HEPATOLOGY

Congenital veno-venous malformations of the liver: Widely variable clinical presentations

Peter Witters,*† Geert Maleux,‡ Christophe George,¹ Marion Delcroix,§ Ilse Hoffman,¹ Marc Gewillig,¹ Chris Verslype,*§ Diethard Monbaliu,*** Raymond Aerts,** Jacques Pirenne,** Werner Van Steenbergen,§ Frederik Nevens,*§ Johan Fevery*§ and David Cassiman*§

*Laboratory of Hepatology, Catholic University of Leuven, Leuven, and Departments of †Paediatrics, ‡Radiology, §Hepatology, ¶Pulmonology and **Transplantation Surgery, University Hospital Gasthuisberg, University of Leuven, Leuven, Belgium

Abstract

Background and Aim: Congenital portosystemic veno-venous malformations are rare abnormalities that often remain undiagnosed. Typically they are classified by their anatomical characteristics according to Morgan (extrahepatic, Abernethy malformations type Ia,b and II) and Park (intrahepatic, types 1–4). However, their clinical presentation is less dependent on the anatomical type.

Method: We reviewed the clinical characteristics of six cases drawn from our files (from 1970 to 2006).

Results: One patient, a 25-year-old male, had extrahepatic shunting whereby the liver receives only arterial blood because the portal vein (PV) connects with the inferior caval vein (ICV) (Abernethy Ib); he presented with episodes of jaundice and pruritus. Three patients had extrahepatic shunting with patent intrahepatic portal veins, but with shunting of splenomesenterial blood towards the ICV (Abernethy II); these included a 66-year-old male with hepatic encephalopathy, a 17-year-old female with (porto-)pulmonary hypertension without portal hypertension, and a 33-year-old female with episodes of acute pain secondary to spontaneous bleeding within a primary liver tumor. Two patients had intrahepatic shunting; these included an 8-year-old boy who was diagnosed incidentally during work-up for abnormal liver enzymes with a communication between right PV and ICV (Park type 1), and a 59-year-old male with multiple PV-ICV–shunts in several liver segments (Park, type 4) who presented with hepatic encephalopathy.

Conclusion: Patients often present with signs of hepatic shunting (encephalopathy, pulmonary hypertension, hepatopulmonary syndrome, and/or hypoglycemia) with relative sparing of the synthetic liver function in the absence of portal hypertension. Some shunts present with space-occupying lesions (focal nodular hyperplasia, hepatocellular carcinoma, nodular regenerative hyperplasia, etc.) or biliary atresia. Finally, some cases are detected incidentally.

Key words
congenital extrahepatic portosystemic shunt, congenital intrahepatic portosystemic shunt, encephalopathy, portocaval, veno-venous malformations.

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Correspondence
Dr Peter Witters, Afd. Hepatologie, O&N, Herestraat 49-bus 703, BE-3000 Leuven, Belgium. Email: Peter.witters@gmail.com

Introduction

Aberrant vascularization of the liver is a common feature, especially in patients with advanced liver cirrhosis where various anatomic routes (intra and extrahepatic) of shunting are described. However, besides this acquired portosystemic shunting, rare congenital abnormalities also occur. The complicated embryonic development of the inferior caval vein and its close relationship with the development of the vitelline veins, and the existence of intrahepatic embryonal anastomoses, are held responsible for their anomalies.

Anatomically, portosystemic shunts are divided in intra and extrahepatic shunts. Extrahepatic portosystemic shunts were studied for the first time by Abernethy in 1793 and are therefore called Abernethy malformations. Morgan and Superina1 classified extrahepatic portosystemic shunts into two types (See Table 1).

Until now, 39 type I and 22 type II cases have been described in the literature.2 Intrahepatic portosystemic shunts are defined as communications between the portal and systemic venous circulation, measuring more than 1 mm in diameter and at least partially located inside the liver. Park et al.3 described four distinct types (see Table 1). A total of 21 type 1, nine type 2, 29 type 3, and six type 4 shunts have been described in the literature.5 Some authors4 classify a patent ductus venosus (OMIM 601466) as a fifth type.

In this article, we add six cases (one type Ib, three type II, one type 1, and one type 4), and highlight the clinical cues that can lead to their diagnosis. Most papers describing venous portosystemic shunts are radiological descriptions and therefore do not provide much information for the clinician. Here, we review the literature and summarize the clinical presentations.
Table 1 Classification of congenital hepatic shunts

<table>
<thead>
<tr>
<th>Extrahepatic portosystemic shunts</th>
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<tbody>
<tr>
<td>Type I</td>
<td>Absence of intrahepatic portal veins</td>
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<tr>
<td>Type Ia</td>
<td>Superior mesenteric and splenic vein drain separately into inferior caval vein</td>
</tr>
<tr>
<td>Type Ib</td>
<td>Superior mesenteric and splenic vein form a common trunk before draining into the inferior caval vein</td>
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<tr>
<td>Type II</td>
<td>Important collateral, patent intrahepatic veins</td>
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</table>

<table>
<thead>
<tr>
<th>Intrahepatic portosystemic shunts</th>
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<tbody>
<tr>
<td>Type 1</td>
<td>Single tubular connection between right portal vein and inferior caval vein</td>
</tr>
<tr>
<td>Type 2</td>
<td>Multiple connections between peripheral portal and hepatic veins within one segment</td>
</tr>
<tr>
<td>Type 3</td>
<td>Aneurysmal connection between portal and hepatic vein</td>
</tr>
<tr>
<td>Type 4</td>
<td>Multiple connections between peripheral portal and hepatic veins diffusely in both lobes</td>
</tr>
</tbody>
</table>

Method

We reviewed the clinical characteristics of six cases drawn from our files (from 1970 to 2006), at the University Hospital Gasthuisberg, University of Leuven, Belgium. Further, we have reviewed the literature by medline search and by extensive bibliographic research.

Results

See Table 2.

Discussion

Portosystemic shunts are increasingly recognized due to the evolution and expansion of medical imaging. However, the total number of reports remains small. Early recognition of portosystemic shunts is important, given the detrimental effects of shunting on the liver and other organs. This damage can be prevented if a timely diagnosis is made. In the early course of this congenital disease there are few, if any symptoms. Those symptoms are usually not liver related, which delays referral and diagnosis. Furthermore, a clinical suspicion will alert the radiologist and increase the diagnostic yield of for instance echo Doppler, allowing a diagnosis to be made. Here we review the possible clinical presentations.

The liver’s synthetic functions are usually well preserved and symptoms secondary to portal hypertension (splenomegaly, ascites, varices) are typically absent. This is due to the fact that portal hypertension is prevented from developing, since blood is easily pushed through the congenital portosystemic shunt. In the course of the disease, nodular lesions can develop. Focal nodular hyperplasia, adenoma, hyperplastic nodules, diffuse nodular regenerative hyperplasia, hepatocellular carcinoma, and hepatic sarcoma have all been documented.

In patient three, we identified focal nodular hyperplasia lesions, in patient four a hepatocellular carcinoma within an adenoma, and in patient five we identified an increase in echo graphic nodularity. Some portosystemic shunts coincide with other congenital abnormalities, for example biliary atresia (six Abernethy type I and one Abernethy type II cases).

As is seen in patients two and six, congenital shunts can present with neurologic symptoms without abnormal clinical findings (no gynecomastia, vascular spiders, jaundice, or portal hypertension). An elevated ammonia level will suggest hepatic encephalopathy. Given its origin (due to portosystemic shunting instead of cirrhotic-altered liver function) portalsystemic (instead of hepatic) encephalopathy is a better term. This degree of encephalopathy is suggested to be dependent on an age-dependent increase in the sensitivity to the deleterious effects of the shunt and to the fraction of blood that is shunted.

In patient two, dyspnea due to pulmonary hypertension was the presenting symptom. Previously only one similar case has been described (in a 3-month-old female). Probably this pulmonary hypertension can be interpreted as portopulmonary hypertension without portal hypertension (given the congenital transjugular intrahepatic portosystemic shunt variant). Pulmonary hypertension is thought to result from the effect of vasoactive substances produced in the splanchic bed, bypassing the normal liver metabolism and exerting a vasoconstrictive effect on the small pulmonary arteries. A separate entity is the hepatopulmonary syndrome that has been described in four cases of Abernethy malformations.

Congenital hepatic shunts can also present with metabolic dysregulation such as hypoglycemia. In one case, an early hyperglycemia after an oral glucose tolerance test was described. This was presumably caused by defective liver uptake of glucose followed by hyperinsulinism, and finally hypoglycemia, because of reduced hepatic degradation of the insulin secreted in a normal quantity. There are also some reports on hypergalactosemia in the newborn screening test, due to shunting, without evidence of a deficiency of galactokinase or epimerase.

Elevated liver tests sometimes provide the first clue enabling diagnosis. However, it must be emphasized that usually the hepatic function is very well preserved, certainly in the absence of associated conditions such as biliary atresia or the development of hepatic tumors (compared with supra). In our six patients, impaired liver tests indicative of cholestasis were present. Sometimes a portosystemic shunt is an incidental radiologic finding. This should always be considered as clinically relevant. Only an intrahepatic shunt type I (tubular communication between the right portal branch and the inferior vena cava) has been documented as disappearing spontaneously in neonates.

Given its congenital nature, there are often associated malformations, especially in extrahepatic shunts. Various cardiac abnormalities are often reported (atrial or ventricular septal defect, persistent ductus arteriosus, coarctation of the aorta, dextrocardia, etc.), but also polysplenia, biliary atresia, skeletal abnormalities (for example short 5th phalanxes in our first patient), or renal tract abnormalities (for example cystic dysplasia).

Since congenital hepatic shunts are uncommon and underrecognized, few cases have been published – as such no standard treatment is available. While some authors advocate conservative management (lactulose treatment and protein restriction) others prefer embolization or ligation of the shunts.

Conclusion

Typically, portosystemic veno-venous communications are classified by their anatomical characteristics according to Morgan and...
Table 2  Patient overview

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex (M/F), age (years)</th>
<th>Shunt Type</th>
<th>Presenting symptoms</th>
<th>Past medical history</th>
<th>Laboratory</th>
<th>Imaging/Work-up</th>
<th>Biopsy</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>M, 25 years</td>
<td>Extrahepatic, II</td>
<td>Intermittent jaundice (for some weeks)</td>
<td>–</td>
<td>AST 161 U/L, ALT 137 U/L, total bilirubin 2.40 mg/dL (y &lt; 1), direct bilirubin 0.60 mg/dL, ALP 266 U/L, y &lt; 129, yGT 242 U/L, y &lt; 53, ammonia 73 µmol/L, y &lt; 32</td>
<td>MRI: small nodular 12 hepatocellular lesions (FNH), absence of intrahepatic portal branches</td>
<td>Absence of portal venous structures within portal tracts, dilated sinusoids</td>
<td>Focal atrophy of the liver parenchyma with a dilation of the sinusoids and a hypertrophy of the periporal parenchyma. Hypothesis (but not absence) of the smallest branches of the portal vein</td>
<td>Conservative: clinical, biochemical, ultrasonographic follow-up</td>
</tr>
<tr>
<td>2</td>
<td>M, 66 years</td>
<td>Extrahepatic, II</td>
<td>Fatigue, dyspepia</td>
<td>Alcohol hepatitis, hepatitis B, chronic bronchitis, psoriasis, cardiomyopathy, mild chronic renal insufficiency</td>
<td>AST 67 U/L, ALT 3 U/L, total bilirubin 1.06 mg/dL (y &lt; 11), APH 90 U/L, y &lt; 32–62, yGT 58 U/L, y &lt; 6–24</td>
<td>Doppler ultrasonography: ‘liver oedema’ without evidence of portal hypertension, and a suggestive connection between portal vein main stem and inferior caval vein with turbulent signal</td>
<td>Not performed yet</td>
<td>Lactulose enemas</td>
<td>Follow-up by our pneumonologists: Stable clinical situation</td>
</tr>
<tr>
<td>3</td>
<td>F, 17 years</td>
<td>Extrahepatic, II</td>
<td>Right upper quadrant pain</td>
<td>Suspected Holt–Oram syndrome, 3 hypomnoreaemia, iron deficiency anaemia</td>
<td>AST 612 U/L, ALT 240 U/L, total bilirubin 1.06 mg/dL (y &lt; 11), APH 80 U/L, y &lt; 32–62, yGT 52 U/L, y &lt; 35, total bilirubin 1.34 mg/dL, y &lt; 11</td>
<td>Ultrasonography, CT, MR angiography: portohepatic communication between the right intrahepatic portal vein and the IVC</td>
<td>Nodular regenerative hyperplasia, portal fibrosis, and central vein dilatation</td>
<td>Medical treatment of pulmonary hypertension</td>
<td>Two recurrences of bleeding. Underwent liver transplantation. Histology: HCC within a pre-existing adenoma with a metastasis (lesion in the left lobe), arterialized veins, and nodular regenerative hyperplasia in the remainder of the liver</td>
</tr>
<tr>
<td>4</td>
<td>F, 42 years</td>
<td>Extrahepatic, II</td>
<td>–</td>
<td>Quater headaches, mola</td>
<td>APH 612 U/L, ALT 240 U/L, total bilirubin 1.06 mg/dL (y &lt; 11), APH 80 U/L, y &lt; 32–62, yGT 52 U/L, y &lt; 35, total bilirubin 1.34 mg/dL, y &lt; 11</td>
<td>Ultrasonography, CT, MR angiography: intrahepatic communication between the right intrahepatic portal vein and the IVC</td>
<td>–</td>
<td>–</td>
<td>Follow-up by our pneumonologists: Stable clinical situation</td>
</tr>
<tr>
<td>5</td>
<td>M, 8 years</td>
<td>Extrahepatic, I</td>
<td>–</td>
<td>–</td>
<td>AST 80 U/L, ALT 5–37, total bilirubin 1.20 mg/dL</td>
<td>–</td>
<td>–</td>
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<td>–</td>
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<tr>
<td>6</td>
<td>M, 59 years</td>
<td>Extrahepatic, IV</td>
<td>Incidental (workup for multiple fractures)</td>
<td>Meningococcal sepsis</td>
<td>Alkaline phosphatase: with increased bone (730 U/L, y &lt; 96 U/L) and liver fraction (523 U/L, normal &lt;200)</td>
<td>Ultrasonography: normal liver parenchyma with dilatation of hilar, extra- and intrahepatic bile ducts without an apparent cause or portal hypertension</td>
<td>–</td>
<td>Lactulose enemas</td>
<td>Nine years’ follow-up, increased cholesterol (377 512 U/L, bilirubin 1.23 mg/dL, ALP 1972 U/L) Ultrasonography: increase in nodularity (micronodular nodules, some with central scar), compression of the subhepatic veins and intermittent hepatofugal flow in the portal vein</td>
</tr>
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</table>

1Holt–Oram syndrome: absence of distal digital phalanxes V, short palatum molle, mild pectus deformity mixed carinatum and excavatum, perimembranous ventricular septum defect with hemodynamically unimportant shunting.
2Alkaline phosphatases: with increased bone (730 U/L, y < 96 U/L) and liver fraction (523 U/L, normal <200).
3Various immune-mediated conditions: membranoproliferative glomerulonephritis with nephrotic syndrome (41 years), protein losing enteropathy (42 years), cerebrovascular accident (48 years) secondary to vasculitis of left internal carotid artery resulting in right hemiparesis, with recurrence and recurrent coma with spontaneous recovery within 24–48 h, exophthalmia because of retrobulbar inflammatory pseudotumor cerebri (52 years).
4Focal atrophy of the liver parenchyma with dilatation of the sinusoids and a hypertrophy of the periporal parenchyma. Hypothesis (but not absence) of the smallest branches of the portal vein.
5Serious developmental abnormalities; short palatum molle, mild pectus deformity mixed carinatum and excavatum, perimembranous ventricular septum defect with hemodynamically unimportant shunting.
6Meningococcal sepsis: obtundation, convulsions, DIC, DIC.
7Focal atrophy of the liver parenchyma with dilatation of the sinusoids and a hypertrophy of the periporal parenchyma. Hypothesis (but not absence) of the smallest branches of the portal vein.
8Giant cell arteritis.
9Doppler ultrasonography: demonstrated various shunts directly, showed cardiac modulations of the portal flow signal and absence of a retrogade phase in the hepatic veins (characteristic of increased flow).
10ALT, alanine aminotransferase level; APH, alkaline phosphatase; AST, aspartate aminotransferase level; CT, computed tomography; FEV1, forced expiratory value in the first second; FPH, focal nodular hyperplasia; yGT, gamma-glutamyltransferase; MRI, magnetic resonance imaging; Ni, normal; PFO, patent foramen ovale; RBBB, right bundle branch block; RVH, right ventricular hypertrophy; Tiff, Tiffeneau index; VQ, ventilation perfusion scan; VSD, ventricular septal defect; y, year.
Superina (extrahepatic, Abernethy malformations type Ia,b and II) and Park (intrahepatic, types 1–5). (Table 1) However, their clinical presentation is less dependent on the anatomical type. Patients often present with hepatic shunting (encephalopathy, pulmonary hypertension, hepatopulmonary syndrome, hypoglycemia) with relative sparing of the synthetic functions of the liver in the absence of portal hypertension. Some shunts present with space-occupying lesions (focal nodular hyperplasia, hepatocellular carcinoma, nodular regenerative hyperplasia, etc.) or biliary atresia.

Finally, some cases are detected incidentally during work-up for abnormal routine liver tests or while performing medical imaging for other reasons.

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References


