Case Report

Extra hepatic portal vein obstruction due to combined protein 'C' and 'S' deficiency - A case report

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Abstract

Extra-hepatic portal vein obstruction (EHPVO) is an important cause of non-cirrhotic portal hypertension, in Third World countries like India. In this disorder, it results in obstruction and cavernomatous transformation of portal vein with or without the involvement of intra-hepatic portal vein, splenic vein, or superior mesenteric vein resulting in portal hypertension and esophagogastric varices. Extensive collateral circulation develops, involving paracholecystic, paracholedochal and pancreaticoduodenal veins which results in formation of ectopic varices, and portal biliopathy. Besides variceal bleeding, patients may have symptoms of portal biliopathy, hypersplenism, and growth retardation. Although the liver may appear normal, functional compromise develops in the long term. Patients with extra-hepatic portal vein obstruction are usually young and belong to India and other Asian countries. The variceal bleeding in EHPVO can be managed by endoscopic obliteration of varices, or by portosystemic shunt surgery. In this case report, we present a case of 15 year old male, with extra-hepatic portal vein obstruction due to combined deficiency of Protein C and Protein S recanalized by short-term low molecular heparin plus oral Rivaroxaban therapy.

Key words

Extra-hepatic portal vein obstruction (EHPVO), Protein C and protein S deficiency.

Introduction

Thrombosis of the portal vein is an uncommon disorder comprising of thrombosis of the extra-hepatic portion of the portal vein and/or its branches. It can occur concomitantly with mesenteric and/or splenic vein thrombosis.

Portal vein thrombosis (PVT) is defined as complete or partial obstruction of blood flow in the portal vein, associated with a thrombus in the vessel lumen [1]. PVT has different clinical presentations in acute Vs chronic onset and collateral circulation, both its development and extent. Symptoms and signs due to intestinal congestion and ischemia, like abdominal pain, diarrhea, rectal bleeding, abdominal distension, nausea, vomiting, anorexia, fever, lactic acidosis, sepsis, and splenomegaly are common in acute PVT. Chronic PVT is more challenging to diagnose, can be completely asymptomatic, or present as splenomegaly, pancytopenia, varices, and, ascites [2].

PVT is classified into four categories:
(1) Thrombosis confined to the portal vein beyond the confluence of the splenic and superior mesenteric vein (SMV);
(2) Extension of thrombus into the SMV, but with patent mesenteric vessels;
(3) Diffuse thrombosis of splanchnic venous system, but with large collaterals; and
(4) Extensive splanchnic venous thrombosis, but with only fine collaterals.

Presently this anatomical classification is mainly used to determine operability, but it may also have etiological and prognostic relevance, as patients with thrombus interference with mesenteric vasculature risk bowel infarction and have a lower risk of variceal bleeding than those with isolated PVT. All patients with PVT should be tested for an underlying thrombophilic condition [3]. Hereditary thrombophilias known to predispose for PVT include mutations of the prothrombin, or factor V, genes, and deficiency of one of the natural anticoagulant proteins C, S, or anti-thrombin. Fisher, et al. [4] in a study of 29 patients with portal hypertension caused by PVT, found that 18 patients (62%) had deficiencies in one or more of the natural anticoagulant proteins, and 6 (21%) had combined deficiency of all three proteins. Of these, 8 cases (28%) had combined C and S protein deficiency, 9 (31%) had C protein and anti-thrombin deficiency, 7 (24%) showed protein S and anti-thrombin deficiency. Due to advances in non-invasive imaging techniques in diagnostic evaluation of abdominal pain, acute portomesenteric venous obstruction is an increasingly recognized disorder [1, 2, 5, 6].

Etiology

Virchow's triad of hypercoagulability, endothelial injury, and stasis lead to PVT, although the etiology of these alterations is quite different. Local factors often contribute to PVT and these include Liver cirrhosis (28% of PVT), Abdominal malignancy (27-44% PVT), abdominal inflammatory (10% of PVT) conditions. Abdominal infections, and portal vein injury (e.g. during splenectomy, surgical shunts, trauma, gastric bypass surgery, colectomy, post liver transplant, umbilical vein catheterization cholecystectomy) [7, 8, 9-11].

Systemic causes include [7, 12, 13] Inherited thrombophilia (20% of PVT) [7, 12, 13] like Factor V Leiden mutation, Prothrombin gene G20210A mutations and methyl tetra hydro folate reductase (MTHFR) mutations, Protein C, S and AT III deficiency Hyperhomocystinemia. Acquired thrombophilia [7, 13] like Myeloproliferative disorders (11% of PVT): JAK2 mutation (JAK2V617F), essential thrombocythemia, Polycythemia vera, myelofibrosis, Antiphospholipid antibody syndrome / lupus anticoagulant, Pregnancy, Hormonal therapies(OCP's), Non-abdominal malignancy, Paroxysmal nocturnal hemoglobinuria, and other causes like Burns, DIC, Sepsis, etc.

Prevalence and epidemiology

There is no accurate epidemiological data on PVT. PVT is rare disorder, has been reported

with mean age-standardized incidence and prevalence rates of 0.7 and 3.7 per 100000 inhabitants, respectively [14].

However in patients with cirrhosis, these rates jump to between 4.4%-15%, and cause 5%-10% of overall cases of portal hypertension [15], 22%-70% of patients without cirrhosis have prothrombotic states and local factors are present in 10%-50% [14-16], although more than one factor is often present [17].

Pathophysiology

Portal venous obstruction is usually well tolerated and patients are often asymptomatic. There are two important mechanisms which play a role in portal venous obstruction.

1. Arterial vasodilation or arterial rescue, which preserves the liver function in acute settings, also allows other mechanisms to operate the venous rescue.
2. Venous rescue allows several collaterals to develop, to bypass portal vein obstruction. This neovascularization or neoangiogenesis takes around 4–6 weeks, [18, 19] and an obstructed portal vein is replaced by collateral network called cavernoma. The portal cavernoma bypasses the obstructed portal vein and thus a thrombosed portal vein turns into a fibrotic cord [20, 21]. The network is seen around structures near the obstructed portal vein such as the bile duct, gall bladder, pancreas, gastric antrum, and duodenum. The bile duct may be difficult to locate within the network of collaterals on abdominal ultrasonography.

Formation of collaterals can also occur rapidly, and described as early as 12 days after an acute thrombosis, though the average time to formation is approximately 5 weeks. The development of collateral circulation, with it risk of variceal hemorrhage, is responsible for the complications and is the most common manifestation of portal vein obstruction. The other sequelae such as ascites, are less frequent. Rarely, the thrombosis extends from the portal vein to the mesenteric arcades, leading to bowel ischemia and infarction.

Biopsy of liver is usually normal except hemosiderosis related to porto systemic shunt. In advanced states of PVT, hypoperfused cells of the liver die by apoptosis as a result of increased apoptotic signals and enhanced mitotic activity in normally perfused cells. This process finally leads to reduced synthetic function of the liver in later stages of EHPVO [22].

There is a an increased risk of recurrent venous thrombosis in patients with Protein C and Protein S deficiency such as Deep vein thrombosis with or without Pulmonary embolism seen in 50 percent of patients by the age of 30-45 years, Cerebral vein thrombosis, mesentric vein thrombosis, superficial thromboplebitis, portal vein thrombosis (abdominal pain, rectal bleeding, diarrhea, abdominal distension, ascites, anorexia, fever, lactic acidosis, sepsis, spleenomegaly), hepatic vein thrombosis (Budd Chiari Syndrome).

Non-cirrhotic, non-malignant acute portal vein thrombosis

Currently the American College of Chest Physicians (ACCP) and American Association for the Study of Liver Disease (AASLD) have separate clinical guideline recommendations for treatment of PVT [23, 24]. The ACCP recommends anticoagulation for symptomatic PVT with a grade 1B level of evidence, which is a fairly scientifically robust recommendation; however, they do not suggest anticoagulation for asymptomatic, incidentally diagnosed PVT, which has a grade 2C level of evidence – a very weak recommendation given the lack of good data in this group of patients [24]. The AASLD clinical guidelines suggest anticoagulation for all acute PVT regardless of symptomatology [23]. There is clearly equipoise in the treatment of PVT, even between different thrombotic society guidelines.

PVT in non-cirrhotic and non-malignant individuals can occur in the setting of abdominal inflammatory processes such as pancreatitis, infections, and inflammatory bowel diseases, and after abdominal surgeries. Literature is very sparse regarding this group of PVT, and there are no randomized controlled trials. Baril, et al. identified pylephlebitis in 44 patients with PVT on CT scans. Of these, 18 were hypercoagulable due to clotting factor deficiencies (6/18), malignancy (8/18), or AIDS (4/18). Fifteen patients had mesenteric vein thrombosis in addition to PVT. Five of the 32 cases that were not anticoagulated died compared to none in the remaining 12 patients who were anticoagulated [25]. Kanellopoulou, et al. reviewed and reported that complete recanalization was higher in anticoagulated cases compared to those with no anticoagulation; no recanalization was also seen less commonly in those who were anticoagulated, with lower death rates [26]. In a meta-analysis of 315 patients by Hall, et al., 12 were not anticoagulated and only two had spontaneous recanalization, and both of those patients had selflimiting conditions that provoked thrombosis.22 Of the 228 cases that were anticoagulated, 38.3% had complete and 14% had partial recanalization of the portal vein. On follow- up, 20% demonstrated cavernous transformations, 47 patients developed esophageal varices, and upper gastrointestinal bleeding was seen in five cases, all of whom had not recanalized completely. Seventy-one patients underwent thrombolysis with or without thrombectomy 34 had failed a trial of anticoagulation), with a majority having an indication of increasing pain on anticoagulation or thrombus extension. Complete recanalization occurred in 40.8% and partial recanalization occurred in 45.1%, and 14.1% remained occluded. Among 111 of the 315 patients in which long-term follow-up were available, 26 cases had complete recanalization and all of them had no complications of portal hypertension. Up to 50 cases had partial recanalization, of which four had varices, two had ascites, and one had a small bowel obstruction [27].

Acute portal vein thrombosis in the setting of cirrhosis of liver

PVT in cirrhosis has adverse outcomes as it is associated with variceal bleeding. Thrombophilic disorders are common with cirrhosis, but there is also a unique balance of hemostasis related to cirrhosis that includes both hyper and hypocoagulable states [28, 29–31].

In liver cirrhosis, not only the procoagulant proteins (vitamin K-dependent proteins and factor V) reduced but the anticoagulant proteins (protein C and S) are impaired, often in equilibrium, thereby creating a hemostatic balance in the majority of cases [4, 28, 32, 33].

The effects of vitamin K deficiency seen with warfarin use is that factor VIII and von-Willebrand factor are elevated in cirrhosis, creating a procoagulant milieu at times [33, 34].

Patients with cirrhosis have a relatively high risk of PVT compared with the general population. Up to half of the patients presenting with PVT in this setting can be asymptomatic and incidentally diagnosed [35]. Studies have shown that PVT can lead to worsening of liver function and increased mortality, and the presence of PVT may negatively impact morbidity and mortality at the time of liver transplant [36, 37, 38].

To treat PVT in patients with cirrhosis, many factors should be taken into consideration: acuity of thrombosis, transplant candidacy, presence of an inherited coagulopathy, bleeding risk factors, and co-morbidities. There is ample data regarding the safety and efficacy of anticoagulation in patients with cirrhosis. Francoz, et al. reported a higher incidence of partial or complete recanalization of thrombus burden with anticoagulation over no anticoagulation [36]. Amitrano, et al. reported that with therapeutic doses of low-molecular weight heparin (LMWH), complete recanalization was seen in 33% of patients and partial recanalization was seen in 50% of patients with no increased bleeding risk [39].

A study by Senzolo, et al. utilizing therapeutic doses of LMWH for treatment of PVT showed a higher rate of variceal bleeding in patients not on anticoagulation (five) than those on anticoagulation (one) [40].

TIPS has shown to completely recanalize portal veins in up to 57% of cases; but is associated with a high incidence of low stent patency rates as well as hepatic encephalopathy.(41,42), Hence, the benefits of TIPS need to strongly weigh against the risks of hepatic decompensation, hepatic encephalopathy, and risk of embolization [40, 43, 44].

Anticoagulation of patients with liver cirrhosis can be complicated. Warfarin is often difficult to manage since some of these patients have baseline elevated international normalized ratio (INR) levels, and hence, the ideal INR goal to maintain a therapeutic range is difficult to assess [32]. LMWH is an excellent alternative to warfarin that is safe and efficacious for these patients [39, 40].

Direct oral anticoagulants (DOACs) such as apixaban, dabigatran, and rivaroxaban have not been studied well. Case series using rivaroxaban and apixaban have been reported; larger studies are required for large-scale utilization, as there is increased risk of gastrointestinal bleeding with some DOACs and their metabolism through the cytochrome P450 3A4 pathway [45–47].

Acute portal vein thrombosis in the setting of malignancy

PVT is identified in patients with hepatocellular carcinoma (HCC) and with pancreatic adenocarcinoma [48–53]. PVT is an independent predictor of increased mortality among patients with HCC. Untreated HCC with PVT was reported to be associated with decreased survival time [54, 55]. It is recommended to use LMWH rather than warfarin in treatment of thrombosis in the setting of malignancy [56]. DOACs have not yet been studied in the setting of malignancy.

Case report

On 25th March 2014 - A 15 year old male student, came to the OPD with Chief complaints of one episode of hemetemesis, non projectile, non bilious, 1 tea spoonful in quantity, associated with retrosternal burning sensation and 1 episode of melena, sticky, non foul smelling of one day duration. No history of fever, diarrhea, giddiness.

Past history: Patient had similar episodes of on and off hematemesis episodes since 8 years. No history of HTN, TB, DM, Thyroid disorders, Epilepsy, CRHD, MI.

On General examination, Patient was conscious, coherent and cooperative. Moderately built, moderately nourished. Pallor ++, no icterus, no cyanosis, no clubbing, no koilonychia, no lymphadenopathy, no pedal edema. No signs of liver cell failure. Patient was stable at presentation with BP - 110/70mm Hg, PR - 84/min and respiratory rate -18/minute.

On Systemic examination: Abdomen was symmetrical with umbilicus inverted in position, with all quadrants moving equally with respiration. There were no visible pulsations, swellings or sinuses. On palpation, there was splenomegaly 2cm below the left coastal margin. On percussion, tympanic resonance was noted. Normal bowel sounds were heard on auscultation. Other systems were normal.

Investigations: Hb - 7.2g/dl, WBC count-4000cells/cumm, Platelet count - 92,000, MCV - 68.9fl (79-98), MCH - 20.8 pg (27-32), MCHC – 30.2% (31-36), Blood urea – 68 mg/dl, Serum creatinine -1.5mg/dl. Dengue serology (NS1, IGM, IGG) - negative, Smear for Malarial parasite-negative. Widal test - negative. X - Ray chest PA view – normal, USG abdomen - Moderate splenomegaly. Upper GI Endoscopy (**Figure - 1a, b, c, d**) - Esophageal varices grade 3 along with fundal varices were noted. Patient was transfused 2PRBC (A + positive). Sclerotherapy was done twice in the month of March 2014 and April 2014.

Figure - 1 (a, b, c, d): Upper GI Endoscopy (25th March 2014).

Figure - 1a: Oesophagus – Grade III varices.

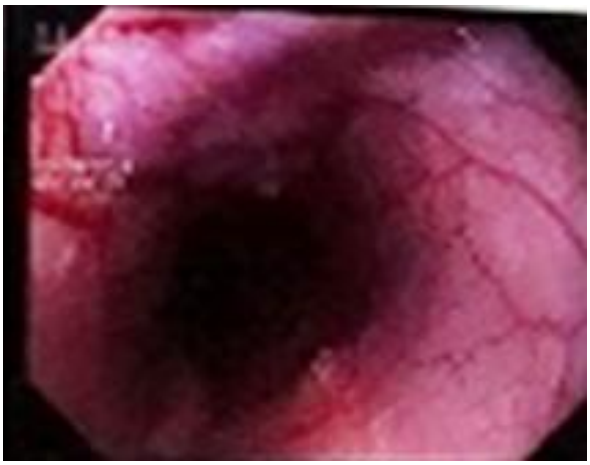


Figure - 1b: Cardia – Grade III varices.

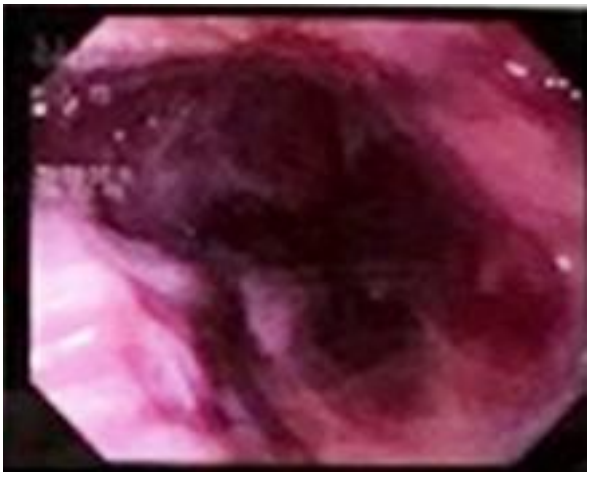
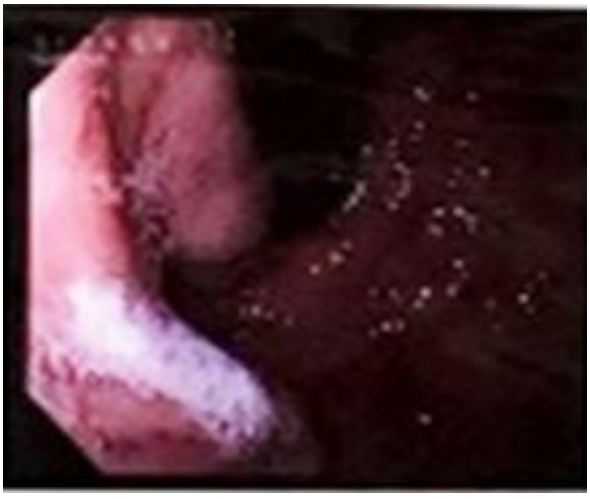
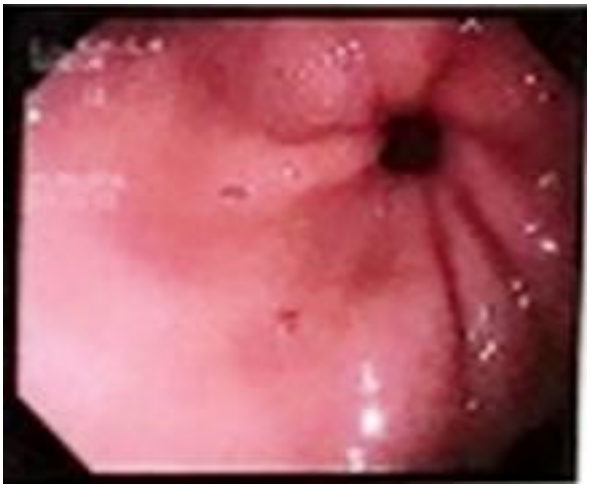


Figure - 1c: Stomach – Fundal varices.



On 31/8/14 - After 5 months the patient presented with 5 episodes of hematemesis, 2 teaspoonful in quantity, and 5 episodes of melena since 2 days. No h/o fever, yellowish discoloration of eyes. On examination, Pt had Pallor. LFT, RFT was normal. Repeat USG abdomen showed Portal vein with decreased calibre, Splenomegaly.

Figure - 1d: Duodenum – Normal.



On 2/9/14 - Upper GI endoscopy was done esophageal varices Grade 2 were noted and Patient underwent EVL banding. On 9/9/14

After 5 years, on 30/7/19 - Patient presented with fever of 5 days duration associated with chills and rigors with hematuria since 3 days. No hematemesis/ melena. On examination, Pallor and splenomegaly was noted. CBP showed HB - 7.2 g/dl, Platelet - 66,000/cumm, WBC - 4,200cells/cumm. 4/8/19 - complained loose stools of 6 days duration, 2-3 episodes per day with Pain abdomen around periumbilical region. Treated conservatively.

On 21/1/20 Follow up - Upper GI endoscopy was again done and Grade 1 Esophageal varices were noted.

19/3/20-Follow up -There were no fresh complaints.

9/11/21 - Patient complained of Pain abdomen and on endoscopy Grade 2 esophageal varices were noted and EVL banding was done on 23/11/21.

23/1/22 - Patient complained of Bilateral pain from loin to groin region of 3 days duration, gradually progressive dragging type of pain,

radiating to left iliac fossa. History of fever of 3 days duration associated with 1 episode of vomiting non projectile, non bilious not blood stained. Investigations- CBP Hb - 8.9g/dl, WBC-1,100 cells/cumm Platelets 63000/cumm, MCV - 31.4fl, MCH - 66.4 pg. BT - 2min 25 secs (2-5 min), CT – 6 min 35 secs (5-10 min) RBS - 92 mg/dl, Blood Urea – 28 mg/dl, Serum Creatinine - 1.0 mg/dl, CUE- normal., Serum sodium - 137mmol/l, Potassium - 4.7mmol/l , Chloride – 105 mmol/l, Calcium - 1.19 mmol/l, viral markers – negative, LFT – Normal. USG abdomen - Left ureteric calculus causing mild hydroureteronephrosis, Left kidney lower pole calyx 8.8 mm and Upper pole calyx 5.5mm. Left upper ureteric calculus 7 mm. Gross splenomegaly (20 x 7.8 cm). Liver showed mild coarse echotexture of the liver, periportal fibrotic changes noted in portahepatis with main portal vein replaced by collateral vessels. Upper GI endoscopy (**Figure - 2, a, b, c, d, e**) was done there were no varices noted.

26th Jan 2022 - He presented with pain in the abdomen from loin to groin region associated with 1 fever spike 3 days back subsided on taking medication. Decreased appetite since 1 month. On examination- pallor was present and splenomegaly was noted 4 cm below the left costal margin. Pt was investigated further which revealed, HB - 8.2 g/dl, Platelet count - 60,000, WBC -2,100cells/cumm. RBS - 99mg/dl, l, RFT – Normal, LFT – Normal, Serum folic acid - 3.7mg/dl (3.5-7.2), Bone marrow was hypoproliferative, erythroid hyperplasia with micronormoblastic picture, Reticulo cyte count - 0.8%, Cardiolipin Ab IgA - 1.5 u/ml(neg) (N - < 12u/ml), Cardiolipin Ab, IgG-2.0 u/ml(neg) (N - < 20 GPL U/ml), Cardiolipin Ab - IgM-2.5u/ml (neg) (N < 13MPL U/ml), Beta 2 Glycoprotein IgG Ab -0.46u/ml(neg) (N - <12u/ml), Beta 2 glycoprotein IgM ab-0.2u/ml8 (neg) (less than 12u/ml), Lupus anticoagulant - 39.50 secs (n - 39.20 secs), Factor 5 Leiden mutation – RT PCR not detected, Protein C-42% (N -70-140), Protein S - 28.3% (N - 63.5-149), USG Abdomen - showed gross splenomegaly with splenic hilar collaterals and peri gall bladder collaterals, Portal vein - periportal fibrotic changes noted in the porta hepatis with main portal vein replaced by collateral vessels Altered liver parenchymal echotexture. Bilateral renal calculi- right 2 renal calculi - largest measuring 4.2 mm noted in midpole, left measuring 3mm noted in midpole. CT Abdomen (**Figure - 3, 4**) – liver - caudate lobe hypertrophied, segments 2, 3, and 6, 7 atrophied, left upper ureteric calculus, causing upstream mild hydronephrosis is seen. Bilateral renal caculi, and gross splenomegaly was also present.

Figure – 2 (a, b, c, d. e): Upper GI Endoscopy (23rd Jan 2022).

Figure - 2(a): Oesophagus – Normal.

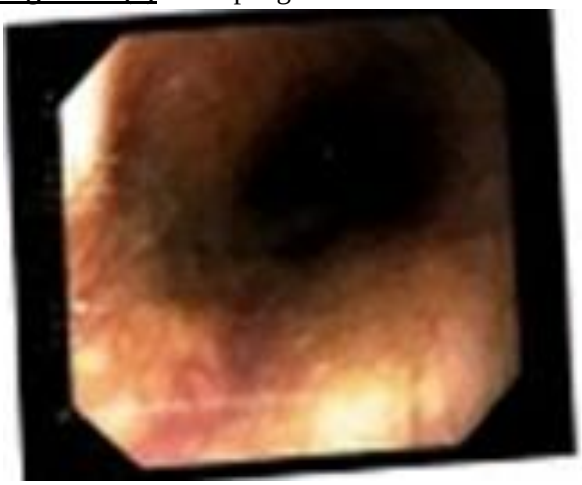


Figure - 2(b): Cardia – Post banding no residual varices.

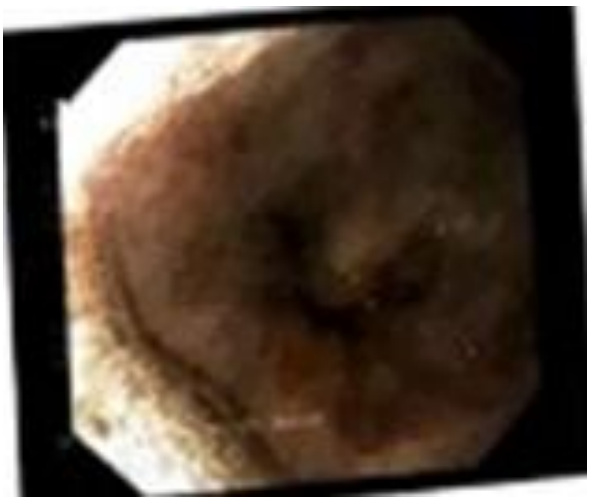


Figure - 2(c): Stomach – Normal.

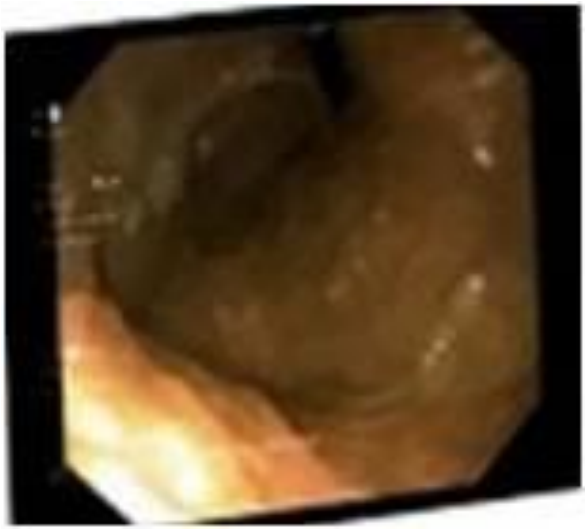


Figure - 2(d): Duodenum – Normal.

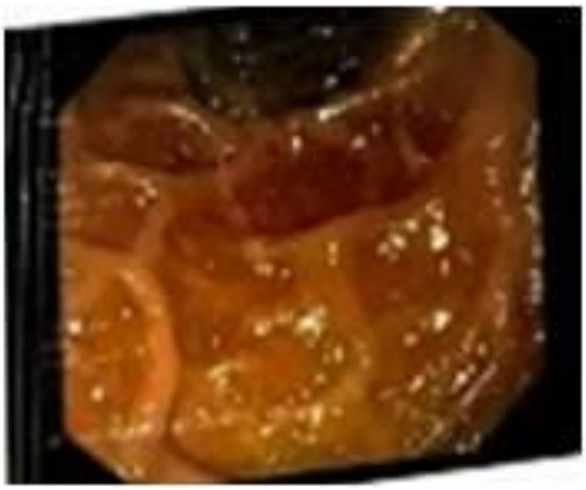


Figure - 2(e): Duodenal bulb – Normal.

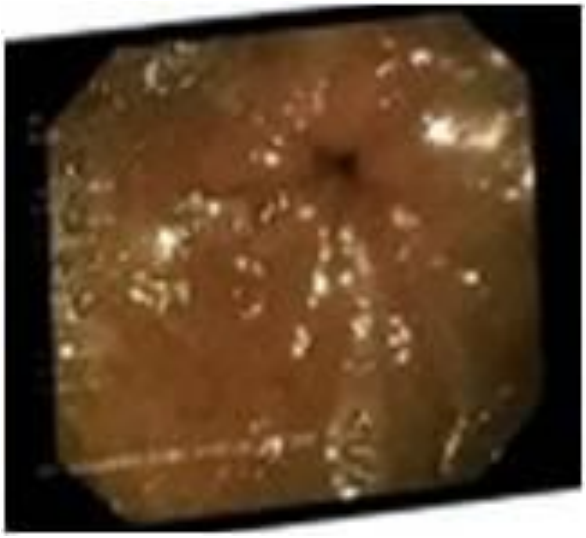


Figure – 3: CT Abdomen – liver - caudate lobe hypertrophied, segments 2,3,and 6,7 atrophied, left upper ureteric calculus,causing upstream mild hydronephrosis is seen. Bilateral renal caculi, and gross splenomegaly is also present.

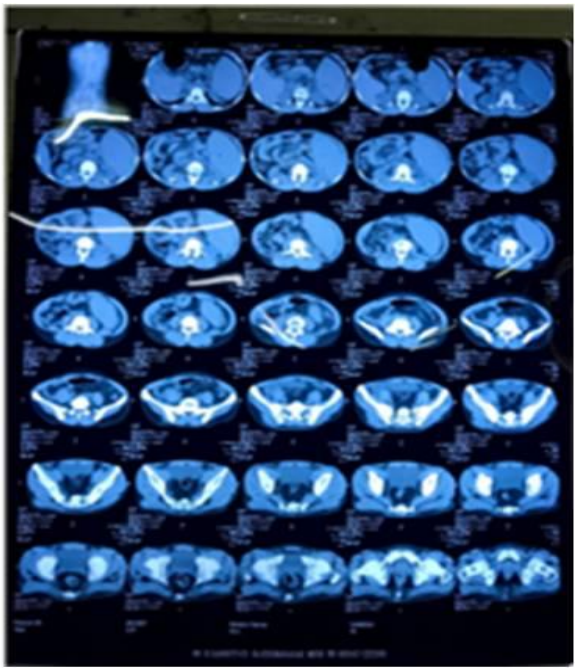
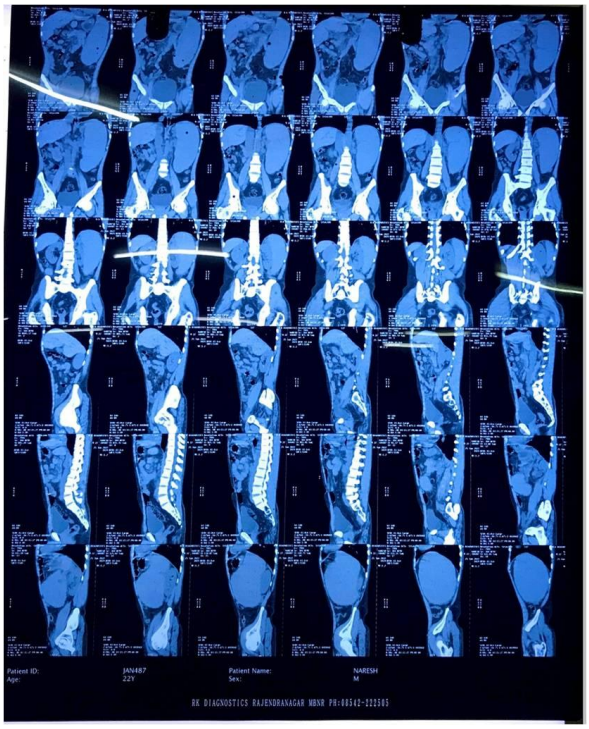


Figure – 4: CT Abdomen – liver - caudate lobe hypertrophied, segments 2, 3, and 6,7 atrophied, left upper ureteric calculus, causing upstream mild hydronephrosis is seen. Bilateral renal caculi, and gross splenomegaly is also present.



Diagnosis

Extra Hepatic Portal Vein Obstruction (EHPVO) due to combined PROTEIN 'C' and 'S' deficiency

Treatment

Injection Clexane 60 mg (low molecular weight heparin) s/c bd X two weeks followed with Tab rivaroxaban 10 mg /bd.

Discussion

PVT interrupts blood flow to the liver and causes portal hypertension [3]. Phlebothrombosis is caused by local, genetic, or acquired thrombophilic factors [57]. Local factors include local inflammatory lesions such as neonatal funiculitis, diverticulitis, appendicitis, pancreatitis, duodenal ulceration, tuberculous lymphadenitis, portal vein injury by surgical operations, thrombokinesis, pressure mass effect by an abdominal neoplasm, and portal hypertension by liver cirrhosis [57]. Denninger, et al. reported that 6% to 11% of PVT is attributed to liver cirrhosis, and 35% is related to hepatocellular carcinoma [3]. Webb, et al. reported that 40% of PVT is caused by intraperitoneal or systemic septicemia. In other reports, 7% of PVT was reported to be caused by chronic pancreatitis [58]. Primary myeloproliferative disorder, anti-phospholipid antibody syndrome, paroxysmal nocturnal hemoglobinuria, oral contraceptives, pregnancy, childbirth, malignant tumor, and hypercysteinemia are reported as acquired thrombophilic factors [5]. Genetic thrombophilic factors can be divided into the frequent type, such as factor V Leiden mutation and mutation IIG20210, in which PVT is rarely associated, and the rare type, such as protein C, S, and antithrombin III, in which PVT is more likely to occur [57].

Protein C is a thrombin-dependent anticoagulant enzyme known to deactivate coagulation cofactors V and VIa and to stimulate fibrinolysis [59]. Protein C deficiency, inherited as an autosomal dominant trait and is a risk factor for venous thrombosis. The prevalence of protein C deficiency is 1 in 200-500 persons in the general population. This number may be unreliable as many affected individuals are asymptomatic throughout their lives. However, protein C deficiency is present in 2%-5% patients presenting VTE. Severe homozygous or compound heterozygous protein C deficiency is found in 1 in 500000-750000 live births. Protein S deficiency occurs in 1.35% of the patients with venous thrombosis. There is evidence to suggest that thrombosis in unusual sites, such as cerebral sinus venous thrombosis, mesenteric vein thrombosis, PVT, and suprahepatic vein thrombosis (Budd-Chiari syndrome), in young individuals is associated with inherited thrombophilia. Liver function impairment, which can be a result of PVT, cannot account for the low C and S protein levels in our patient.

Clinically, PVT is classified as acute or chronic. But,it is difficult to identify when the symptoms begin and the temporal criteria about chronicity is not established [60]. Malkowski, et al. classified PVT as acute or chronic according to symptom onset time before admission (60 days) [60]. Acute PVT typically provokes pain abdomen, nausea, vomiting, and fever. The symptoms can be more severe if mesenteric thrombosis provokes infarction of the bowel or liver. Nonspecific symptoms such as diarrhea, anorexia, weight loss, and abdominal distention may develop [61]. The symptoms of chronic PVT are similar to the acute ones, but such symptoms may be related to portal hypertension and splenomegaly [62]. Splenomegaly, anemia, leukopenia, thrombocytopenia, and variceal bleeding can be provoked [62].

Duplex, Doppler ultrasound, and abdominal CT scan, and abdominal MRI can be used to make a accurate diagnosis of PVT in the early stages [63]. Abdominal MRI is more useful than Doppler ultrasound in identifying venous collateral development and cavernoma [63]. In patients with PVT, local factors such as liver cirrhosis and pancreatitis should be suspected. If no local factor can be identified, it is necessary to

investigate genetic or acquired thrombophilic factors [61].

Regarding the treatment of PVT, long-term anticoagulant therapy and invasive methods such as surgical thrombectomy, local thrombolytic therapy, thrombolytic agent based selective portography, and intrahepatic stent insertion via the jugular vein can be applied [62]. In many cases, chronic PVT is accompanied by gastroesophageal varix, which can result in variceal bleeding during anticoagulation therapy [61]. In acute PVT, early anticoagulant therapy prevents the spread of thrombi and promote blood reperfusion [62]. Sheen, et al. used anticoagulant therapy to 9 acute PVT patients with a target INR of 2 to 4 for 3 months and reperfusion was achieved in 78% [64]. However, there are no clear guidelines on the choice of anticoagulant drugs, the period of administration, and even the need for anticoagulant therapy [60]. In our case, we successfully treated our acute PVT patient with a 2-week subcutaneous injection of low molecular weight heparin, followed with oral anticoagulant therapy.

Conclusion

In conclusion, our case EHPVO shows that PVT can be provoked by protein C and S deficiency and that the PVT can be recanalized by short-term low molecular heparin plus oral rivaroxaban therapy. Further large studies are needed to investigate the target INR, the period of administration, and the dosage and duration for relapse prevention in treatment with oral anticoagulants.

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