflammatory markers, INR, haematinics, serum copper, ceruloplasmin, alpha-antitrypsin levels . Ascitic tap was done and ascitic fluid work up was done . An autoimmune screen, viral screen, leishmaniasis screen and serum protein electrophoresis were also done. Her PT-INR range was very high , 4.5 at the time of admission. No other abnormalities were detected. Ultrasonography also showed sinusoidal dilatation suggestive of portal vein thrombosis or Budd-Chiari syndrome. CT scan confirmed portal vein thrombosis as shown. The patient was started on anticoagulants, with a target INR of 2-2.5. A thrombophilic screen was done; this confirmed protein S deficiency .She was started on 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. She was discharged on subcutaneous enoxoparin, with regular follow-up .



USG showing PVT



CT Scan showing PVT

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 (MTHR) gene mutation.[5-7]

Table 1

Inherited Prothrombotic State -Protein C deficiency -Protein S deficiency -Antithrombin III Deficiency -Factor V Leiden mutation -Factor II gene mutation - Methylene – tetrahydrofolate reductase (MTHR) Gene mutation
Acquired Prothrombotic state -Primary myeloproliferative disorder (e.g polycythemia 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
Infectious - Cytomegalovirus - Bacteroides fragilis
Pregnancy
Drugs (e.g oral contraceptives)
Idiopathic

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]

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 PVT and 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.

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.

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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