Heparin-perfusion therapy for thrombosis of the intra- and extrahepatic portal and mesenteric vein.

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Abstract

Background:

Although as stated many times in the literature, the initial treatment of acute and subacute portal vein thrombosis (PVT) consists of intravenous anticoagulation with heparin, but there is still a huge uncertainty among physicians regarding whether the patient should be better taken to more invasive therapies.

Case Presentation:

We henceforth report on a 61-year-old patient, who presented in our emergency room with a subacute thrombosis of the intra- and extrahepatic portal and superior mesenteric vein (SMV) and venous congestion of 20-30 cm of the small intestine with a quick and complete remission of the PVT under sole i.v. Heparin-perfusor therapy with repetitive CT-follow-ups 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.

Conclusion:

Early diagnosis and immediate initiation of heparinization in patients with PVT and SMVT, could not only reverse the initial intestinal ischemia but also suffice as the sole mode of treatment, preventing the subsequent need for radiological and surgical interventions. Furthermore, molecular genetic counseling should be always taken under consideration when the cause of PVT remains unknown.

Background

Portal vein thrombosis (PVT) 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 techniques (MRI). According to Organ et al., the reported lifetime risk of developing PVT in the general population is approximately 1% [1]. Some of the most common causes contributing to the development of PVT are inherited hyper-coagulopathy disorders, cirrhosis, hepatocellular carcinoma (HCC), abdominal infection, or inflammation.

Case Presentation

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 (46,6 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 h) under complete bowel rest and total parenteral nutrition. After a scheduled 48-h follow-up CT we planned a second discussion, to escalate the treatment in case of failure of the Heparin therapy to a TIPS 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 SMV (Fig.4 and 5).

As the most common coagulation disorders were ruled out beforehand (e.g. factor V Leiden), 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.

**Conclusion**

Portal vein thrombosis (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 [2]. The thrombosis can affect the portal vein and its branches and additional veins of the splanchnic area (e.g. splenic or superior and inferior mesenteric vein) and
accounts for 5-15% of intestinal ischemia [3] in its acute form, which further complicates its management as e.g., venous congestion [4].

The incidence of PVT can be as high as 16% [5] 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 complications after intervention [6]. For chronic PVT, mortality for 5 years is significantly lower as 5-10%, which is mostly related to age, underlying disease, and etiology of PVT, rather than PVT complications [7, 8].

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 nausea, vomiting, diarrhea, fever, and tachycardia. Characteristically patient 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 with signs and symptoms of portal vein hypertension e.g., hypersplenism and ascites [9].

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 transjugular portosystemic shunt (TIPS), 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. Guglielmi et al. suggested in 2005 therapeutic superiority of the exclusive systemic i.v. anticoagulation over surgical therapy in terms of mortality and morbidity [10]. But operative therapy may be still necessary for patients, who present with signs of bowel infarction or perforation and patients, who fail to improve under conservative management.

The prognosis of patients with PVT who responded to conservative management has been reported to be as high as 93% at 3 years [11]. 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.

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 is controlled by repetitive CT-Follow-ups without any complications. Coagulation disorders are very common in PVT cases (e.g. factor V Leiden). Therefore, molecular genetic examinations should be taken into consideration.
Abbreviations

PVT: Portal vein thrombosis
CT: computed tomography
MRI: Magnetic resonance imaging techniques
TIPS: Transjugular portosystemic shunt
IR: Interventional radiology
SMV: Superior mesenteric vein

Declarations

Ethics approval and consent to participate All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication written and signed consent for publication was acquired

Availability of data and material Data sharing does not apply to this article as no datasets were generated or analyzed during the current study

Competing interests The authors declare that they have no competing interest

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Authors' contributions ML performed the literature review. ML, BR, AM, KD, and MM were all major contributors in writing the manuscript. BA, MR, and CB were directly involved in the care of this patient and assisted with editing the manuscript. All authors read and approved the final manuscript.

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References


Figures
Figure 1

a.-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.-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.

Figure 2

a. Unchanged extensive portal vein thrombosis (white arrow) in the CT after 48h. b. Regression of congestion-related segmental swelling of small intestine loops (white arrowheads) located in the left lower abdomen.
Figure 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.

Figure 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.
Figure 5

a.-b. Complete regression of the PVT in the CT after 12 months.