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Portal Vein Thrombosis in Liver Cirrhosis – An Updated Review

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ABSTRACT

Portal Vein Thrombosis (PVT) is a frequent complication in cirrhosis and its prevalence increases with disease severity. Several factors are involved in the development and progression of PVT. Portal Vein Thrombosis is the condition in which the obstruction of the portal vein due to the thrombus formation which can lengthen to the superior mesenteric and splenic veins. It is the common complication of advanced liver disease.[1,4] Clinical examination, Laboratory investigations and imaging are helpful to provide a swift diagnosis. However, decreased blood flow related to portal hypertension appears to increase PVT risk as per Virchow's triad. There is a higher incidence of PVT in cirrhosis with a higher MELD and Child Pugh Score. Treatment options include anticoagulants, and interventional thrombolytic therapies, which are chosen almost on a case-by-case basis depending on the characteristics of the patient and thrombus. In this review article we shall aim to discuss the etiology, pathophysiology, Clinical presentation, diagnosis and therapeutic management of portal vein thrombosis. [2,3,]

KEYWORD: Portal Vein Thrombosis, Liver cirrhosis, Bleeding, Anticoagulation, Thrombectomy, Shunt surgery

INTRODUCTION

Portal vein thrombosis (PVT) may be best defined as syndrome in which the presence of a thrombus in the portal vein or its branches presents either as an incidental finding on abdominal imaging or with abdominal signs and symptoms that represent complications of portal hypertension or a composite of both acute abdominal and portal hypertensive manifestations in the presence or absence of cirrhosis and /or malignancy. Patient who are suffering from liver cirrhosis are at great risk of developing portal vein thrombosis, which has a complex multifactorial cause. This condition may occur with very large number of symptoms and can sometimes cause severe complications. PVT is frequent in advanced liver Cirrhosis often associated with hepatocellular carcinoma, it is less frequent in compensated cirrhosis. The main challenge of managing PVT in cirrhosis is analyzing the risk of thrombus in extension leading to complications. [3] Thrombophilic conditions, abdominal inflammation and liver cirrhosis are among the most common causes of PVT, whereas its been less affected after bariatric surgery, radiofrequency ablation or fine needle aspiration. [4] PVT prevalence is estimated to be 0.6-15.8% in patients with liver cirrhosis or portal hypertension. [6, 9] The prevalence of PVT increases with the severity of cirrhosis. A prevalence of 10-25% has been reported by ultrasonography. [18, 20]

Classification of PVT [18,19]

Grade 1 : Thrombus at main portal vein affecting less than 50% of the lumen with or without minimal extension into superior mesenteric vein (SMV).

Grade 2 : Thrombus at PV affecting more than 50% including complete thrombus with or without minimal extension into SMV.

Grade 3 : Complete PVT plus thrombosis extending to the proximal SMV with patent distal SMV.

Grade 4 : Complete PVT affects both proximal and distal SMV.

Risk factors for PVT[20]

Inflammation of the pancreas

Appendicitis

Navel infection

Polycythemia

Cancer

Cirrhosis of the liver

Trauma or injury

Oral contraceptives

Child-pugh class B and C

Oesophageal varices grade > 2

Portal vein blood flow < 15cm

Local vascular damage

Previous splachnic vein thrombosis

Sclerotherapy of oesophageal varices

Partial splenic embolization

Altered Portal Venous blood flow

A threshold portal vein flow <15 m/sec has been described as the most predictive of PVT. [8,19] An increase in portal blood flow through portosystemic collaterals also seems to influence PVT development. Indeed, a large flow volume (>400ml/min) and velocity (>10cm/sec) in the largest porto-collateral vessel visualized by Doppler ultrasound have been shown to predict PVT.[9] Non- selective beta blockers (NSBB's), by reducing portal venous blood flow, could increase the risk of PVT. [19,21]

Altered Coagulation

Haemostatic alterations associated with cirrhosis

Patients with cirrhosis have a well-described derangement of the haemostatic balance due to a reduction of both anticoagulant and procoagulant factors, together with increased levels of several procoagulant factors such as factor VIII and von Willebrand factor (vWF).[20] Overall, these alterations indicate that the homeostatic balance leans toward hypercoagulability, which would favour the development of PVT.

Inherited and acquired prothrombotic disorders

nherited and acquired prothrombotic disorders can contribute to the development of portal vein thrombosis (PVT), particularly in patients without cirrhosis. Mutations in genes like prothrombin or factor V, deficiencies in proteins C, S, or antithrombin, are known factors. However, their significance in patients with cirrhosis is less clear. [22,27]

Local portal vein alterations

In patients with cirrhosis and portal hypertension, several factors contribute to the development of a hypercoagulable state in the portal venous system. Bacterial translocation, which involves the migration of bacteria from the gut lumen to the mesenteric lymph nodes and other organs, is a significant contributor. This process is facilitated by increased intestinal permeability, altered gut microbiota, and impaired immune function in cirrhosis.[23,24]

Other factors associated with PVT development

Several risk factors contribute to the development of portal vein thrombosis (PVT) in cirrhotic patients. Endoscopic therapies for esophageal varices, such as sclerotherapy or variceal band ligation, have been associated with an increased risk of PVT. This could be due to endothelial damage or endotoxemia following the procedures.[25,26]

Furthermore, a history of variceal bleeding increases the risk of PVT development. Previous abdominal surgeries, splenectomy, and portosystemic shunt surgeries are also known determinants of PVT due to potential venous injury or alterations in portal venous flow.[27]

Additionally, certain underlying liver conditions such as cryptogenic cirrhosis and non-alcoholic steatohepatitis (NASH) cirrhosis are associated with a higher risk of PVT compared to other etiologies of cirrhosis.[24,25] This increased risk is attributed to factors such as increased thrombin generation and hyperfibrinolysis, which contribute to a prothrombotic state in these patients.[29]

CLINICAL PRESENTATION [30]

Splenomegaly, Fever

Ascites

Abdominal pain

Hematemesis

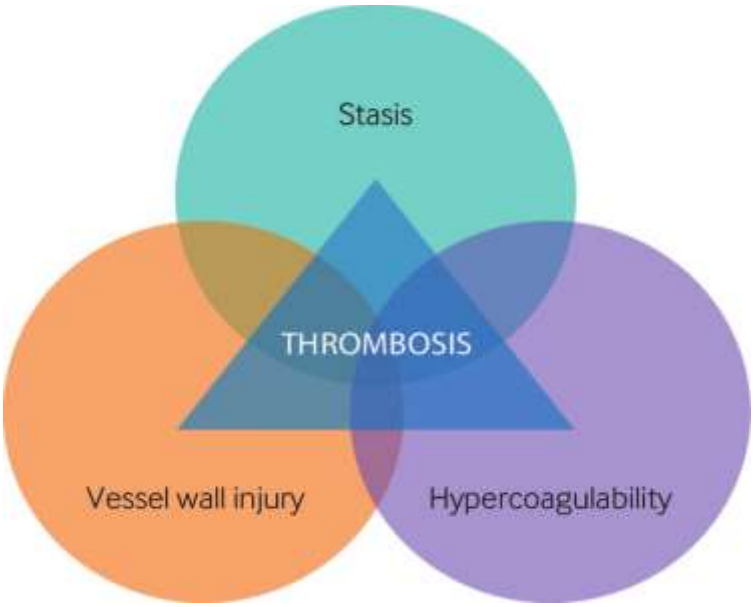
Weight loss

PATHOPHYSIOLOGY

As the part of cessation of portal blood flow, the liver losses two third of its blood supply. Captivating, this condition is generally well tolerated, in addition patients become more asymptomatic, when an acute arterial obstruction always leads to severe hepatic dysfunction which is sometimes fatal. [7,34] An immediate activation of two compensatory mechanism that is arterial vasodilation of the hepatic artery likewise to that portal vein clamping during the surgery of liver. Another one is the arterial rescue is a kind of vascular reflex present in every organ with both an arterial and venous circulation and is able to preserve liver function in the acute stages of PVT.[42] The final compensatory mechanism is venous rescue consisting of the rapid development of collaterals to bypass the obstruction. Usually the original portal vein become a thin, fibrotic cord but which is difficult to visualize. [30] Despite the activation of the complex system support, the impairment of the portal flow has an important consequences on liver tissue. [32,33]

Pathophysiology of portal vein thrombosis encompasses one or more features of Virchow's triad, which includes reduced portal blood flow, a hypercoagulable state, or vascular endothelial injury.[34,35]

VIRCHAW'S TRIAD



DIAGNOSIS

There are no laboratory findings for PVT, however combination of D-dimers and elevated protein and plasma concentration to exclude PVT in cirrhotic patients. [35] Majority of patients with cirrhosis PVT is an incidental findings during routine ultrasound , CT or MRI evaluation. First technique for PVT detection is Doppler ultrasound .Doppler allows noninvasive diagnosis of acute PVT. At ultrasound, the thrombus appears as hypo or iso-echoic material inside the vessel, more hyperechoic if chronic.[42,43] However, evaluation of the extension and occlusion of all portal vein branches (superior mesenteric and splenic veins) by Doppler ultrasound can be limited by the presence of ascites, obesity, and bowel gas and therefore, the use cross-sectional imaging (angio-CT or angio-MRI) is recommended to confirm the presence of PVT and for complete PVT staging.[35,37] Surgical exploration is done in some patients to have a part of the detection. [35,11]

COMPLICATIONS

Portal Hypertension

Portal hypertension is responsible for the majority of the complications seen in patients with chronic PVT.[34] It presents with splenomegaly, varices, ascites. Portal vein thrombosis commonly forms varices in sites other than the esophagus and stomach (ectopic varices).[35]

Intestinal Ischemia

Intestinal ischemia is typically seen when acute PVT progresses to obstruction of mesenteric venous outflow with reflex arterial constriction and occlusion.[35]

Septic Portal Vein Thrombosis

Septic Portal Vein Thrombosis (acute Pyle phlebitis) occurs when PVT develops in a patient with an abdominal focus of an infection like appendicitis, diverticulitis, among others.[36]

Portal Cholangiography

Portal cholangiography is a complication that may develop with longstanding PVT due to extrinsic compression of large bile ducts from venous collaterals around portal vein. [37]

MANAGEMENT

The management of portal vein thrombosis (PVT) in cirrhotic patients typically involves several approaches, including anticoagulation therapy, thrombolysis, and transjugular intrahepatic portosystemic shunt (TIPS) placement.[40] However, some cirrhotic patients with PVT may experience spontaneous recanalization without the need for antithrombotic therapy or other interventions. This phenomenon is termed transient PVT in liver cirrhosis.[41]

Identifying patients who will undergo spontaneous recanalization and determining the appropriate interval for follow-up imaging examinations can be challenging.[42,43] On the other hand, studies have shown that initiating anticoagulation therapy promptly after diagnosing PVT is associated with a higher rate of recanalization.[43]

Understanding the factors that influence spontaneous recanalization and the effects of early anticoagulation therapy initiation can help guide clinicians in managing PVT in cirrhotic patients more effectively. [45]

Anticoagulation

The aim of the treatment is to reverse or prevent advancement of thrombosis in the portal venous system and to treat complications of established PVT. Low-molecular-weight heparin and direct oral anticoagulants are relatively safe and effective in patients with compensated liver cirrhosis and PVT.[41] But the safety and efficacy of direct oral anticoagulants in cirrhotic patients with Child–Pugh C cirrhosis need further evaluation. Anticoagulants encompass vitamin K antagonists, heparins, and direct oral anticoagulants, with warfarin being a prominent vitamin K antagonist. Achieving the therapeutic dosage of warfarin necessitates close monitoring of the International Normalized Ratio (INR). Traditionally, maintaining the INR at 2–3 times the upper limit of normal (ULN) is recommended. However, patients with end-stage liver disease often exhibit elevated INR levels even without warfarin use. Consequently, accurately monitoring warfarin usage in patients with liver cirrhosis remains uncertain. Furthermore, the INR can be easily influenced by dietary habits and concurrent medication, exacerbating the challenge of assessing warfarin efficacy.[42]

The efficacy and safety of early anticoagulation therapy for acute nonmalignant and noncirrhotic PVT have been widely recognized .[39,40] By comparison, cirrhotic patients are at a high risk of bleeding from gastroesophageal variceal rupture and other sources, and often manifest as coagulation disorders, such as prolonged prothrombin time, elevated international normalized ratio (INR), and decreased platelet count. Therefore, whether and when to start anticoagulation therapy, as well as the methods of anticoagulant administration, should be cautiously evaluated.

Thrombolysis

Thrombolytic therapy in very recent non-cirrhotic portal vein thrombosis can be done via indirect intraarterial infusion of tissue plasminogen activator, urokinase or streptokinase into the superior mesenteric artery (SMA) or directly via the catheter introduced into a portal vein either transhepatically or through transjugular approach. Prolonged catheterization of SMA may itself pose a risk of embolizing SMA and its arterial branches. Hence, direct access to portal vein via transjugular or percutaneous intrahepatic route is preferred mode as being less time consuming and more efficient technique with a requirement of a reduced dose of thrombolytics, thereby reducing thrombolysis related complications.

Thrombectomy

Surgical thrombectomy or mechanical thrombectomy by percutaneous transhepatic route is associated with recurrence of thrombosis from intimal or vascular trauma to the portal vein. Percutaneous transhepatic thrombo aspiration within 72 hours has been done successfully in some patients.

Transvenous Intrahepatic Portosystemic Shunt

Transvenous intrahepatic portosystemic shunt (TIPS) placement in the setting portal vein thrombosis is technically challenging. However, when placed successfully, there is a possibility of achieving recanalization by disrupting the thrombus and mechanical thromboectomy.

Treatment for acute portal vein thrombosis which includes,

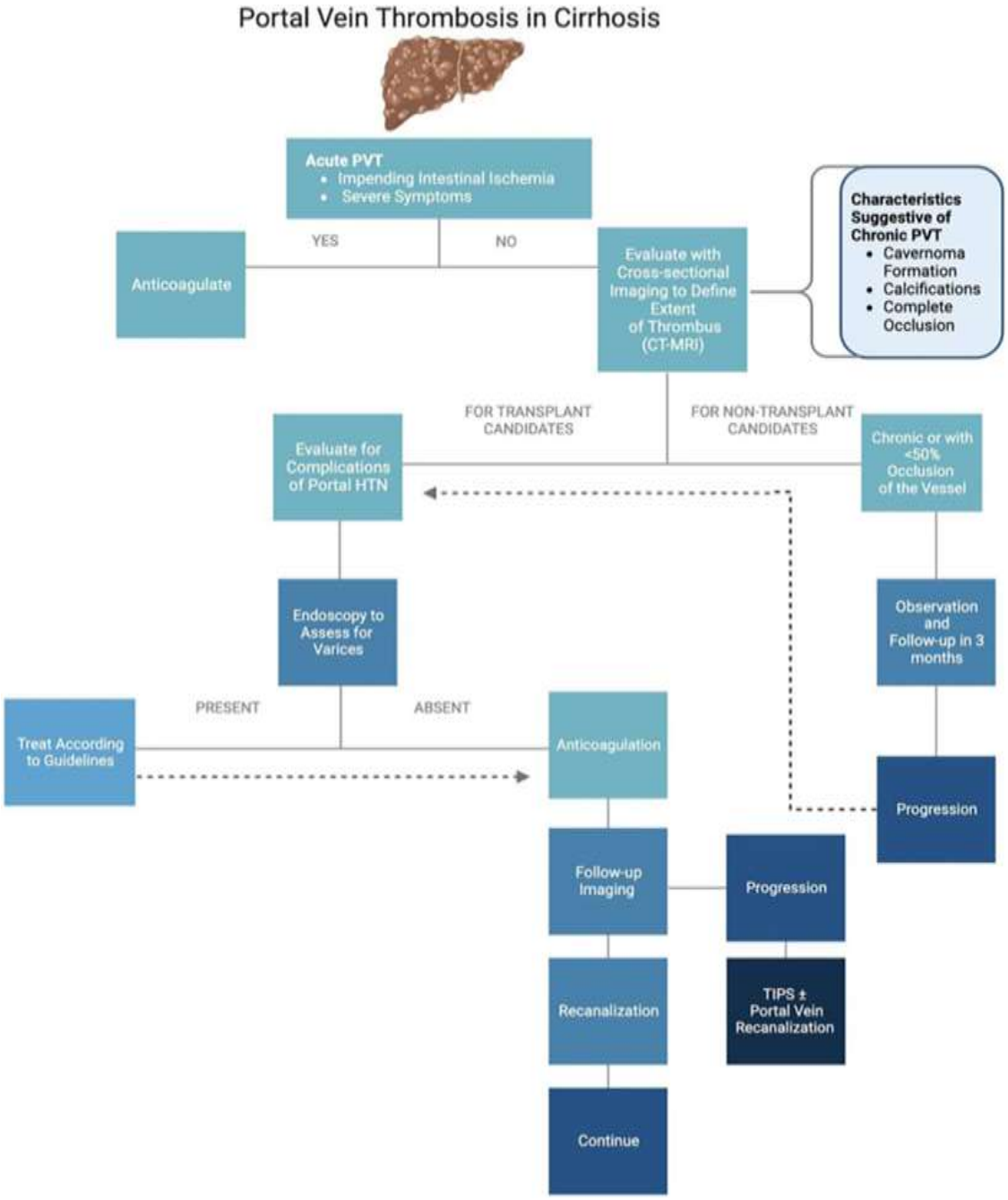
Anticoagulation is initiated with subcutaneous low molecular weight heparin which is effective as intravenous unfractionated heparin, so it has low risk of adverse effect reactions. After 2-3 weeks it is shifted to vit K antagonist targeting INR range of 2-3, Surgical thrombectomy is generally not indicated unless laparotomy is needed because bowel infarction is suspected. [12] Anticoagulation is done in atleast 3 and 6 months. In acute onset of PVT, sooner the treatment should be given the result will be improved ,the rate of recanalization is about 69%, if anticoagulation is instituted with in the first week after diagnosis when it falls 25% when instituted at the second week. [13] Sign of ischemia and infarction or an underlying prothrombotic disorder should be considered an indication for anticoagulants in cirrhotic patients. [14]

Treatment of chronic portal vein thrombosis

The last stage of portal vein thrombosis have certain symptoms such as bleeding from o esophagus, gastric ectopic varices. It is reasonable to manage acute bleeding episode as in cirrhotic patients with vasoconstrictors, Endoscopic treatment, Glue injection for fundal varices and antibiotic therapy. [15] The bleeding should be managed with Beta blockers as prophylaxis .Shunt surgery also be considered if endoscopic therapy failure occurs. [16] Although when lacking of clinical evidence occurs portal bilopathy can be treated with ursodeoxycholic acid. Liver transplantation may be the last option for severe biliary complications. [17]

Treatment of portal vein thrombosis in patients with cirrhosis

The long term use of anticoagulant in cirrhotic patients with PVT should not be considered as a correct practice. [40] Thrombolytic therapy is given either into the systemic venous circulation the superior mesenteric artery or the portal vein via triangular route. [41] Despite high incident of side effects, thrombolysis should be considered when initial anticoagulant therapy fails. [20] Surgical thrombectomy is usually not recommended because it has high morbidity and mortality have been reported.[42,43] Another method is to transjugular intrahepatic portosystemic shunt placement should be reserved for patients developing PVT before or after liver transplantation or in alternative to thrombolysis when anticoagulation fails. Shunt surgery (distal splenorenal shunt or rex shunt in children) might be applied as the final choice, however it applicable only in the absence of splenic or superior mesenteric vein thrombosis. [45]



CONCLUSION

PVT was a clinical rare deep venous thrombosis but highly occurred in liver cirrhotic patients. Local or systemic factors alone or in combination make contribution to the formation of PVT. In clinical, PVT should be given enough attention due to its severe threat to the patients life and health. The overall treatment principles are early diagnosis, early treatment and prevention combined with treatment.This review focus on the knowledge of diagnosis, pathophysiology, risk factors management of portal vein thrombosis in cirrhosis. It helps in reducing portal hypertensive complications.

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