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SPLANCHIC VENOUS THROMBOSIS

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INTRODUCTION:

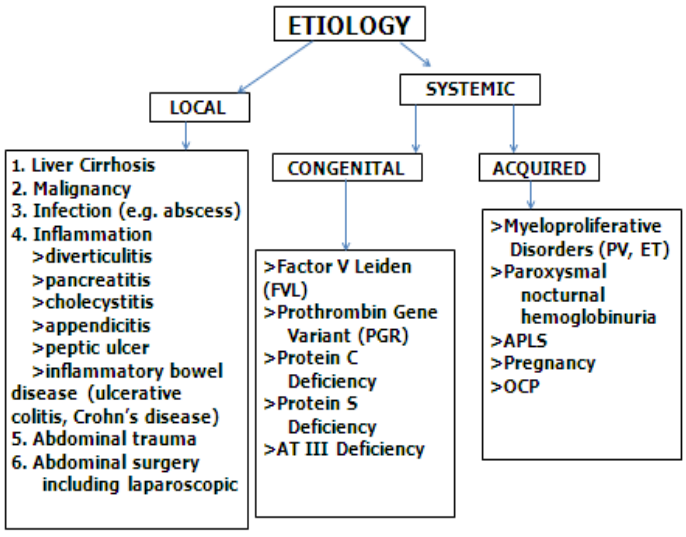
Abdominal venous thrombosis may present as splanchnic venous thrombosis (SVT) including occlusion of portal, splenic, superior or inferior mesenteric veins or Budd- Chiari Syndrome (BCS), thrombosis of inferior vena cava and/or hepatic veins.

Splanchnic vein thrombosis is rare. Annual incidence of BCS is less than one per million individual. Portal vein thrombosis (PVT) is a little more common, abut 3-4 cases per million. Presentation may be different from asymptomatic to life-threatening cases.

RISK FACTORS:

There are many similarities, as well as differences in risk factors for patients with common deep vein thrombosis such as DVT and PE, as well as SVT. Inherited thrombophilia and acquired risk factors are common in both patient groups.

Risk factors for SVT can be local or systemic, inherited or acquired, but multiple factors are commonly present.



The most common risk factors for DVT/PE include hospital admissions, immobility, surgeries and central venous catheters. However, myeloproliferative neoplasms (MPN) are the leading systemic cause of SVT. Polycythemia Vera, essential thrombocythemia, and idiopathic myelofibrosis, also known as Philadelphia-negative chronic myeloproliferative neoplasms, represent the most common causes of SVT including BCS and PVT. The molecular marker *JAK2 V617F* gene mutation is detectable in a large majority of patients with overt MPN, and up to 40% of patients without overt disorder. Patients with MPN have a high risk of thrombotic complications. PVT in many cases appears at the onset of the disease. The risk factors are related to the presence of qualitatively altered thrombocytes and leukocytes, leading to their activation and appearance of leukocytes-platelet-aggregates. *JAK2 V617F* mutation screening should be an initial test for MPN in patients with SVT and is now a part of the standard work up in BCS and PVT.

Paroxysmal nocturnal hemoglobinuria, another rare acquired hematologic clonal disorder frequently associated with SVT, is more common in patients with BCS than PVT. Several mechanisms may play a role in the pathogenesis of thrombosis in these patients including hemolysis, increased platelet activation, increased tissue factor expression and complement mediated damage. Testing for PNH, flow cytometry for CD55 and CD59, should be performed on all patients with BCS and PVT.

Inherited thrombophilia is present in at least one-third of the patients with SVT. Factor V Leiden mutation has been reported to be more commonly associated with BCS and the prothrombin G20210A mutation more commonly found in patients with PVT. Deficiencies of protein C, S and antithrombin III may also predispose to SVT; however the prevalence of inherited deficiencies of these natural anticoagulants is difficult to determine in patients with SVT since acquired deficiencies of these proteins occur due to liver dysfunction, which is a frequent complication in patients with SVT. In addition, many of these patients are treated with long term anticoagulation therapy which also results in acquired deficiency of protein C and S.

Antiphospholipid antibody syndrome, although considered to be a risk factor for BCS and PVT, its importance as a risk factor is difficult to evaluate because anticardiolipin antibodies are frequently positive in patients with chronic liver disease.

An underlying prothrombotic disorder has been demonstrated to be an independent risk factor for recurrent SVT.

Local precipitating factors are more common in patients with PVT. They are present in about one third of patients with PVT and are rare in patients with BCS.

The leading cause of PVT is liver cirrhosis. Local malignant tumors are also a common risk factor for PVT. Other frequent local risk factors include inflammatory process in the abdomen, including infections and inflammations such as in cases of inflammatory bowel disease, including ulcerative colitis and Crohn's. Acute pancreatitis, cholecystitis, diverticulitis etc. may also predispose to PVT. Abdominal trauma including surgical trauma even with laparoscopic surgeries is also a known risk factor for PVT.

Oral contraceptives, hormone replacement therapy and pregnancy are also known risk factors for SVT; however, an additional prothrombotic condition is frequently present in these women.

Acquired risk factors play a more prominent role than congenital in promoting thrombotic events. Prevention of thromboembolism should be aimed at minimizing the acquired/reversible risk factors (e.g., inflammation, immobility, hospitalization, central intravenous catheters, smoking, and oral contraceptives).

CLINICAL PRESENTATION:

BCS is an obstruction of the hepatic venous outflow from the level of the small hepatic veins to the entrance of the inferior vena cava into the right atrium. Presentation may include abdominal pain, ascites, and hepatomegaly with fulminant hepatic failure; however, it may also be asymptomatic in the case of developed collateral circulation. BCS is considered primary in cases of obstruction by thrombus, or secondary when obstruction is due to extrinsic compression by tumor, cyst, or abscess. Symptoms depend on the extent and rapidity of obstruction. Fulminant disease is associated with hepatic necrosis, liver failure, and encephalopathy. An acute form may also present with liver failure and ascites. The chronic form is most common and presents with symptoms of portal hypertension and cirrhosis.

PVT is the obstruction of the extrahepatic portal veins, but involvement of intrahepatic portal, superior mesenteric and splenic veins may also occur. PVT can also be acute or chronic. Acute thrombosis is characterized by sudden onset of abdominal pain, nausea/vomiting, abdominal tenderness, fever. In the absence of an underlying liver disease, liver function tests may be initially normal. If thrombosis extends to the mesenteric veins, there is a risk of bowel infarction. The most common clinical presentation of PVT is chronic and includes portal hypertension with gastrointestinal bleeding, esophageal varices, development of collateral circulation, ascites, and splenomegaly.

TREATMENT:

Immediate anticoagulation with heparin is used to treat patients acutely which is followed by oral anticoagulation with warfarin. Catheter-directed thrombolysis may be used in conjunction with anticoagulation in some cases. In the acute phase, anticoagulation is used to avoid extension of thrombosis and decrease risk of portal hypertension. In cases of clinical deterioration, invasive procedures including transjugular intrahepatic portosystemic shunt should be considered.

Beyond the acute phase, duration of anticoagulation should be individualized, based on the underlying etiology of SVT, risk of recurrence, and risk of bleeding complications, particularly in patients with underlying liver disease.

Long-term oral anticoagulation with vitamin K-antagonists should be considered in all BCS patients, and in the patients with irreversible prothrombotic state associated with an unprovoked PVT. In patients with underlying thrombophilia, the risk of recurrent thrombosis is higher. In an unprovoked PVT and no prothrombotic conditions, or in those with a provoked PVT, anticoagulant treatment is recommended for a minimum of 3-6 months. This applies to patients with no evidence of liver cirrhosis.

Portal vein thrombosis is not uncommon in patients with liver cirrhosis. The objective for these patients is to recanalize the vein and prevent further clot extension; however, using systemic anticoagulation in patients with liver cirrhosis is controversial since these patients are at increased risk of GI bleeding, form esophageal varices, and coagulopathy of an underlying liver disease, thrombocytopenia, and impaired platelet function. Treatment of these patients should target complications related to portal hypertension

Consideration for long term anticoagulation therapy should be individualized for each patient.

SUMMARY:

SVT, including BCS and PVT are rare. Risk factors include local and systemic, congenital and acquired. Chronic myeloproliferative disorders represent the most common cause. Determination of JAK2 mutation is useful for investigation of etiology of SVT, particularly if the etiology of thrombosis is not obvious since SVT may be a first manifestation in patients with MPN. Liver cirrhosis is a common cause of PVT. Patients without liver cirrhosis should be started on anticoagulation therapy, but anticoagulation therapy in patients with underlying liver cirrhosis is controversial.

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