Case Report

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A rare delayed onset of esophageal varices and portal vein thrombosis in a ten-year-old patient following umbilical vein catheterization

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Introduction and significance: Portal vein thrombosis (PVT) is not commonly observed in patients, particularly those who have gone through neonatal intensive care unit (NICU) stays and had umbilical catheters. Although PVT can potentially cause hypertension and gastrointestinal bleeding it is highly unusual for this condition to manifest during childhood.

Case presentation: The authors present a case of a 10-year-old child who developed portal hypertension, esophageal varices, and multiple thrombophilia associated mutations. This child was born prematurely. Had to stay in the NICU, where an umbilical venous catheter was used which likely triggered the development of PVT. At the age of 7 he started experiencing distension, anemia and low platelet count, which eventually led to splenectomy. On at the age of 10 he began experiencing episodes of bleeding. Was diagnosed with esophageal varices and portal gastropathy. Through procedures, like Histoacryl glue injection and band ligation bleeding was successfully controlled. Genetic analysis revealed mutations associated with thrombophilia.

Clinical discussion: This case highlights how rare it is for older children to develop PVT and emphasizes the possibility of delayed onset symptoms following catheterization. The placement of catheters in NICUs can disrupt blood flow and increase the likelihood of clot formation. The presence of hypertension resulting from PVT can lead to complications such as varices. Effective control, over bleeding was achieved through interventions. Importantly, the presence of ACE I/D, FXIII Val34Leu, and Factor V Leiden mutations introduces an aspect to this scenario. It is worth noting that these mutations are not commonly linked to thrombophilia or clotting disorders.

Conclusion: This case highlights pediatric PVT, emphasizing the need for a collaborative approach among gastroenterologists, hematologists, and geneticists. Further research is required to understand PVT mechanisms and long-term implications, aiding in diagnosis and management, especially when it appears in late childhood. Evaluation is crucial in deciphering thrombophilia-related complications in the context of hypertension.

Keywords: esophageal varices, pediatric gastrointestinal bleeding, portal vein thrombosis, thrombophilia mutations, umbilical catheterization

Introduction

Portal vein thrombosis (PVT) is a rare disorder in the pediatric population, and it is more common in neonatal intensive care unit (NICU) patients with reported incidence rates varying between 1.3 and 43%[1]. Patients are generally asymptomatic in the neonatal period[2]. There are two major risk factors for PVT: sepsis and exposure to umbilical catheters[2]. Although neonatal PVT is considered the major cause of portal hypertension and subsequent gastrointestinal bleeding, bleeding from varices due to PVT resulting from an umbilical catheter is considered a relatively rare complication, particularly when presenting later in childhood[2,3].

Case presentation

This case is about a 10-year-old child who has been diagnosed with portal gastropathy and esophageal varices. The patient's medical history includes being born prematurely at 35 weeks with a birth weight of 2.800 kg. In addition to his prematurity, he required NICU admission for 17 days due to severe indirect

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Table 1

Lab tests for the splenomegaly

Test	Results
Hemoglobin	9.2 mmol/l
Platelet	25 000 platelets per microliter (mcl)
Prothrombin time	18 s
Partial thromboplastin time (PTT)	30.4 s
The international normalized ratio (INR)	1.5
Liver function tests (LFTs)	Normal
Reticulocyte	4.3%
Direct and indirect Coombs	Negative
Antinuclear Antibody (ANA), and Anti-Sm antibodies	Negative
Electrophoresis	Normal

hyperbilirubinemia. During the NICU stay, the child underwent a double-volume blood exchange procedure through an umbilical venous catheter twice to address the hyperbilirubinemia.

At the age of 7 years, the child's family sought medical advice due to progressive abdominal distension. Physical examination revealed a significantly enlarged spleen, and blood tests showed anemia and thrombocytopenia. Abdominal ultrasound indicated massive splenomegaly (measuring 22×9 cm) with no focal lesions, and blood film analysis revealed peripheral destruction of platelets, which led to the decision for splenectomy. Table 1 shows lab test results before the surgery.

Then, the patient underwent a splenectomy, without any complications. At that time bone marrow aspiration was done to exclude malignancy and metabolic causes of splenomegaly (Table 2: bone marrow biopsy result). The results came back normal. Other than frequently getting bruises and ecchymosis the patient did not have any bleeding issues and remained without symptoms.

The patient's health remained stable until he was 10 years old when he experienced pain and fatigue for 2 days. Later on, he began to experience bleeding while vomiting and in his stool. Consequently, he was admitted to another hospital where he received a blood transfusion with packed red blood cells to address his condition before being transferred to the current hospital for a gastrointestinal (GI) endoscopy. Endoscopy was performed by the head of the endoscopy department at the hospital who has 10 years of experience in this field.

On physical examination, the patient was alert and had pale lips and conjunctivae with no jaundice or cyanosis. Vital parameters were normal (BP: 115/71, HR: 128, RR: 26, temperature: 37, and SpO2: 100% on room air). His abdominal exam was normal except for mild abdominal distension with no hepatomegaly. Further physical examination revealed no abnormalities.

The differential diagnosis at that point included esophagitis, gastric ulcer, vascular malformation, Mallory Weiss lesion, clotting disorder, and most probably bleeding from esophageal varices resulting from portal hypertension. Evaluation at presentation showed severe anemia (hemoglobin: 4.5 mmol/l; MCV: 65 fl) and a platelet count of 170 000 platelets per microliter (mcl). Liver function tests and coagulation profile were all normal (Table 3: lab results at admission).

The results of the endoscopy showed that the boy had large esophageal varices without any active bleeding or recent signs of bleeding. Additionally, two gastric fundal varices were identified with blood leakage (Fig. 1A, B). A small amount of Histoacryl glue was injected into each varix to address the issue.

The patient continued on octreotide infusion for 72 h, followed by band ligation for the varices, where 12 bands were applied without any complications. Propranolol was started for long-term management.

At that time abdominal computed tomography scan was also done, which confirmed the presence of transformation of the vein indicating PVT (Fig. 2A–D).

Following this, another band ligation session was conducted after 4 weeks, during which six bands were applied to the esophageal varices with minimal red spots. The gastric fundal varices were successfully treated, and there was no evidence of bleeding or recent episodes.

Overall, after evaluating the GI endoscopy and other investigations, the final diagnosis consisted of esophageal varices and portal gastropathy. To address this condition, the patient was discharged with a treatment plan that involved taking propranolol twice daily at a dosage of 10 mg and nexium once daily at a dosage of 40 mg. Additionally, the doctor recommended the patient to undergo a thrombophilia study and scheduled a repeat endoscopy after 6 months for further evaluation and monitoring.

Eventually, a consulted hematologist ordered a panel PCR test for the patient to test the presence of common mutation in thrombophilia. Upon analysis, it was discovered that the patient had multiple mutations. These included being homozygous for the ACE I/D mutation, heterozygous for the FXIII Val34Leu mutation, and also heterozygous for the Factor V Leiden mutation. These mutations are associated with plasma ACE activity, fibrin cross-linking, and fibrinolysis regulation, as well as thrombosis and thrombophilia.

Table 2

Bone marrow aspiration results

Bone marrow biopsy result
• Hyper cellular marrow with trilineage hematopoiesis
• No morphologic evidence for leukemia, lymphoma or storage disorders.
• Estimated cellularity in the marrow spaces seen is 95%.
• Myeloid cells to nucleated erythroid cells ratio is 5:1
• All hematopoietic cell lines are present with increased erythroid and megakaryocytes.
• No evidence for foamy or wrinkled paper histiocytes;
• Ruling out Niemann Pick disease and Gaucher disease; respectively
• No blast cells seen.
The overall findings are suggestive of peripheral destruction.

Table 3

Lab results at admission

Test	Result
Prothrombin time (PT)	14.8 s
Partial thromboplastin time (PTT)	21 s
The international normalized ratio (INR)	1.15
Hepatitis B surface antigen (HBsAg)	Nonreactive
Hepatitis C antibody (HCV Ab)	Nonreactive
Inflammatory markers	Negative
Ceraluplasmin level and anti-tissue transglutaminase antibody	Negative
anti-smooth muscle antibody (ASMA), Antinuclear Antibody (ANA), Antimitochondrial antibodies (AMA)	Negative
protein c. protein s, anti-thrombin 3	Nonreactive

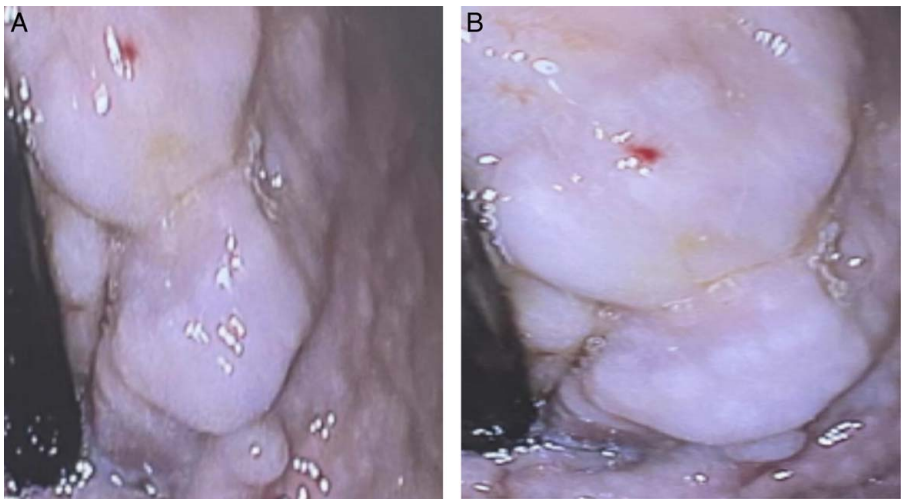

Figure 1. Two Gastric fundal varices with oozing of blood.

Discussion

The case we are looking at involves a boy who is 10 years old and has portal hypertension, esophageal varices and complications that followed. It is quite uncommon and interesting to see such a scenario, in someone young. Initially, the doctors who managed the case did not think of portal hypertension as a cause of splenomegaly thrombocytopenia because of absence of chronic liver disease stigmata, which is the case in posthepatic portal hypertension. Usually, portal hypertension and esophageal varices are

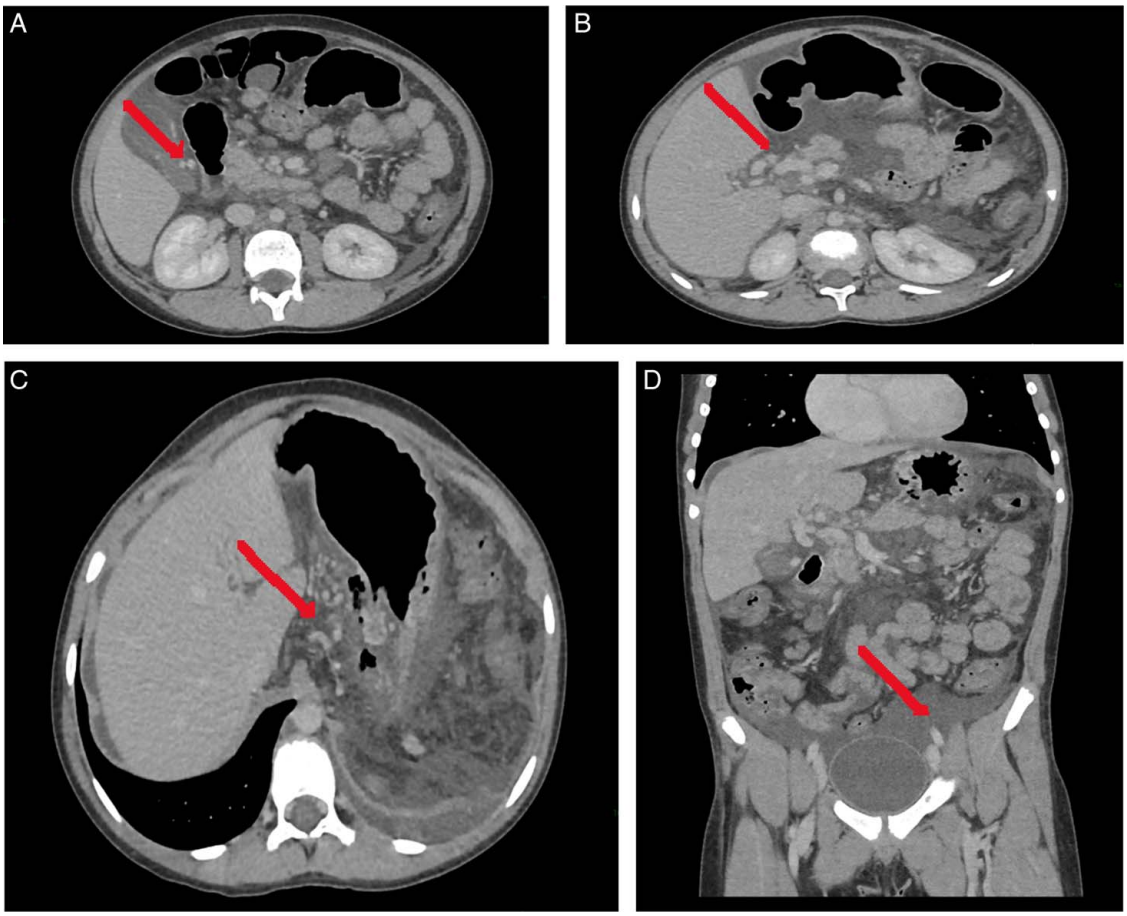

Figure 2. A pericholecystic varices. B cavernous transformation. C gastric varices. D Ascites.

seen in patients with liver disease or other underlying causes. In this case, the use of an umbilical venous catheter (UVC) for double-volume blood exchange at the NICU can explain the origin of PVT in such a young age[4]. Especially when placed malposition. According to another study, in a total of 257 neonates had UVC implanted; following first insertion, 158 (61%) and 99 (39%), respectively, were in central and noncentral placements. On a subsequent X-ray, 35 (22%) of the initial centrally positioned UVCs were pulled back or moved to a malposition[5]. PVT occurs when a blood clot develops in the vein, which is responsible for transporting blood from the GI tract and spleen to the liver.

Comparatively, our study underscores the prominent role of UVC as a significant risk factor for PVT in pediatric patients[6]. The presence of a catheter in the vein poses potential risks, including vessel wall irritation and clot formation, which can disrupt blood flow patterns and significantly impact liver function[4]. Notably, our findings align with a larger study, where 13.5% of patients previously exposed to UVC as neonates experienced PVT, with cases ranging from partial to full occlusion[7]. Furthermore, a comparative study involving 187 patients highlighted the prevalence of UVC in cases of portal hypertension, with a notable 65% incidence rate[8]. Our case, involving a 10-year-old patient, stands out for its rarity, challenging the conventional notion that such conditions manifest at an earlier age. The distinctive time gap between catheter placement and the onset of PVT symptoms adds an additional layer of uniqueness to our findings, emphasizing the need for heightened awareness and tailored approaches to the diagnosis and management of portal hypertension in older pediatric patients.

The effective management of the patient's varices through a combination of Histoacryl glue injection and band ligation procedures underscores the critical role of interventions in mitigating bleeding and averting complications. In comparison, a separate investigation revealed that endoscopic variceal ligation is a secure and markedly successful procedure in children with portal hypertension, irrespective of its cause[9]. Notably, this earlier study reported a cessation of bleeding for a significant duration of 16 months following the removal of esophageal varices. However, the persistence of varices and the subsequent development of PVT in our case introduce pertinent inquiries into the underlying factors, necessitating continuous scrutiny and follow-up examinations[9].

The discovery of mutations associated with thrombophilia, including the ACE I/D mutation, FXIII Val34Leu mutation and Factor V Leiden mutation adds a genetic element to this case. These mutations are rarely identified[10]. These mutations have been linked to the regulation of ACE activity in plasma fibrin cross-linking fibrinolysis and the development of clotting disorders. The presence of these mutations in a patient with hypertension and esophageal varices enhances our understanding of the complex relationship between genetic factors and vascular complications.

The reason why the authors decided to share this case is not just because its rare but because it has implications, for patient care. By describing the situation of a 10-year-old with hypertension, esophageal varices, and related complications this case report adds to the existing medical knowledge by showing a less common occurrence that challenges what we typically expect about when these conditions develop. Moreover, the discussion about the impact of catheterization and subsequent PVT backed up by relevant studies offers valuable insights for healthcare professionals and researchers. Collaboration among gastroenterologists, hematologists, and geneticists is crucial, in order to thoroughly assess the underlying risk factors, optimize treatment strategies and develop personalized long-term management plans. So, beyond its rarity this report provides an opportunity to explore connections ask questions about underlying causes and support a comprehensive approach, to managing patients.

Further investigation is necessary to explore the links between these mutations and the occurrence of portal hypertension in children. It is also crucial to understand how these findings may impact prognosis and the effectiveness of treatment options.

Limitation

While this case study offers insights, into the occurrence of portal hypertension, esophageal varices and the complications they entail in a 10-year-old patient it is important to acknowledge certain limitations. Firstly, we must recognize the challenges posed by the study's nature and its reliance on medical records. These factors make it difficult to obtain a comprehensive and real time understanding of the patient's condition. Additionally, because this study focuses on a case with a sample size, we must be cautious in generalizing its findings to a broader population. The uniqueness of the patient's history, which includes prematurity and neonatal interventions adds complexity. Might not be representative of typical patients with portal hypertension. Furthermore, although we have identified mutations associated with thrombophilia in this context, we should interpret these findings cautiously due to our understanding of such mutations in children with portal hypertension. Despite these limitations this case highlights the importance of conducting research and fostering collaboration among medical specialties to enhance our understanding of complex vascular conditions, in pediatric patients.

Conclusion

In conclusion, this interesting case involves a 10-year-old boy who developed portal hypertension at an early age, along with esophageal varices and multiple mutations associated with thrombophilia. There was an exceptionally long interval between catheter placement and experiencing PVT symptoms[1]. This case highlights how complex this condition is and emphasizes the need for a team approach to its management. The successful use of endoscopic interventions combined with the identification of factors offers insights into how portal hypertension can be treated in children. Further research is necessary to uncover the underlying mechanisms, identify therapy targets, and improve our understanding of the long-term outcomes in such cases.

Disclaimer

This work has been reported in line with the Surgical Case Report (SCARE) criteria[11].

Ethical approval and consent to participate

The manuscript's conduct and publication have received approval from the university's IRB.

Patient consent

Written informed consent was obtained from the patient's parents (patient's guardian) for publication of this case report and accompanying images.

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Author contribution

A.D., M.A., M.A., D.N., and M.A.: wrote the manuscript; Q.A. and M.A.: diagnosis, management, and follow-up of the case. All authors read and approved the final manuscript the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Research registration unique identifying number (UIN)

We obtained verbal approval from the Ethical Review Committee at An-Najah University, as the patient's ethical consent to conduct the research is sufficient to raise the case report.

Guarantor

Not applicable.

Data availability statement

The corresponding author will provide the data sets used and/or analyzed during the current study upon reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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