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Case Report

Superior Mesenteric venous thrombosis in a patient with protein C deficiency

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Abstract

Mesenteric venous thrombosis causing small-bowel infarction is an extremely rare cause of acute abdomen and often difficult to diagnose. Both congenital and acquired causes are responsible. Protein C deficiency is a rare genetic abnormality that predisposes the patient to thrombophilia and leads to thrombosis, often at unusual sites. It mimics clinically with many differentials.[1] This paper presents a case of superior mesenteric venous thrombosis caused by protein C deficiency, which is a rare disease. A 68-year-old foreigner female presented with complaints of constant, diffuse abdominal pain of 7 days associated with nausea, vomiting, and anorexia. Even with all sorts of conservative management, pain was not subsiding. Contrasted computed tomography of the abdomen revealed SMV thrombosis. Immediate anticoagulant was started & hypercoagulability workup revealed protein C deficiency. It is concluded that the mesenteric venous thrombosis might be caused by underlying protein C deficiency, while protein S and antithrombin III levels were normal.

Key words: *Superior mesenteric vein (SMV), Mesenteric venous thrombosis (MVT), Protein C deficiency, Protein S deficiency, Antithrombin III deficiency, Intestinal infarction.*

Introduction:

Mesenteric venous thrombosis is an uncommon cause of mesenteric ischemia accounting for 5-15% of the cause.[2] It usually involve superior mesenteric vein & rarely inferior mesenteric vein.[3] It can be presented either as acute with abdominal pain or as chronic- presenting with features of portal HTN. The diagnosis often delayed & most common cases are identified either at laparotomy or at incidental findings on abdominal CT scan or at autopsy. Contrast enhanced CT scan of abdomen is quite accurate for diagnosis & differentiating two types of mesenteric vein thrombosis. Diagnosis is often delayed due to nonspecific clinical presentation & low degree of clinical suspicion. Prothrombotic factor, haematological malignancy & local abdominal inflammatory conditions, use of oral contraceptive are common predisposing conditions. Use of Anticoagulant is treatment of choice in acute MVT. Early diagnosis can be made by advanced radiological technique; immediate anticoagulation can improve the outcome. SMV occlusion can be either primary (Idiopathic) or secondary to diverse conditions, one of them being secondary to Protein C and Protein S deficiency.[4] Protein C and Protein S are natural anticoagulants and their deficiency can lead to venous thrombosis.[5]

The prevalence of protein C deficiency in a healthy population is 0.2%– 0.4%, whereas in patients with venous thrombosis it is 3%–4%.[6]

Protein C-deficient patients have a significant risk of a thrombotic event over the general population, up to a 7-fold increased risk. Up to 63% of affected individuals will have recurrent venous thrombosis in need of lifelong anticoagulation.[7] However, some evidence suggests that thrombosis, in patients with a genetic hypercoagulable dysfunction, is more properly thought of as a multicausal disease, requiring an acquired risk factor for expression like pregnancy, oral contraception, immobilization, and inflammatory conditions such as pancreatitis.[8]

Case Report:

A 68-year-old female presented with complaints of constant, diffuse abdominal pain of 7 days marked at umbilical & right lumbar region, associated with nausea, vomiting, and anorexia. Pain was moderate in severity & colicky in nature, no specific site of radiation or aggravating & reliving factor. No history of melaena, hematochezia, hematemesis, diarrhea, or fevers/chills was given. The patient had no history of intravenous drug abuse, toxic ingestions, or prolonged

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nonsteroidal anti-inflammatory medication use. She is a known case of DM, HTN, NAFLD related compensated CLD. She had history of abdominoplasty 25 years back & following that she developed DVT & post thrombotic syndrome of both lower limb. The patient's family history was significant, her father & daughter suffered from DVT.The patient reported that she was not taking any medications currently for postthrombotic syndrome.

On physical examination, the patient was afebrile, nonicteric, moderately dehydrated, mildly tachycardic and hypertensive (BP-150/90mmof Hg), and appeared to be in mild distress. Abdominal examination showed a diffusely tender and soft abdomen without peritoneal signs, no deep point tenderness, McBurney's point tenderness & Murphy's sign were negative, no renal angle tenderness, hypoactive bowel sounds, and tympanatic percussion of at paraumbilical region.

Laboratory work revealed amylase and lipase, LFT, S electrolytes & S. creatinine within normal limits. Also of note, the patient had a white blood cell count of 6.0×10.3/μL,Neutrophil-57.8%, ESR-22mm/1st hr. Random blood glucose of 10.65mmol/L,. Radiographic abdominal series-revealed no ileus. abdominal ultrasound showed - Chronic liver disease with evidence of portal hypertension. The patient managed conservatively with intravenous hydration & bowel rest.

After an initial mild improvement in symptoms, the patient's clinical status worsened, with increased nausea and vomiting, abdominal pain, abdominal distension, and fever. The patient received antispasmotic and antiemetic drugs, but on following day the abdominal pain worsened with repeated vomiting, but without constipation or fever. Abdominal examination revealed only diffuse tenderness, particularly in the para umbilical & right lumbar region, without rigidity and bowel sound was sluggish. Computed tomography (CT) with contrast of the abdomen (Figure-1 & Figure 2) was performed on the 2nd hospital day. This revealed superior mesenteric vein thrombosis as well as a Chronic liver disease with evidence of portal hypertension & circumferential wall thickening of ileo-caecal region with partial narrowing of lumen. The findings on CT scan combined with the patient's past history & family history of DVT prompted a search for a hypercoagulable syndrome. Patient's viral screening for CLD was negative, albumin level & all tumor markers (Ca-19.9,Ca-125,CEA,AFP) were within normal limit. The patient was placed on anticoagulant with subcutaneous LMW heparin(Enoxaparin), which was continued until oral warfarin therapy came to therapeutic level. The patient improved clinically & wanted to go abroad for further management & refused to do Oesophago Gastro Duodenoscopy for evaluation of oesophageal varices & Duplex study of both lower limb vessels. Patient gave blood samples for Protein C & Protein S, but report was not available as patient was discharged against medical advice. The patient was lebelled as a case of Superior mesenteric vein thrombosis with advice to continue warfarin & advised for follow up in 3 months with report of Protein C & Protein S. As patient did not come for follow up we looked for the report in laboratory & found that she had an abnormally low level of protein C (46%; normal range 70%–140%). Screening for protein S revealed normal values.

Fig-1 shows axial section of CT abdomen indicating complete obstruction of SMV

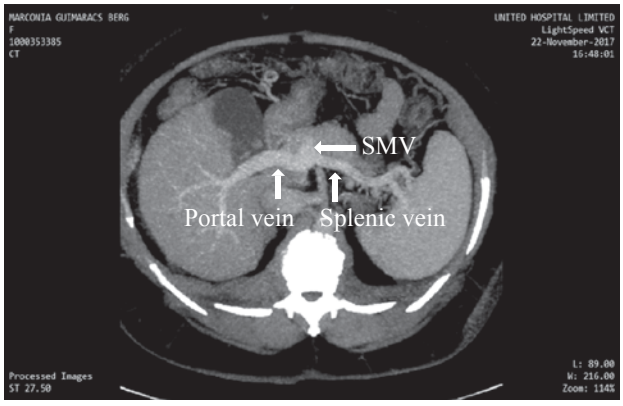

Fig 1

Fig-2 shows coronal section of CT abdomen showed complete obstruction of SMV

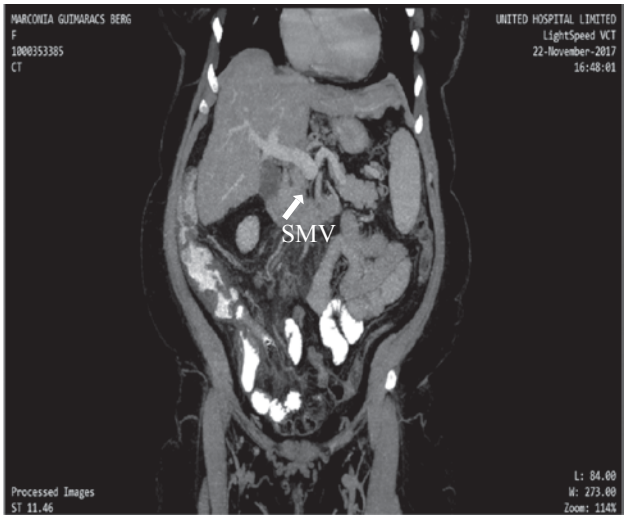

Fig 2

DISCUSSION:

Mesenteric venous thrombosis (MVT) is a rare cause of acute abdomen. MVT has been a recognized clinical entity since 1935, when it was first formally described by Warren and Eberhardt. [9]At that time, they reported a mortality rate of 34%, with only a 5% survival rate of patients who did not undergo surgical treatment.[10] Now, with the aid of new imaging techniques such as Computed tomography (CT) scan, diagnosis can be made at an earlier stage in the disease, allowing for more conservative management. The overall mortality rate, though still high, has decreased to approximately 20% by some reports[11] . MVT is often difficult to diagnose because of its rarity and lack of specific symptoms on presentation. The most common presenting complaint is abdominal pain, usually vague in character. Contrast-enhanced abdominal CT scanning currently holds a

diagnostic sensitivity of greater than 90% and the diagnostic test of choice[11].However, magnetic resonance imaging and ultrasound have also been used in making the diagnosis.[12]The combination of Doppler ultrasonography and CT increases the sensitivity.[13]Prompt recognition is important because early and aggressive treatment can limit progression of the thrombotic process. Classification of MVT falls into three categories, based on the time course of the patient's abdominal pain: acute, subacute, or chronic. The acute form is associated with the highest risk of bowel infarction and peritonitis.[11] Therefore, early recognition and treatment is critical in these patients. Previously patients were treated surgically for this diagnosis. More recently, anticoagulation alone and close follow-up have become acceptable means of treatment when bowel ischemia has not led to transmural necrosis and bowel perforation.[13] Thrombolytic therapy has also been used successfully in a few case reports. [11]however, long delays in the diagnosis of this condition often make thrombolytic therapy obsolete. Mesenteric venous thrombosis are classified as either primary or secondary depending on etiological factor, patients are said to have secondary mesenteric venous thrombosis where etiological factors are found (Table 1). Once MVT has been confirmed, patients should be screened for hereditary or acquired thrombophilia. First, we should search for predisposing factors, such as congestive heart failure, atrial fibrillation, myeloproliferative disorders, oral contraceptive use and abdominal infection. In our case we searched for acquired causes but found none. Second, in spite of a finding of acquired factors, screening for genetic factors should be performed. Protein C is a physiologic anticoagulant because it inactivates Factor Va and Factor VIIIa, which are two essential cofactors in the coagulation cascade. This system is a major regulator of blood fluidity and prevents thrombus formation. Protein C deficiency is a rare genetic abnormality that is responsible for thrombophilia, often in conjunction with other genetic or acquired risk factors. The prevalence of protein C deficiency in a healthy population is 0.2%– 0.4%, whereas in patients with venous thrombosis it is 3%–4%.[6]

Before labeling a patient with inherited protein C deficiency, it is mandatory to rule out acquired causes of the deficiency such as liver disease, vitamin K deficiency, renal insufficiency, disseminated intravascular coagulation and postoperative states. Thus it is essential to repeat an assay after 4–6 weeks to confirm the deficiency. The treatment of MVT involves anticoagulation alone or in combination with surgery. In patients with acute or sub acute mesenteric venous thrombosis, treatment with heparin should be started immediately even intraoperatively or even in the presence of GI bleed. The duration of treatment is based on the presence of identifiable reversible risk factor in which case anticoagulation can be given for 3-6 months. Otherwise, indefinite anticoagulation should be considered. Surgery is required in case of transmural infarction & with the presence of peritoneal sign.

In many cases of MVT, prompt anticoagulation will preserve bowel viability. In cases of bowel infarction, the prognosis correlates well with the length of intestine remaining after resection of the ischemic bowel. In selected patients, thrombectomy in addition to bowel resection may be successful.[14] But it is only indicated in patients with recent and limited thrombus. Use of intra-arterial or intramesenteric venous lytic therapy has been reported, with a low success rate and a high hemorrhagic risk that may restrict its use. Anticoagulation therapy with tissue plasminogen activator was used in one case, and despite the total cessation of superior mesenteric venous flow, the authors reported that they found only a short segment of necrotic intestine at laparotomy, which suggests that this treatment was effective.[15]

In the context of massive mesenteric venous thrombosis, intravenous protein C concentrate has been used successfully.[16]It should be considered in patients with congenital protein C deficiency with major thromboembolic complications. In each case, early anticoagulation with heparin followed by long-term warferin is recommended.

Outcomes are mainly determined by underlying prothrombotic state, recurrence of the thrombosis & development of short bowel syndrome.

Table 1.

Prothrombotic States
• Protein C deficiency
• Protein S deficiency
• Factor V Leiden
• G20210A mutation in Prothrombin gene
• Antiphospholipid antibodies
• Hyperhomocysteinemia
• Oral-Contraceptive use*
• Pregnancy
• Neoplasm's*
Hematologic Disorder
• Polycythemia Vera*
• Essential thrombocythemia*
• Paroxysmal nocturnal hemoglobinuria*
Inflammatory Diseases
• Pancreatitis*
• Peritonitis & intraabdominal sepsis*
• IBD
• Diverticulitis
Postoperative state
• Abdominal operations*
• Splenectomy
• Sclerotherapy for esophageal varices
Cirrhosis & portal hypertension
Miscellaneous Causes
• Blunt abdominal trauma
• Decompression sickness

*This factor is among the more common causes of mesenteric venous thrombosis

Conclusion:

Our patient had a multifactorial thrombotic event. Given the patient's family history of thrombotic events in a first-degree relative, coupled with low protein C level, our patient probably had a genetic defect that predisposed her to this SMV thrombosis. SMV thrombosis should always be considered in the setting of vague abdominal pain in a patient with hypercoagulable risk factors.

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