

## NONCIRRHOTIC PORTAL HYPERTENSION – A CASE REPORT ON A SEQUELA OF PORTAL VEIN CAVERNOMA

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### Abstract

**Introduction:** Increased pressures in the portal vein (portal hypertension) which occurs following portal vein thrombosis, results in cavernous transformation of the portal vein. Though portal vein thrombosis (PVT) is a frequent complication in cirrhotic patients, it may also exist as a basic vascular condition without any liver damage. Among the predisposing factors for portal vein cavernoma are deficiencies in protein C, S & antithrombin III, antiphospholipid syndrome and mutations in factor V Leiden and JAK2. Determination of the aetiology aids in the management plan to not only relieve symptoms of the patient but also to treat the underlying cause. Gastroesophageal variceal bleeding, splenomegaly, portosystemic collaterals, and ultimately hematologic abnormalities are among the prominent clinical features.

**Case Presentation:** We present a case of a 16-year-old

male with portal vein cavernoma complicated by bleeding oesophageal varices presenting with a second episode of hematemesis and melena within a 10-year period. He underwent endoscopic variceal band ligation and was put on oral warfarin and propranolol. The patient was followed up once at the outpatient clinic after discharge without the laboratory investigations we requested due to financial constraints. He has since been lost to follow up.

**Conclusion:** Bleeding oesophageal varices from noncirrhotic causes are common and a high index of suspicion is needed to make a diagnosis. Though investigations tailored towards identifying the underlying cause presents a challenge in a resource constrained setting like ours, management of complications and symptoms to reduce morbidity and mortality cannot be over-emphasized.

**Keywords:** Portal vein cavernoma, endoscopic variceal band ligation, esophagogastroduodenoscopy, anticoagulant

### Introduction

Portal vein thrombosis (PVT) is an obstruction of the portal vein by a thrombus.<sup>1</sup> This leads to the creation of multiple collaterals to bypass this obstruction. Clinically, PVT may be acute or chronic, though symptoms and signs are different, one remains a sequela of the other.<sup>2</sup>

Local and systemic pathogenetic factors have been identified as possible causes of PVT. Infections (commonly umbilical cord sepsis), toxins, immunologic & prothrombotic tendencies, genetic disorders (low levels of protein C, protein S, and anti-thrombin III, increased VIII endothelial factor) are possible causes of portal vein thrombosis.<sup>3</sup> Prothrombotic<sup>4</sup> and local factors around the portal vein may lead to extrahepatic portal vein obstruction and thus portal hypertension.<sup>5</sup> PVT may be associated with liver cirrhosis but it can also be the result of other disorders, such as inherited thrombocytopaenia, malignancies, abdominal infections, or bowel diseases.<sup>6</sup>

Presentation of portal vein cavernoma varies from asymptomatic, yellowing of the sclera, abdominal mass, abdominal distension, recurrent torrential hematemesis

and consequently symptoms of anaemia (dizziness, easy fatigue, palpitations).

Ultrasound is the initial screening modality in investigating PVT.<sup>7</sup> The absence of portal vein with presence of cavernoma formation which is seen as multiple tubular anechoic structures surrounding the porta to non-visualization of portal vein is diagnostic. However, colour doppler is considered superior as it demonstrate periportal collaterals, a recently formed anechoic thrombus and or reduced or absence of flow in the portal vein.<sup>8</sup> CT scan clearly depicts the cavernous transformation of the portal vein, presence of the intra and extrahepatic portions of the parabiliary and peribiliary plexuses, and gallbladder varices. Though not preferred because of radiation exposure, CT is also useful in providing additional information about the cause of portal vein obstruction and excluding neoplastic causes such as tumoral thrombosis.<sup>9</sup> MRI has replaced direct cholangiography as the imaging investigation of choice for PVC with direct cholangiography being reserved for interventional purposes.<sup>8</sup>

Patients with portal cavernoma usually present with upper gastrointestinal haemorrhage, a complication of the disease process. This requires emergency resuscitation with intravenous fluids (crystalloids and or colloids), intravenous octreotide<sup>10</sup> and gram negative intravenous antibiotic cover. Once haemodynamically stable, an upper GI endoscopy is performed to confirm the presence of oesophageal varices and ligate them. The

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ASGE and ESGE guidelines recommend the use of the Glasgow Blatchford score<sup>11</sup>, pre-endoscopic Rockall score<sup>12</sup> or AIMS-65 score to prognosticate each patient. Preferably, all cases should have an oesophogastroduodenoscopy (OGD) done within 24 hours of admission to the emergency room, where either endoscopic sclerotherapy (EST) or endoscopic variceal band ligation (EVL) is performed.<sup>13</sup> Nonselective beta-blockers are used for secondary prophylaxis to reduce hepatic venous portal gradient by inducing splanchnic vasoconstriction and reducing cardiac output. Multiple systematic reviews and meta-analyses state that carvedilol is more effective in decreasing hepatic venous pressure than propranolol with fewer side effects.<sup>14</sup>

Anticoagulation initiation with unfractionated heparin or low molecular weight heparin (LMWH) is recommended for patients with portal vein cavernoma. This is followed by maintenance of anticoagulation with either LMWH or the vitamin K antagonist, warfarin, is the treatment of choice.<sup>7</sup> The use of direct oral anticoagulants (DOACs) has also proven to be a promising alternative to traditional anticoagulants in patients with PVT with or without cirrhosis. However, there is the need for further randomized controlled trials in this area.<sup>15</sup> Transjugular intrahepatic porto-systemic shunt (TIPSS) is considered for patients with variceal bleeding that cannot be controlled by medical and endoscopic treatment.<sup>16</sup>

### Cases Presentation

We report the case of a 16-year-old male who was referred to the emergency unit of the Eastern Regional Hospital as a case of anaemia secondary to upper gastrointestinal bleeding. He presented to the referral site with a second episode of haematemesis and melaena. The patient was resuscitated at the referring hospital and then sent to the Eastern Regional Hospital for further management. At presentation, he was symptomatic of anaemia (easy fatigability, palpitations) and complained of nonspecific abdominal pain but no jaundice. This was his second episode of haematemesis; the first had occurred 10 years prior. Following the first episode, OGD was performed, but neither he nor his relatives remember the findings. He did not have sickle cell disease, neither was he diabetic nor hypertensive. He had no history of umbilical cord sepsis or childhood exchange transfusion.

At the emergency unit, the patient was alert and not in distress. There was moderate conjunctival pallor, no icterus, and his temperature was 36.5°C. Physical examination revealed a flat abdomen, no caput medusae. His liver span was normal (10cm) with massive splenomegaly (11cm) below the left costal margin. Both kidneys were not ballotable. Examination of other systems were essentially normal with BP 101/50mmHg and pulse 100bpm. These signs raised a high suspicion for bleeding oesophageal varices from non-cirrhotic portal hypertension. For laboratory investigations haemoglobin was 7.6g/dL<sup>-1</sup>; MCV 76.5fL MCH 26.7

HCT 45; Platelets 52x10<sup>9</sup>, white cell count and its differentials were all normal. Likewise renal function test, liver panel and clotting profile was also all normal. The HB electrophoresis of our patient is AS and G6PD test showed no defect. An abdominopelvic ultrasound scan revealed non-visualization of portal vein with multiple periportal collaterals and massive splenomegaly which is suggestive of cavernous transformation of portal vein was seen on abdominal ultrasound. Both Pre-endoscopic Rockall score and AIMS-65 score were 0 pts which means 0.2% mortality risk and 0.3% in-hospital mortality respectively. However, his Glasgow-Blatchford score was 8 pts which placed him at a high risk of GI bleed.

He was transfused with a unit of packed cells and an upper gastrointestinal endoscopy was performed. Multiple columns of grade III oesophageal varices were seen and 8 bands were deployed to ligate these varices with a recommendation of repeat band ligation in 6 weeks. Liver biopsy has long been regarded as the gold standard to diagnose cirrhosis. However, there exists the problem of sampling error and interobserver variability. Cirrhosis can still be diagnosed in the absence of liver biopsy. An APRI score of greater than 2 strongly suggests cirrhosis. As does a Bonacini cirrhosis discriminant score of greater than 7. In the case of our patient, his APRI score was 1.4, and his Bonacini discriminant score was 6. Coupled with this was the ultrasound findings that did not suggest cirrhotic changes. The patient and his relatives were thus, counselled on the condition and need to do the requested laboratory investigations which included antithrombin III, protein C and protein S deficiencies, mutations in JAK2 and factor V Leiden however they could not do them due to financial constraints. He was put on anticoagulation therapy with a possible surgical intervention (Transjugular intrahepatic portosystemic shunt) if need be. With an initial INR of 1.2, he was started on propranolol, warfarin 2mg, ferrous iron haematinics on day 5 of admission and discharged home to see the gastroenterologist for review with a repeat international normalized ratio.

### Discussion

Portal hypertension is not always from a hepatic pathology but can also be from non-cirrhotic causes which are often underdiagnosed.<sup>7</sup> Neonatal events (prematurity) have been implicated as a cause of PVT. This is similar to what was found in Egyptian children but contrary to our case, he had no known perinatal attributable risk factors.<sup>17</sup> Splenomegaly followed by thrombocytopenia, hepatomegaly and sarcopenia are the most common features.<sup>7</sup> We similarly identified thrombocytopenia and massive splenomegaly in our patient. Upper gastrointestinal bleeding is one of the commonest presentations of portal hypertension. It may spontaneously stop but rebleeding is common as was seen in our patient.<sup>18</sup> Emergency resuscitation with intravenous fluids and vasoactive agents should be

instituted to raise the haemoglobin while monitoring vital signs closely. Excessive resuscitation should be avoided because of the risk of rebound portal hypertension and rebleeding.<sup>19</sup> Whilst correcting anaemia, an attempt to control bleeding is instituted pharmacologically and endoscopically. Pharmacological agents such as somatostatin analogues help to reduce bleeding by reducing splanchnic blood flow.<sup>20</sup> The use of tranexamic acid, which acts by inhibiting fibrinolysis by inhibiting the action of plasmin, in acute gastrointestinal bleeding has shown not to reduce mortality but is rather linked with unwanted blood clots and seizures.<sup>21</sup> To prevent bacterial translocation across the gut wall, patients with suspected or confirmed variceal bleeding may be placed on prophylactic gram negative antibiotic treatment<sup>22</sup> however, antibiotics were not administered to our patient. As soon as our patient was haemodynamically stable, we performed an upper gastrointestinal endoscopy to confirm our suspicion of variceal bleeding and ligate oesophageal varices. Besides variceal band ligation, endoscopic sclerotherapy with ethanol can be used albeit an inferior option.<sup>23</sup>

Post endoscopy, our patient was counselled on his diagnosis and put on a nonselective beta-blocker to reduce hepatic venous pressure gradient by decreasing cardiac output (beta1-receptor antagonism) and inducing splanchnic vasoconstriction (beta 2- receptor antagonism). The expected aim would be reduction in the portal pressures.<sup>24</sup> Other patients have received carvedilol and it was found to be more efficient in decreasing hepatic portal vein pressure gradient with less drug adverse effects.<sup>14</sup> He was also put on warfarin to prevent further thrombi from developing in the future while the specific cause of his diagnosis is investigated.<sup>15</sup> Several mandatory labs like mutations in factor V Leiden and JAK2 that are required for investigating portal cavernoma are unavailable in Ghana others deficiencies in protein C,S and antithrombin III which were initially being run at the time of patient presenting were not being run in Ghana. However, patients' samples are often sent to South Africa, at a high cost to the patient.

## Conclusions

Bleeding oesophageal varices secondary to portal hypertension from either cirrhotic causes or otherwise is not uncommon however there presents a challenge in investigating and diagnosing noncirrhotic causes like PVT in resource constrained setting. That notwithstanding managing complications and symptoms should be done to reduce morbidity and mortality.

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