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Acute Portal Vein, Superior Mesenteric Vein and Splenic Vein Thrombosis Secondary to JAK2 V617 Mutation- A Case Report

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ABSTRACT

Portal vein thrombosis (PVT) is a rare finding which usually occurs in association with local factors such as cirrhosis, malignancy, pancreatitis, intraabdominal infections or systemic hypercoagulable states. It may present acutely as abdominal pain, ascites, fever or exist in a chronic state which is generally asymptomatic and an incidental finding. With advancement in Imaging and laboratory studies, PVT cases are diagnosed more frequently along with its predisposing factors. The invention of JAK2 mutation and it's addition to the WHO criteria for Myeloproliferative neoplasm (MPN) diagnosis, has increased the number of MPN cases which were previously labelled idiopathic. We present a case of 54 year old female diagnosed with unprovoked PVT with bowel ischemia and JAK 2 mutation positive, managed surgically and with long term anticoagulation.

KEYWORDS: Portal Vein Thrombosis, JAK 2 Mutation, Myeloproliferative Neoplasm.

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INTRODUCTION

Portal vein thrombosis (PVT) is a condition in which thrombosis develops within the extrahepatic portal venous system and can extend to the intrahepatic portal vein branches or upstream to the superior mesenteric and splenic veins.[1] Prevalence is estimated to be 1% with 0.6%-16% occurring in asymptomatic liver disease, 15% of patients awaiting liver transplant, and 35% in the cases of cirrhosis with hepatocellular carcinoma.[2] The PVT is an uncommon disease, nowadays being diagnosed more frequently because of the increasing use of imaging techniques in clinical practice. Several risk factors are involved in the pathogenesis of acute PVT, both of local and systemic origin.[3] Local causes includes underlying malignancy, mostly hepatocellular carcinoma and others of pancreatic, biliary origin or metastatic, intra abdominal inflammation and liver cirrhosis.[4][5] Systemic causes include congenital and acquired thrombophilic states and sepsis. Myeloproliferative disorders such as thrombocythemia, polycythemia vera, and myelofibrosis with myeloid metaplasia can also cause the thrombophilic state associated with a large proportion of portal vein thrombosis cases previously diagnosed as "idiopathic".[6] V617F mutant JAK2 protein is positive in nearly all cases of PCV and in approximately 50% of cases of ET and primary myelofibrosis, thus it is routinely tested when myeloproliferative neoplasm is suspected.[7] In our case report we present a case of non-cirrhotic, non-malignant portal venous thrombosis with small bowel gangrene associated with JAK2 V617F mutation.

CASE REPORT

A 54 year old female, first presented to a local hospital with history of abdominal pain and vomiting since 15 days. Abdominal pain was diffuse, non-radiating in nature. There

was no history of melaena, hematochezia. Her blood work up showed anemia with leucocytosis and thrombocythemia, same findings found in her peripheral blood smear. Ct abdomen showed subacute thrombosis of portal vein (PV), splenic vein(SV) and proximal superior mesenteric vein (SMV) with partial recanalization of SMV and edematous appearance of wall of small bowel loops. Patient was started on anticoagulation with intravenous heparin. As symptoms not relieved and patient developed constipation with abdominal distension, a diagnostic laparoscopy was done which showed thickened, edematous and congested ileal segment. Patient came to our hospital for further management. On arrival patient had bilious vomiting, with abdomen distension and constipation. Significant lab findings included leukocytosis, elevated CRP, d-dimer, serum lactate levels. A CECT abdomen was repeated which in addition to previous findings showed reduced wall enhancement in the edematous bowel loop, s/o bowel ischaemia. A diagnostic laparoscopy confirmed the above findings, resection anastomoses of gangrenous bowel loops was done and appropriate antibiotics were started. On Post operative day 1, patient was started on anticoagulation after confirming adequate hemostasis. Eventually patients clinical condition improved and she was switched to vitamin k antagonist for long term prophylaxis. JAK2 V617F mutation which was sent as a part of her prothrombotic state workup, was found positive. Blood counts were normal before discharge. Patient was asked to follow up a month later for definite diagnosis of MPN, evaluation regarding recanalization via imaging, and to rule out other causes contributing to her prothrombotic state.

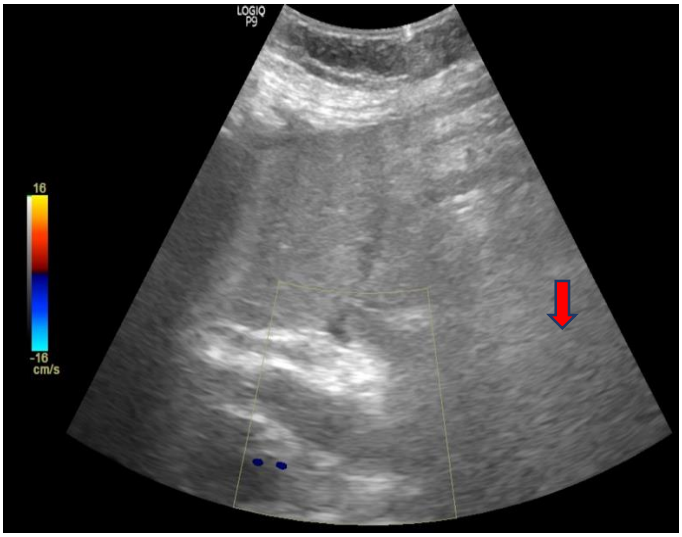

Figure 1. Usg abdomen colour doppler showing absent colour uptake by portal vein

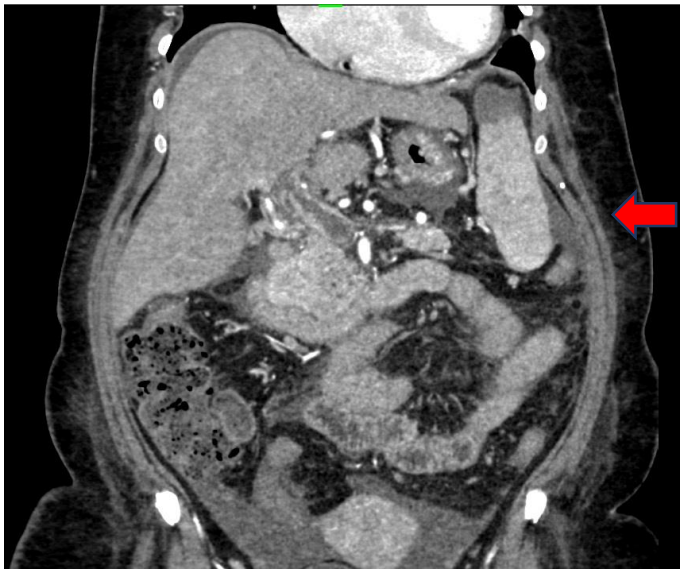

Figure 2. portal venous phase- CECT abdomen, coronal reformatted image showing portal venous obstruction

DISCUSSION

Acute PVT presents with symptoms of acute abdominal pain, fever, ascites, or splenomegaly.[8] Chronic PVT is generally asymptomatic and is more commonly an incidental finding on radiological imaging. The presence of collateral veins surrounding the region of obstruction, thrombus calcifications, or signs of portal hypertension are often found in the cases of chronic PVT.[9] Local factors giving rise to PVT includes cirrhosis, malignancies and intraabdominal infections. Systemic factors such as hypercoagulable states and sepsis predispose the formation of PVT. In non-cirrhotic cases of PVT, also termed extrahepatic portal vein obstruction, where no other local causes are identified, other factors like hormonal contraception, pregnancy, systemic thrombophilic states are assessed.[8]

Table 1: causes of thrombotic states[10]

Acquired thrombophilic factors
Myeloproliferative disorders (polycythaemia vera, essential thrombocytosis, idiopathic myelofibrosis) Antiphospholipid syndrome Paroxysmal nocturnal haemoglobinuria Hyperhomocysteinaemia Elevated Factor VIII Genetic variation in the thrombin-activatable fibrinolysis inhibitor gene
Hereditary thrombophilic factors
Factor V Leiden mutation Protein C deficiency Protein S deficiency Antithrombin deficiency Prothrombin G20210A mutation MTHFR C677T mutations

The JAK2 V617F mutation which is found in 97.6% cases with PV, 54.5% with ET and 53.44 % patients with PMF is now a routinely done screening test for myeloproliferative neoplasms.[11]

In suspected PVT cases, ultrasound is recommended as first-line imaging with an accuracy of 88%-98% and a specificity of 60%-100%. Contast enhanced CT(CECT) is preferred in acute scenarios for better visualization of anatomy and extension of occlusion. In addition to it, CT imaging provides advantages of visualizing bowel ischemia, presence of malignancy, or cirrhosis. [2] Magnetic resonance imaging (MRI) is equally useful for detection of thrombus. MRI additionally can be used to detect the biliary system abnormalities.[8] Patients with myeloproliferative neoplasms (MPN) increase the risk of developing PVT by 30-40 %. The diagnosis of MPN should be based on the 2017 WHO diagnostic criteria which includes specific findings like raised counts on the CBC, blood smear, and bone marrow analysis, correlated with clinical history with the presence of certain molecular markers and the exclusion of other disorders.[12] Characteristic peripheral blood cell changes (i.e. high haemoglobin levels and thrombocytosis) may be masked as a consequence of hypersplenism which is found in cases of PVT and make diagnosis of MPN difficult. Patients were diagnosed with occult MPN in case of typical bone marrow changes, but in whom blood cell counts were normal.[13]

Treatment of PVT is to reduce the advancement of thrombosis and prevent portal hypertension or intestinal infarction.[14] The mainstay therapy immediately of acute noncirrhotic nonmalignant PVT is low molecular weight heparin followed by long-term use of vitamin K antagonists with targeted INR of 2-3. The duration of anticoagulation therapy depends on recurrence risk. Life long anticoagulation is recommended in a patient with portal vein thrombosis with an underlying prothrombotic risk factor.[15]

In acute non-cirrhotic portal vein thrombosis with an early diagnosis and use of early anticoagulation, the 5-year survival rate has now improved to 85%. The outcome of PVT is good, and mortality is mostly due to an underlying cause or as consequences of portal hypertension.[16]

CONCLUSION

In conclusion, this case is an example of portal vein thrombosis, with JAK2 mutation without any other identifiable etiology for her prothrombotic state. Her blood picture did not meet the WHO criteria at this admission but patient was asked to follow up a month later and discharged with oral anticoagulants. Thus with timely identification of the portal vein thrombosis along with its causative factor and prompt management, mortality and morbidity associated with such cases can be reduced. Studies regarding usage of DOACs (direct oral anticoagulants) in the management of PVT are limited and is much needed with the increasing number of cases of PVT.

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