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Case Report

Successful heparin-perfusion therapy for complete thrombosis of the intra- and extrahepatic portal and mesenteric vein. A case report and literature review ☆

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ABSTRACT

The initial treatment of acute and subacute portal vein thrombosis, which is the most common cause of portal vein occlusion, consists of intravenous anticoagulation with heparin, but there is still a huge uncertainty among physicians regarding the role of more invasive therapies. We report a 61-year-old male patient, who presented in our emergency room with a subacute complete thrombosis of the intra- and extrahepatic portal vein, mesenteric vein, with associated venous congestion of 20-30 cm length of the small intestine with a quick and complete remission of the portal vein thrombosis under sole i.v. heparin-perfusor therapy without any complications. Molecular genetic analysis found combined genetic mutations of the gene factor 2 (c.20210G>A, heterozygotic), SERPINE1 (-675 5G>4G, heterozygotic), and the MTHFR gene. Along with this interesting case, we also present the recent status of portal vein thrombosis and portal vein occlusion in the literature.

☆ Competing Interests: The authors declare that they have no competing interest.

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Introduction

In literature, portal vein occlusion (PVO) was first reported in 1868 by Balfour and Stewart, who described a patient presenting with an enlarged spleen, ascites, and dilated varices [1]. In patients with chronic liver disease, the incidence of PVO is 8.16%-12.92%, and prevalence is 11.18%-16.91% [2]. Besides chronic liver diseases, PVO is seen in patients suffering from neoplasms, that is, hepatocellular carcinoma, coagulation disorders, myeloproliferative diseases, inflammation, and infections (pancreatitis, perforated diverticulitis, cholangitis, necrotizing enterocolitis, pylephlebitis), congenital anomalies (eg, portal vein atresia), post-surgical complications (eg, after liver transplant, Billroth-II, splenectomy, cholecystectomy, surgery of duodenum, pancreas or bile duct and after neonatal umbilical vein catheterization) and post-trauma [3].

PVO is most often caused due to portal vein thrombosis (PVT), which is a very important acute to chronic hepatobiliary disease that all physicians should be familiar with. Given the advanced technology of today's time, PVT is being more frequently diagnosed with the help of sonography, computed tomography (CT), and magnetic resonance imaging (MRI) techniques. According to Organ et al., the reported lifetime risk of developing PVT in the general population is approximately 1% [4]. Some of the most common causes contributing to the development of PVT are inherited hyper-coagulopathy disorders, cirrhosis, hepatocellular carcinoma, abdominal infection, or inflammation.

Case report

A 61-year-old male without any known pre-existing conditions presented to the emergency unit with a 2-day-long and increasing abdominal discomfort with nausea and flatulence. Clinically, a soft abdomen with tenderness on palpation on the upper left and middle quadrant with no rigidity and guarding sign was reported. The laboratory parameters revealed a moderate increase in the CRP value of 46.6 mg/L (>5 mg/L) without any other pathological findings.

Sonography showed diffusely distended and thickened loops of the small intestine measuring up to 2.4 cm in diameter with a "pendulum peristalsis sign." A subsequent multiphase contrast-enhanced (MDCT, Revolution HR, GE Healthcare, USA) of the abdomen (Fig. 1) revealed a diffuse wall thickening of a 20-30 cm long segment of the small intestine (see white arrowheads) with mesenteric venous engorgement as a sign of venous congestion. This was revealed to be caused by a complete and massive intra- (see black arrowhead) and extrahepatic thrombosis of the portal vein with thrombotic material also in the superior mesenteric and splenic vein (see white arrow). Due to the beginning cavernous transformation of the left main portal branch (see black arrow) and the acute symptoms, the PVT was considered subacute. The CT also showed venous perfusion defects of the right liver lobe but ruled out any acute bleeding and pneumatosis intestinalis.

After an interdisciplinary discussion (Surgery, Gastroenterology, and Radiology), we started with controlled continuous i.v. heparin therapy (PTT value 60-70; controlled every 4 hours) under complete bowel rest and total parenteral nutrition. After a scheduled 48-hour follow-up CT, we planned a second discussion to escalate the treatment in case of failure of the heparin therapy to a transjugular-intrahepatic-portosystemic-stent-shunting (TIPSS) implantation (combined with a mechanical thrombectomy). In addition, i.v. antibiotic treatment with a combination drug with 4 g piperacillin and 0.5 g tazobactam (Actavis Group PTC, Norway) was infused to eradicate any intestinal contamination. Within the first 48 hours, his condition improved (abdominal discomfort, nausea, and flatulence dissolved). The following day, the planned contrast-enhanced follow-up CT scan (Fig. 2) revealed an almost complete decrease in the edema of the small intestine walls (see white arrowheads), without progression of the PVT (see white arrow), so we decided to continue the conservative treatment. Antiemetic therapy brought steady improvement in intestinal activity and a decline in nausea. Follow-up CT findings on day 30 showed further recovery (Fig. 3) and the follow-up CT after 6 and 12 months established complete remission of pre-existing PVT with small residual thrombosis in the superior mesenteric vein VMS (Figs. 4 and 5).

As the most common coagulation disorders were ruled out beforehand (eg, factor V Leiden, HIT, hemophilia, von Willebrand disease, clotting factor deficiency, hypercoagulable states, and deep venous thrombosis), molecular genetic counseling to exclude rarer congenital coagulation disorders was recommended. It revealed a combined genetic mutation of the gene factor 2 (c.20210G>A, heterozygotic), SERPINE1 (-675 5G>4G, heterozygotic), and most important of the MTHFR gene (c.1298A>C, heterozygotic), which lead in their combination to an increased thrombotic risk. Given the potentially fatal complications, lifelong anticoagulation with Rivaroxaban (XARELTO; Bayer AG) was recommended. Moreover, regular clinical, and laboratory controls, as well as annual endoscopic checks were recommended, too.

Discussion

PVT, which is the most important reason for PVO, is also one of the most important causes of prehepatic portal hypertension. PVT describes a partial or complete thrombotic occlusion of the intra- and/or extrahepatic portal venous system due to malignant, cirrhotic, non-malignant, and non-cirrhotic thrombosis or thromboembolism [3]. The thrombosis can affect the portal vein and its branches and additional veins of the splanchnic area (eg, splenic or superior and inferior mesenteric vein) and accounts for 5%-15% of intestinal ischemia [5] in its acute form, which further complicates its management by, for example, venous congestion [6]. Ultrasound for PVT offers a sensitivity of 89%-93% and a specificity of 92%-99%, but its findings are operator dependent and vary due to patients' characteristics, such as obesity, ascites, bowel gas, and decreased portal flow velocity [2], so the use of contrast-enhanced CT is obligate.

The incidence of PVT can be as high as 16% [7], and without former liver disease for acute PVT, the 5-year mortality rate is up to 15%, which is mostly related to underlying disease or

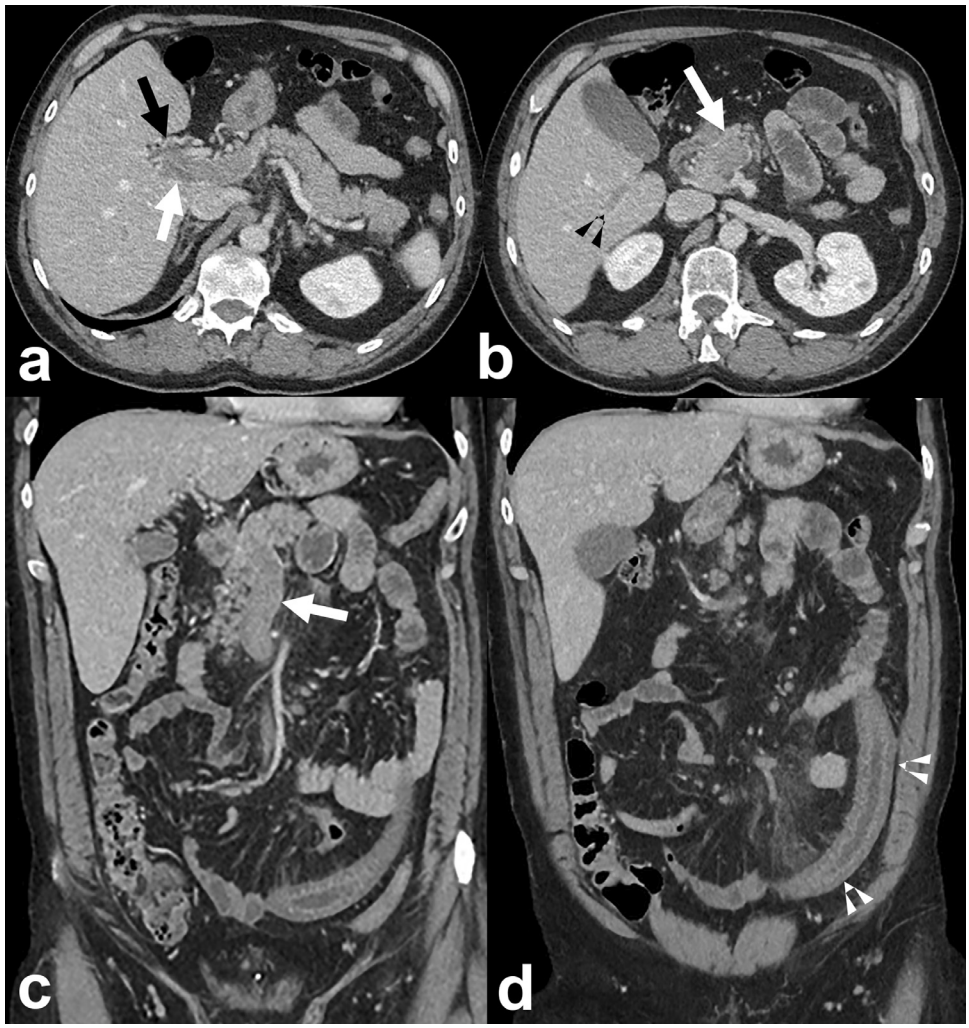

Fig. 1 – (A and B) The contrast-enhanced MDCT examination showed extensive thrombosis of the vena portae (white arrow) with the involvement of the right (black arrowhead) and also left intrahepatic branches. (C and D) In the coronal reconstruction of the portal venous phase expansion of the thrombosis up to the superior mesenteric vein (white arrows) and the small branches with signs of mesenteric congestion as well as wall thickening/edematous representation of small intestine loops (white arrowheads) in the left middle to lower abdomen.

complications after intervention [8]. For chronic PVT, mortality for 5 years is significantly lower at 5%-10%, which is mostly related to age, underlying disease, and etiology of PVT, rather than PVT complications [9,10].

The pathogenesis of PVT can be assigned to the Virchow triad consisting of (1) hypercoagulability due to change in viscosity, (2) hemostasis due to low portal flow, and (3) vasculopathy of the vascular wall. The clinical picture is remarkably diverse and can present itself acutely-subacutely or chronically. In the acute and subacute phases, there are non-specific symptoms such as abdominal pain, nausea, vomiting, diarrhea, fever, rectal bleeding, bowel distension, sepsis, and lactic acidosis with or without splenomegaly. Characteristically, patients present with abdominal pain, which can suddenly start or develop progressively over several days. Furthermore, an ileus can manifest with existing intestinal obstruction or even with infarction of the intestine following peritonitis. Suppose there is no remission of an acute/subacute PVT by spontaneous remission or therapy, in that case, it progresses to the chronic stage and can be asymptomatic or with signs and symptoms of portal vein hypertension, that is, splenomegaly, pancytopenia, varices, and ascites [11].

When the acute PVT becomes chronic; the occluded portal vein gradually atrophies, fibrosis develops and chronic PVO ensues, eventually leading to the cavernous transformation of the portal vein. However, these collaterals are usually not completely effective in decompressing the portal system, and many patients have persistent portal hypertension and develop serious portal hypertensive complications, such as variceal bleeding and ascites, which is the rationale for the use of TIPSS dealing with PVT [12].

The treatment methods for PVT mentioned in the literature vary greatly and have mostly only been observed in small study groups. Minimally invasive treatment options for PVT include recanalization of the occluded veins with local thrombolytic therapy, potentially with the creation of a TIPSS

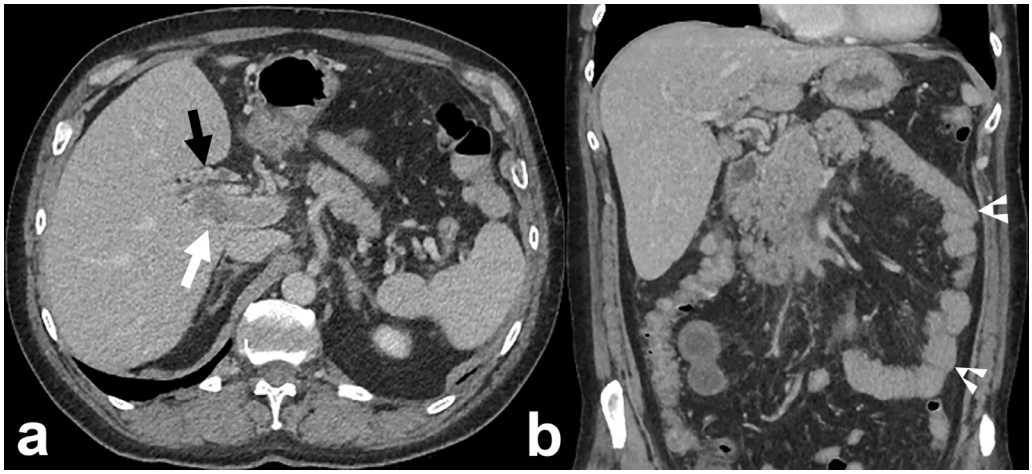

Fig. 2 – (A) Unchanged extensive portal vein thrombosis (white arrow) in the CT after 48 hours. (B) Regression of congestion-related segmental swelling of small intestine loops (white arrowheads) located in the left lower abdomen.

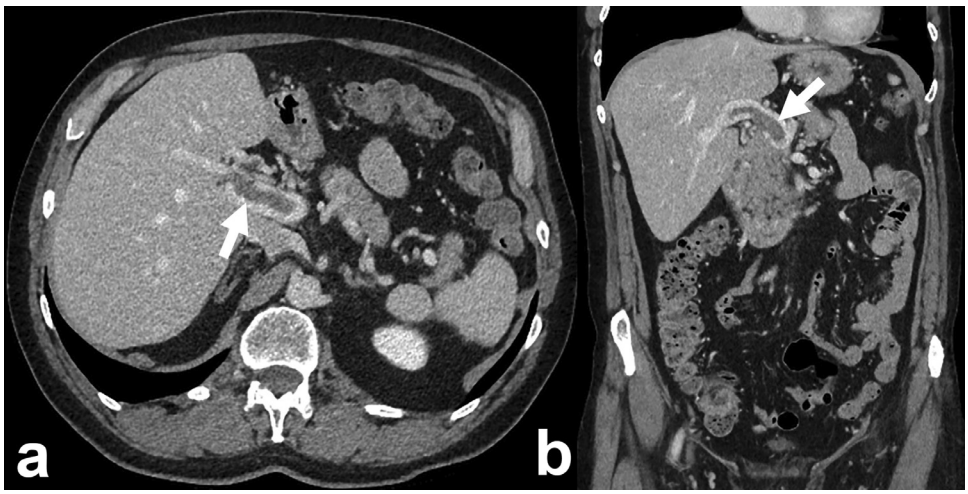

Fig. 3 – Partial regression of thrombosis of the portal vein and superior mesenteric vein with complete regression of thrombosis (white arrow) in the right and left intrahepatic branches in the CT after 30 days.

tract, and additional mechanical thrombectomy. Due to the invasivity of the IR techniques most patients with PVT are treated with immediate anticoagulation therapy at diagnosis. This is most often performed through continuous intravenous heparin infusion, but some authors report using s.c. low-molecular-weight heparin. The prognosis of patients with PVT who responded to continuous intravenous heparin infusion has been reported to be as high as 93% at 3 years [13]. However, it is often limited by the severity of the potential underlying disease. Long-term complications such as recurrence of thrombosis and intestinal ischemic strictures can also develop with variably reported incidences in small studies.

Before discussing and planning therapy of PVT the most common coagulation disorders should be ruled out beforehand (eg, factor V Leiden et al.). In cases with negative findings regarding the typical coagulation disorders, molecular genetic counseling to exclude rarer congenital coagulation disorders is recommended.

Reaching out for a standardization of therapy, Sarin et al. proposed in 2016 a new classification of PVT in patients with cirrhosis. A recent functional PVT (still patent flow), which is asymptomatic, may or may not be treated with anticoagulation, whereas an acute symptomatic PVT requires anticoagulation. A chronic asymptomatic functional PVT without cavernoma requires anticoagulation and there is no prerequisite for anticoagulation in patients with cavernoma formation. The complications of portal hypertension should be treated in all symptomatic patients of chronic PVT. In patients with procoagulant status anticoagulation is recommended to prevent the extension of PVT [14]. In case of a PVO, anticoagulation and TIPSS are the mainstays of treatment. There is no recanalization treatment recommended in malignant liver tumor-related PVO.

In the 2022, the Baveno VII consensus it was stated that the risk of intestinal infarction and organ failure is increased in patients with recent PVT and (1) persistent severe abdom-

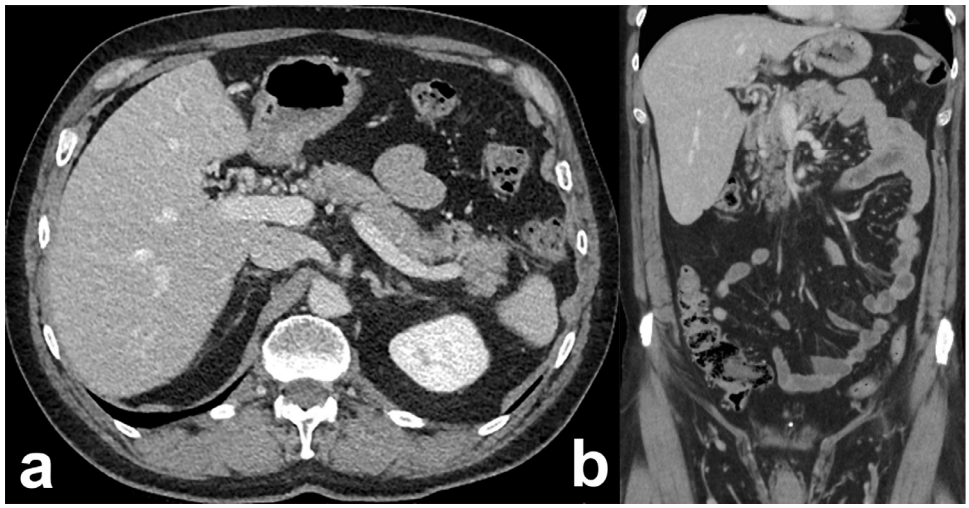

Fig. 4 – (A) Progressive regression of the PVT with complete regrading of the thrombus in the confluence, vena portae, and regredience of the thrombus in the superior mesenteric vein in the CT after 6 months. (B) In the coronal reconstruction, complete regression of the wall swelling in the left lower abdomen located in small intestine loops.

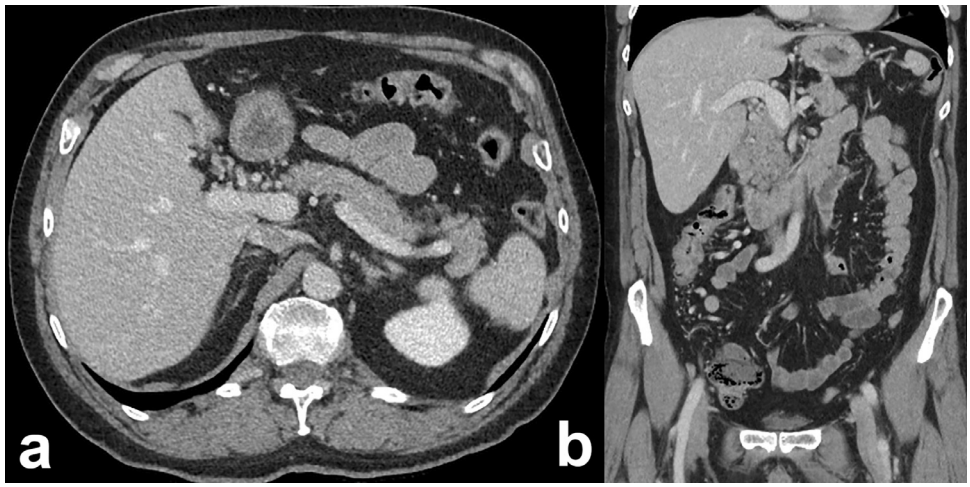

Fig. 5 – (A and B) Complete regression of the PVT in the CT after 12 months.

inal pain despite anticoagulation therapy, (2) bloody diarrhea, (3) lactic acidosis, (4) bowel loop distention, or (5) occlusion of second order radicles of the superior mesenteric vein. These are the patient at risk and therefore, a multidisciplinary approach with early image-guided intervention, thrombolysis, and/or surgical intervention should be considered in referral centers [15].

In case of extrahepatic portovenous obstruction (EHPVO), the technical success rate of percutaneous portal vein recanalization was found to be 92% in patients with chronic EHPVO and patent intrahepatic portal veins, while this procedure failed in 100% of patients with obstructed intrahepatic branches [16]. In case of a recurrent thrombosis already treated with anticoagulation management, a second intervention for recanalization is still controversial. The most common causes for recurrent thrombosis are poor adherence to the treatment regimen, inappropriate dosing and/or drug interactions. Second, it is important to reconsider an underlying disease associated with EHPVO and treat it [15]. Surgical attempts are used infrequently but may be still necessary for patients who present with signs of bowel infarction or perforation and patients, who fail to improve under conservative or interventional-radiologist management.

Conclusion

PVT is a potentially life-threatening situation if not dealt with swiftly. Therefore, timely diagnosis and therapy are important. Varied treatment options exist, which must be tailored according to the patient's condition, in this case with a quick and complete remission of the PVT under sole i.v. heparin-perfusor therapy controlled by repetitive CT

follow-ups without any complications. Coagulation disorders are quite common in PVT cases (eg, factor V Leiden et al.). Therefore, molecular genetic examinations should be taken into consideration too.

Patient consent

I state that written and informed consent was taken from the patient for publication of this case. The patient was informed that no personal details will be revealed in the publishing of this case.

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