

## CASE NOTE

# Protein C deficiency and mesenteric venous thrombosis

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**M**esenteric venous thrombosis causing small-bowel infarction is an extremely rare cause of acute abdomen and is 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.

**CASE REPORT**

A 22-year-old woman with a history of gestational toxicosis and oral contraceptive use for 3 years reported progressive vague abdominal pain and vomiting over a 2-day period, without constipation, followed by rectal bleeding. On physical examination in the emergency department, the patient was afebrile, her blood pressure was 110/70 mm Hg and her pulse rate was 80 beats/min. There was diffuse abdominal tenderness with no rebound or abdominal rigidity. Findings on digital rectal examination were normal. An abdominal radiograph showed no air–fluid levels in the small bowel. An abdominal ultrasound showed pelvic and parietocolic extravasation. A computed tomography (CT) scan confirmed ascites but did not reveal venous thrombosis. Blood test results showed hyperleukocytosis with granulocytosis. Amylase and lipase values were within their normal ranges, fibrinogen levels and metabolic parameters were normal. The patient received antispasmodic and antiemetic drugs, but the following day the abdominal pain worsened with involuntary vomiting, but without constipation or fever. Abdominal examination revealed only diffuse tenderness, particularly in the iliac fossa, without rigidity.

At exploratory laparotomy, we found that the ileum was necrotic (Fig. 1, Fig. 2), and we resected 20 cm of bowel, which, histologically, showed ischemic necrosis with venous thrombosis. The final diagnosis was small-bowel infarction secondary to mesenteric vein thrombosis. Her postoperative outcome with “bridging” heparin therapy was good, and she left the hospital fully anticoagulated, with a prescription for long-term coumadin.

On investigation for possible thrombophilia, we found that the patient had an abnormally low level of protein C (42%; normal range 70%–140%). Screening for protein S, antithrombin III, Factor V Leiden, prothrombin mutation, activated protein C resistance, plasma homocysteine, lupus anticoagulant and cardiolipin antibodies revealed normal values. Paroxysmal nocturnal hemoglobinuria was absent. A repeat assay 6 weeks after presentation, while the patient was on bridging heparin therapy, reproduced low protein C levels. She remains well on lifelong anticoagulation therapy and has had no further thrombotic event.

**DISCUSSION**

Mesenteric venous thrombosis is a rare cause of acute abdomen. The diagno-



**Fig. 1.** Surgical view shows the necrotic bowel; 20 cm required resection.



**Fig. 2.** Endoscopic view of the necrotic bowel.

sis may be difficult and treatment delayed because patients usually have nonspecific abdominal symptoms. Contrast-enhanced CT allows venous thrombosis to be detected by a noninvasive method; Morasch and colleagues<sup>1</sup> were able to make the diagnosis in 90% of their patients, but there were false-negative results. The combination of Doppler ultrasonography and CT increases the sensitivity.<sup>2</sup> Prompt recognition is important because early and aggressive treatment can limit progression of the thrombotic process.

First, we should search for predisposing factors, such as congestive heart failure, atrial fibrillation, myeloproliferative disorders, oral contraceptive use and abdominal infection. We searched for acquired causes but, with the exception of oral contraception, found none. Second, and in spite of a finding of acquired factors, screening for genetic factors should be performed. In Mediterranean countries we should bear in mind the possibility of Behçet disease. Our patient had no aphthosis or pseudofolliculitis with either an ocular or a vascular manifestation.

Protein C is a physiologic anticoagulant because it inactivates Factor Va and Factor VIIIa, which are 2 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%.<sup>3</sup>

Before labelling 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.

In many cases of mesenteric venous thrombosis, 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,<sup>4</sup> 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.<sup>5</sup>

In the context of massive mesenteric venous thrombosis, intravenous protein C concentrate has been used successfully.<sup>6</sup> 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 coumadin is recommended.

## CONCLUSION

Deep vein thrombosis, especially mesenteric thrombosis, in young people, even in conjunction with acquired factors like oral contraceptive use, should prompt physicians to perform full screening for thrombophilia.

**Competing interests:** None declared.

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