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Review Article

PORTAL VEIN THROMBOSIS: ETIOLOGY, DIAGNOSIS AND MANAGEMENT A REVIEW

[*]Waseem Raja Dar, Najeeb Ullah Sofi, Imtiyaz Ahmad Dar, Muzamil Latief, Manzoor Ahmad Wani, Prof. Jaswinder Singh Sodhi

Department of Internal Medicine, Division Gastroenterology
Sheri Kashmir Institute of Medical Sciences, Soura J & K India 190011.

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For Correspondence
Email ID:
drwaseem.mw@gmail.com

Abstract
Portal Vein Thrombosis (PVT) is a common clinical problem often found in Gastroenterology Clinics. It may occur with or without a pre-existing chronic liver disease. Clinical course may be acute or chronic. Clinical features vary in acute and chronic Portal Vein Thrombosis. Acute PVT usually presents with pain abdomen while as chronic PVT presents with features of Portal Hypertension. Management also differs—acute PVT is managed with anticoagulants while as chronic PVT is managed as portal hypertension.

Key Words: Portal Vein Thrombosis, Cirrhosis, Anticoagulants, Varices, Portal Hypertension

Introduction

Portal Vein Thrombosis is the commonest cause of portal hypertension in children; in adults it is one of the common causes of portal hypertension beside cirrhosis, particularly in developing countries. [1] In India, Portal Vein Thrombosis has been found responsible in about 50% cases of Portal Hypertension [2]. In a study of 517 children, Dilwari et al found that EHPVO was responsible for 54% cases of portal hypertension. [3]In another study of 75 children of variceal bleed, extrahepatic portal vein obstruction was found in 92% of them.

We here present a case series of three patients, each with a diagnosis of portal vein thrombosis due to different etiologies. A discussion of etiology, diagnosis and treatment follows.

Case No 1

A 40 year old male, nonalcoholic, craftsman by occupation presented to our OPD with complaints of progressive distension of abdomen of two months duration. Examination revealed an averagely built male with mild icterus; per abdomen spleen was palpable and ascites was present. Baseline investigations revealed bicytopenia (leukopenia and thrombocytopenia), hyperbilirubinemia and very high ALP

(Table 1). Ascitic fluid analysis revealed no cells with SAAG of 1.79. Ultrasound of abdomen showed coarse liver with nodular surface with dilated Portal Vein (15mm) with echogenic thrombus in it with Doppler showing no flow through it. Spleen was 18cm. Endoscopy revealed severe portal hypertensive gastropathy with Grade II×I, III×I, I×I esophageal varices. Hepatitis B, C, D/Wilsons Profile/ANA/ were negative. A CT portovenogram was done that revealed dilated Portal Vein with ill-defined thrombus in it extending up to Superior Mesenteric Vein (Fig 1). Our full diagnosis was Chronic Liver Disease (CLD) with Portal Vein Thrombosis. Endoscopic variceal ligation was done and other treatment (Aldactone, Lasix, Lactulose and Propranolol) also prescribed for CLD. Following eradication of varices, anticoagulation was started. Oral Vitamin K antagonists were given with overlap of low molecular heparin (LMWH). INR was maintained within a range of 2-3. Meanwhile patient is on waiting list for Liver Transplant. On follow up after 2 months of anticoagulation, his CT portovenogram shows minimal thrombus in Portal Vein with no obstruction to blood flow.

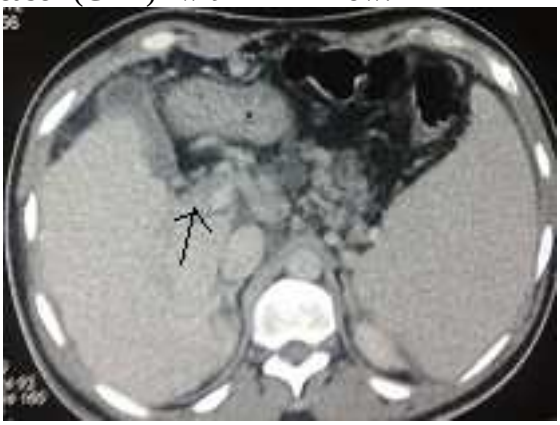

Fig 1. CT portovenogram showing dilated Portal Vein with thrombus in it (arrow)

Table 1: Baseline investigations of three patients.

Parameter	**Case 1**	**Case 2**	**Case 3**
Hb	11.5 g%	6.2 g%	10.6 g%
TLC	3100/mm^3	3400/mm^3	1690/mm^3
PLT	50,000/mm^3	274 lacs/mm^3	51,000/mm^3
MCV	88fL	70fL	83fL
MCH	25.9	20.9	24.9
Urea	28 mg/dl	16 mg/dl	25 mg/dl
Creatinine	1.3 mg/dl	0.8 mg/dl	0.6 mg/dl
Bilirubin	5.31 mg/dl	0.97mg/dl	0.67mg/dl
ALT	45 U/L	28 U/L	30 U/L
AST	39 U/L	39 U/L	39 U/L
ALP	1493 U/L	396 U/L	514 U/L
Total Protein	7.76 g/dl	5.76 g/dl	7.71 g/dl
Albumin	2.99 g/dl	2.3g/dl	3.38g/dl

Case No 2:

A 60 year old female was admitted in our Gastroenterology Department with complaints of right upper quadrant abdominal pain of 20 days duration. This pain had no relation with food and was not relieved by proton pump inhibitors or antispasmodics. On examination she was cachectic female with pallor; per abdomen there was mild epigastric tenderness with an ill-defined lump felt in epigastrium. Periumblical (Sister Mary) nodules were present. Baseline investigations revealed microcytic anemia (Table 1). Endoscopy showed an ulcero-infiltrative growth involving antrum and pylorus. Biopsy revealed moderately differentiated adenocarcinoma. USG abdomen revealed dilated Portal Vein with echogenic thrombus inside, seen extending into right and left branches and into the Superior Mesenteric Vein. Contrast CT revealed circumferential thickening of Pylorus and associated transient hepatic attenuation density (THAD) of surrounding liver parenchyma. Portovenogram showed no enhancement of Portal vein with thrombus inside it extending into Superior Mesenteric Vein (Fig 2). Our full diagnosis was Adenocarcinoma stomach with portal vein thrombosis. Patient was started on anticoagulation –Oral Vitamin K antagonists with LMWH heparin overlap; INR kept between 2 to 3. Patient declined any palliative treatment for her malignancy.

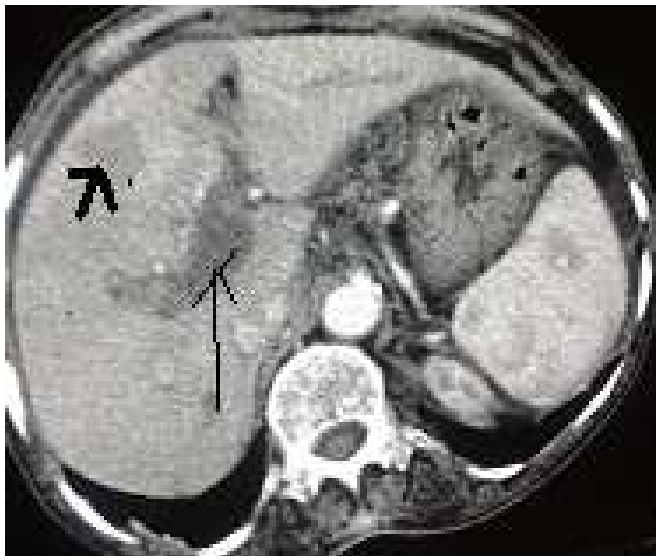

Fig 2. CT Portovenogram with Rt. Portal Vein showing Thrombus inside (arrow). THAD (Bold Arrow)

Case No 3

A 55 year old female presented to our Gastroenterology OPD with complaints of dyspepsia and dragging sensation in left hypochondrium for past 6 months. Patient had no history of jaundice, weight loss or bleeding from any orifice. On examination she was an averagely built female with mild pallor, per abdomen there was hepatosplenomegaly was present. Baseline investigations revealed bicytopenia (Table 1). Ultrasound abdomen showed dilated Portal Vein with thrombus inside with poor flow on Doppler. Endoscopy revealed high grade esophageal varices and gastric varices. CT Portovenogram showed partially occluding organized thrombus in main Portal Vein extending into right Portal Vein,

small periportal collaterals, splenic vein replaced by collaterals, splenomegaly and gastric varices (Fig 3).Liver Biopsy showed no features of cirrhosis. Bone Marrow examination revealed hypercellular marrow. JAK 2 Mutation was positive. Endoscopic variceal ligation (EVL) was done and patient planned for anticoagulation after eradication of varices. Unfortunately patient developed a massive GI bleed following Post EVL ulcer and succumbed.

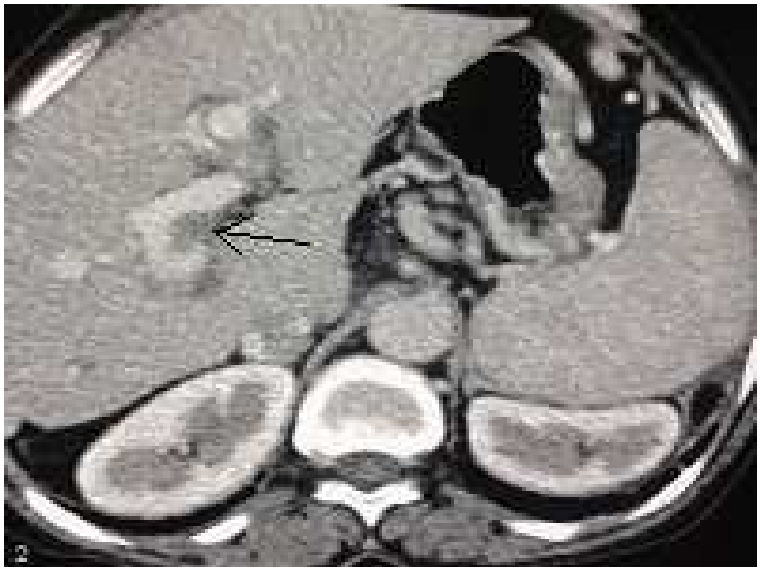

Fig. 3. Thrombus extending into Rt. Portal Vein. (Arrow)

Discussion:

Anatomy of Portal Vein:

Portal vein is formed in the retroperitoneum by confluence of Superior Mesenteric Vein and Splenic Vein behind the duodenal bulb. [4, 5]The portal bifurcation may be extrahepatic (48% of cases), intrahepatic (26%), or located right at the entrance of the liver (26%). Inside the liver, right portal vein divides into two sectoral branches—anterior and posterior; left portal vein has two parts—intrahepatic and extrahepatic parts. Sectoral branches divide into segmental branches; segmental veins then divide into subsegmental branches, which further divide into small veins leading to the portal venules of the liver acinus.

Definition

Portal vein thrombosis refers to the development of thrombosis within the extra-hepatic portal venous system draining into the liver. Sometimes however the thrombosis may extend into Superior Mesenteric Vein or into the Splenic Vein. The thrombosis may also extend into the intrahepatic portal veins.

Etiology

Etiology of Portal Venous Thrombosis is quite varied. Both local as well as systemic factors have found to play a role in the generation of thrombus in the portal vein. All the three variables of Virchow's triad—endothelial trauma, turbulent blood flow and hypercoagulability play role in portal vein thrombosis.

Table 2: Causes of Portal Vein Thrombosis

Hypercoagulable States	Malignancies
Myeloproliferative Disorders Antiphospholipid Syndrome Antithrombin deficiency Factor V Leiden Mutation Nephrotic Syndrome Oral Contraception ProteinC, S deficiency PNH Sickle Cell disease	HCC Gastric Malignancy Cholangiocarcinoma Bladder Cancer
Infections	Others
Appendicitis Cholangitis Diverticulitis Umblical vein infection	Inflammatory disease Pancreatitis Choledochal Cyst Umblical Vein Catheterisation Liver Transplantation TIPS Hepatic Vein Chemoembolization
Impaired Portal Vein Flow	
Cirrhosis HCC Budd-Chiari Syndrome	

Thrombophilic disorders form an important cause of portal vein thrombosis, particularly in cases previously considered as idiopathic. Out of these, Myeloprolierative disorders are the most predominant; 20% portal vein thrombosis cases may have an underlying MPD. Frequently, they are the initial presentations of Myeloprolierative disorders. [6-10] The discovery of JAK2V617F mutation, found in approximately 90% of patients with polycythemia vera (PV), and in 50% of those with essential thrombocythemia (ET) or primary myelofibrosis (PMF), has modified the diagnostic approach to Myeloproliferative disorders which previously relied on bone marrow biopsy (BMB) findings and endogenous erythroid colony (EEC) formation assessment, both of which have limitations. In addition newer molecular markers, particularly for JAK2-ive MPD patients have also emerged. [11-14] W515L and W515K mutations in the thrombopoietin receptor, MPL, deserve mention in this regard.

Portal vein thrombosis is an important complication of cirrhosis. The exact mechanism is unknown but several factors seem to be involved. Stagnant blood flow within the splanchnic circulation and imbalance in the procoagulant state in chronic liver disease has been proposed as possible mechanisms. PVT is encountered in 0.6 to 26% of individuals with liver cirrhosis. [15-17]The prevalence of PVT increases with the severity of liver disease, being 1% in individuals with compensated cirrhosis and up to 8–25% in candidates for liver transplantation.

Clinical Features

The clinical presentation of portal vein thrombosis can be acute or chronic. An acute episode may be asymptomatic or patient may present with abdominal pain, particularly if the thrombus extends to superior mesenteric veins and mesenteric venous arcade resulting in bowel infarction. Patients may then have severe abdominal pain, hematochezia and ascites. Commonest presentation however is a bout of hematemesis from ruptured esophageal varices due portal hypertension.[18, 19]Mortality from gastrointestinal bleeding secondary to variceal rupture amounts to approximately 2-5% in PVT patients. Patients usually have splenomegaly, but ascites is uncommon. Occasionally asymptomatic patients may be diagnosed on a routine abdominal scan. Children with portal vein hypertension may present with growth deficits. It has been assumed that chronic anemia due to intestinal venous congestion with secondary malabsorption may interfere with growth rate.

Patients with chronic portal vein thrombosis can have ectopic varices; commonest sites being bile duct, gallbladder, duodenum, and rectum. Patients may then present with obstructive jaundice, cholangitis and even choledocholithasis late in the natural course of the disease because of pseudosclerosing cholangitis or portal hypertensive biliopathy.

Diagnosis

1. **Ultrasound**
   Sonograms usually show an echogenic thrombus within the portal vein. However, recently formed thrombi may be anechoic or hypoechoic. Besides, intravascular red cell roleaux may appear as echogenic structures within patent vessels. Color Doppler shows attenuation of the flow signal normally obtained from the portal vein. Other findings include extensive collateral vessels in the portahepatis, an enlarged spleen, and occasionally nonvisualization of the portal vein. [24]The diagnostic sensitivity and specificity for Colour Doppler Ultrasound (CDUS) in detecting portal vein thrombosis vary from 66% to 100%. [25]Contrast Enhaced Ultrasound seems to be the most sensitive and specific test for diagnosing malignant portal vein thrombosis in patients with cirrhosis.
2. **CT Scan**
   CT scan shows a non-enhancing filling defect within the lumen. The thrombus is usually hypodense or isodense to surrounding soft tissues; a recent onset thrombus can however be hyperdense.
3. **MRI**
   Diagnosis is based on identification of a defined low-signal structure within the main portal vein adjacent to a high signal gadolinium-containing lumen or inability to detect a main portal vein accompanied by collateral vessels (cavernous transformation) or the detection of diminutive main portal vein. [27]Sensitivity and specificity of MRI for detecting main PVT were 100% and 98%, respectively.

Treatment

The treatment of acute and chronic portal vein thrombosis differs. In Acute PVT, main aim is to prevent or reverse portal vein thrombosis while in chronic PVT treatment is aimed at managing the complications of portal hypertension.

Acute PVT:

Thrombolytic therapy in acute PVT is reserved for patients with severe disease. Approaches include transhepatic and transjugular. [28]In a retrospective study of 20 patients, Hollingshead et al found that 15 patients exhibited some degree of lysis of the thrombus; 3 patients had complete resolution, 12 had partial resolution, and five had no resolution. Sixty percent of patients

developed a major complication. i.e. bleeding. [29] De Santis et al that thrombolytic treatment of recent portal vein thrombosis with i.v. r-tPA and LMWH in patients with cirrhosis appears to be safe and effective and can significantly reduce pressure in esophageal varices.

Patients of acute PVT are treated with anticoagulants since spontaneous recanalisation is rare except in acute pancreatitis and umbilical vein sepsis. Anticaogulation is started within 30 days as rates of recanalisation decrease with time. [30, 31] When cirrhotic individuals with PVT are treated with anticoagulation, complete recanalization has been described in 33–45% while partial PV recanalization is observed in 15–35% of cases. The optimal anticoagulation regimen has not been determined yet. The choice of anticoagulation regimen is particularly difficult in cirrhotics. With regards to Vit K Antagonists, INR has only been validated in individuals with normal liver function on stable anticoagulation. LMWH dose depends on weight. Cirrhotics have large volume of distribution, so dose determination is difficult. Length of anticoagulation therapy for PVT in cirrhotic individuals is not known.

Thrombectomy in PVT can be done by 1) Surgical and 2) Mechanical methods. Surgical thrombectomy is not recommended. Mechanical thrombectomyis done by percutaneous transhepatic route. Drawbacks include intimal or vascular trauma to the portal vein that may promote recurrent thrombosis.

Chronic PVT

There is no role of primary prophylaxis in PVT associated portal hypertension. Management is to treat portal hypertension and its consequences. However there is a concern of extension of thrombosis with b-blockers as well as vasopressors because of decrease in splanchnic blood flow. Endoscopic variceal ligation is safe and highly effective in children and adults with PVT. Shunt surgeries are indicated in 1) Failed endotherapy 2) Symptomatic Portal Biliopathy and 3) Symptomatic Hypersplenism. Distal splenorenal shunts have been shown to be effective in control of bleeding and long-term survival in patients with PVT.

First successful liver transplant in the presence of PVT was done in 1985. Liver transplant in portal vein thrombosis is associated with greater operative complexity, rethrombosis and reintervention, but has no influence on overall morbidity and mortality.

Conclusion

Portal Vein Thrombosis is a common clinical condition with varied etiology. Although chronic liver disease is the leading cause of PVT, other causes particularly Myeloprolierative disorders should be excluded. Besides malignancies deserve special mention because they change the prognosis of a patient with PVT. Acute PVT should be treated with anticoagulants to maintain an INR of 2 to 3, thrombolysis being reserved for selected few. Chronic PVT should be managed like any patient of portal hypertension. Prognosis largely depends on the underlying disease.

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