Case Reports in Gastroenterology

Case Rep Gastroenterol 2018;12:322–326

DOI: 10.1159/000488191
Published online: June 25, 2018

Single Case

A Patient with Ulcerative Colitis Complicated by Systemic Vein Thrombosis

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Keywords
Ulcerative colitis · MTHFR gene mutation · Vein thrombosis

Abstract
Crohn's disease and ulcerative colitis (UC) patients have an increased risk for thromboembolic complications, the most common of them are deep venous thrombosis and pulmonary embolism. Other locations and genetic mutations of coagulation factors are not so common in these patients. Here we present a case of a young woman with exacerbation of previously diagnosed mild UC complicated by multiple thrombotic incidents due to MTHFR gene mutation.

Introduction

Crohn's disease and ulcerative colitis (UC) are 2 major forms of inflammatory bowel disease (IBD) which affect more than 2 million people in Europe [1]. These patients have an increased risk for thromboembolic complications. Deep venous thrombosis and pulmonary embolism are recognized consequences of a hypercoagulable state in patients with IBD [2, 3]. The risk for these most common thromboembolic events is estimated to be three-fold increased when compared to control subjects [4, 5]. Other locations such as hepatic veins (Budd-Chiari

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syndrome), mesenteric veins, portal veins, and others are not so common [6]. Genetic mutations of coagulation factors often trigger thrombosis. Furthermore, disseminated intravascular coagulation is also rare in patients with IBD [7]. Mutations in methylenetetrahydrofolate reductase (MTHFR) gene with subsequent increase in homocysteine levels are a very well-known inherited cause of thrombophilia [8]. Here we present a case of a 37-year-old woman with exacerbation of previously diagnosed mild UC complicated by multiple thrombotic incidents due to MTHFR gene mutation.

Case Report

A 37-year-old woman with a previous history of total alopecia and mild UC in remission was admitted to the Department of Gastroenterology and Hepatology, University Hospital Split, with nausea, vomiting, and severe abdominal pain, 1 day after her control colonoscopy showed exacerbation of previously diagnosed mild UC (Mayo score 7). Physical examination revealed abdominal distension and dull abdominal percussion sound. Plain abdominal X-ray did not show any signs of perforation or bowel obstruction. Blood analysis revealed an elevated leukocyte count (11.9 × 10^9/L), a normal erythrocyte count (4.38 × 10^{12}/L), low platelets (44 × 10^9/L), elevated C-reactive protein (137.4 mg/L), low albumin (17 g/L), and increased LDH (430 U/L), AST (269 U/L), and ALT (346 U/L). Hepatitis B, hepatitis C, EBV, and CMV serology was negative. Coagulation panel was pointing towards disseminated intravascular coagulation development. Prothrombin time was 0.22, INR was 2.75, and fibrin degradation products (D-dimers) were significantly elevated (33.26). Multislice computed tomography (MSCT) angiography revealed portal thrombosis (Fig. 1), upper mesenteric vein thrombosis, thrombosis of the hepatic veins (Budd-Chiari syndrome), splenic vein thrombosis with spleen infarction, and ascites. She was treated with fresh frozen plasma, low molecular weight heparin, vitamin K, metronidazole, ciprofloxacin, pantoprazole, and methylprednisolone. After a short period of time she developed partial complex epileptic seizures followed by left hand paresis. MSCT of the brain revealed ischemia of the right precentral gyrus, occipital hemorrhage, superior sagittal and straight sinus thrombosis (Fig. 2). She received carbamazepine and phenobarbitone for epileptic seizures. Due to the worsening of the patient's clinical condition and development of acute liver failure (AST 8,870 U/L, ALT 3,932 U/L, ammonia 150.4 μmol/L, MELD score 31), she was immediately transferred to the liver transplantation center, but due to the inability to perform liver transplantation in a patient with occluded portal and hepatic veins, she was transferred back to the intensive care unit. Molecular analyses were performed as follows: DNA was isolated from whole peripheral blood, using a High Pure PCR Template Preparation kit (Roche Diagnostics, Mannheim, Germany). Genotyping of FV Leiden (Arg506Glu), Factor II G20210A, MTHFR (C677T), and plasminogen activator inhibitor 1 (PAI-1; 4G/5G) was performed on the LightCycler® 2.0 Instrument (Roche Diagnostics), using Cobas LC kits, according to the manufacturer's recommendations (Roche Diagnostics). Angiotensin-converting enzyme (ACE I/D) genotyping was performed using a modified method described by Oike et al. [9]. Results revealed a normal type of the gene for factor V, normal type of the gene for factor II, homozygous mutation type (TT) of the gene for MTHFR, insertion type of the genotype for PAI-1 and ACE. Homocysteine level was increased (12 μmol/L). Control MSCT showed progression of thrombosis with both renal veins occluded. Her health condition severely deteriorated and 1 month after admission she died because of multiple organ failure.

Discussion

In this case report, we presented a patient with previous history of mild UC complicated by severe thrombosis of visceral and cerebral veins during exacerbation of UC. Genetic analysis discovered a homozygous MTHFR C677TT gene mutation. Arterial and venous thrombosis are recognized complications of IBD. Meta-analyses, case series, and case reports show various patterns of thrombosis, although the most common locations are the deep veins of the leg. Less frequently, thrombosis occurs in the visceral veins of the abdomen and cerebral veins. Reviewing the literature, we did not find any case report with this pattern of thrombosis and gene mutations. Our patient was on oral and rectal mesalazine therapy since 2005. The main question that remains is what triggered such a severe thrombosis in a patient with only mild UC. Paraneoplastic syndrome or infection could start this coagulation cascade, but no malignancy or infection was detected. High CRP levels and previous colonoscopy suggest more severe UC flare in the background. Several studies showed that IBD itself shifts the balance of coagulation homeostasis in favor of hypercoagulability. There are various reasons for that shift, such as elevated levels of TNF-alpha and interlukin-6, which contribute to platelet activation [10, 11] and subsequent thrombosis. It is still debated if this condition is just a consequence of the inflammatory state and its intensity or if it is a feature of intestinal involvement regardless of disease activity. In conclusion, prophylactic anticoagulation against thromboembolic complications is currently not fully defined in these patients. Our case report shows that a more liberal approach for heparin use is recommended in patients with IBD and persistent abdominal symptoms. More research is needed to establish a closer link between a hypercoagulable state and IBD.

Statement of Ethics

Written informed consent was obtained from the patient's closest relative for publishing purposes.

Disclosure Statement

The authors declare no conflict of interests.

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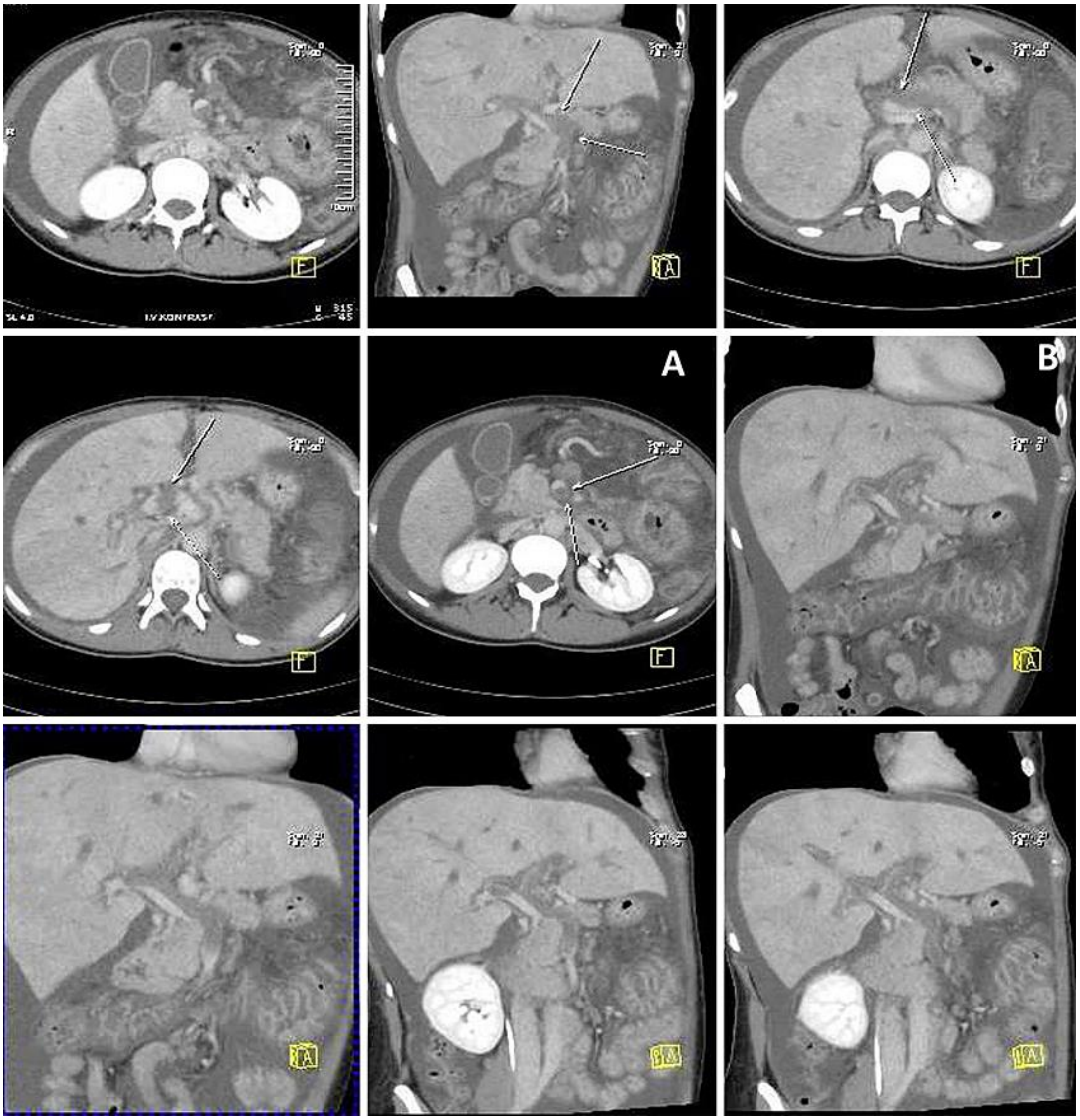

Fig. 1. MSCT angiography indicating portal vein thrombosis (A and B, white arrows).

DOI: 10.1159/000488191

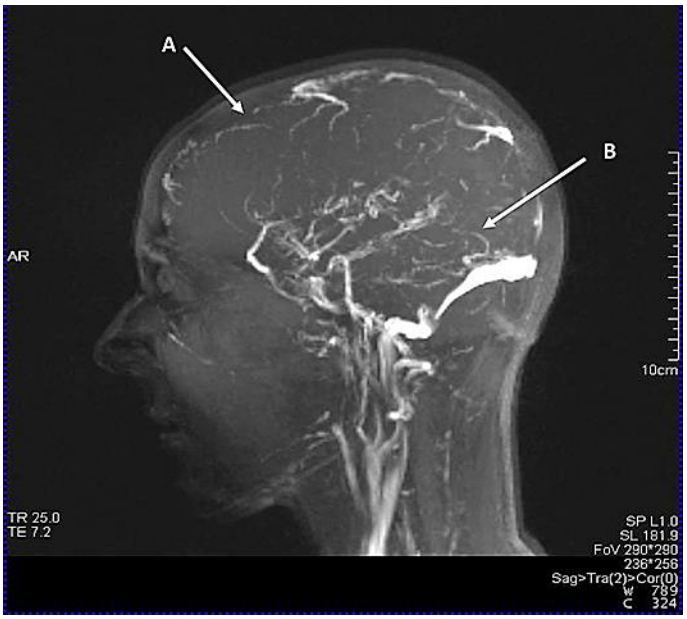

Fig. 2. CT angiography revealed superior sagittal sinus (arrow A) and straight sinus (arrow B) thrombosis.