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Case Report

Multiple Thrombi in Portal Vein with Protein C and Protein S Deficiency: A Case Report

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Abstract:

Background: Portal vein thrombosis (PVT) is a rare but significant cause of the gastrointestinal bleeding, often leading to delayed diagnosis due to its subtle presentation. PVT can result in portal hypertension, which cause the formation of portosystemic collaterals as a compensatory mechanism. Deficiencies in protein C and protein S are recognized as risk factor for PVT. This study aims to describe a rare underlying condition of PVT in children.

***Case*:** A 14-year-old boy presented with recurrent hematemesis and melena over the past eight years. Physical examination revealed no epigastric pain but showed splenomegaly. Laboratory findings showed pancytopenia, mildly elevated AST, prolonged plasma prothrombin time and partial thromboplastin time, increased INR, and low protein C and S. Endoscopic evaluation revealed esophageal and fundal varices, with portal hypertensive gastropathy. Multi-slice CT (MSCT) confirmed thrombosis in the main, right, and left portal veins, supporting the diagnosis of PVT. The patient was also diagnosed with an underlying myeloproliferative disorder, further contributing to his condition.

***Discussion*:** Protein C and S deficiency is a prominent risk factor of PVT. Identification of risk factors is essential to accurately treat the condition and prevent worse outcomes. Imaging modalities remain essential for diagnosing PVT. Management focuses on treating complication, particularly those related to portal hypertension, with endoscopic variceal ligation as the preferred treatment.

Conclusion: Comprehensive investigation on etiology and risk factors, close monitoring and individualized treatment are essential in PVT management, especially in pediatric patients.

Keywords: children, portal vein thrombosis, protein C, protein S

Introduction

Portal vein thrombosis (PVT) is an uncommon condition, occurring in approximately 1 in 100,000 live births or between 1 and 36 per 1000 newborns.[1-3] PVT is characterized by the formation of a thrombus in the main trunk of the portal vein, along with its right and/or left intrahepatic branches.[4] The main clinical manifestations of PVT are upper gastrointestinal bleeding and splenomegaly.[1, 2, 5] Splenomegaly results from portal hypertension.[3, 6] The cause of PVT in children is unknown, but several factors were found to predispose this pathology. These can be divided into three groups: local factors that may lead to portal vein injury (such as abdominal infections, surgical procedures in the abdomen, or the use of umbilical catheters), general factors (such as a procoagulant state), and, occasionally, vascular abnormalities. The most common cause is umbilical vein catheterization (UVC), with prevalence ranging from 20% in low-income countries to 60% in developing countries. The general factors predisposing to venous thrombosis are thrombophilia, sepsis, and dehydration. Deficiency or qualitative abnormalities of anti-coagulation factors (antithrombin III, protein C, protein S, and activated protein C resistance) and chronic myelodysplasia syndrome often predispose to thrombotic events, including extrahepatic PVT (EHPVT).[1, 4, 6]

The fundamental pathophysiology of portal hypertension resulting from a prehepatic obstruction of portal blood circulation, while liver function remains well-preserved without any cirrhotic alterations in the liver. This increase in blood volume within the venous portal system causes an elevation in hepatic venous pressure. As a compensatory mechanism, portosystemic collaterals are formed, resulting in increased flow in splenorenal, paraumbilical, or gastric and esophageal veins. Additionally, cavernomatous transformation of the portal vein (CTPV) arises from the formation of hepatopetal collateral vessels surrounding the obstructed portal vein.[3, 6]

Currently, studies on pediatric portal vein thrombosis are still limited. Thus, this study aims to report the rare occurrence of portal vein thrombosis on a 14-year-old with protein C and protein S deficiency.

Case

A 14-year-old boy was admitted to the hospital with a history of recurrent hematemesis and melena. These episodes occurred 2-3 times yearly over the past 8 years. The last time hematemesis and melena occurred was on Mei 2024. He had a history of polyps and neonatal infection. Figure 1 shows colonic polyps observed during a colonoscopy performed in 2017.

During his hospital visit, physical examination revealed normal vital signs, no epigastric pain, and splenomegaly classified as Schuffner stage 2. He also had a history of pancytopenia and slightly elevated SGOT and normal SGPT, with an increase in plasma prothrombin time (1.58x), partial thromboplastin time (1.42x), and INR (2.04x). Endoscopy in 2020 identified grade 2-3 esophageal varices, grade 1-2 fundal varices, and portal hypertensive gastropathy **(Figure 2)**.

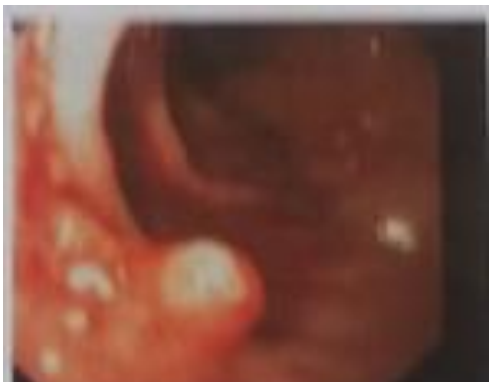

Figure 1. Colonoscopy performed in 2017 revealed hyperemic mucosa with extensive ulcerative lesions in the rectum, sigmoid colon, ascending colon, transverse colon, descending colon, and cecum. Additionally, three polyps measuring 2–3 mm in diameter were identified 10 cm from the anal verge.

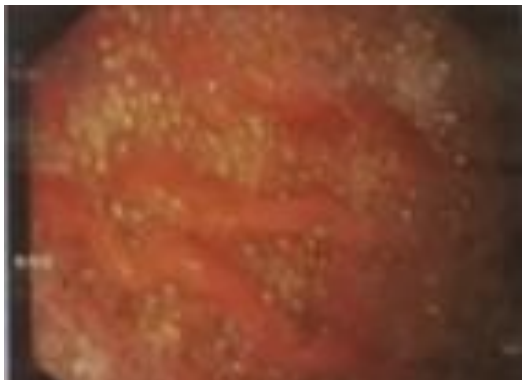

Figure 2. Gastroscopy revealed grade 2-3 esophageal varices, snake-skin appearance with erythema in gaster, erythema and petechiae in the antrum, normal bulbous duodenum, and grade 1-2 varices in the fundus.

Abdominal MSCT with contrast was conducted in December 2023 and revealed thrombi in the main, right, and left portal veins, with the largest thrombus measuring 1.1 cm in thickness and 5.7 cm in length **(Figure 3).**

A subsequent bone marrow puncture confirmed the diagnosis of hypoplastic myelodysplastic syndrome (hMDS) **(Figure 4)**. The patient also exhibited low levels of protein C (27 IU/dL) and protein S (36 IU/dL).

The patient was initiated on maintenance doses of propranolol, a non-selective beta blocker, to reduce portal pressure and received treatment for portal vein thrombosis. Varices ligation was also planned.

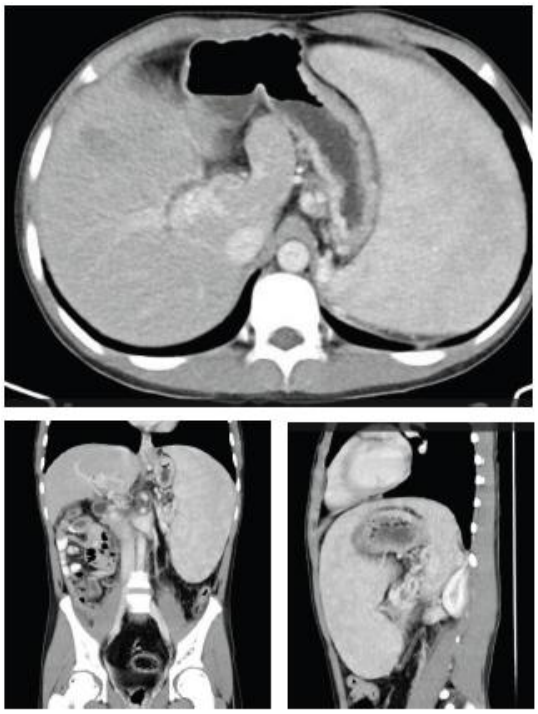

Figure 3. MSCT scan exhibited thrombi in the main, right, and left portal veins, with the largest thrombus measuring 1.1 cm in thickness and 5.7 cm in length. Splenomegaly was observed, with splenic widening and tortuosity of splenic vein, oesophagal vein, left gastric vein, right gastric vein, gastroduodenal vein, and gastroepiploic vein. Furthermore, multiple lymphadenopathies were found in paraaorta, interaortocava, and left and right inguinal region, with the largest measuring around 1.7 × 0.7 cm in the interaortocaval region.

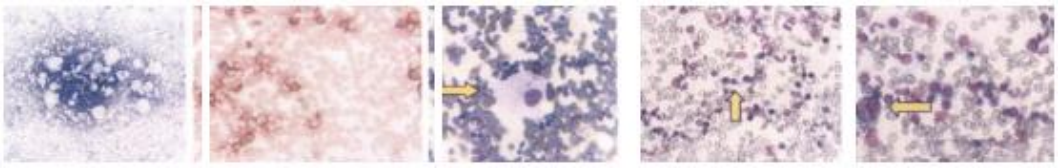

Figure 4. Bone marrow puncture showed hypocellular bone marrow with trilineage dysplasia and mild erythroid hyperplasia, suggesting a myelodysplastic syndrome (hypoplastic MDS)

Discussion

In this case, a 14-year-old boy presented with recurrent hematemesis and melena for 8 years, along with a history of polyps in the colon and splenomegaly. The patient also exhibited pancytopenia, as well as esophageal and gastric varices. Esophageal varices (EV) are present in 90% to 95% of patients with portal vein thrombosis, and gastric varices (GV) in 35% to 40%, which extrahepatic thrombi is one of the rare causes of

esophageal varices. Initial obstruction of the PV by thrombus formation is followed by compensatory vasodilation of the hepatic artery and the formation of collateral vessels that bypass the thrombosed PV and constitute the "cavernous transformation" or "portal cavernoma" which leads to varices formation.[2] The endoscopic result showed gastropathy portal hypertension in this patient, which worsens the prognosis of this patient.[2, 7] This patient then underwent bone marrow puncture due to its pancytopenia, and the result suggests a myelodysplastic syndrome. Myeloproliferative disorders account for 30% to 40% of PVT in adults but are uncommon in children.

Interestingly, the patient exhibited low protein C and protein S. These proteins are natural vitamin K-dependent anticoagulants, which may result from either hereditary or acquired causes.[1, 8] Deficiency in these proteins has been associated with the occurrence of thrombosis at multiple sites, as well as childhood stroke.[8, 9] Notably, a study by Grama et al. reported a high prevalence of protein C and S deficiency in children with extrahepatic portal vein thrombosis. The decreased level of proteins S and C can be secondary to the thrombosis or as the result from their consumption in portosystemic shunts. Neovascular formations (cavernoma) will generate hepatopetal flow that is insufficient to reduce the pressure, which may cause the formation of spontaneous natural portosystemic shunts. These shunts function as "release valves" to relieve the pressure in the portal space. However, this compensatory mechanism is insufficient and does not allow adequate reduction of portal pressure, thus causing the consumption of these anticoagulant proteins. Another cause of protein C or S deficiency is the hepatic injury caused by reduced flow through the portal vein.[1] In this patient, the occurrence of bleeding due to the portal hypertension had occurred for several years. This highlights the importance of extensive investigation for the etiology and risk factors, which should be conducted thoroughly to prevent prolonged manifestation which may worsen the prognosis of the patient.

In patient with PVT, history taking and physical examination, imaging studies are the mainstay for diagnosis. Ultrasonography is the initial modality due to its noninvasive technique. The results expected for PVT are detection of hyperechoic thrombi in the PV lumen, collateral vessels, and portal cavernous. Portal cavernoma constitutes a tangle of tortuous vessels in the porta hepatis. Contrast-enhanced computed tomography and magnetic resonance angiography are valuable tools for evaluating the degree of thrombosis.[2] MSCT abdomen was performed in this patient and showed multiple thrombi in the portal vein.

Treatment includes pharmacologic, endoscopic, and surgical modalities. Nonselective b-blockers reduce hepatic venous pressure gradient by decreasing cardiac output (b-1 receptor antagonism) and inducing splanchnic vasoconstriction (b-2 receptor antagonism).[2] Endoscopic techniques, including sclerotherapy and endoscopic variceal ligation (EVL), are very effective for managing acute variceal hemorrhage and

eliminating varices. EVL is preferred because it has limited complications and requires fewer endoscopic treatments. EVL facilitates portal decompression either by forming collateral vessels or by surgical portosystemic shunting, when vessels grow to the proper diameter for anastomosis.

The medical management of PVT involves the use of beta-blockers for initial prevention.[10, 11] Sclerotherapy and variceal band ligation are essential treatment methods both in severe life-threatening bleeding and in preventing possible bleeding in those with high-grade varices. Children who have significant varices should be evaluated for primary prevention using endoscopic treatment. Children with recurrent bleeding, despite these measures, will be suitable for surgical treatment (shunts or bypass). PVT can arise following a transplant, but the best approach to management remains unclear.[12]

Surgical portosystemic shunts are typically utilized only in severe cases due to considerable risks and technical challenges. Transjugular portosystemic shunts are gaining importance in treating portal hypertension resulting from PVT.[13] Portosystemic shunts can either alleviate pressure throughout the entire splanchnic area (including portacaval, mesocaval, or proximal splenorenal shunts) or specifically relieve pressure in the gastroesophageal veins while maintaining a steady flow from the superior mesentery (as seen in distal splenorenal shunts). The role of portosystemic shunts is well known in controlling variceal bleeding and symptoms related to hypersplenism.

The primary reasons for considering surgical intervention include uncontrollable severe bleeding despite endoscopic treatment, ongoing high-grade varices, significant splenomegaly accompanied by notable thrombocytopenia, or hindered growth.[12] Various factors, such as the overall health of the child, the presence of other medical conditions, the vascular structure, and the capabilities and experience of the surgical team influence the selection of the type of shunt. Only a small number of children experienced complications, including complete or partial narrowing of the shunt.

Another surgical option that shows excellent outcomes is the mesenteric-left portal bypass (Meso-Rex bypass).[14] This procedure seeks to restore blood flow in the portal vein by establishing an anastomosis between the superior mesenteric vein and the left portal vein. This technique was first employed for portal vein thrombosis following liver transplant surgery. It is utilized in children with extrahepatic portal vein thrombosis (EHPVT) who have a weight-to-portal vein diameter ratio exceeding 10. The meso-Rex shunt reduces the portal vein pressure, the degree of esophageal and gastric varices, or the splenomegaly and significantly improves the prognosis in children with EHPVT.[14, 15] Doppler ultrasound has demonstrated a remarkable intrahepatic portal flow following the Rex-bypass shunt.

The transjugular intrahepatic portosystemic shunt (TIPSS) is a non-surgical method by which a metallic stent is inserted between the hepatic and intrahepatic portal veins.[16, 17] The experience with TIPSS in pediatric patients is restricted to a few case reports or small series that highlight complications, which may hinder the viability of alternative surgical interventions.[18] TIPSS may be used when surgical shunting is contraindicated or as a bridge to liver transplantation.[16, 17]

Conclusion

Portal vein thrombosis should be considered a potential cause of gastrointestinal bleeding, with a thorough investigation into its underlying etiology and risk factors. Treatment strategies must be individualized to address the patient's underlying condition and any contributing factors.

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Conflict of Interest

None declared

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