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【 CASE REPORT 】

Successful Nonsurgical Treatment of Acute Peritonitis Caused by a Large Thrombosis of the Superior Mesenteric Vein in a 25-year-old Woman

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Abstract:
Superior mesenteric venous thrombosis (SMVT), which results from various etiologies, including coagulation disorders, can be diagnosed early using advanced imaging technology. However, few reports have described the nonsurgical treatment of acute peritonitis caused by SMVT. We encountered a young woman whose history included abdominal pain and daily oral contraceptives and who presented with acute peritonitis caused by SMVT. We administered nonsurgical treatment that included thrombolysis and anticoagulation for the peritonitis (without mesenteric ischemia as confirmed by contrast-enhanced computed tomography). In addition, we showed the importance of investigating persistent risk factors for thromboembolism in young patients to determine the duration of anticoagulation.

Key words: superior mesenteric venous thrombosis, acute peritonitis, nonsurgical treatment, anticoagulation

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Introduction

Superior mesenteric venous thrombosis (SMVT) is a rare disease that, in the early stage, manifests as nonspecific abdominal symptoms, such as nausea, vomiting, and diarrhea (1). Thus, the diagnosis is often delayed until bowel ischemia becomes evident (1). Although mesenteric venous thrombosis (MVT) has historically been associated with a poor prognosis, with about 10% of affected patients presenting with bowel ischemia, recent advances in imaging technology have enabled us to diagnose and perform early anticoagulation without the need for surgery (2, 3). Common causes of SMVT are coagulation disorders, malignancies, abdominal inflammatory conditions, postoperative states, and liver diseases (1).

We herein report the successful nonsurgical treatment for acute peritonitis caused by SMVT in a young woman who was suspected of being in a hypercoagulable state caused by the ingestion of contraceptive pills and hereditary thrombophilia.

Case Report

A 25-year-old woman with no significant medical history presented to our hospital with a 5-day history of continuous abdominal pain accompanied by abdominal distention, nausea, and vomiting. Before coming to our hospital, she had visited another hospital and was prescribed oral loxoprofen and butylscopolamine, neither of which alleviated the pain. She had been taking oral contraceptives (levonorgestrel and ethinyl estradiol), prescribed at a local gynecology clinic, for 18 months. Her family history was significant with respect to thromboembolism in her paternal uncle.

Her initial vital signs were stable, including a heart rate of 79 beats per minute, blood pressure of 112/68 mmHg, respiratory rate of 14 breaths per minute, peripheral oxygen saturation of 98% on room air, and body temperature of 36.3°C. A physical examination revealed significant peritoneal signs with diffuse abdominal tenderness and guarding.

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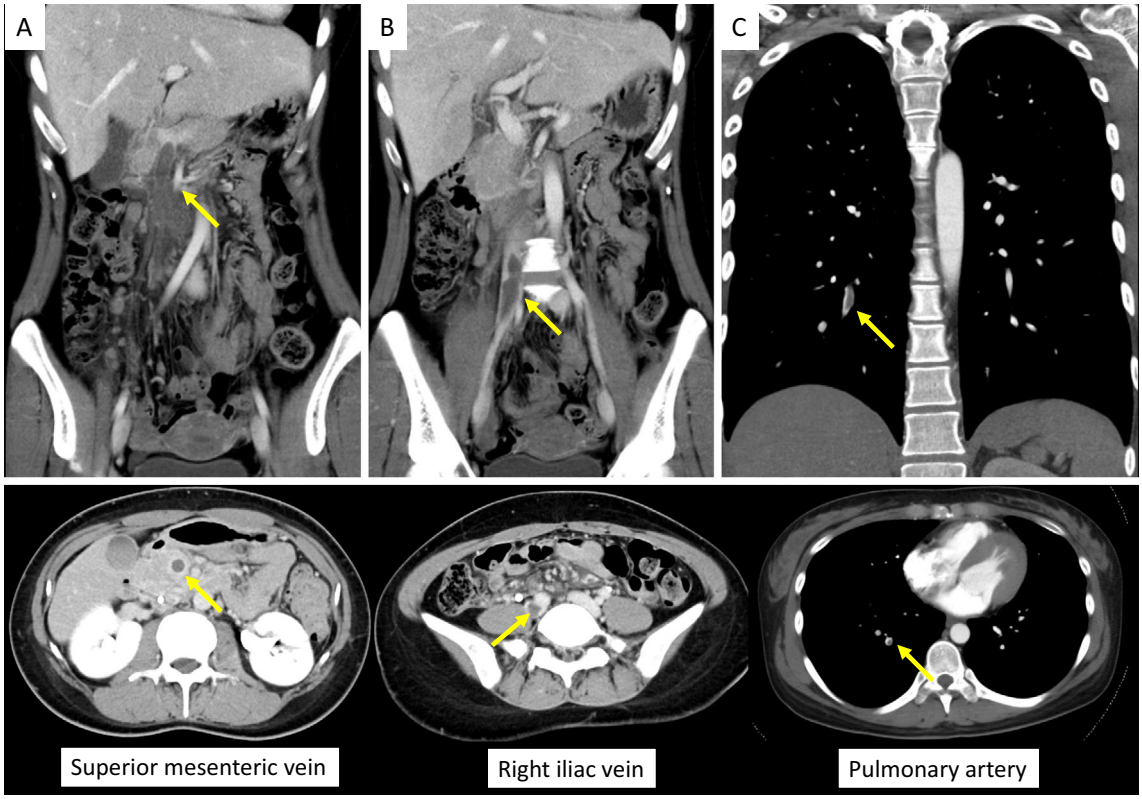

Figure 1. **Contrast-enhanced computed tomography images. Coronal (top) and axial (bottom) images of the chest and abdomen at admission. Yellow arrows indicate thrombi in the (A) superior mesenteric vein, (B) right iliac vein, and (C) peripheral branch of the right inferior pulmonary artery. (A) and (B) show increased fat concentration in the intestinal membrane without bowel wall thickening or intestinal pneumatosis. CECT: contrast-enhanced computed tomography**

Blood tests showed an elevated white blood cell count (13,990/mm^3), C-reactive protein concentration (4.45 mg/dL), and D-dimer concentration (8,000 ng/mL). An arterial blood gas analysis showed a pH of 7.42, partial pressure of oxygen of 56 mmHg, partial pressure of carbon dioxide of 29 mmHg, bicarbonate concentration of 18.8 mmol/L, and lactate concentration of 1.1 mg/dL. Additional blood tests revealed low levels of protein S activity (15%), free protein S antigen (41%), and antithrombin (70%). Other coagulation markers were within the normal range (protein C activity, 102%; lupus anticoagulant, 1.2; and anticardiolipin antibody, <8.0 U/mL).

Contrast-enhanced computed tomography (CECT) showed large thrombi in the superior mesenteric vein (Fig. 1A), right common iliac vein (Fig. 1B), and right branches of the pulmonary arteries (Fig. 1C). CECT additionally showed increased fat concentration in the intestinal membrane without bowel wall thickening or intestinal pneumatosis. No signs indicating intra-abdominal cancer were present. We suspected that SMVT had caused acute peritonitis because the CECT findings showed no potential causes of peritonitis other than SMVT, such as perforation or obstruction of the bowel and intra-abdominal inflammation.

Interventional therapy was immediately performed. A temporary filter (Neuhaus Protect®; Toray Industries, Tokyo, Japan) was placed in the inferior vena cava (IVC) below the bifurcation of the renal veins to prevent lethal pulmonary thromboembolism. We also initiated continuous intravenous thrombolysis and anticoagulation (urokinase at a dose of 240,000 units/day and heparin to control the activated partial thromboplastin time at 60-80 seconds) to avoid systemic venous thromboembolism.

Follow-up CECT at seven days showed that a large thrombus had been captured in the IVC filter and that a thrombus in the right common iliac vein had slightly regressed (Fig. 2A). Therefore, local thrombolysis with infusion of urokinase (60,000 units twice daily) was started through a catheter device (Fountain® Infusion System; Merit Medical Systems, South Jordan, USA) inserted via the right femoral vein to approach the thrombus in the IVC filter. We maintained continuous intravenous infusion of urokinase (120,000 units daily) and peripheral administration of heparin to control the activated partial thromboplastin time at 60 to 80 seconds. Follow-up CECT at 12 days showed slight regression of the thrombus in the superior mesenteric vein and marked regression of the thrombi in the IVC filter and right common iliac vein (Fig. 2B). After removing the IVC filter and catheter device, oral anticoagulation therapy commenced with 15 mg of rivaroxaban.

The patient's abdominal pain gradually decreased and finally disappeared 9 days after starting nonsurgical treatment. The C-reactive protein concentration peaked at 13.17 mg/dL

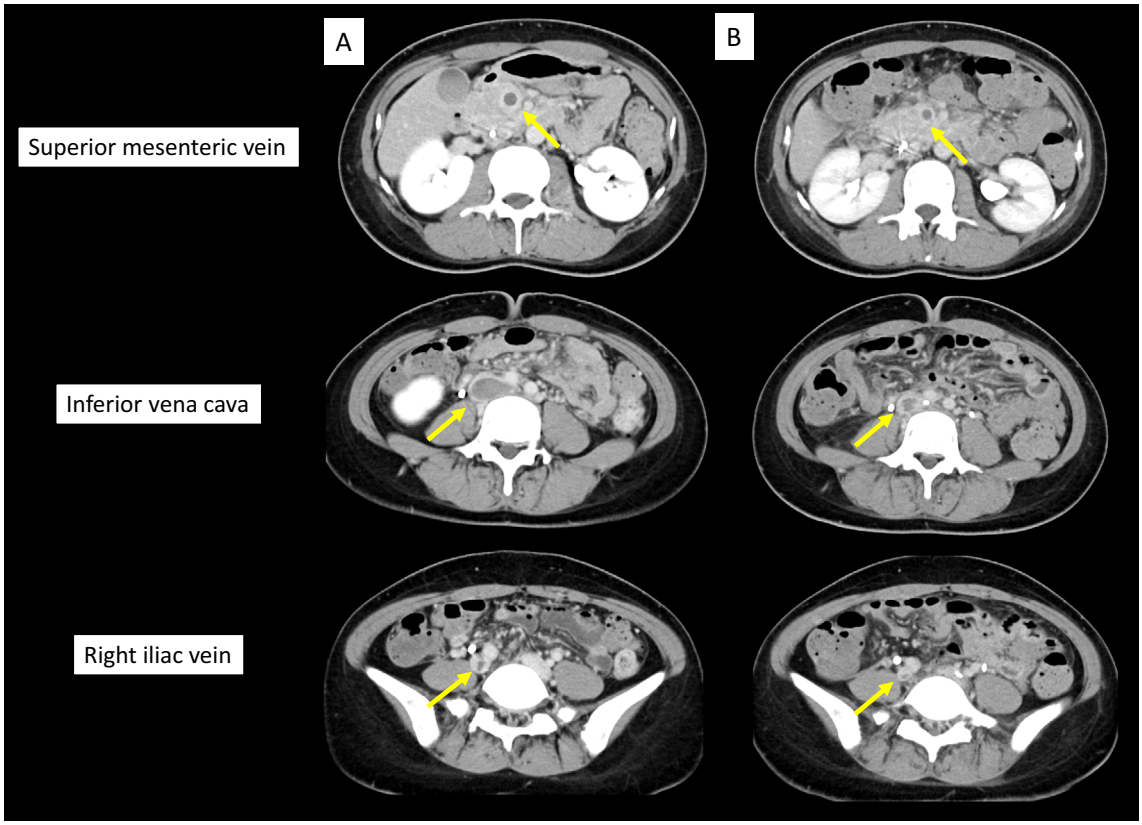

Figure 2. **Follow-up CECT axial images of the abdomen. (A) Follow-up CECT at 7 days shows little regression of the thrombus in the superior mesenteric vein (arrow, top image), a large thrombus captured in the IVC filter (arrow, middle image), and slight regression of the thrombus in the right common iliac vein (arrow, bottom image). (B) Follow-up CECT at 12 days shows slight regression of the thrombus in the superior mesenteric vein (arrow, top image) and marked regression of the thrombus in both the IVC filter (arrow, middle image) and right common iliac vein (arrow, bottom image). CECT: contrast-enhanced computed tomography, IVC: inferior vena cava**

at 4 days postoperatively and became negative at 21 days. The patient was discharged without symptoms at 25 days.

Follow-up CECT at 56 days after discharge showed no thrombi in the superior mesenteric vein, common iliac vein, or the right branches of the pulmonary arteries (Fig. 3). A blood test at 8 months after discharge showed normalization of the antithrombin level to 95% and protein S activity to 73%; however, the free protein S antigen level remained consistently low at 32%. A genetic test revealed the presence of two heterozygous mutations: c.234+1G>T located in intron 2 and c.2001A>G (p.Pro667Pro) located in exon 15. The intron 2 mutation is a newly discovered mutation, while the exon 15 mutation is a common genetic polymorphism. Our patient seemed to have a persistent risk of venous thrombosis because of the protein S genetic mutation, which would have continued even if she had ceased oral contraceptives. Thus, we considered the patient to require long-term anticoagulation. We have been checking on the patient regularly to monitor her for any adverse events associated with the long-term use of oral anticoagulants.

Discussion

We administered successful nonsurgical treatment for acute peritonitis caused by SMVT without complications of bowel ischemia or transmural necrosis, as confirmed by CT. Our case indicates that SMVT can be a cause of acute peritonitis. Nonoperative management of acute MVT is feasible when the bowel infarction has not led to transmural necrosis or bowel perforation (4). CT is a useful and widely used tool for detecting mesenteric ischemic changes (5), and it allowed us to diagnose and treat SMVT at an early stage (2). When CT shows intestinal pneumatosis, mesenteric venous gas, bowel wall thickening, and/or a focal lack of bowel wall enhancement, mesenteric ischemia should be considered because it requires bowel resection (5). The severity of acute peritonitis must therefore be assessed via a comprehensive examination that includes physical findings, laboratory data, and imaging results.

The indications for placement of a temporary IVC filter for venous thromboembolism are controversial. In this case, we decided to use a temporary IVC filter because a serious pulmonary embolism would have occurred if thrombolysis

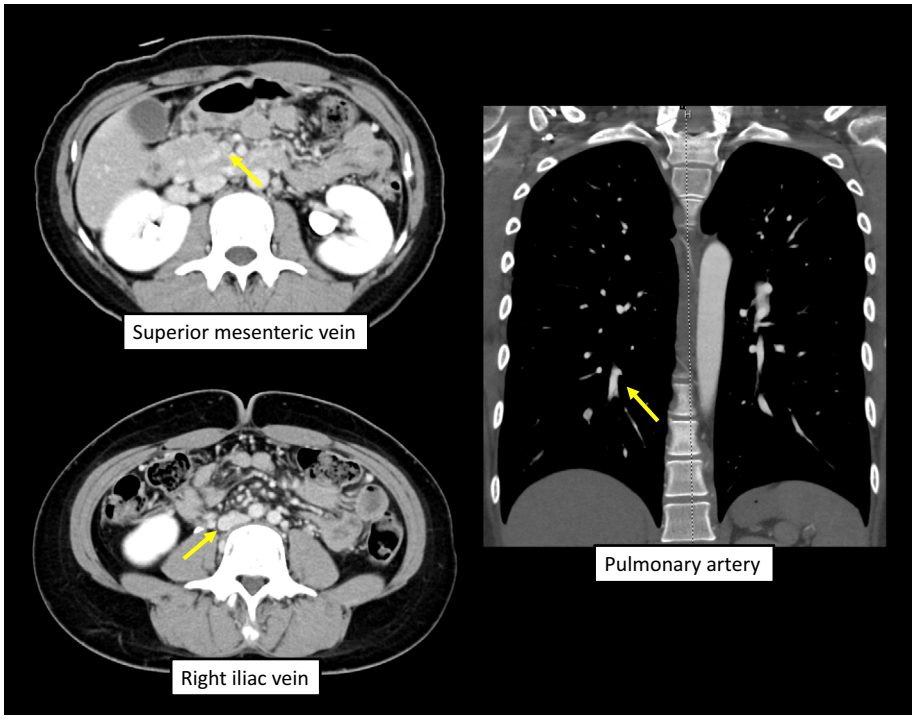

Figure 3. **Follow-up CECT axial image at 56 days after discharge shows disappearance of the thrombi in the superior mesenteric vein and common iliac vein. CECT coronal image obtained the same day shows disappearance of the thrombus in the right inferior pulmonary artery. Yellow arrows show sites where previously large thrombi existed. CECT: contrast-enhanced computed tomography**

had caused the large thrombus in the right common iliac vein to move. We believe that placement of the IVC filter was highly effective for preventing serious pulmonary embolism in this case because follow-up CECT at seven days showed that a large thrombus had been captured in the IVC filter.

This patient was suspected to have hypercoagulability due to ingestion of contraceptive pills and hereditary thrombophilia. Her laboratory data suggested protein S abnormality. Plasma protein S levels can be inherited or acquired due to medications, including oral contraceptives, as well as pregnancy and various disorders, such as liver disease or nephritic disease (6). Whenever clinicians encounter young women with MVT, they should consider the possibility of not only intra-abdominal inflammation but also a hypercoagulable state related to drugs or hereditary thrombophilia.

The etiology of MVT can be identified in about 75% of patients, with the use of oral contraceptives accounting for 9% to 18% of MVT in young women (1). The main causes of MVT are reportedly intraperitoneal inflammation (65.9%), malignancy (17.1%), and unknown causes (17.1%) (7). Among patients with intraperitoneal inflammation, the most common causes are appendicitis (51.9%), diverticulitis (25.9%), and ileus (7.4%) (7). Laboratory tests for thrombophilia include inherited factors (e.g. factor V Leiden mutation; prothrombin gene mutation; and deficiencies of protein C, protein S, and antithrombin) and acquired thrombophilic factors, such as Janus kinase 2 V617F (*JAK2*) mutation, lupus anticoagulant, and cardiolipin antibodies. These tests are recommended in patients with thromboembolism if there is no provocative factor, such as a structural disorder revealed by CT (8).

The duration of anticoagulation should be determined only after a careful evaluation of the risk factors for venous thromboembolism. The European Society of Cardiology guideline states that long-term use of oral anticoagulation should be avoided unless a patient has persistent risk factors other than antiphospholipid antibody syndrome (9). Although our patient had a protein S mutation, we should attempt to stop the anticoagulation medication in the future, considering her young age and complaints of heavy menstrual bleeding. In addition, we recommended that our patient undergo measurement of her protein S level again after ceasing oral anticoagulation to evaluate the need for the long-term use of oral anticoagulation. Protein S antigen is a more reliable marker than protein S activity due to its lower rate of inaccurate results (10). However, the protein S level can reportedly be falsely low under various conditions, such as during an immediate post-thrombosis state, during pregnancy, and during anticoagulation (10). The cause of the low level of free protein S antigen at 8 months after discharge in this case was supposed to be not only the patient's gene mutation but also the use of oral anticoagulants.

Conclusion

We successfully managed a case of SMVT (with no signs of bowel ischemia on CECT) in a young woman using non-surgical management involving thrombolysis and anticoagu-

lation for SMVT-related acute peritonitis. This case illustrates that SMVT can be the etiology of acute peritonitis, which is important for making a diagnosis at an early stage and preventing surgical treatment. In our case, hypercoagulability due to the use of oral contraceptives and hereditary thrombophilia was suspected of being the cause of SMVT. We should keep monitoring the patient for any adverse events caused by anticoagulation, even though the patient has a risk factor for thromboembolism.

The authors state that they have no Conflict of Interest (COI).

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