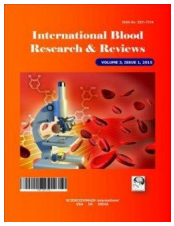

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Case Report: Portal Vein Thrombosis as a Cause of Haematemesis in a Healthy African Adolescent

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Authors' contributions

This work was carried out in collaboration between all authors who managed the patient. Author FAF designed the study and wrote the first draft of the manuscript. Author FAF managed the literature searches. Authors FAF and AA participated in revising the writing up. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: Thromboembolic incidents typically occur as deep vein thrombosis of the limbs and pulmonary embolism but can also occur in unusual sites such as cerebral or sinus, mesenteric, portal, hepatic renal and retinal veins. When thromboembolism occurs in any of these unusual sites, diagnosis is often unsuspected and missed. The relatively low incidence of thrombosis in healthy children further presents a potential diagnostic dilemma. High index of suspicion is therefore required for timely diagnosis in order to prevent complications.
Presentation of Case: We report a case of a 15 year-old girl with 10 years history of recurrent haematemesis. She was managed initially as a case of upper gastrointestinal bleeding of unknown aetiology and subsequently as a case of chronic liver disease and then later, as case of bleeding diathesis. The patient had several oesophageal variceal band ligation, courses of propranolol, omeprazole, livolin and several units of blood transfused. Abdominal ultrasound, Computed Tomographic scan of abdomen and angiography revealed portal vein thrombosis with periportal collaterals. The proteins C and S levels were low. A diagnosis of portal vein thrombosis (PVT)

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secondary to Proteins C and S deficiencies was then made. Patient has been symptom free since commencement of anticoagulation but there was no recanalization of the vessels.
Conclusion: The potential role of prothrombotic risk factors and PVT should be explored in paediatric age group with gastrointestinal bleeding for early diagnosis and management to reduce complications.

Keywords: Portal vein thrombosis; protein C; protein S; anticoagulant; children.

ABBREVIATIONS

PVT – Portal vein thrombosis.

1. INTRODUCTION

The first report of portal vein thrombosis (PVT) was in 1868 [1]. Since then there has been several reports due to greater availability of diagnostic methods. Despite this, the diagnosis is often missed in clinical practice and treatment is delayed [1]. In PVT, thrombus formation occurs in the portal vein and may extend to other branches of the portal system [2]. The involved blood vessels can be partially or totally occluded resulting in portal hypertension, organization of the thrombus and tortuous collaterals [2]. The incidence in the general population is approximately 1% [2] while it is up to 26% in some risk groups [3]. In some countries the prevalence is not well defined due its rarity and initially asymptomatic nature [4].

There are differences in etiological and clinical presentations between children and adults [1]. In adults, liver cirrhosis play a leading role, hypercoagulability and intra-abdominal inflammatory conditions are the main causes of PVT not associated with cirrhosis. In children and adolescents, the main causes are direct injury of the vein and intra-abdominal infections. The natural history of PVT may range from asymptomatic to non-specific symptoms and acute massive haematemesis. In acute PVT, abdominal pain may be marked with abrupt variceal bleeding. Symptoms abate as collaterals develop and diagnosis may be missed. Patients with chronic PVT often present with clinical features of complication such as portal hypertension. Growth retardation may occur in children [1]. Diagnosis of PVT depends on imaging-studies including Doppler ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and portography. A variety of treatment could be administered, which include anticoagulation, portal venography with infusion of streptokinase or urokinase and open surgical thrombectomy. The prognosis of PVT depends on the aetiology. However, it is much better in children than in adults because of low incidence of malignancy and cirrhosis and a 10 year survival rate of 70% in them [1]. Portal vein thrombosis is an infrequent diagnosis in children and adolescent nevertheless it is an important cause of upper gastrointestinal (UGI) bleeding in children [5]. We hereby present a case of PVT in an adolescent.

2. PRESENTATION OF CASE

A 15 year-old girl was referred to the haematology clinic with 10 years history of recurrent haematemesis. Her body mass index was 27 kg/m^2. Patient was the only child and the father was late. Patient's first episode of haematemesis was at 5 years and was associated with abdominal pain. Thereafter, haematemesis became recurrent and were managed with ranitidine and gastric lavage. At 13 years, she had the worst episode of haematemesis, associated with haematochezia and melaena for 3 days during which she received 7 units of stored blood before being referred to our hospital for further management. This patient could not undergo endoscopy prior to presentation at our centre because, all along she was being managed at a secondary health centre where there was no endoscopic facility. At presentation at our centre, she was febrile with a temperature of 38ºC. Peripheral blood film for malarial parasite was positive. Abdominal examination then revealed vague epigastric tenderness with mildly tender, soft liver and spleen, 2 and 4cm below coastal margin respectively confirmed by abdominal ultrasound. An urgent upper gastrointestinal (GI) endoscopy revealed multiple bleeding oesophageal varices occupying the entire diameter of the oesophagus. Diagnosis then was upper gastrointestinal bleeding (UGIB) from oesophageal varices secondary to portal hypertension probably due to chronic liver disease. She was managed with rabeprazole and mist magnesium trisilicate. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were 14 and 40 seconds for the patient with

control result of 13 and 33 seconds respectively. The PT, INR was 1.1. Full blood count (FBC) revealed anaemia with haematocrit (hct) of 32% and platelet count of 55,000/mm3. Liver function test (LFT) result was: Total Bilirubin , 0.1mg/100ml; Conjugated bilirubin, 0.05/mg/100ml; Total protein, 7.9g/100ml; Albumin, 3.7/g/100ml; SGOT, 23u/L; SGPT, 20/u/L; ALP, 68u/L; blood urea, creatinine and electrolytes were within normal range. Oesophageal variceal band ligation was performed and platelet concentrate was transfused. She was also placed on propranolol for secondary prophylaxis. After discharge from hospital admission, FBC at follow up clinic showed hct of 44%, platelet count was 320 x 10^9/l, LFT, was normal, PT and aPTT results showed that PT,INR was 0.96 (test -13sec control 13.5), APTT (test,27 sec control,33sec). Screening for HIV, hepatitis B and C viruses were negative. Request for liver biopsy was declined. Hepatic venous pressure gradient was not done.

Because the abdominal ultrasound done did not reveal much information about the portal system, CT angiography of the portal vein was requested for as a secondary diagnostic test at 15 years during an episode of haematemesis, revealed intraluminal clots in the portal vein with its intrahepatic branches and portal hepatis as well as tortuosity of vessels in the region of the porta hepatis consistent with periportal collaterals (Fig. 1). Other test results were PC; 56% (70-140%), PS; 49% (60-140%) while antithrombin, homocysteine and fasting lipid profile were normal. Based on this, a diagnosis of portal vein thrombosis secondary to proteins C and S deficiencies was made and she was commenced on subcutaneous clexane which was later changed to dabigatran. So, our diagnosis was based on the finding of clots in the portal vein on angiography which was probably secondary to the deficiency of proteins C and S. This diagnosis is a form of non-cirrhotic portal hypertension because, the liver in this patient was normal. Abdominal Ultrasound after one year of dabigatran showed overall appearance in keeping with chronic portal vein thrombosis with development of collaterals at the portal hepatis (Fig. 2).

Follow up endoscopy showed post oesophageal variceal ligation scars. Patient has not had any episode of haematemesis since the commencement of anticoagulation. Surgical modalities of treating this condition include splenectomy, splenic artery ligation and azygoportal disconnection. But, none of these was offered to the index patient since she has responded to the medical treatment offered so far.

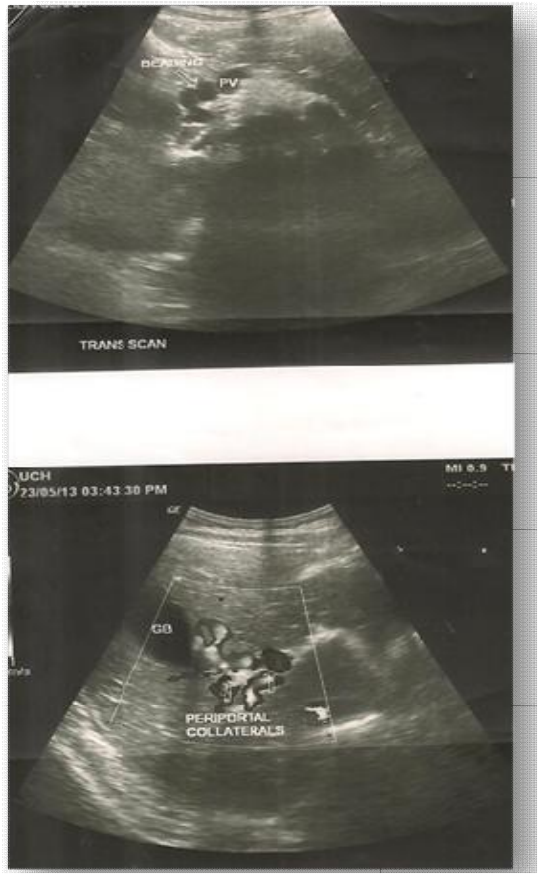

Fig. 1. Abdominal ultrasound report before anticoagulation

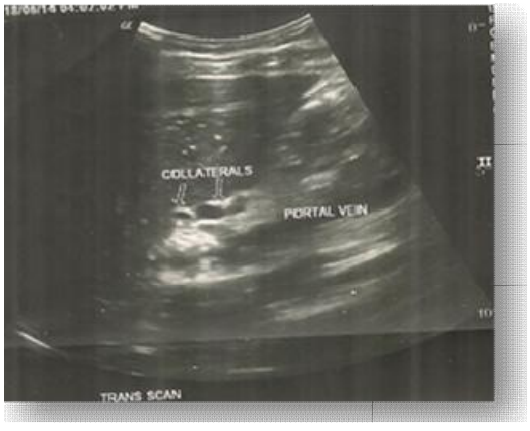

Fig. 2. Abdominal ultrasound report one year after anticoagulation

3. DISCUSSION

Thromboembolic disorder is uncommon in children and adolescent (0-18 years) [6]. This is because of age related reduction in thrombin generation and increased ability to inhibit thrombin [7]. Unlike in adults, the diagnosis of both spontaneous and risk related thromboembolic complications such as portal vein thrombosis is rare. When thromboembolic event occurs, it is often seen in hospitalized sick children with cancer, prolonged immobilization, cardiovascular surgery and venous cather insertion [8]. The observation of a thromboembolic event, diagnosed as portal vein thrombosis in our patient who was healthy is unusual. Protein C (PC) and protein S (PS) are natural anticoagulants that regulate the coagulation cascade through the selective inactivation of Factors Va and VIIIa. The principal mode of presentation of patients deficient in proteins C and S is with deep vein thrombosis and pulmonary embolism [9]. Portal vein thrombosis (PVT) as seen in our patient is uncommon. More so, this is an infrequent diagnosis in children and adolescent hence, the reason for delayed diagnosis in our patient. When acute portal vein thrombosis goes unrecognized, symptoms resolve and collateral vessels develop to progress to portal hypertension with varices which is not a desirable outcome. Clinical diagnosis is challenging due to the non-specific nature of its signs and symptoms [10]. Even though, doppler ultrasound is considered to be effective as first line diagnostic test, this was not so in our patient in whom the first doppler ultrasound performed at the age of 13 years did not detect portal vein thrombosis. This might be because the sensitivity and specificity of the test are dependent on the expertise of attending radiologist. Also, the presence of a detectable flow through a partially occluded portal vein may contribute to misdiagnosis [1].

Another source of confusion was the thrombocytopenia at presentation which was probably due to haemodilution as result of multiple blood transfusions she received or as a result of platelet consumption due to the thrombosis [10,11]. The presence of splenomegaly at the time of thrombosis might have also contributed to the thrombocytopenia [1,6]. The low suspicion of PVT in our patient could also be explained by the scarcity of reports and rarity of this condition, particularly in an African population. There is no doubt a high index of suspicion for thromboembolism is required for timely diagnosis. Bleeding oesophageal varices due to PVT in the absence of liver disease is rare with a different clinical course and management strategy [10]. A differential diagnosis to consider in this patient is noncirrhotic portal hypertension (NCPH)/idiopathic portal hypertension (IPH) which is common in developing countries. The aetiopathogenesis of NCPH/IPH includes infections, immunological abnormalities, exposure to arsenic and drugs [12]. Patients with IPH have been reported to have higher incidence of protein C and S deficiencies or factor V Leiden mutations Similar to our patient, the patients with IPH often present with more than one episode of well tolerated haematemesis but in contrast to our patient, massive splenomegaly with anemia is characteristic in IPH [12]. The association of abdominal pain with the sudden onset of upper gastrointestinal bleeding and negative viral serology may further support the diagnosis of PVT. The clinical feature of PVT could be ill-defined [11] hence, the diagnostic dilemma and eventual detection of portal vein thrombosis with low levels of PC and PS after several years of haematemesis in the index case. The age of our patient and duration of symptoms are suggestive of inherited rather than acquired aetiology of PC /PS deficiencies particularly as the LFT were normal [13]. However, the inherited aetiology could not be substantiated because family study was not carried out. But, it appears the patient had recurrent acute thrombosis on a chronic portal vein thrombosis. Acquired deficiencies of these proteins can occur with oral anticoagulants, liver disease, renal disease, disseminated intravascular coagulopathy, pregnancy and certain hormonal therapy [14]. These conditions were not evident from the clinical and laboratory findings in our patient. Hereditary thrombophilia contribute substantially to the development of VTE in the young particularly when the VTE is unprovoked [14] besides coinheritance of prothrombotic factors is not uncommon [13] and this increases the risk of primary VTE considerably. Therefore, combined deficiency of both PC and PS might be responsible for the early presentation as well as the severe symptoms observed in our patient [13,15,].

Reports on combined deficiency of PC and PS resulting in portal hypertension from PVT are few and in non-Africans [16,17]. Pooled prevalence of PC deficiency in portal vein thrombosis is 5.6% while that of PS is 2.6% [18]. The risk of

recurrent VTE in children is highest in those with combined prothrombotic risk factors [19] as demonstrated in our patient by the recurrent haematemesis. The implication of this risk of recurrent thrombosis is that she will require lifelong anticoagulation. This patient was probably having acute on chronic PVT given the clinical presentation.

Rate of recanalization is poor if anticoagulant is not instituted early as observed in our patient [20]. Therapeutic options in chronic PVT are controversial and vary significantly. These include endotherapy (endoscopic band ligation or sclerotherapy) and shunt surgery [21]. Splenectomy could also be performed. Patients with chronic portal vein thrombosis with ongoing thrombotic risk factors will require treatment with long-term anticoagulation [22,3].Early diagnosis is paramount, because early treatment could encourage recanalization. Also most of the pathological changes of PVT are irreversible and prophylactic measures would minimize the risk of complications such as hepatic dysfunction and ascites.

4. CONCLUSION

This case represents an unusual scenario of recurrent haematemsis from childhood to adolescence due to portal vein thrombosis and protein C and S deficiencies in an adolescent. It also illustrates one of the consequences of delayed diagnosis and institution of anticoagulant. This report is aimed to increase physician's index of suspicioon of the potential role of prothrombotic factors in the aetiology of portal vein thrombosis in children and adolescent patients with upper GIT bleeding particularly when it becomes recurrent. It should be considered in clinical practice for early intervention.

CONSENT

Consent was obtained from patient and mother for publication of this case report.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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