INTRODUCTION

We describe a patient with protein C deficiency presenting as subacute intestinal obstruction due to ischaemic small bowel stricture. Review of world literature revealed only seven cases presenting with subacute intestinal obstruction due to ischaemic strictures secondary to mesenteric vein thrombosis. One case was due to protein C deficiency, one due to anti-thrombin (AT) deficiency and one was part of antiphospholipid antibody syndrome. No underlying cause was found in other four cases. To the best of our knowledge we report the first such case from India of protein C deficiency presenting with subacute intestinal obstruction due to mesenteric vein thrombosis. He also had left sided iliofemoral thrombosis. Protein C deficiency is an autosomal dominant disorder found in 3-4% patients with venous thrombosis. Deep vein thrombosis (DVT) of the lower extremities and pulmonary embolism are the most frequent clinical manifestations. More unusual sites include cerebral venous sinus and mesenteric vein thrombosis and upper limb deep vein thrombosis.

CASE REPORT

Thirty eight years male patient presented with colicky pain in epigastrium with abdominal distension and recurrent vomiting of one month duration. The pain worsened post-prandially and was partially relieved by vomiting. He also had pain and swelling of left lower limb. Clinically he was afebrile with no icterus, pallor or lymphadenopathy. Abdomen was distended with visible peristalsis and mild epigastric tenderness. There was no guarding or organomegaly. Local examination of left lower limb revealed clinical findings suggestive of deep venous thrombosis (DVT). Blood counts, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen and metabolic parameters were normal. X-ray abdomen showed multiple air-fluid levels in the small bowels with distension. Enteroclysis showed a 3.5 cm long mid-ileal stricture. Ultrasound and computerised tomography (CT) scan of abdomen revealed portal and superior mesenteric vein thrombosis with splenomegaly. There was no evidence of pulmonary thrombo-embolism clinically; colour Doppler flow imaging (CDFI) of left lower limb revealed ileo-femoral thrombosis. Chest X-ray, electrocardiography (ECG) and echocardiography were normal. Patient was investigated for thrombophilia and an abnormally low level of protein C of 40% was found on functional assay (normal 70-140%). Protein S, AT-III, Factor V Leiden (FVL), plasma homocysteine, lupus anticoagulant (LA) and anti-cardiolipin antibodies (ACA) revealed normal values. Paroxysmal nocturnal haemoglobinuria (PNH) workup was normal. History of DVT in the lower limbs was elicited in his only sibling, a sister, who however, refused screening. There was no other family member available for screening. Patient was anti-coagulated with low molecular weight heparin (LMWH) for one week followed by oral anticoagulant Acitrome (Acenocoumarol) targeting an international normalized ratio (INR) of 2.5 to 3.0. Surgical resection of the ileal stricture was done after switching from oral anticoagulant to bridging heparin therapy for a week. Histopathologically this resected ileal segment revealed ulceration, fibrosis and thrombosis of intramural veins. Patient was thereafter maintained on oral anticoagulants and was relieved of his abdominal symptoms and on
4 years follow-up did not reveal any recurrence of his prior complaints.

**DISCUSSION**

Ischaemic small intestinal strictures complicating mesenteric vein thrombosis are rare. The summary of 7 such cases reported in literature is shown in Table 1.1-3 Majority of patients reported are males and except for one patient with ileal stricture, all reported patients had jejunal strictures. Colon seems to be spared due to a well-developed collateral circulation. The median length of the stricture was 7.6 cm (range 2 to 20 cm) and the strictures were regularly contoured at barium studies. An underlying thrombophilic state could be demonstrated only in three patients out of whom only one had underlying protein C deficiency. Symptoms of bowel obstruction appeared 3 weeks to 2 months after presumed onset of mesenteric venous thrombosis. None of these patients had a family history of thrombosis. Only one patient had associated venous thrombosis in the calf veins.2 In our patient not only was there a history of left ilio-femoral thrombosis but also in addition there was family history of DVT in the lower limbs in his only sister (Table 1).

The prevalence of protein C deficiency in healthy population is 0.2-0.4%, while in patients with DVT it is 3.7% and in patients with thrombophilia it is 4.8%.4 Protein C deficiency is an uncommon genetic abnormality that may be a contributory cause for thrombophilia, often in conjunction with other genetic/acquired risk factors. The other genetic factors causing thromboph embolism are FVL defect with activated protein C resistance (APCR), protein S and AT-III deficiency. Raised plasma homocysteine with methyl tetrahydrofolate reductase (MTHFR) mutations, ACA and LA are the other common risk factors for thrombophilia.

Hereditary thrombophilia should be suspected in the following situations:-

1. Age < 45 years
2. Spontaneous/unprovoked thrombotic episodes
3. Recurrent thrombotic episodes without any obvious cause
4. Trivial trigger factors leading to life-endangering thrombotic episodes
5. Thrombosis at unusual sites, such as cerebral, mesenteric and upper limb venous thrombosis
6. Family history of thrombosis

Prior to labeling a patient with inherited protein C deficiency it is mandatory to rule out acquired causes of protein C deficiency like liver disease, vitamin K deficiency, renal insufficiency, disseminated intravascular coagulation (DIC), postoperative states with ARDS and patients on oral anticoagulants, all of which can cause low levels of these factors. To establish a hereditary thrombophilia, family studies are mandatory.5

A thorough search for these acquired causes was made in our patient but none were detected. Multiple deficiencies are seen following acute thrombosis, hence, whenever more than one natural anticoagulant (protein C, protein S, AT-III, FVL, APCR) is found deficient it is essential to repeat an assay after 4-6 weeks to reconfirm the deficiency. If the patient is on oral anticoagulant therapy, the same should be withheld for at least two weeks and patient put on bridging heparin therapy prior to repeating an assay for all defects except AT, which is interfered with by heparin therapy.5

Patients with thrombophilia who develop spontaneous life endangering major thrombotic episodes such as abdominal catastrophes or cerebral sinus venous thrombosis, need life-long anticoagulation, while if it follows exposure to a reversible trigger factor such as surgery, pregnancy, trauma, drugs etc. a shorter course of six months of anticoagulation followed by close follow up may be sufficient.

In our patient, a repeat assay six months after presentation, while on bridging heparin therapy, reproduced low protein C levels of 43% with all other natural anticoagulants being in the normal range. The patient is presently asymptomatic on long term follow up of over four years with oral anticoagulation, targeting an INR of 2.5. Though his only sister had history of DVT in her lower limbs, she did not agree for screening, hence the hereditary nature could not be established in this case.

Protein C is a rare genetic abnormality, which predisposes to thrombophilia and leads to thrombosis, often at unusual sites. Hence in all cases of mesenteric vein thrombosis, a thrombophilia screen should be done along with family screening, where possible, to establish

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<th>Authors</th>
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<th>Age (Y)</th>
<th>Sex</th>
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</table>

Table 1: Description of reported patients with small intestinal stricture complicating mesenteric venous thrombosis
a diagnosis of hereditary thrombophilia.

REFERENCES


Announcement

ECG Learning Course

INDIAN SOCIETY OF ELECTROCARDIOLOGY

Indian Society of Electrocardiology is organizing 3rd ECG Learning Course at Rapicon Hall, Central Railway Headquarters Hospital, Byculla, Mumbai 400 027 on 21st and 22nd July 2007. Registrations open upto 15th July 2007 only.

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