

Extended Mesenteric Thrombosis in a Splenectomised Young Man with Myeloproliferative Syndrome

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Abstract

Mesenteric vein thrombosis (MVT) is not an uncommon cause of acute mesenteric ischemia yet its diagnosis is often delayed due to its nonspecific abdominal symptoms, low incidence, and low awareness among clinicians. A 21-year-old man who underwent splenectomy after a traumatic injury four years prior to presentation, presented with subacute epigastric pain associated with mild fever, not responding to symptomatic treatment. Based on the initial imaging studies done, he was found to have mesenteric vein thrombosis. Further workup showed myeloproliferative syndrome with JAK2 mutated wild type allele. The patient was successfully treated with long term anticoagulant. Three months later, control studies documented the disappearance of thrombotic lesions. This report is to highlight the importance of suspecting a MVT in patients with unexplained recurrent abdominal pain and looking for specific etiologies for secondary MVT such as JAK2 mutation even if the patient has an obvious reason for thrombocytosis.

Keywords: Mesenteric vein thrombosis; Splenectomy; Myeloproliferative syndrome

1. Case Presentation

A 21-year-old man presented for two-week history of epigastric pain associated with mild fever not responding to symptomatic treatment. He denied any episode of nausea, vomiting or diarrhea. He had no known drug and food allergies, worked as military cook. He was a non-alcoholic but a five pack-year smoker. He has been splenectomised four years ago secondary to a traumatic lesion of the spleen and since that accident he used to have high platelets count on peripheral blood without any thrombotic episodes. His physical showed normal vital signs, and epigastric abdominal pain and tenderness.

In the ER, his blood pressure was 130/70 mmHg and the blood tests showed : WBC = 30.000 (N = 54 – L = 25 – M = 8 – Eo=8 B = 2 – myel=2- Metamyelocyte = 1) – Ht = 29 – MCV = 69 – Plat = 2.266.000 – CRP = 30 – Liver enzymes = Normal – Lipase = 35 – TP = nl – PTT = nl; The chest X-ray was normal and the abdominal US showed a slightly enlarged liver with a thrombus in the superior mesenteric vein; Abdominal angio CT Scan showed thrombosis of the portal vein (18 mm) and the proximal segment of the SMV (12 mm) associated with an infiltration of the mesenteric fat and multiple mesenteric adenopathies.

The coagulopathy studies (Prot C, Prot S, anti-thrombin, Factor V Leyden) was normal as well as ANA and antibody anti-phospholipids. Gastroscopy showed an oesophageal varices grade 2 with fundic erythematous lesions. The specific etiology was not yet diagnosed. Hence, bone marrow aspirate was done and showed a very rich myeloid cellularity suggestive of myeloproliferative syndrome. Moreover, bone marrow biopsy revealed pleomorphic megakaryocytic hyperplasia. The molecular biology revealed the presence of a JAK2 mutated wild type allele (73% positive).

Thus after his diagnosis, he was successfully treated with long term anticoagulant and cytoreduction. The disappearance of the thrombotic lesions was confirmed by a control CT scan after 3 months after presentation.

2. Introduction

Mesenteric vein thrombosis (MVT) is responsible of 10% to 20% of cases of acute mesenteric ischemia. Its diagnosis is often delayed due to its nonspecific abdominal symptoms, low incidence, and low awareness among clinicians. The primary or idiopathic form of MVT represents 50% of cases and in the remaining secondary MVT types, myeloproliferative disorders are responsible of 25% of cases; JAK2 mutation has emerged as an accurate biomarker for diagnosis of myeloproliferative neoplasm and represents 20% of their causes. Therapeutic modalities are variable and may include a specific treatment for the underlying disease with or without a long term anticoagulation [1].

3. Discussion

The most common clinical presentations of venous thromboembolism (VTE) are deep vein thrombosis (DVT) and pulmonary embolism(PE), yet, they can occur in any location of the venous system, such as in the cerebral veins, retinal veins, and abdominal and pelvic veins [1].

Splanchnic vein thrombosis refers to VTE occurring in portal, mesenteric, and hepatic venous segments, either in isolation or in different combinations [2]. Mesenteric vein thrombosis (MVT) is usually suspected in the later stages of the disease after multiple diagnostic tests fail to identify the cause of the patient's symptoms [3]. The late diagnosis has been attributed to multiple factors including features that overlap those of more common intestinal disorders, the relative rarity of the disease, insufficient clinical awareness, the lack of sensitivity for clot detection and the poor specificity of ancillary signs at noninvasive imaging [4].

The advancement of diagnostic modalities resulted in an increase in number of diagnosed MVT, which now accounts for 6%-9% of all cases of acute mesenteric ischemia, and 1/1000 emergency department admission [5]. The mean age of patients at presentation ranges between 40-60 years with a minute male to female predominance [6].

MVT is either primary or secondary. Primary MVT, which accounts for up to 50% of the cases, is a diagnosis of exclusion, in which no specific etiologic factor is found [3]. On the other hand, secondary MVT is associated with an underlying disease [7]. 70% of cases of secondary MVT are attributed to hyper-coagulable states that include thrombophilic defects, primary or secondary thrombocytosis, nocturnal paroxysmic hemoglobinuria, heparin induced thrombocytopenia, oral contraceptive drugs and pregnancy, whereas 25% are due to local factors such as abdominal trauma, surgery, severe infections, severe inflammation (ex. IBD, pancreatitis, behcet, sarcoidosis) and neoplasia (ex. colorectal, pancreas or hepatocarcinoma) [7]. The remainder 5% are due to local venous stasis resulting from factors such as portal hypertension (ex. cirrhosis, hepatocarcinoma), hypersplenism and congestive heart failure [7].

For management purposes, MVT are also classified as acute, subacute, or chronic [3]. Typical signs and symptoms in patients with acute MVT are nonspecific and include abdominal pain that is out of proportion to physical exam, nausea, vomiting, constipation with or without melena [4]. If not treated, gradually mesenteric ischemia takes place [3]. In subacute MVT, the patient presents with days to weeks duration of the aforementioned symptoms [3]. Chronic MVT are a challenge for physicians and are often considered only after exclusion of more common and less urgent causes of abdominal pain [4]. Often patients are asymptomatic until late stages of the disease where complications mainly due to portal hypertension occur [3,4].

In a closer look into the most common cause of secondary MVT, the hyper coagulable states, the two most common etiologies are thrombophilic defects thrombocytosis, with each attributing to 25% of such cases.

Thrombocytosis is either primary (primary myeloproliferative diseases) or a secondary to diseases affecting the bone marrow, such as infections, severe iron deficiency, neoplasm, hemorrhage, hemolysis, inflammatory conditions, and splenectomy [9]. MPNs are a group of hematopoietic stem cell disorders characterized by clonal proliferation of myeloid-lineage cells and they include polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF), and chronic myeloid leukemia (CML) [8].

In splanchnic vein thrombosis specifically, the most common underlying prothrombotic disorder is MPN [7]. Risk factors for MPN-associated SVTs include younger age, female sex, concomitant hypercoagulable disorders, and the *JAK2 V617F* mutation [7].

JAK2 mutation analysis and bone marrow biopsy are the two main procedures to diagnose primary thrombocytosis in adults with persistent thrombocytosis after excluding the causes of secondary thrombocytosis [10]. After 12.6 years follow up, Landgren et al. [11] found that on the basis of 8,149 cancer-free splenectomized patients, excluding those who were diagnosed with cancer <1-year post-splenectomy, there was a 50% increased risk of solid and hematologic malignancies, and they concluded that cancer-free splenectomized patients have an increased risk of infections, thromboembolism, and possibly cancer [11].

Based on the aforementioned information, we suspected an underlying MPN and JAK2 mutation despite the fact that our patient had been previously splenectomised, and work-up confirmed our suspicions.

The management of SVT associated with JAK2 mutation is very complex. Cytoreduction is often poorly tolerated due to side effect profile or cytopenias in this group. Treatment with anti-platelets or anticoagulation agents is also debatable [12]. Some patients with segmental venous thrombosis recover without any specific therapy, some others improve with anticoagulation therapy and others may require surgery. However, De Stephano et al. [13], in the largest study cohort of MPN related SVT describing in detail the treatments before and after the SVT, reported that factors associated with a significantly higher risk of recurrence were Budd-Chiari syndrome, history of previous thrombosis, splenomegaly, leukocytosis and the absence of vitamin K-antagonists (VKA) treatment.

Intracranial and extracranial major bleeding was recorded mainly in patients on VKA [13]. Despite the fact that our patient was splenectomised, he has at least 3 major risk factors for SVT recurrence like the history of previous thrombosis, the high level of leukocytosis and thrombocytosis and the presence of portal vein hypertension well documented by the presence of esophageal varices on gastroscopy. The long term treatment with VKA and cytoreduction was clearly justified knowing the fact that he may develop a major bleeding at anytime, and control CT Scan after 3 months showed the disappearance of thrombotic lesions.

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