Outcome of Extrahepatic Portal Vein Obstruction in Children

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Abstract

Background: Extrahepatic portal vein obstruction (EHP-VO) developing due to thrombotic occlusion of the portal vein in children is generally a benign disease. The aim of this retrospective study was to describe clinical presentation, risk factors, complications and treatment in children with EHPVO presented to the Pediatric Hepatology Unit, Cairo University Children’s Hospital, Egypt.

Materials and Methods: The medical records of 145 children (89 male, median age 10 years, range 7 months -18 years) presenting with EHPVO between 1988 and 2008 were reviewed retrospectively.

Results: Clinical presentation included bleeding in 59% and splenomegaly in 100%. Prolonged prothrombin time was seen in 26% and elevated liver enzymes in 6%. On first endoscopy, oesophageal varices were present in 131 (90%) patients; of those subjects, 101 (77%) received sclerotherapy, 7 (5.3%) had band ligation and 14 (10.6%) received both. Thrombophilia investigation was performed in 40 patients revealed: factor V Leiden mutation in 12, protein C deficiency in 11, factor II mutation in 6 and antithrombin III deficiency in 1 patient. Liver biopsies were performed in 6 patients and revealed mixed portal cirrhosis in two and chronic hepatitis with minimal fibrosis in four patients.

Conclusion: The aetiology of EHPVO in the majority of these children is unknown. The overall prognosis is good. Sclerotherapy and banding are effective treatments for bleeding varices with good long term outcome. Prophylactic beta-blocker decreased the risk of esophageal bleeding.


Introduction

EXTRAHEPATIC portal vein obstruction (EHP-VO) is a vascular disorder of the liver and is defined as obstruction of the extrahepatic portal vein with or without involvement of the intrahepatic portal veins or splenic or superior mesenteric veins. In children EHPVO is an important cause of portal hypertension. It is usually an isolated condition and only is recognized when the child develop symptoms [1].

Asymptomatic cases may be easily overlooked. Gastrointestinal bleeding and an abdominal mass caused by splenomegaly are the most prominent symptoms and signs. Approximately 79% of children with EHPVO will have at least one episode of upper gastrointestinal bleeding in their lifetime [2].

The precise aetiology of the development of EHPVO in the majority of these children is unknown. The predisposing factors are believed to be the following: condition that directly injure the vessel, rare portal vein congenital anomalies, and a group of systemic causes such as neonatal sepsis, abdominal sepsis, dehydration, multiple exchange transfusions, and hypercoagulable states [3].

The aim of this retrospective study was to describe clinical presentation, risk factors, complications and treatment in children with EHPVO in the Pediatric Hepatology unit, Cairo University Pediatric Hospital.

Materials and Methods

The medical records of 145 patients with EHPVO presenting between 1988 and 2008 to the Pediatric Hepatology unit, Cairo University Pediatric Hospital, Egypt; were examined retrospectively. The diagnosis was based on the following:

1- Clinical suspicion of prehepatic portal hypertension by the presence of splenomegaly and/or hematemesis in the absence of hepatomegaly and clinical signs of liver disease.

2- Presence of gastroesophageal varices on upper gastrointestinal endoscopy.
3- Ultrasonographic detection of portal vein obstruction confirmed by Doppler study.
4- Normal liver by ultrasound examination.
5- Normal biochemical liver function tests.
6- Absence of histological abnormalities on liver biopsy examination (when done).

Data collected from each chart included: date of birth, sex, date of onset, date of referral, risk factors (umbilical catheterization, umbilical sepsis, abdominal surgery, severe gastroenteritis and dehydration); symptoms (gastrointestinal bleeding, jaundice, fever, abdominal distension); family history (similar condition, parental consanguinity); and clinical examination (hepatomegaly, splenomegaly, pallor, jaundice, ascites, lower limb edema, visible abdominal veins).

Thrombophilia investigation was performed for 40/145 (27.5%) patients in addition to 20 age and sex-matched controls. Protein C and antithrombin III were determined chromogenically. Activated protein C resistance and protein S were measured using a commercially available kit. Molecular study of factor V Leiden mutation and factor II mutation were carried out using polymerase chain reaction technique.

Therapy consisted of propranolol (1mg/kg/day orally, twice a day) for decreasing the portal pressure. Management of bleeding varices included hemodynamic stabilization (fluid resuscitation; blood transfusion [if hemoglobin <9g/dl] and continuous octreotide infusion [1 μg/kg/hour]); endoscopic sclerotherapy and endoscopic variceal ligation. Oesophageal gastroduodenoscopy was performed with sclerotherapy and/or ligation until variceal obliteration was achieved. Patients were regularly examined every 3-6 months or when active bleeding occurred.

Statistical methods: Data were entered into SPSS version 11 (SPSS, Chicago, IL) and descriptive analysis was made. Results are presented as median (range).

Results

The median age of the first symptom was 3 years (1 month-12 years). Eighty-nine (61%) were males and the median age at diagnosis was 10 years (7 months-18 years) and the median age of the female patients was 11 years (1.3-18 years). Eighty-six patients (59%) their first presentation was hematemesis and/or melena; in which fifty-six of them were 5 years old or younger with a median age of 2 years (1 month-5 years). Six patients (4%) had a second bled and six had bled for the first time during the follow-up. Fifty three (36%) did not experience gastrointestinal bleeding during their follow-up. Fifty-four patients (37.2%) presented with abdominal distension due to splenomegaly.

The demographic profile of patients is shown in Table (1) and laboratory indices in Table (2).

In the majority of patients the etiology of EH-PVO was obscure. The etiology of portal vein thrombosis was possibly due to neonatal sepsis in seven patients (4.8%) and umbilical vein catheterization in nine patients (6%).

During follow-up, nine patients (6%) had elevated both ALT and AST, thirty-eight patients (26%) had prothrombin concentration less than 75%, serum albumin was low in 3 patients (2%), and platelets counts less than 150 (10 9/L) in 73 patients (50%). Sixteen patients (11%) had splenectomy due hypersplenism.

Thrombophilia investigation was performed in 40/145 patients. Twenty five had detectable hereditary thrombophilia (62.5%), 12 had factor V Leiden mutation (30%), 11 had protein C deficiency (27.5%), 6 had factor II mutation (15%), 1 had antithrombin III deficiency (2.5%) and none had protein S deficiency. Five children had concurrence of more than one defect. Factor V Leiden mutation was the most common hereditary thrombophilia associated with portal vein thrombosis (PVT) and the relative risk of factor V Leiden mutation, as a cause of PVT, was six times more than in controls.

Liver biopsy was performed in six patients. Four of them demonstrated chronic hepatitis with mild activity and minimal fibrosis and two patients had mixed portal cirrhosis.

Endoscopy was performed in all expect four patients. Oesophageal varices were present in 131/141(93%) patients with fundal extension in 31 (22%). Of these patients 101 received sclerotherapy, 7 were banded and 14 had both. Complications of sclerotherapy were seen in 17 (17%) patients in the form of stricture in 4, hypertensive gastropathy in 10 and both in 3. At the time of the study, eradication of oesophageal varices was achieved in 60 patients. A median of 2 (1-5) sclerotherapy sessions with or without banding was required to eradicate the varices. For decreasing portal pressure, all patients received beta-blocker (propranolol) 1mg/kg/day.
Table (1): Demographic and clinical profile of the patients at presentation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>89/145 (61)</td>
</tr>
<tr>
<td>Presentation</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Hematemesis</td>
<td>41/145 (28)</td>
</tr>
<tr>
<td>Melena</td>
<td>4/145 (2.7)</td>
</tr>
<tr>
<td>Hematemesis &amp; melena</td>
<td>41/145 (28)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>54/145 (37)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5/145 (3.4)</td>
</tr>
<tr>
<td>Physical examination</td>
<td></td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>145/145 (100)</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>0</td>
</tr>
<tr>
<td>Ascites</td>
<td>0</td>
</tr>
<tr>
<td>Upper endoscopy</td>
<td></td>
</tr>
<tr>
<td>Esophageal varices</td>
<td>131/141 (93)</td>
</tr>
<tr>
<td>Fundal extension</td>
<td>31/141 (22)</td>
</tr>
</tbody>
</table>

Table (2): Laboratory data.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (IU/L)</td>
<td>29 (10-218)</td>
<td>139</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>38 (12-207)</td>
<td>139</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.8 (1.4-6.5)</td>
<td>95</td>
</tr>
<tr>
<td>PC %</td>
<td>85 (37-100)</td>
<td>125</td>
</tr>
<tr>
<td>Haemoglobin g/L</td>
<td>10.3 (4.8-15)</td>
<td>144</td>
</tr>
<tr>
<td>Platelets 10^9/L</td>
<td>146.5 (50-582)</td>
<td>144</td>
</tr>
</tbody>
</table>

Data presented as median (range).
ALT (alanine aminotransferase); normal value (5-46 IU/L).
AST (aspartate aminotransferase); normal value (5-46 IU/L).

Discussion

The result of the present study support earlier publications in that the cause of EHPVO in the majority of patients remains unknown [4]. In neonates, EHPVO most commonly occurs following umbilical vein catheterization, with or without concurrent infection [8]. Umbilical vein catheterization and neonatal sepsis were noted as possible causes of EHPVO in a small number of children in the present series.

Tests of liver function are generally within the normal range in patients with EHPVO. In our study, biochemical features of hepatic dysfunction in the form of prolonged prothrombin time, low serum albumin, raised ALT and AST levels were evident in a small percentage of patients. In EHPVO, hepatic dysfunction could be due to prolonged reduction in portal blood flow and/or development of portal biliopathy which raised the possibility that idiopathic EHPVO of childhood could be a progressive disease [6].

In our study, factor V Leiden mutation was the most common hereditary thrombophilia associated with PVT. Factor V Leiden mutation, which is the most prevalent of the heritable thrombophilias, increased the relative risk of venous thrombosis in adults by 4 to 6 fold [7,8]. Although its association with hepatic vein thrombosis has been described, its association with EHPVO is questionable [6,9]. Inherited deficiencies of proteins C and S and antithrombin III increase the risk of venous thrombosis, but they occur at a lower incidence than factor V Leiden [10].

Outcome of patients with EHPVO depends on the control of gastrointestinal bleeding from varices. Sclerotherapy has emerged as an effective and safe treatment for oesophageal varices both in adults and children [11]. The results of our study show that sclerotherapy is an effective and safe treatment for oesophageal varices in children. Although the majority of patients had varices on admission, about 60% were free of varices at the time of follow-up. In 2006, Itha and Yachha 12, reported that among 183 had sclerotherapy, 89% achieved oesophageal varices eradication. The overall prognosis of EHPVO is good, and mortality has been reported at less than 10%. Mortality is mostly related to underlying diseases.

Treatment with beta-blockers has been reported to be effective for variceal bleeding especially if it is started before the first bleeding episode [13]. Fifty three of the fifty nine (90%) in our patients with primary prophylaxis did not experience gastrointestinal bleeding during their follow-up. This is in accordance with Gürakan et al. [14] and Abd El-hamid et al. [15].

In the present study all patients had splenomegaly at their initial presentation. During follow-up sixteen patients had splenectomy due to hypersplenism. Splenomegaly is the second most common initial manifestation of EHPVO and eventually develops in almost all patients. Mild hypersplenism as manifested by thrombocytopenia, and leukopenia is seen in 40 to 80% of patients and raises the issue of splenectomy, even prior to variceal bleeding. Hypersplenism is rarely severe enough to require specific treatment. Only patients with spontaneous ecchymosis or bleeding or severe anemia requiring blood transfusions, require treatment for hypersplenism [16].

The liver histology could be studied in 6 of 145 (4%) patients, only two patients had cirrhosis and four had chronic hepatitis with minimal fibrosis. Rangari, et al. [6], reported that none of their
patients with EHPVO showed features of cirrhotic liver and in a series studied by Gurakan et al. [14], only one patient had minimal hepatic fibrosis.

In conclusion, the overall prognosis of patients with EHPVO in the absence of cirrhosis is good. Although it is mostly manifested with gastrointestinal bleeding, it can be managed successfully with endoscopic sclerotherapy and lately with banding without bleeding related mortality. The aetiology of EHPVO in the majority of patients remains unknown.

References