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Acute intestinal infarction caused by initially unexplained splanchnic venous thromboses in a patient with protein C deficiency: A thought-provoking emergency case

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ABSTRACT

INTRODUCTION AND IMPORTANCE: Splanchnic venous thrombosis (SVT) originating in the superior mesenteric vein (SMV) is rare and may cause acute intestinal infarction (AII). Protein C deficiency (PCD) results in thrombophilia.

PRESENTATION OF CASE: Acute unexplained SVT originating in the SMV and portal vein was detected in 68-year-old man. Pan-peritonitis and AII were diagnosed and emergency surgery performed. Part of the small intestine was necrotic and partial resection without anastomotic reconstruction was performed. Heparin was administered intravenously continuously from postoperative day (POD) 1. Hereditary, heterozygous, type 1 PCD was diagnosed postoperatively. The anastomosis was reconstructed on POD 16. Warfarin was substituted for heparin on POD 22. No recurrent thrombosis occurred during 2 years of follow-up.

CLINICAL DISCUSSION: Patients with the rare condition of SVT require prompt diagnosis and treatment and may have underlying disease. PCD can cause SVT even in intact veins and anticoagulation therapy should be administered immediately postoperatively. Misdiagnosis and/or delayed treatment of SVT can result in AII, a life-threatening condition with a high mortality rate. Insufficient clinician awareness can result in serious mismanagement of patients with PCD and SVT; emergency patients with AII caused by unexplained SVT should therefore be further investigated for prothrombotic states and assessment of coagulation–fibrinolysis profiles to clarify the underlying mechanism.

CONCLUSION: We here present a thought-provoking emergency case of AII associated with acute SVT caused by underlying PCD that was successfully treated by two-stage surgery and anticoagulation therapy. This case provides a timely reminder for emergency clinicians and gastrointestinal surgeons.

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Abbreviations: AII, acute intestinal infarction; PC, protein C; PCD, protein C deficiency; POD, postoperative day; PV, portal vein; SMV, superior mesenteric vein; SVT, splanchnic venous thrombosis.

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1. Introduction

The superior mesenteric vein (SMV) and splenic vein flow into the portal vein (PV); these veins provide hepatopetal splanchnic flow [1,2]. Although PV thrombosis in patients with cirrhosis [3,4] and post-splenectomy splenic venous thrombosis [5] are common, splanchnic venous thrombosis (SVT) in the SMV is rare [1,2,6]. Reported causes of SMV thrombosis include abdominal inflammatory conditions, hypercoagulation disorders, malignancies, pregnancy, post-splenectomy, and heparin-induced thrombocytopenia [2,6].

Protein C deficiency (PCD) results in thrombophilia [7,8] and this specific hypercoagulable state is a rare cause of SVT [6]. Though acute mesenteric ischemia readily causes acute occlusive ischemia of the digestive tract, SVT can also cause acute intestinal infarction (AII) [9]. Importantly, patients with the rare condition of SVT, which

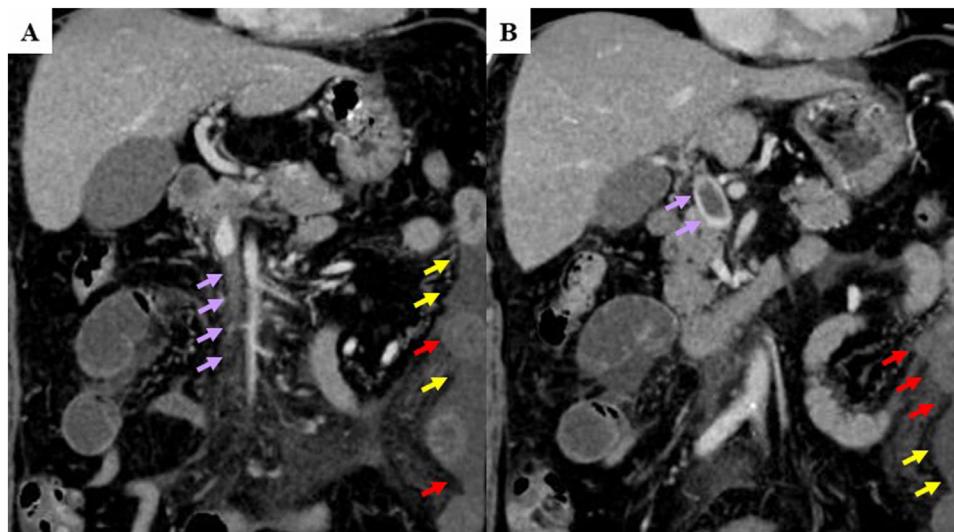


Fig. 1. SVTs in the SMV and PV.

Contrast-enhanced computed tomography images revealing SVTs originating in the SMV (A, purple arrows) and PV (B, purple arrows). Enhancement is clearly decreased in the small intestine (A and B, red arrows). Additionally, ascites is apparent (A and B, yellow arrows). Abbreviations. SVT, splanchnic venous thrombosis; SMV, superior mesenteric vein; PV, portal vein.

requires prompt diagnosis and adequate treatment, are likely to have a causative underlying disease [6].

Here, we report a thought-provoking emergency case of All associated with acute SVT caused by PCD that was successfully treated by two-stage surgery and anticoagulation therapy. This case was reported in accordance with the SCARE 2020 Guideline [10].

2. Presentation of case

A 68-year-old man presented to our emergency unit because of sudden onset of progressive abdominal pain. Physical examination revealed an acute abdomen with rebound tenderness. Although blood tests showed a high white cell count (18,500/ μ L) and C-reactive protein (15.8 mg/dL), conventional coagulation variables, namely prothrombin time and activated partial thromboplastin time, were within the normal range. Contrast-enhanced computed tomography revealed SVTs in the SMV and PV (Fig. 1), and the plasma concentration of D-dimer was high (6.0 μ g/mL). There was clear reduced enhancement in the small intestine and ascites was detected (Fig. 1); however, serum concentrations of lactate dehydrogenase and creatine phosphokinase were within the normal range. He had no history of thrombotic episodes such as venous thromboembolism or purpura fulminans. Blood samples for detailed investigation of prothrombotic states and his coagulation–fibrinolysis profiles were collected before surgery because his SVT was unexplained and might be attributable to an underlying coagulation disorder. Pan-peritonitis and All caused by SVTs originating in the SMV and PV were diagnosed and emergency surgery performed. Abundant bloody ascites was found and the intestinal mesentery was obviously congested and swollen. A total of 50 cm of small intestine located approximately 2 m from the Treitz ligament was necrotic (Fig. 2) and therefore resected. Transvenous thrombectomy was not performed for the PV thrombosis, our intention being to initiate anticoagulation therapy postoperatively to treat that thrombosis and prevent further venous thrombosis. Because we considered that second-look laparotomy might be required because the cause of our patients SVTs was unknown, we did not construct an anastomosis of the digestive tract during the emergency surgery but created an end-fashioned stoma. Full-dose unfractionated heparin was continuously administered intravenously from postoperative day

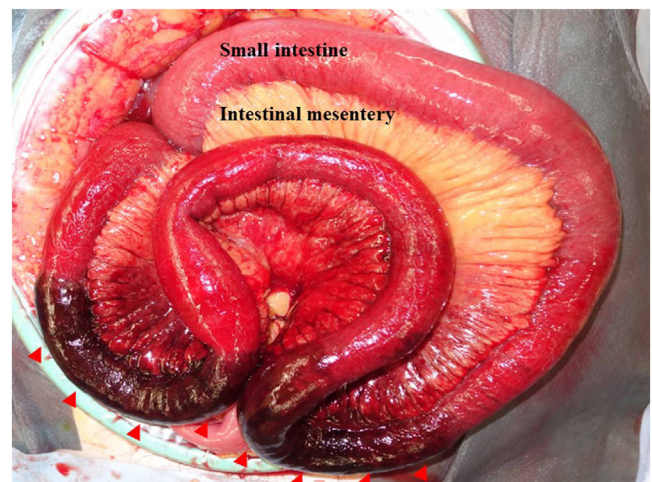


Fig. 2. Intraoperative findings.

Abundant bloody ascites is apparent. The intestinal mesentery is obviously congested and swollen. A total of 50 cm of small intestine located approximately 2 m from the Treitz ligament is necrotic. This All is accompanied by whole layer necrosis (red arrow heads). The necrotic intestine associated with SMV thrombosis was resected.

Abbreviations. All, acute intestinal infarction; SMV, superior mesenteric vein.

(POD) 1. Testing of the preoperative blood samples revealed low protein C (PC) activity and antigen concentration (Table 1), resulting in a definitive postoperative diagnosis of PCD. The temporary stoma was closed and a small intestinal anastomosis constructed on POD 16. Oral warfarin was substituted for the intravenous heparin on POD 22. The postoperative course was uneventful and the patient was discharged on POD 57. He has continued on warfarin and the SMV and PV have remained patent (Fig. 3). There has been no recurrent thrombosis or venous thromboembolism during the 2 years since emergency surgery.

3. Discussion

PC and protein S are vitamin K-dependent glycoproteins, which act as natural anticoagulants [8]. Proteolytic activation of PC by thrombin occurs on the surface of endothelial cells and involves

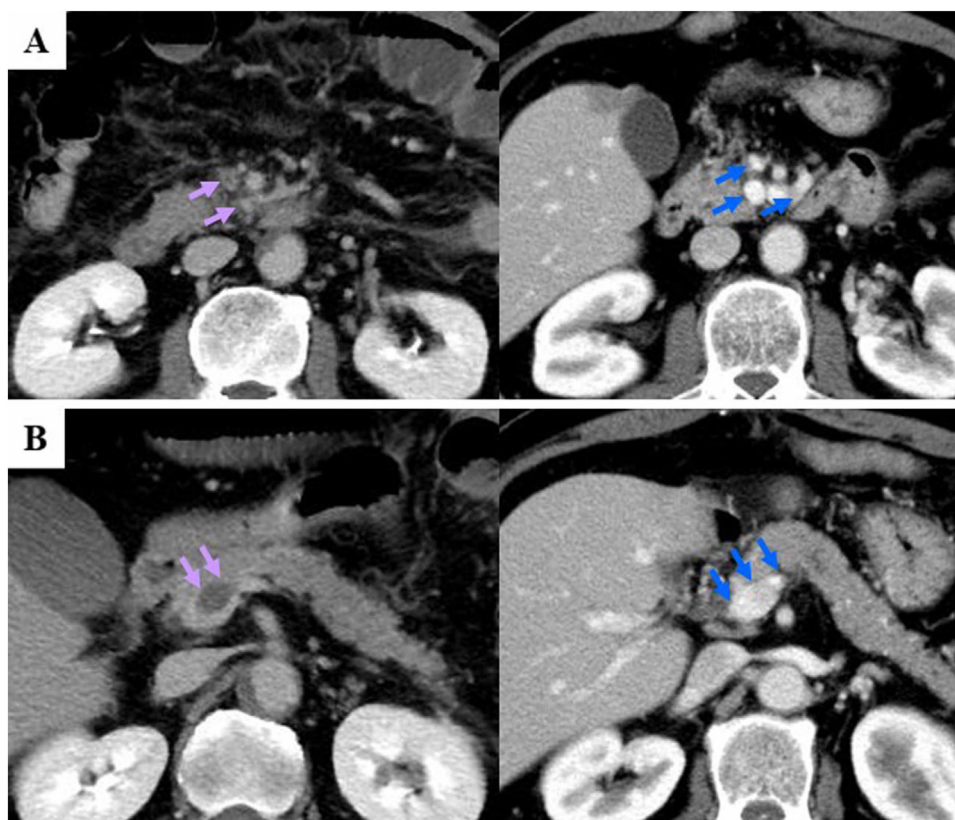


Fig. 3. SVTs before and after treatment.

Contrast-enhanced computed tomography images 2 year after emergency surgery. The SVTs (A and B, purple arrows) have completely resolved and the SMV (A, blue arrows) and PV (B, blue arrows) are patent.

Abbreviations. SVT, splanchnic venous thrombosis; SMV, superior mesenteric vein; PV, portal vein.

Table 1

Coagulation-fibrinolysis profiles and antibodies.

Antithrombin III	96	%
Antigen amount of PC	52	%
Activity of PC	46	%
Antigen amount of protein S	123	%
Activity of protein S	97	%
Coagulation factor II	95	%
Coagulation factor VII	84	%
Coagulation factor IX	164	%
Coagulation factor X	84	%
Antinuclear antibody	<40	times
Anti-cardiolipin antibody	<8	U/mL
Lupus anticoagulant	1.12	second

Abbreviations. PC, protein C.

thrombomodulin and endothelial PC receptor [8]. In the presence of protein S, phospholipids and calcium, activated PC inactivates membrane bound complexes (Factors Va and VIIIa) [8]. Hence, PCD causes a specific hypercoagulable state. PCD is a heritable or acquired risk factor for thrombophilia and recurrent venous thromboembolism [7,8]; lifelong oral anticoagulation is generally required [8]. Manifestations of PCD range from being asymptomatic to developing venous thromboembolism, purpura fulminans and other life-threatening thrombotic disorders [7,8]. Hereditary PCD, an autosomal dominant disorder, is caused by a mutation in the PC gene [7]. Heterozygous and acquired PCDs are more common than homozygous PCD [7,8]. PCD is classified as Type 1, which is characterized by low PC activity and antigen concentrations, and Type 2, which is characterized low PC activity and normal PC antigen concentrations. Accurate diagnosis of PCD is challenging [7,8]. Our

patient was diagnosed as having hereditary, heterozygous Type 1 PCD.

Wallen et al. first coined the term ‘SMV thrombosis’ in 1935 [11]; this cause of SVT is rare [1,2,6]. Misdiagnosis and/or delayed treatment of SVT can result in development of AII, a life-threatening condition with a high mortality rate [6]. Intestinal infarction caused by SVT is distinct from that caused by acute mesenteric ischemia [9]; however, both conditions require prompt diagnosis and treatment and are life-threatening conditions with high mortality rates [9]. Even after AII has occurred, serum concentrations of lactate dehydrogenase and creatine phosphokinase may be normal because of the obstruction of venous drainage and resultant congestion [6]. Indeed, the concentrations of these enzymes were normal in our case despite clear evidence of AII caused by SVT.

PV thrombosis in cirrhotic patients is associated with endothelial injury, not with intestinal barrier disruption or increased platelet aggregability [4]; however, PCD can cause SVT even in intact veins [7]. We chose two-stage surgery with second-look laparotomy and did not construct a small intestinal anastomosis during the initial emergency surgery because further AII caused by progressive SVT may occur repeatedly, even after emergency surgery. In our view, this decision was appropriate for the emergency management of a patient with unexplained SVT, the crucial intervention being initiation of anticoagulation therapy immediately postoperatively to prevent progressive SVT and subsequent further AII.

Let us remember coagulation disorders may contribute to acute intestinal infarction of unknown cause, and moreover, delayed diagnosis and/or treatment can result in acute intestinal infarction. From the viewpoint of management, our clinical choices of avoidance of digestive anastomosis during emergent surgery and

employment of postoperative anticoagulation therapy might be key points for successful management in our patient.

Insufficient clinician awareness can result in serious mismanagement of PCD patients with SVT [6]. Emergency patients with AI caused by unexplained SVT, in whom underlying disease should be suspected, require further investigation for prothrombotic states and assessment of coagulation–fibrinolysis profiles despite such detailed investigation being time-consuming.

4. Conclusions

We here present a successfully treated case of AI caused by an initially unexplained SVT in a patient with underlying PCD. We hope our thought-provoking case will provide a timely reminder for emergency clinicians and gastrointestinal surgeons.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

Data were retrospectively evaluated. This report was approved by the Institutional Review Board of Shiga General Hospital, Moriyama, Japan.

Consent

The patient involved in this study provided written informed consent authorizing the use and disclosure of his protected health information. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author contribution

Yudai Sasaki collected the data. Masahiro Yamada and Tomohide Hori analyzed the data, and wrote the manuscript. Yudai Sasaki, Masahiro Yamada and Tomohide Hori contributed equally to this work.

All authors discussed therapeutic options, reviewed previous papers, and provided important opinions.

Masahiro Yamada and Tomohide Hori supervised this report.

Registration of research studies

Not applicable.

Guarantor

None.

Provenance and peer review

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