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Case Report

Portal vein thrombosis due to inherited combined deficiency of protein C and S in a young adult: A case report ☆

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ABSTRACT

Protein S and C deficiency is a rare inherited thrombophilia that predisposes individuals to a hypercoagulable state, leading to clot formation in various locations, such as the deep veins of the legs, cerebral veins, and rarely the portal vein. We present the case of a 21-year-old male who came to the ER with hematemesis and melena secondary to chronic portal vein thrombosis (PVT) without any evidence of cirrhosis. Diagnostic investigations, including ultrasonography and computed tomography, confirmed the presence of thrombosis and cavernous transformation of the portal vein, splenic vein thrombosis, and splenomegaly. Coagulation profiling revealed diminished Protein S and C levels, thus confirming the diagnosis of a combined Protein S and C deficiency. Management involved indefinite anticoagulant therapy with direct oral anticoagulants to mitigate thromboembolic risks associated with the inherited thrombophilia. This case underscores the importance of considering rare coagulation disorders in young patients with unexplained thrombotic events, emphasizing the need for a comprehensive diagnostic approach and timely therapeutic interventions to minimize morbidity and mortality.

Introduction

Protein S and C are crucial in maintaining effective anticoagulation within blood vessels. These proteins are vitamin K-dependent plasma serine protease enzymes synthesized in the liver and are essential for hemostasis. Specifically, protein S works synergistically with activated protein C to inhibit factors Va and VIIIa, thereby impeding tissue plasminogen activator and enhancing fibrinolysis [1].

The deficiency in proteins S and C is either congenital or acquired. Congenital cases are typically associated with

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Complete blood count (CBC) + P/F

Test Name	Results	Unit	Normal Range
HAEMOGLOBIN (Hb.)	**7.7**	g/dL	12 - 17
E.S.R. (Westergren Method)	05	mm/1st Hour	00 - 18
TOTAL W.B.C.	4600	/Cu.mm.	4000 - 11000
TOTAL R.B.C.	**3.51**	Mill/Cu.mm.	4.5 - 6.5
PLATELET COUNT	**127000**	/Cu.mm.	150000 - 400000
P.C.V (Hematocrit)	**25.1**	%	40 - 54
M.C.V.	**71.5**	fL	76 - 96
M.C.H.	21.9	Pg.	20 - 32
M.C.H.C.	30.7	g/dL	30 - 35
DIFFERENTIAL CELLS :			
NEUTROPHILS	75		
LYMPHOCYTES	18		
MONOCYTES	05		
EOSINOPHILS	02		

PERIPHERAL BLOOD FILM :

RBCs are microcytic and hypochromic. No immature cell is seen. No haemoparasite is seen. Platelets are reduced.

Test Name	Results	Unit	Normal Range
L.F.T. (Liver Function Test)			
BILIRUBIN TOTAL	1.2	mg/dl	0.1 - 1.0
BILIRUBIN CONJUGATED	0.4	mg/dl	0.0 - 0.5
BILIRUBIN UNCONJUGATED	0.8	mg/dl	0.1 - 0.75
ALKALINE PHOSPHATASE	90	U/l	Adult : 35-130 Children : Upto 462
SGPT (ALT)	21	U/l	00 - 41
SGOT (AST)	26	U/l	08 - 40

Fig. 1 – Baseline Lab values of the patient at admission with low Hemoglobin, MCV, RBC, platelet counts, and normal Liver function tests.

autosomal dominant mutations in the PROS1 and PROC genes respectively [2]. Acquired deficiencies, on the other hand, can result from various factors such as vitamin K insufficiency, chronic liver diseases, nephrotic syndrome, chronic infections, systemic lupus erythematosus, oral contraceptive use, or pregnancy. Congenital deficiencies of the natural coagulants are rare, with a prevalence of about 1 in every 200–500 individuals for Protein C deficiency and 1 in every 500 individuals for Protein S deficiency [3]. Combined deficiency of protein C and protein S is even more rare, and only a few confirmed cases have been reported, so its prevalence has not yet been established.

Individuals with these deficiencies are predisposed to thrombophilia, increasing the risk of venous thromboembolic events such as deep venous thrombosis, portal vein thrombosis, pulmonary embolism, and disseminated intravascular coagulation.

PVT is the rarest form of venous thrombosis with mean age-standardized incidence and prevalence rates of 0.7 and 3.7 per 100000 inhabitants, respectively [4]. Thrombosis causes narrowing of the portal vein compromising the blood supply to the liver and can also spread to the splenic and mesenteric veins [5]. leading to splenomegaly and bowel ischemia.

Case summary

A 21-year-old male patient presented in the ER with complaints of 2 episodes of hematemesis along with melena for 2 days. There was no history of drug or alcohol intake and no other signs of liver injury. Vitals were stable at presentation. Baseline investigations were ordered which showed low Hemoglobin, Platelets, MCV, and Red Blood cell count but the Liver Function panel was within normal reference ranges (Fig. 1).

The patient was given IV crystalloids, IV proton pump inhibitors, and admitted to the hospital. Esophagogastroduodenoscopy (EGD) revealed large esophageal varices (Fig. 2) that

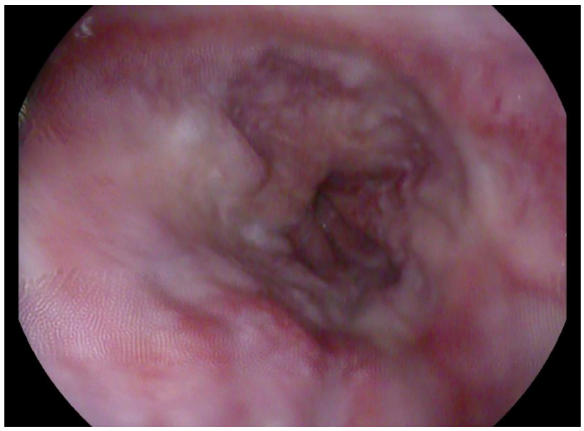

Fig. 2 – Esophagogastroduodenoscopy image showing esophageal mucosa with large varices.

were subsequently ligated via Esophageal Variceal Band Ligation (EVBL).

USG abdomen (Fig. 3) of the patient revealed chronic portal vein thrombosis involving the splenic vein with cavernous transformation at the Porta-hepatis without any signs of cirrhosis or irregularities in the liver parenchyma.

CT abdomen with IV contrast was requested that confirmed noncirrhotic chronic Portal vein thrombosis with cavernous transformation and splenomegaly (Figs. 4 and 5).

After confirmation of thrombosis on imaging and before initiation of any anticoagulant therapy, a coagulation profile (Fig. 6) was sent to check for levels of Antithrombin III, Protein C & S, Lupus anticoagulant, Anti-Cardiolipin antibodies, Anti-Beta 2 glycoprotein antibodies, and Homocysteine levels to figure out the primary etiology. The results revealed a combined deficiency of both Protein S and C which was confirmed by repeat testing on follow-up appointments.

The Patient was prescribed Direct Oral anticoagulants for an indefinite period due to his inherited thrombophilic state.

Discussion

Portal Vein Thrombosis (PVT) occurs when a thrombus partially or completely occludes the lumen of the Hepatic Portal Vein. Due to the widespread utilization of Doppler Ultrasonog-

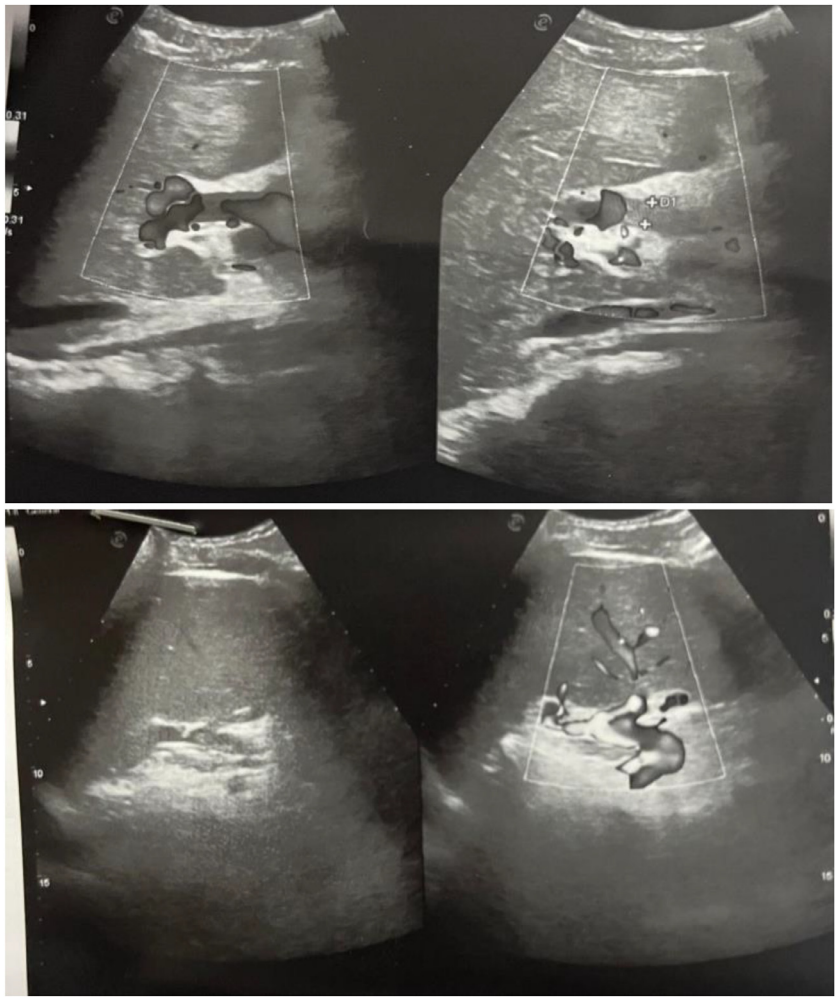

Fig. 3 – USG Doppler abdomen/hepatobiliary suggestive of Portal and Splenic Vein thrombosis.

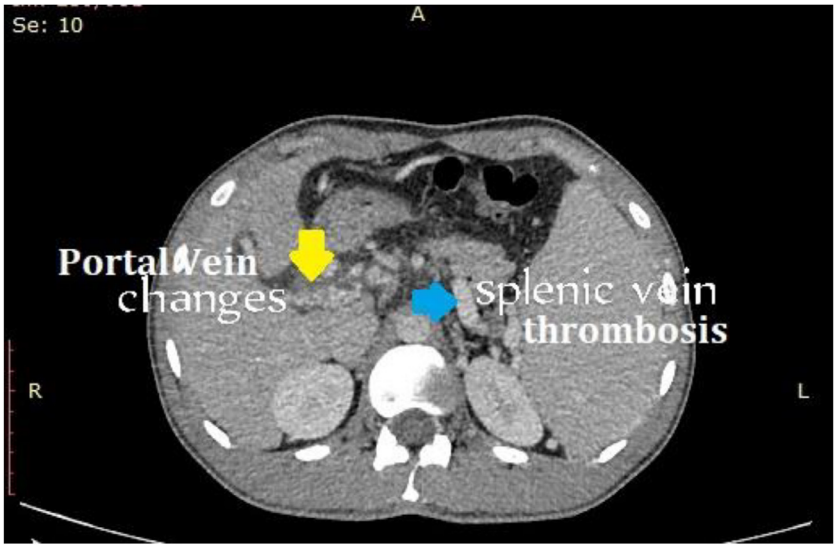

Fig. 4 – CT Abdomen & Pelvis axial view shows thrombosis of the Portal (yellow arrows) and Splenic (blue arrows) veins along with splenomegaly, and without any signs of cirrhosis.

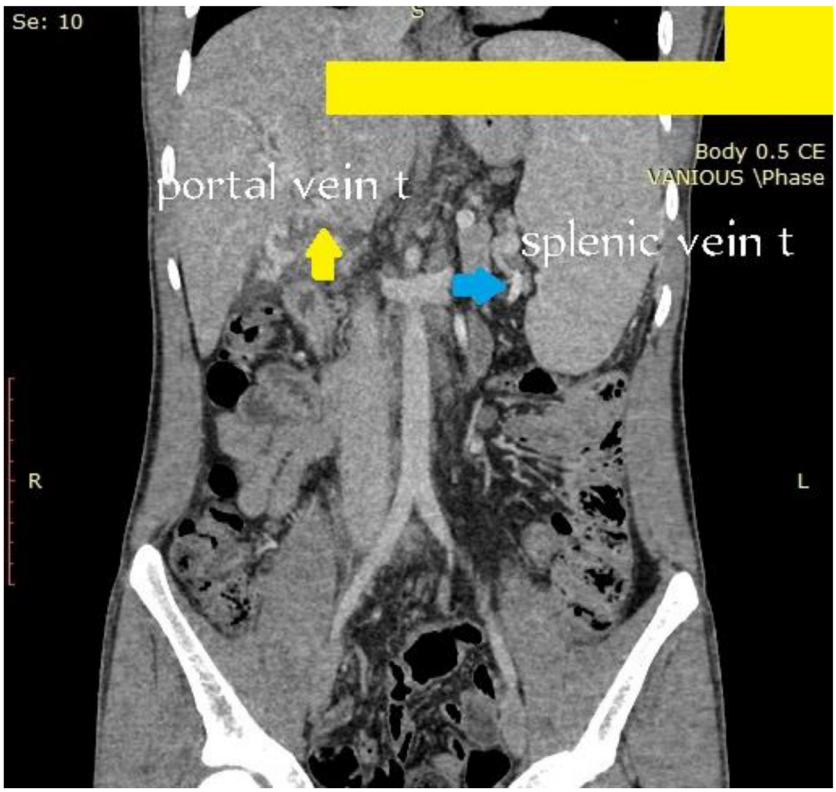

Fig 5 – CT Abdomen & Pelvis coronal view shows thrombosis of the Portal (yellow arrows) and Splenic (blue arrows) veins, splenomegaly, and no signs of cirrhosis.

raphy in recent times, the diagnosis of PVT has become more prevalent. Still, in individuals without cirrhosis, PVT is a rare occurrence [6].

PVT can present either acutely or chronically. Acute PVT presents with abdominal pain, nausea, emesis, fever, new-onset ascites, and metabolic acidosis. Chronic PVT, as in our patient, leads to the development of collaterals and portosystemic shunting occurs leading to esophageal and rectal varices, rectal bleeding, hematemesis, and splenomegaly.

Detecting abnormalities related to portal vein thrombosis (PVT) is essential for accurate diagnosis and timely intervention. In approximately one-third of patients with PVT,

Fig. 6 – The patient's coagulation profile shows low Free Protein S and Protein C levels.

cavernous transformation of the portal vein occurs which indicates an old thrombus. The ultrasonographic diagnostic triad includes failure to visualize the extra-hepatic portal vein, demonstration of high-level echoes in the porta hepatis, and visualization of multiple serpiginous vascular channels around the portal vein [7]. Contrast-enhanced computed tomography (CT) is the optimal method for diagnosing portal vein thrombosis (PVT) and assessing potential underlying diseases. Key findings of PVT on dynamic CT include filling defects that partially or completely occlude the vessel lumen and rim enhancement of the vessel wall.

Etiologically, PVT can occur due to underlying malignancy, infection, use of oral contraceptives, acute pancreatitis, pregnancy, Liver disease, or coagulopathies [6]. Pro-coagulative states leading to PVT can either be acquired due to myeloproliferative disorders, antiphospholipid syndrome, and Paroxysmal Nocturnal Hemoglobinuria (PNH) [4,6] or inherited due to mutations in Prothrombin, anti-thrombin, protein C, protein S, or Factor V [8].

Fisher et al. [9] investigated twenty-nine adult patients with portal hypertension due to PVT. Their findings revealed that 62% of the patients exhibited deficiencies in one or more natural anticoagulant proteins. Among these cases, only 28% had combined deficiency of C and S proteins, 31% had deficiency in C protein and antithrombin, while 24% showed deficiencies in protein S and antithrombin. Additionally, 21% of cases had deficiencies in all 3 proteins simultaneously. Therefore, in cases of PVT, especially without any evidence of underlying cirrhosis or other risk factors, it is imperative to test for deficiencies of anticoagulant proteins.

The initial treatment for portal vein thrombosis (PVT) involves anticoagulation. If needed, subsequent approaches include mechanical thrombectomy, thrombolysis, and interventional radiographic procedures or surgery [10]. Anticoagulant therapy is currently the most effective approach for achieving portal vein recanalization. However, its universal acceptance remains a topic of debate. After 6 months of therapy, approximately 50% of patients experience complete recanalization, with minimal complications. Importantly, in acute portal vein thrombosis (PVT), early treatment significantly impacts prognosis. The rate of recanalization is approximately 69% when anticoagulation is initiated within the first week after diagnosis, but it drops to 25% if treatment begins in the second week. [11]. Thrombolytic therapy may offer some effectiveness, but its efficacy is notably lower, and it is associated with increased mortality compared to conservative treatment [12]. As patients with an unprovoked episode of venous thrombosis and potent thrombophilia have a higher risk of recurrent VTE (>10 %), anticoagulants should be continued indefinitely [13].

Patient consent

Written, informed consent was obtained from the patient for publication of their case.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) used CHAT GPT / OPEN AI in order to improve language and readability. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

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