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Acute Portal Vein Thrombosis in Obesity: A Case Report and Review of Literature

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Abstract

Portal Vein Thrombosis (PVT) without non-cirrhosis is of low incidence. However, obesity may aggravate PVT and induce a high mortality rate. Herein, we present a case of a 66 years old woman with obesity who presented with fever and progressively worsening abdominal pain. Diagnostic workup resulted in Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI) showed PVT extends to the superior mesenteric vein. A diagnosis of PVT was made, and antibiotic as well as anticoagulant were administrated. However, obesity retard the recovery in this patient compare to general patients with normal weight. In addition to presenting risk factors of obesity in PVT, we offer a review of literature and draw important precise mechanisms to assist in the diagnostic workup and treatment of PVT in obesity.

Keywords: Portal Vein Thrombosis (PVT); Obesity; Abdominal infection

Introduction

Portal Vein Thrombosis (PVT) refers to the development of thrombus within the portal vein and can extend to splenic and the superior mesenteric veins. PVT, a well-known complication of cirrhosis, mainly due to rebalance of coagulation-anti-coagulation system and reduction of portal venues velocity (<15 cm/s). Acute PVT in non-cirrhosis patients is of low incidence while with a high mortality. Risk of non-cirrhosis related PVT including inherited gene mutation, like Factor V Leiden or Prothrombin G20210A mutation [1,2]. Moreover, other causes of intraabdominal inflammation (colitis, pancreatitis, cholecystitis, appendicitis) and myeloproliferative disorders (thrombocythemia, polycythemia Vera, myelofibrosis with myeloid metaplasia) may as risk factors for PVT development. Obesity, which will cause cardiovascular or cerebrovascular diseases *via* induction of atherosclerosis, now has been a public health challenge worldwide [3]. Several studies have observed obesity as a risk factor for venous thromboembolism, abdominal obesity in particular, due to visceral fat accumulation, appears to be a major risk factor for VTE [4,5]. However, risk of obesity on PVT is still controversial. Here we present a case of portal vein thrombosis in obesity, and review the available mechanisms of obesity involved in PVT.

Case Presentation

A 66-year-old female presented with persistent mild abdominal pain for 4 days. Four days before her admission, she had mild pain in the right upper abdomen without any obvious cause, accompanied by diarrhea, and passed yellow loose stools twice, accompanied by nausea and vomiting. She took berberine and Montmorillonite powder as symptomatic treatment, but without success. The patient reported aggravated abdominal pain and persistent fever up to 39.3°C with chills and rigor. For this reason, she was admitted to our hospital.

Her past medical history was one of asthma and hypertension, but her blood pressure was well controlled. On physical examination, the patient is obese with a weight of 78 kg, a height of 158 cm, and a BMI of 31.24 kg/m^2. Abdominal palpation suggests right upper abdominal pain. No enlargement of the liver or spleen was found during inspiration.

Laboratory tests showed an elevated white blood cell count (WBC: 13.75 × 10^9/L), predominantly neutrophils (94.1%), a marked increase in c-reactive protein (CRP: 286.22 mg/L), and a marked increase in D-dimer concentration (D-D, 18.64 ug/ml). Liver and kidney function tests showed no significant abnormalities (AST 44 U/L, ALT 56 U/L, BUN 8.32 mmol/L, creatinine 99 μmol/L). Fast serum glucose test of 6.5 mmol/L indicated impaired fasting glucose. Serology tests for hepatitis A,

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Table 1: Summary of clinical features of acute PVT reported.

Reference	Age	Gender	Past medical history/risk factor	Clinical presentation	CECT findings
Cecchini et al. [18]	45	Female	Hereditary spherocytosis status post remote splenectomy, gastroesophageal reflux disease, obstructive sleep apnea, nonalcoholic steatohepatitis, hypertension, previous cholecystectomy, and morbid obesity	Severe abdominal pain, nausea, vomiting,	A complex loculated fluid collection with scattered air pockets and thrombosis in a branch of the superior mesenteric vein found in a surgical specimen.
Shirai et al. [19]	22	Male	Acute pancreatitis.	Abdominal pain	Massive PVT extending to the SV and SMV, edematous thickening of the intestinal wall with bloody ascites.
Shirai et al. [19]	48	Male	No significant past illness	Abdominal pain and nausea	PVT extending to the SMV and SV, edematous thickening of the intestinal wall with bloody ascites.
Martin et al. [20]	44	Female	Irritable bowel syndrome, hypertension, hyperlipidemia, obstructive sleep apnea, and anxiety, MTHFR A1298C polymorphism	Abdominal pain, diarrhea, nausea, and anorexia	An acute right portal vein thrombosis that was likely occlusive, with partial thrombosis of the left portal vein and main portal vein.
Shyam et al. [21]	35	Male	Alcohol-associated pancreatitis	Epigastric pain with intermittent fever	Multiple microabscesses in the left lobe of the liver with portal vein thrombosis extending into the splenic and superior mesenteric vein.
Shyam et al. [21]	60	Male	Alcohol-associated pancreatitis	Epigastric pain, fever and loss of appetite	A small microabscess in the right lobe of the liver and portal vein thrombosis extending into the spleen and superior mesenteric vein.
Kalbitz et al. [22]	60	Male	*Escherichia coli* and *Bacteroides uniformis* were detected in the blood culture, positive for Leptospira IgM	High fever, acute renal failure, elevated liver transaminases	Initiated, extensive PVT.
Benmassaoud and Rodger [23]	53	Male	Obesity	Abdominal pain	Acute portal vein thrombosis with complete occlusion of the intrahepatic portal veins, main PV, superior mesenteric vein and splenic vein.
Setaka et al. [24]	30	Male	Hereditary antithrombin deficiency	Abdominal pain, fever	Thrombotic obstruction of the main portal vein and the lumen of the superior mesenteric vein.
Our case	66	Female	High blood pressure, asthma, obesity Blood culture showing *Enterobacter avium*	Abdominal pain, fever, nausea, vomiting	PVT extends into the superior mesenteric vein and splenic vein.

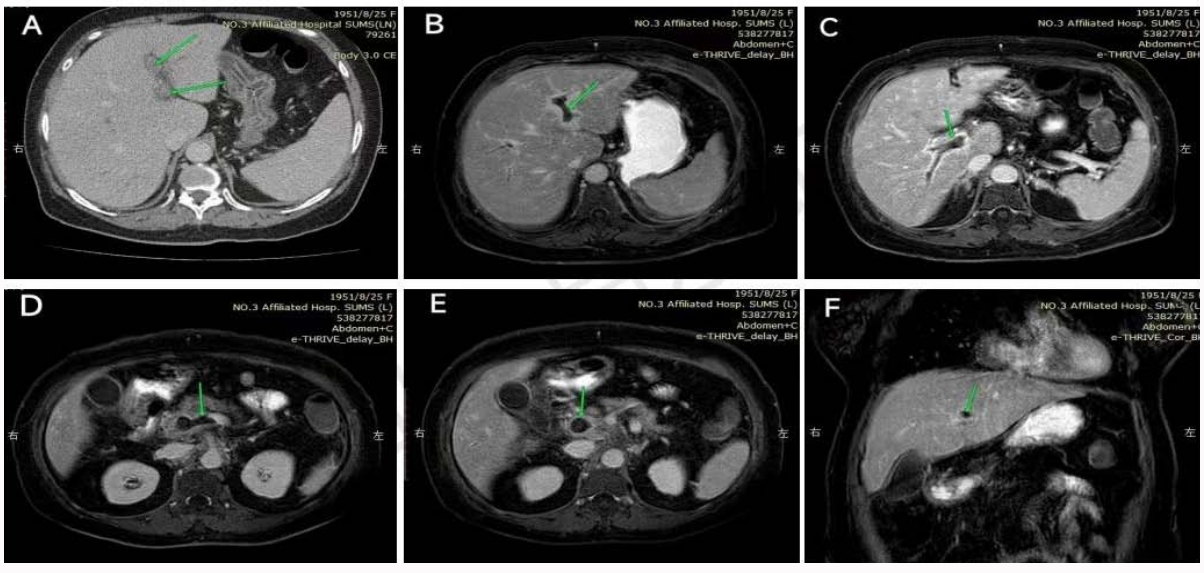

Figure 1: Computed Tomography (CT) imaging and Magnetic Resonance Imaging (MRI) of the patient. CT (A) and MRI (B-F) showed filling defects in the superior mesenteric vein, splenic vein, main trunk of portal vein and its branches, suggesting extensive thrombosis.

B, C, and E, and the *Cytomegalovirus*, Epstein-Barr, and HIV viruses were negative. Oncological indices CEA, AFP, CA19-9, and CA12-5 were normal, as were autoimmune-related indices. The stool liver fluke count was negative. Blood culture was suggestive of *Enterococcus avium*. Color Doppler ultrasound suggested extensive thrombosis of the main trunk and right and left branches of the portal vein, superior mesenteric vein, and splenic vein. Abdominal CT scan and enhanced MRI scan showed a non-enhancing filling defect within the lumen of the portal and superior mesenteric vein, which indicated portal vein thrombosis extended to the superior mesenteric venous (Figure 1). Moderated liver steatosis without neoplasm was found in the liver. Endoscopic examination showed no evidence of gastroesophageal

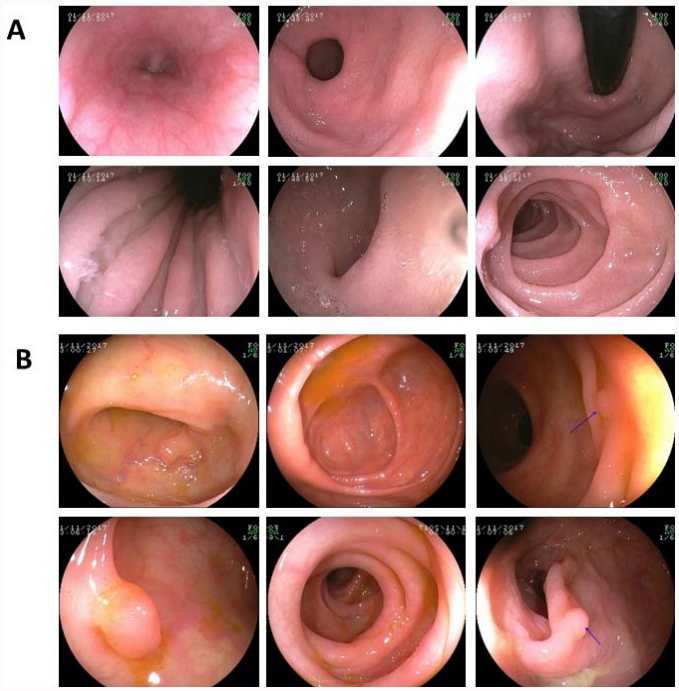

Figure 2: Endoscopic examination of the patient. Gastroscopic examination: A) No evidence of gastroesophageal varices, (B) and no evidence of inflammatory bowel disease on colonoscopy.

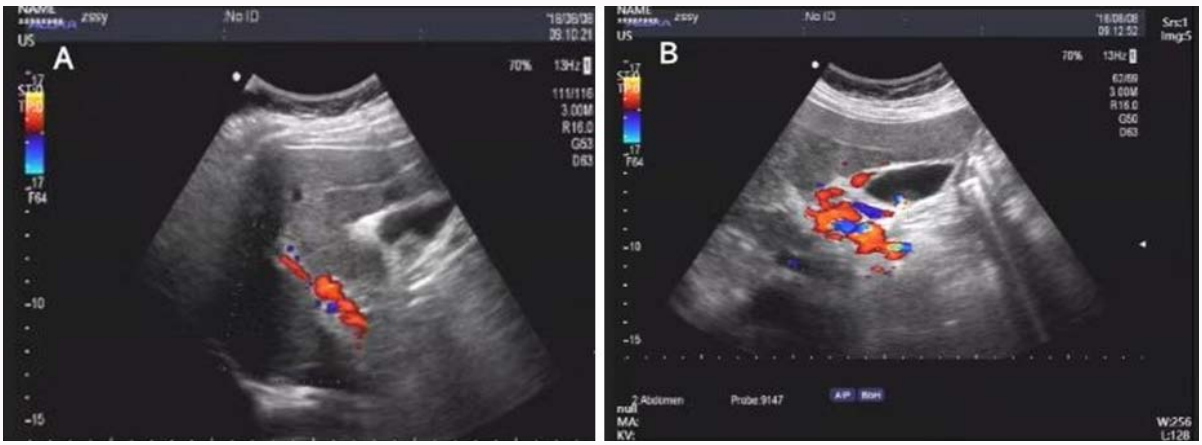

Figure 3: Doppler ultrasound performance of the patient at the 9-month follow-up. Doppler ultrasound showed a thin portal vein with spongy portal vein.

varices and inflammatory bowel diseases (Figure 2).

She was treated conservatively with intravenous imipenem and cilastatin sodium 1 g q8h and the anticoagulant rivaroxaban 20 mg/day. After 4 days of the above treatment, the patient still had mild abdominal pain, loss of appetite, and nausea, and the infection was considered not significantly controlled, so intravenous vancomycin 1 g q12h was added as a combination anti-infection. After a week of continued treatment, her clinical symptoms of diarrhea disappeared, but her temperature was between 37.5°C to 38.0°C. Color Doppler ultrasound showed echogenic, organized thrombotic material in the lumen of the portal vein and superior mesenteric vein. She was continued treated with intravenous imipenem and Cilastatin sodium 1 g q8h and vancomycin 1 g q12h and oral anticoagulant rivaroxaban at 20 mg/d. On day 14 of treatment, the patient was downgraded from imipenem and cilastatin to moxifloxacin 0.4 g QD and metronidazole 0.5 g q12h. After 18 days of treatment in the hospital, her temperature got too normal, and relief of clinical symptoms such as abdominal pain, poor appetite, and nausea. After that, she was treated with rivaroxaban at 20 mg/d for six months. At the 9-month follow-up, the patient's repeat Doppler ultrasound showed that the main trunk and the left and right branches of the portal vein were thin, but the blood flow was smooth and there was no thrombosis, while the splenic vein and superior mesenteric vein were suspected of thrombosis and there is portal vein spongiosis (Figure 3). At the 4-year follow-up, the patient has no symptoms, but Doppler ultrasound showed patent portal venous flow and spongy portal veins.

Discussion

Acute Portal Vein Thrombosis (APVT) is defined as thrombosis of the main portal vein and/or the left and right branches of the portal vein, with or without mesenteric and splenic vein thrombosis. Acute portal vein thrombosis can lead to serious adverse outcomes such as

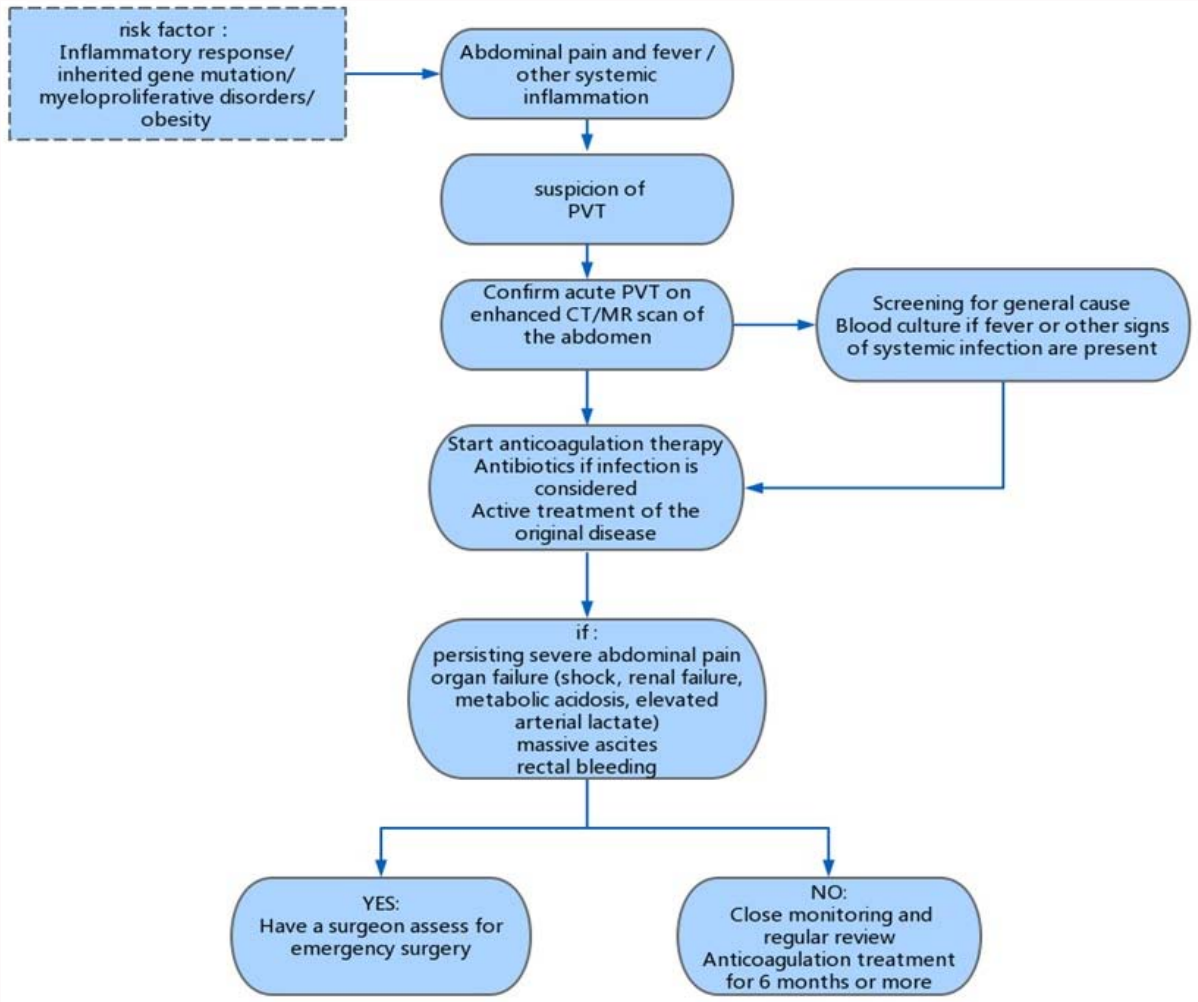

Figure 4: Procedure for the management of acute portal vein thrombosis.

mesenteric ischemia and even intestinal necrosis, with a mortality rate of up to 50% [6]. A large study found a 1% population prevalence of PVT, with most cases associated with cirrhosis and hepatobiliary malignancy, and a low incidence of portal vein thrombosis in non-cirrhotic livers [7]. Another Japanese study showed that the incidence of PVT was 0.05% in patients without cirrhosis [17]. We report a case of a 66-year-old obese female patient with abdominal pain and fever as the main symptoms and review the available literature. The clinical characteristics of these 10 PVT cases are summarized in Table 1. By reviewing the literature, we found that these 10 patients were aged 22 to 66 years, with a 7:3 male-to-female ratio, and 2 of them presented with intestinal infarction and underwent emergency surgery. However, one of these patients developed short bowel syndrome after surgery because of the extent of the intestinal infarction.

There are three elements to portal vein thrombosis, including a hypercoagulable state, endothelial injury, and stasis of blood flow, known as Virchow's triad. Any one of these elements may be affected to promote portal vein thrombosis. In our case, the main risk factors considered for portal vein thrombosis were obesity and abdominal infection. Obesity is a worldwide health problem that induces cardiovascular or cerebrovascular diseases, such as coronary syndrome, cerebral embolism, and encephalorrhagia. The contribution of obesity to vein thrombosis is large evaluated and obesity is a known risk factor in venous thrombosis [8]. Obese individuals have nearly doubled the risk of both pulmonary embolism and Deep Vein Thrombosis (DVT) and obese patients less than 40 years of age have nearly a five-fold risk than those with normal weight.

However, there is limited knowledge about the risk of PVT in obese patients. Previous studies mainly focus on risk factors for PVT development in liver disease patients with obesity. A cohort study in a single center indicated that obesity was an independent risk factor for pre-transplant portal vein thrombosis [9].

Mechanistically, several pathways could underlie a causal relationship between obesity and increased risk of DVT. Studies showed upregulation of inflammation factors, such as IL-6, TNF-α, and IL-1β were observed in obese individuals. These inflammation factors, which trigger the upregulation of procoagulant activity by promoting the synthesis of tissue factors, and suppressing fibrinolytic function via increased PAI-1 expression, facilitate the formation of DVT [3].

Furthermore, adipose tissue is not only a storage site for excess energy but also a multifunctional organ that secretes numerous hormones and cytokines, thus influencing cell functions and gene expression. As a consequence of overnutrition, adipose tissue undergoes remodeling: Adipocytes grow in size and number,

accompanied by altered secretion, angiogenesis, and inflammation. Adipocytes are stimulated to secrete tissue factor (the trigger for blood coagulation), plasminogen activator inhibitor (which impairs fibrinolytic function), and substances responsible for local vessel degradation, all of which may promote clot initiation and formation and increase the risk of developing DVT. It has been found that leptin receptors are expressed on platelets and endothelial cells and can accelerate thrombosis by inducing platelet activation, inhibiting vasodilation, and increasing oxidative stress [10]. From previous studies, it appears that obesity is a prothrombotic factor, favoring chronic inflammation, impairing coagulation and fibrinolysis, increasing hypercoagulability, and thus promoting the formation of venous thrombosis [11-13].

Infections may induce three factors of the Virchow's triad. Pathogenic microorganisms or their endotoxins can activate monocytes, vascular endothelial cells, etc., causing them to release a variety of inflammatory factors, and the local inflammatory response can form portal phlebitis, which promotes endotoxin entry into the blood and damage vascular endothelial cells, thus promoting thrombosis.

According to a review of the literature [7], acute portal vein thrombosis can be symptomatic or asymptomatic, with the most common clinical presentation being mild to severe abdominal pain and fever, but also bloating, diarrhea, nausea, vomiting, anorexia, and ascites, with the severity of symptoms depending on the extent of the thrombus. Acute extension of the thrombus into the superior mesenteric vein is more likely to produce intestinal ischemia and infarction, and the development of intestinal infarction is associated with high morbidity and mortality if there is persistent severe abdominal pain, organ failure (shock, renal failure, metabolic acidosis, and elevated arterial lactate), massive ascites and rectal bleeding all suggest infarction. The diagnosis of APVT is made clinically primarily based on clinical presentation and imaging examinations. A severely obese patient with no specific history who suddenly presents with mild to severe abdominal pain with fever should not be missed as a suspicion for APVT.

Its diagnosis is often delayed due to non-specific abdominal symptoms, low incidence, and low awareness among clinicians. However, portal and superior mesenteric vein thrombosis are being increasingly diagnosed due to the improvement and widespread use of the Computed Tomography (CT) scan technique. The typical abdominal ultrasound presentation of acute portal vein thrombosis is hypoechoic or isoechoic material occupying the lumen of a mildly dilated vein. Enhanced CT or MRI of the abdomen shows an unenhanced filling defect in the lumen of the vein. The presence of features associated with cavernous hemangiomas, venous collateral circulation, or portal hypertension suggests a prolonged period of vessel formation.

The differential diagnosis of acute portal vein thrombosis focuses on differentiating benign from malignant PVT. The first thing to consider is portal vein thrombosis due to malignant tumors in the abdomen (most commonly such as hepatocellular carcinoma), and secondly, tumor encapsulation or compression of the portal vein (such as pancreatic or bile duct cancer), both of which can be secondary to malignant intraportal thrombosis. Imaging can help to differentiate between benign and malignant PVT.

Treatment includes subcutaneous anticoagulant injections or direct oral anticoagulant therapy and intravascular thrombolysis or surgical intervention. EASL recommends anticoagulation as the first-line treatment for acute non-cirrhotic non-malignant PVT [14]. The AASLD guidelines also recommend that all patients with acute PVT, whether symptomatic or not, should be given conventional anticoagulants. Anticoagulation is usually available with low molecular heparin, vitamin K antagonists, and new Direct Oral Anticoagulants (DOACs). Recent data [1,15,16] suggest that the oral anticoagulant rivaroxaban is a reliable and safe treatment for abdominal vascular thrombosis and is increasingly used in patients with abdominal vascular thrombosis. Early anticoagulation is used on the one hand to prevent the thrombus from extending into the mesenteric vein and thus leading to mesenteric vein infarction; on the other hand, to achieve portal vein recanalization, but if intestinal ischemia and intestinal infarction develop, surgical intervention is required.

In Figure 4, we summarize our diagnosis and treatment process based on available guidelines and literature. In our case, the patient was an older obese woman for whom obesity and abdominal infection may have been risking factors for her morbidity, with significant abdominal symptoms and systemic inflammatory manifestations, supported by imaging findings, we diagnosed APVT. She opted for conservative treatment and the patient was discharged after 18 days of combined anti-infective and rivaroxaban anticoagulation therapy.

Conclusion

Portal and superior mesenteric vein thrombosis is a serious but relatively less common complication associated with intraabdominal infection in non-cirrhosis patients. CT scan is an accurate method with excellent sensitivity for the diagnosis of abdominal vein thrombosis, especially as clinical presentation is emergency but vague. Oral anticoagulant rivaroxaban is a reliable and safe treatment for abdominal vessel thrombosis. What is more, endovascular thrombolysis is also a viable option and emergency surgery is required in case of patients with intestinal infarction.

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