



Case report

Protein C deficiency: Report of a challenging case with recurrent multiorgan thrombosis

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ABSTRACT

Introduction and importance: Protein C deficiency is a rare disorder associated with an increased risk of developing abnormal blood clots. Mild and heterozygous cases are usually asymptomatic and may present with recurrent thrombosis. These recurrent thrombi are usually associated with ischemic stroke or concomitant thrombosis during pregnancy and recurrent miscarriage, but arterial thrombosis is relatively uncommon.

Case presentation: In this case report, we introduce an interesting 21-year-old female patient with a protein C deficiency, which presented with a set of symptoms related to ischemia and thrombosis in several different systems, including the colon, brain, and lower extremities.

Clinical discussion: With the diagnosis of ischemic colitis, she underwent medical treatment with hydration, antibiotics, anticoagulant, and GI rest. She was discharged with a suitable response to medical treatment and good general condition. One month later, the patient presented with right upper limb paresis and speech disorder, and at the same time, he had swelling of the left lower limb. The patient was diagnosed with DVT of the common femoral vein and protein c deficiency and treated appropriately with anticoagulant (heparin 1000 IU/h) and was discharged with oral rivaroxaban after symptoms improved.

Conclusion: In young patients with ischemic colitis without a history of previous surgery, increased coagulation should be considered, including impaired fibrinolysis and impaired microcirculation and inflammatory processes. Protein C deficiency is one of several reasons for thrombotic disorders that should be considered in these people, especially if they have a history of DVT or other vascular thromboses.

1. Introduction

Protein C deficiency is a rare disorder associated with an increased risk of developing abnormal blood clots. The active form of protein C (APC) has strong anticoagulant activity, and deficiency in this protein can disrupt the coagulation system, resulting in increased clot production. Protein C deficiency is caused by a mutation in the PROC gene. This mutation is more common in Asian patients and is more common in children than adults. Protein C deficiency may be acquired or congenital, and in terms of disease severity, the prevalence of mild type is estimated to be 1/200 to 1/500, but severe clinical cases are very rare [1]. Deficiency of this protein, which is a type of plasma serine protease, has several symptoms: in severe cases, it occurs in infants with DIC and fulminant purpura; in moderate cases until adolescence, there is no symptom, and it usually presents with recurrent DVT. In mild and heterozygous cases, they are usually asymptomatic and may present with recurrent thrombosis. These recurrent thrombi are usually associated

with ischemic stroke or concomitant thrombosis during pregnancy and recurrent miscarriage, but arterial thrombosis is relatively uncommon [2]. The purpose of this case report is to introduce an interesting case of protein C deficiency, which presents with a set of symptoms of ischemia and thrombosis in several different systems, including the colon, brain, and lower extremities. This case report has been reported in line with the SCARE 2020 Criteria [3].

2. Case presentation

The patient, who was a 21-year-old woman with a complaint of abdominal pain, came to the emergency department of Falsafi Hospital (Gorgan, Iran). The patient had persistent pain in the left side of the abdomen for two days. She did not have nausea and vomiting but had a bloody stool once. The patient reported a history of right lower limb DVT and a spontaneous abortion the previous year that had been treated with warfarin for 6 months but had not been fully evaluated for

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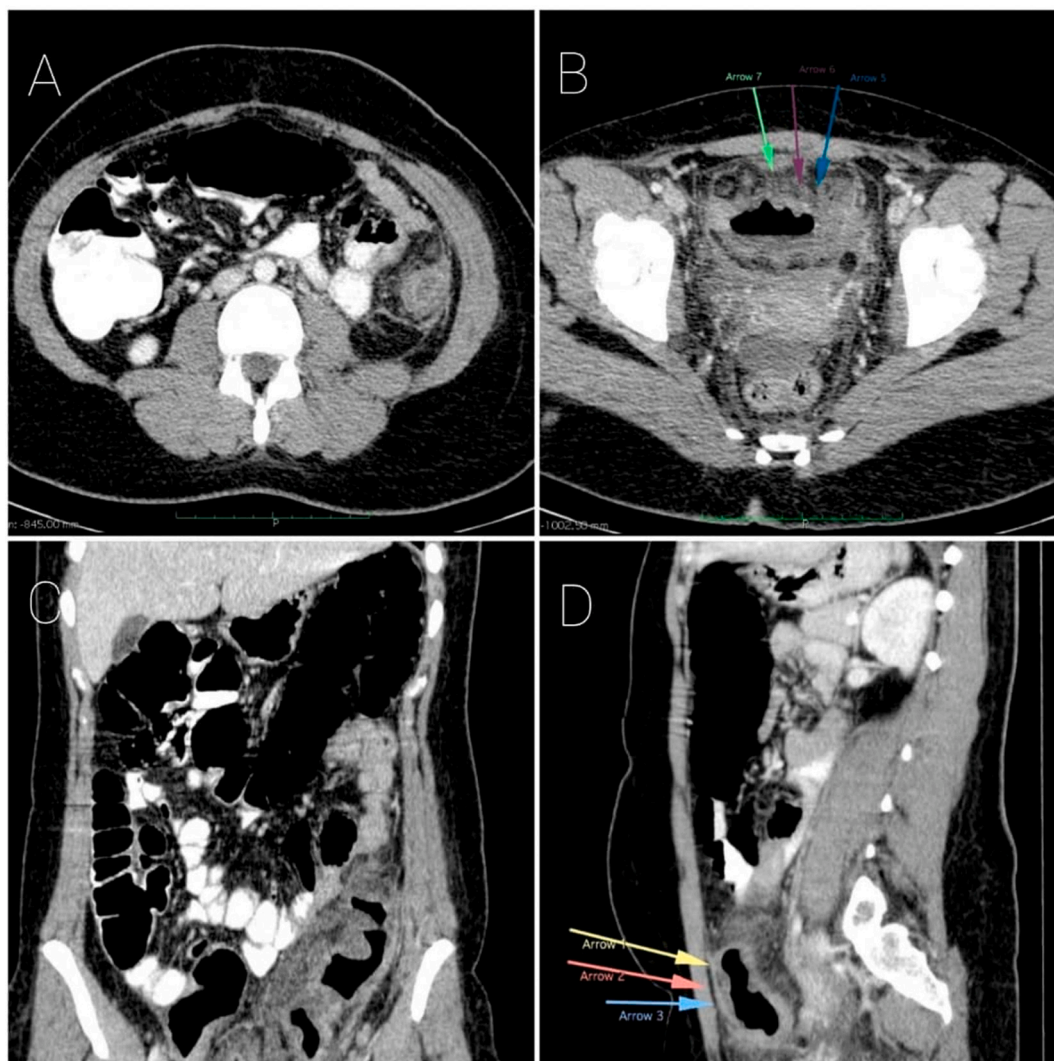


Fig. 1. Axial and coronal reformat post IV and oral abdominopelvic CT scan revealed colonic bowel wall thickening, irregular and segmental, confined to descending (A) and sigmoid colon (B & C). In some portions, there is low density ring of submucosal edema between enhancing mucosa and serosa-target sign (coloured arrows in B & D) associated with pericolic fluid and fat stranding (green arrow in B), in favor of left sided colitis, compatible with ischemic colitis. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

coagulation disorders. On physical examination, she had generalized tenderness predominant on the left side of the abdomen and 39 degrees fever. In the performed lab tests, results were Hb = 11.6 g/dl, WBC: 15700/mm³, PMN: 97%, and LDH: 420, and in the requested abdominal and pelvic ultrasound, a brief free fluid was reported in the LLQ and left gutter. For the patient, a CT scan of the abdomen and pelvis with oral and intravenous contrast was requested and performed (Fig. 1).

With the diagnosis of ischemic colitis, she underwent medical treatment with hydration, antibiotics, anticoagulant, and GI rest. She was discharged with a suitable response to medical treatment and good general condition. One month later, the patient presented with paresis of the right upper limb and speech disorder, and at the same time, he had swelling of the left lower limb. Brain CT scan without contrast and then MRI of the brain with and without injection (MRS and MRV) (Fig. 2), as well as Doppler ultrasound of the lower extremities on both sides, were requested. Doppler ultrasound revealed DVT of the common femoral vein with extension to the saphenous vein and inferior epigastric vein. No lesion in favor of colon tumor was seen on colonoscopy, and the diagnosis of ischemic colitis was confirmed due to fibrinoleukocytoclastic exudate. Coagulation tests were requested for the patient, which declared protein C deficiency and hypercoagulability state. In the additional genetic tests requested, a heterozygous mutation in the PAI-1

gene and 4G/5G polymorphisms were identified. The patient was treated appropriately with anticoagulant (heparin 1000 IU/h) and was discharged with oral rivaroxaban after symptoms improved.

Six months after the initial presentation, the patient was admitted to the hospital with GI obstruction in regular monthly follow-up. Obstruction was complete according to colonoscopy report that could not pass through the narrowing in sigmoid colon and level of the obstruction was distal of sigmoid. Finally, midline laparotomy and resection of the sigmoid colon with Hartman's colostomy were done for her. Histopathology study results confirmed a 10 cm colon stricture due to ischemic colitis' complication with no evidence of malignancy.

3. Discussion

Proteins C and S deficiency and antithrombin III are associated with a high risk of inherited thrombophilia. Protein C deficiency is more common in children and, conversely, protein S deficiency is more common in adults [1]. Protein C deficiency may cause DVT and pulmonary embolism, and it can also cause ischemia in various areas such as the brain and other organs such as the GI tract. Therefore, knowing the body's natural anticoagulants and thrombophilia can help prevent and treat these complications, which are often life-threatening [2].

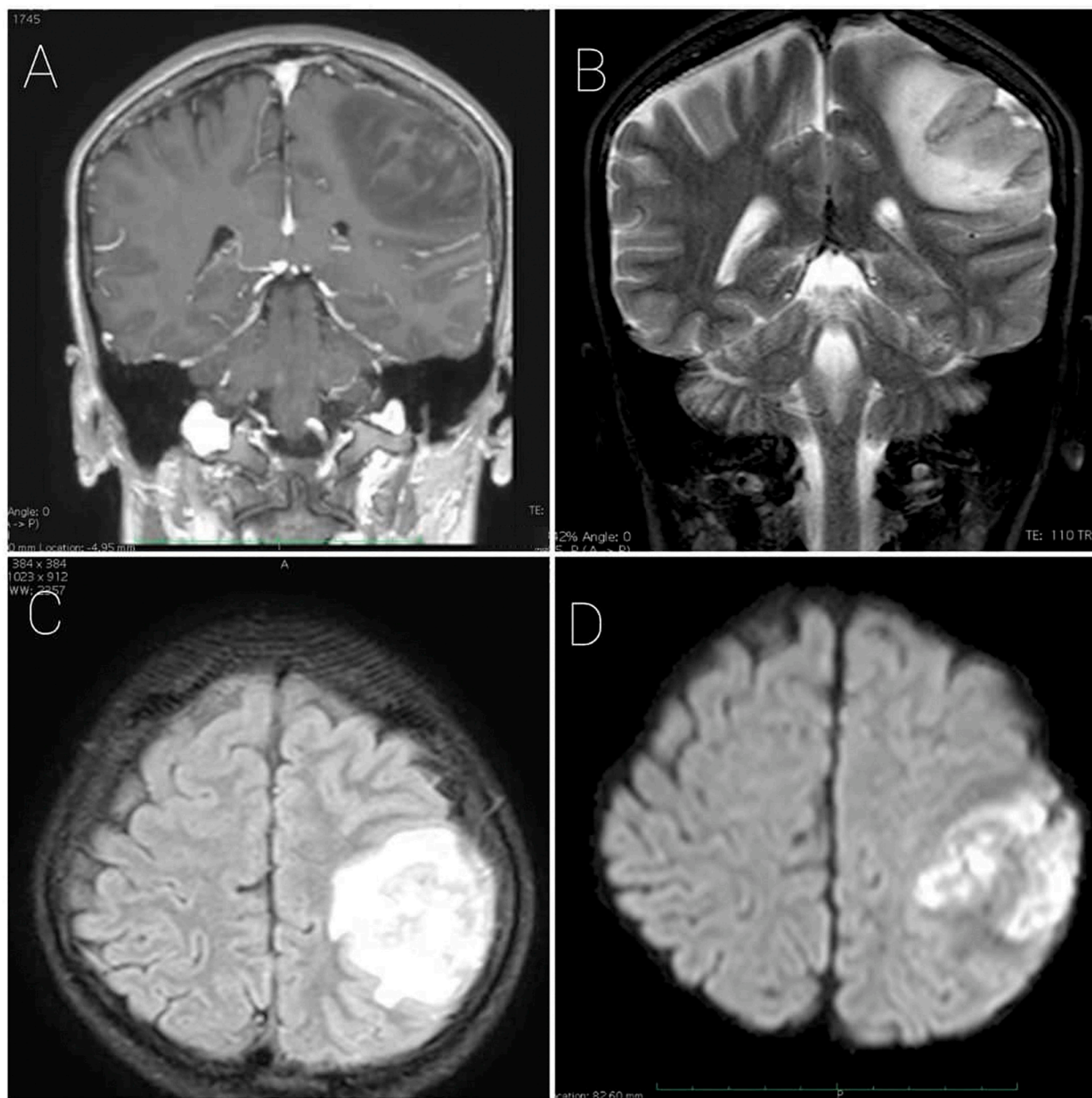


Fig. 2. Contrast enhanced brain MRI shows non enhancing (A) wedge shaped cortical and subcortical high T2/FLAIR signal intensity lesion (B&C), in left high parietal lobe (A & B), demonstrating restriction in DWI (D), consistent with acute ischemic infarct in left parietal lobe.

Many studies have been performed on ischemic symptoms due to protein C deficiency in the brain and DVT of the lower extremities and pulmonary embolism, and various cases have been reported. Lim EYT et al. reported a case of cerebral venous thrombosis in a 19-year-old woman with protein C deficiency who presented with severe headache in the occipital region accompanied by a subdural hematoma on the left [4]. Ghassemi et al. reported a patient that had congenitally deficiency in pro C and presented with ocular manifestations. They suggested that protein C deficiency should be evaluated in all children with leukocoria because early detection can save their eyesight [5].

Nevertheless, ischemic colitis is one of the most common gastrointestinal vascular diseases; the incidence of ischemic colitis in Western

countries is 4.5 to 44 cases per 100,000 people per year. Ischemic colitis results from changes in systemic circulation or anatomical or functional disorders of the mesenteric arteries and appears to be due to local hypoperfusion. In most cases, the specific cause of colon ischemia is unknown and is caused by small vessel disease. However, one of the increasing causes of ischemic colitis is hematological disorders, and protein C deficiency can also be one of the thrombophilic causes of ischemic colitis [6]. Tsimperidis AG et al. conducted a study in which 56 patients with a diagnosis of hospitalized ischemic colitis were compared with 44 patients in the control group with known predisposing factors, but no evidence of ischemic colitis, and they concluded that pro C level in the ischemic colitis group was reduced [6]. In a retrospective study,

Koutroubakis IE et al. compared patients in three groups: ischemic colitis, diverticulitis, and healthy colitis. In the ischemic colitis group, the number of prothrombotic factors such as protein C and S deficiency and APC resistance was higher. However, the amount of factor V Leiden was not significantly different between groups [7]. In another study, 18 patients with a diagnosis of ischemic colitis were evaluated for increased coagulation and concluded that 28% of cases of ischemic colitis had thrombotic disorders. In normal society, this rate is 8.4% [8]. In a study by Theodoropoulou A et al., 19 patients under the age of 55 were analyzed with a diagnosis of ischemic colitis and compared with the healthy control group, they differed only in factor V Leiden, but in terms of other thrombotic and prothrombotic factors, there was no clear difference between the two groups [9]. In our patient, it was also found that the pro C level was reduced, and there was a heterozygous mutation.

4. Conclusion

In young patients with ischemic colitis without a history of previous surgery, increased coagulation should be considered, including impaired fibrinolysis and impaired microcirculation and inflammatory processes. Protein C deficiency is one reason for thrombotic disorders that should be considered in these people, especially if they have a history of DVT or other vascular thromboses.

Sources of funding

There is no funding for the present study.

Ethical approval

This report does not contain any personal information that could lead to the identification of the patient. Therefore, it is exempt from ethical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registration

Not applicable.

Guarantor

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Provenance and peer review

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Credit authorship contribution statement

All of the authors contributed to the case study, research, and writing of the manuscript.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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