

Case report

Abernethy malformation and hepatocellular carcinoma: a serious consequence of a rare disease

Manuel Jaklitsch ,^{1,2} Mafalda Sobral,² Ana Maria Carvalho,³ Hugo Pinto Marques^{2,4}

¹Institut Hépatobiliaire Henri Bismuth, Villejuif, France

²Centro Hepato-Bilio-Pancreático e de Transplantação, Hospital Curry Cabral, Lisboa, Portugal

³Pathology, Hospital Curry Cabral, Lisboa, Portugal

⁴Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisboa, Portugal

Correspondence to

Dr Manuel Jaklitsch; manuel.jaklitsch@gmail.com

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SUMMARY

Congenital portosystemic shunts (CPSS) are a rare vascular consequence of embryogenetic vascular alterations or the persistence of the fetal circulation elements, first described by John Abernethy in 1793 and classified by Morgan and Superina, into complete and partial portosystemic shunts. Its prevalence to this day has not been defined. We present a patient series of a 44-year-old and 47-year-old man and woman, with this rare congenital malformation and underlying hepatocellular carcinoma (HCC) treatment strategies. Over half of the individuals with CPSS have benign or malignant liver tumours, ranging from nodular regenerative hyperplasia, focal nodular hyperplasia, adenomas, HCC and hepatoblastomas. Additionally, it is known that half of individuals with Abernethy malformation type Ib will develop one or multiple types of tumours. There seems to be a direct association with tumorigenesis and CPSS, which is the primary consequence of absent portal flow. Surgery is the treatment of choice, either as a curative resection or orthotopic liver transplantation if recommended as per the criteria, in which replacing the hepatic parenchyma in the setting of an Abernethy malformation will correct the underlying hyper-arterialisation.

BACKGROUND

Congenital portosystemic shunts (CPSS) are a rare vascular consequence from the atypical formation of the splanchnic venous system, in which the portal blood drains entirely or partially into a systemic vein.^{1,2} They are the result of embryogenetic vascular alterations or the persistence of the fetal circulation elements, especially those related to the ductus venosus.³ The first description of CPSS was given by the London surgeon John Abernethy in 1793, known as the Abernethy malformation. His findings were based on a postmortem examination of a 10-month-old child, which revealed the termination of the portal vein (PV) in the inferior vena cava (IVC) at the insertion level of the renal veins. Additionally, presenting polysplenia, dextrocardia and a central liver, her IVC continued above the diaphragm as the azygos vein, with the confluence of the hepatic veins forming a separate single trunk that traversed the left side of the diaphragm and drained directly into the right atrium.^{4,5} Furthermore, CPSS has been associated with cardiac malformation predominating in frequency, heterotaxia, polysplenia syndrome, skeletal malformation, renal malformations and biliary atresia. Regarding

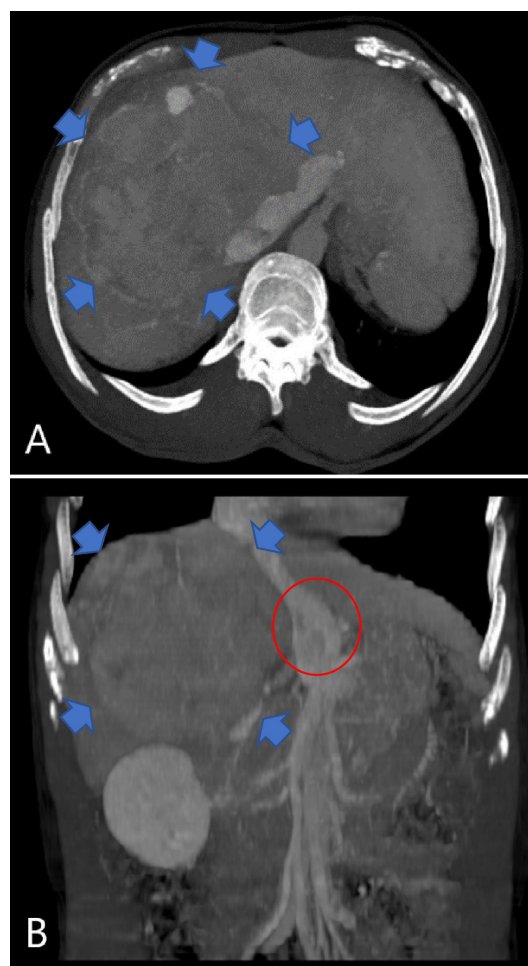


Figure 1 Enhanced CT. (A) Sagittal view of the portosystemic shunt, multiple hypervascular hepatic nodules predominant in right liver lobe (arrows), with late venous washout. (B) Coronal view of hypervascular hepatic nodules (arrows) and portosystemic shunt (circle).

genetical disorders, down syndrome has been the most frequently associated, with 13 cases described. Nevertheless, association with other syndromes have been reported, such as Turner, Cornelia de Lange, Holt-Oram, Goldenhar, Wolf-Hirschhorn and Adam-Olivers.²

The most commonly used classification for CPSS is the Morgan and Superina⁶ classification, which is based on the absence (type I) or presence (type II) of portal liver perfusion. Based on anatomy, CPSS type Ia is defined as having the superior mesenteric vein (SMV) and splenic vein draining separately into the IVC. In type Ib, the SMV and the splenic vein form



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Table 1 Morgan and Supertina classification of congenital extrahepatic porto caval shunts

Type I	Liver not perfused with portal blood flow—complete shunt
	1a: SV and SMV drain separately in IVC
	1b: SV and SMV form a common trunk before draining into the IVC
Type II	Important collateral, patent hepatic portal vein

IVC, Inferior Vena Cava; SMV, Superior Mesenteric Vein; SV, Splenic Vein.

a common trunk and are joined in an end to side shunt between PV and IVC and are also named in the literature as ‘congenital absence of the PV’. Type II is defined as partial shunt having an existing portal liver perfusion, where a side to side shunt PV to IVC prevails with a patent PV^{2,5,6} (table 1).

Several new classifications have been proposed in recent years to further improve clinical and surgical management of CPSS,^{7,8} which remains an infrequently diagnosed condition. Additionally, the actual incidence in the general population is unknown. The diagnosis is mostly incidental⁹ and has been on the rise in recent years owing to advances in imaging techniques and their availability.¹⁰

CASE PRESENTATION

Case report 1

A 44-year-old man, with a history of alcohol consumption in a binge-drinking habit and an abstinence period of 2 years, was diagnosed with cerebral arteriovenous malformation, which was surgically treated 20 years ago. At that time, a concomitant diagnosis of Abernethy malformation was made, and the patient followed with subsequent screening. On a clinical follow-up in June 2017, image studies reported findings of multinodular liver disease and the presence of a pedunculated mass (15×8 cm) in segment V and VI, which is suggestive of hepatocellular carcinoma (HCC). The patient was submitted to an anatomical right hepatectomy, having adequate future liver remnant (FLR), and the surgical specimen confirmed a well-differentiated trabecular HCC staged pT3a N0 M0. Resection margins were R0. On a subsequent clinical follow-up, an enhanced CT showed arterial enhancing lesions in the regenerated liver parenchyma with regenerative nodules and one

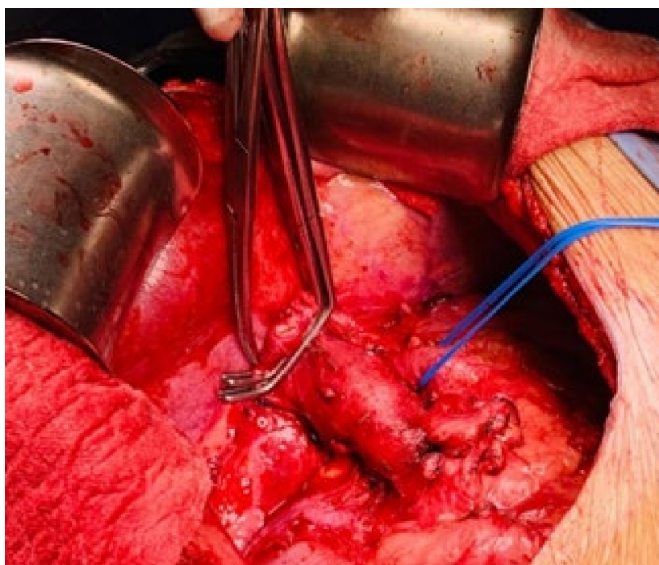


Figure 2 Operative situs in an hepatic phase, showing a congenital portosystemic shunts type 1b (vessel loop).

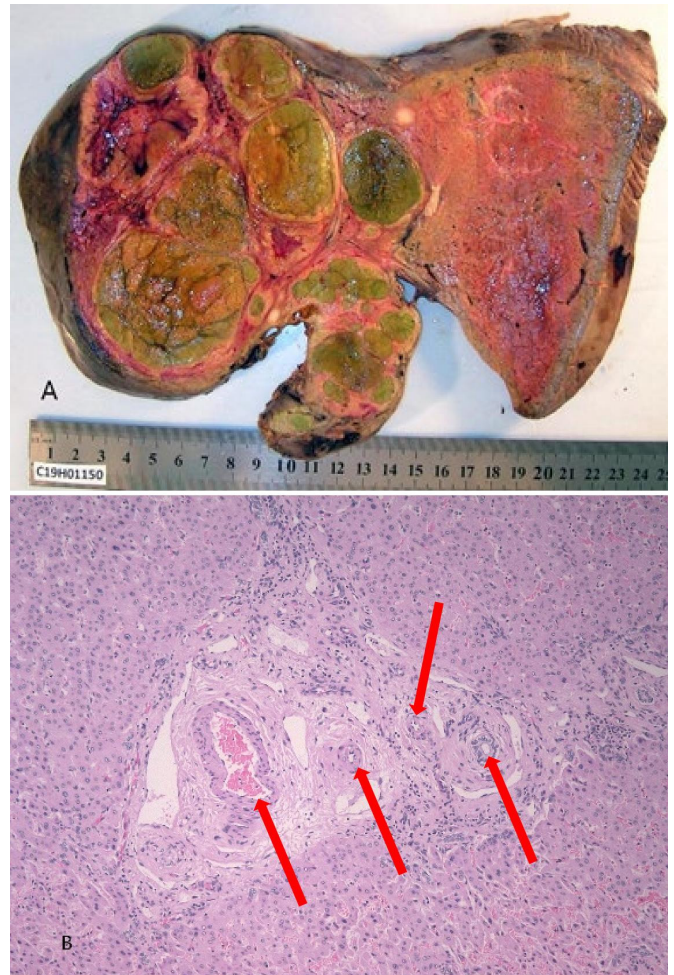


Figure 3 (A) Liver specimen, with multiple regenerative nodes predominantly in the right lobe, (B) portal triad with a noted absence of portal venule and hypertrophic arterial ducts (arrows) with periductal fibrosis.

nodule in contact to prior resection surface presenting HCC characteristics (figure 1). Clinical laboratory values of 1.54 mg/dL total bilirubin (TB), 153 U/L gamma-glutamyl transferase (GGT), 3.68 ng/dL alpha-fetoprotein (AFP), 22 U/mL, carbohydrate antigen 19–9 (CA 19–9) of 22 U/mL and carcinoembryonic antigen (CEA) of 3.9 ng/mL were found. The patient was discussed at the multidisciplinary liver tumour board and proposed to undergo orthotopic liver transplantation (OLT), which followed 3-month post listing.

Intraoperatively, CPSS type 1b was confirmed (figure 2). The transplant was uneventful. On postoperative day 5, a rise in cholestatic parameters and liver transaminase were noticed, and the CT diagnosed hepatic artery thrombosis (HAT) associated with ischaemic lesions bilaterally. Laparotomy with thrombectomy resection and reanastomosis of the hepatic artery was performed. In the absence of clinical improvement, retransplantation was indicated, which was performed at postoperative day 9 of OLT and two of laparotomy, presenting a favourable postoperative evolution. The patient was discharged on day 28.

Histopathological findings consisted of a 1711 g and 23×17×10.5 cm specimen. In the portal triad, the absence of portal venule and hypertrophic arterial ducts with periductal fibrosis was noted. In segment V, there was a dominant mass

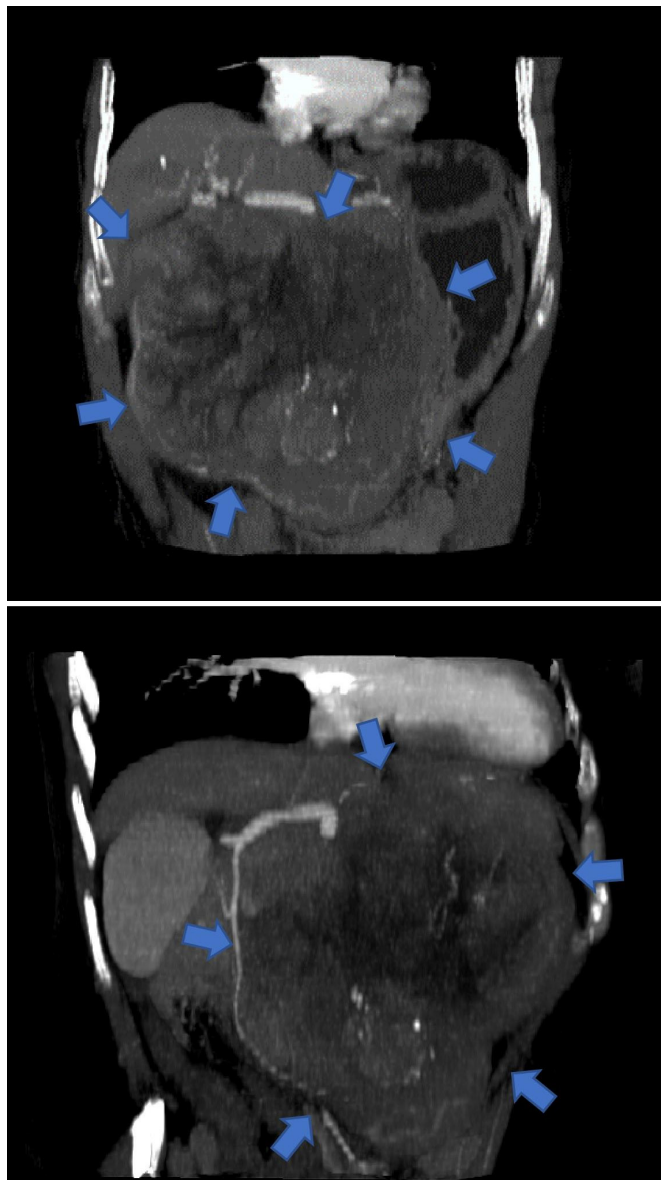


Figure 4 Enhanced CT with a voluminous mass in the left liver lobe (arrows).

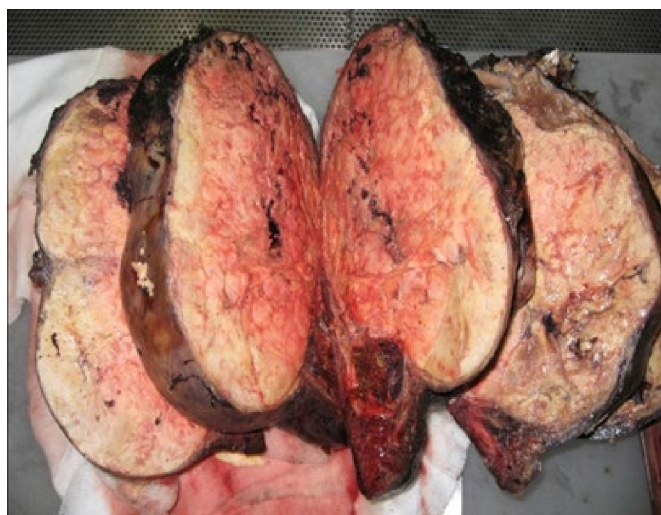


Figure 5 Macroscopic surgical specimen.

of 5×4 cm, where HCC was diagnosed and staged as ypT3 N0 M0 G2. Multiple nodular formations occupying a field of 18×10×14.5 cm in relation to regenerative parenchyma were present (figure 3).

Case report 2

A 47-year-old woman, with known pathological history of an atrial septal defect, with surgical closure during infancy, ischaemic stroke with no sequelae and essential arterial hypertension, presented with pain in the upper right abdominal quadrant in the last 3 months, with no other associated symptoms. On physical examination of the epigastric/hypochondrium region, a painful, elastic and mobile mass was palpated approximately 10 cm in size in the greater axis. On transabdominal ultrasound a heterogeneous irregular mass in the left liver lobe, measuring 11.3 cm in diameter with presence of calcifications, was noted. Biliary ducts were within normal dimensions. The CT study of the abdomen confirmed a single mass in the left lobe with dimensions of 10.5×8×4 cm, with characteristics compliant with HCC and a CPSS type Ib (figure 4). Clinical laboratory reported a TB of 0.8 U/L, AFP: 28.1 U/mL, CA19-9: 43.4 U/mL, GGT: 226 ng/dL. The patient was presented at our multidisciplinary tumour board, and a left hemihepatectomy was considered. Left hemihepatectomy was performed in January 2011. Intraoperatively, the existence of a CPSS type Ib was confirmed. On histology, HCC, Edmondson-Steiner grade 3, with microvascular invasion was confirmed. Resection margins were >1 cm (R0) (figure 5). The patient had an uneventful postoperative course and was discharged on the 11th postoperative day. Yearly follow-up showed no signs of recurrence (figure 6).

DISCUSSION

A study by Franchi-Abella *et al* reported 413 patients in the literature between 1979 and 2017. The respective frequencies of the different types of CPSS are challenging to assess, since most of the reported cases of CPSS are complicated examples and/or spontaneous closures in the first month of life, leading to underestimation of true incidence.² Ponziani *et al* in a literature review stated 178 type I CPSS, presenting a very variable age of diagnosis from prenatal stages to 61 years.¹¹ CPSS type I predominates in females (61%–78%) and includes multiple malformations. Type II has a slight male predominance.¹² A diverse range of clinical manifestations, including hyperammonaemia, hepatic encephalopathy, pulmonary hypertension and hepatopulmonary syndrome have been described. Furthermore, the development of tumour is quite common. Over half of the individuals with CPSS have benign or malignant liver tumours,¹² ranging from nodular regenerative hyperplasia, focal nodular hyperplasia, and adenoma to HCC and hepatoblastoma. It is known that half of the individuals with Abernethy syndrome type Ib will develop one or multiple types of tumours.^{13 14} A diversity of lesions on a single patient have also been reported, and the association between PV agenesis and liver tumours is attributed to the absence of portal flow and compensatory increased arterial blood flow.^{14 15} Whether the time of detection and age of patients explains why some have benign and others malignant tumours is unclear.¹³ Nevertheless, the presence of oncogenic mutations has been recorded in some lesions, and the clinical entity's assortment needs individualised therapy, either surgical or radiological intervention in the environment of partial shunts (type II), which mitigates encephalopathy¹⁵ and can lead to regression of tumour development.^{7 13} At present, resection is the treatment



Figure 6 MRI at 1-year follow-up, visualising the congenital portosystemic shunts type Ib (circle), with no recurrent disease.

of choice for HCC in a non-cirrhotic liver,¹⁶ although carrying a high risk of recurrence of around 20%.¹⁷ For OLT, robust data are lacking, and there is need to refine the indications for transplantation in this setting. Nevertheless, liver transplantation for malignant liver tumours in a context of complete portacaval shunting has been considered.¹ In the first case presented, indication for OLT was based on the presence of multiple non-typical nodules scattered through the parenchyma. Knowing the risk of HCC in underlining Abernethy malformation, advised of the possibility of more HCC harbouring nodules. A second resection was not considered due to borderline FLR, and the anatomical impossibility of preoperative PV embolisation. HAT

Learning points

- ▶ Abernethy malformations type Ib carries a high risk of hepatocellular carcinoma, and transplantation is probably the treatment of choice for these patients. Some evident technical remarks are the eccentric position of the portal vein, which may pose difficulties in the portal anastomosis, and a long vicariant hepatic artery.
- ▶ The risk of hepatic artery thrombosis in this setting is not known, but due to our experience we would advise keeping a short artery after anastomosis to avoid kinking.
- ▶ In the case of resection, vascular control can be done with intermittent arterial clamping in the setting of congenital portosystemic shunts (CPSS) type Ib for type II where arterial clamping is not sufficient vascular control may imply total vascular exclusion.
- ▶ The primary consequence of hyper-arterialisation is linked to the lack of portal blood flow.
- ▶ Surgery is the treatment of choice, either as a curative resection or if criteria suggest orthotopic liver transplantation, in which replacing the hepatic parenchyma in the setting of an CPSS, will correct the underlining hyper-arterialisation.

is a severe complication after OLT which often results in early graft loss having an overall incidence of 4.4% in transplanted patients.¹⁸ It is logical to assume the absence of portal flow to be accompanied by a robust arterial flow. The HAT in this case was due mainly to surgical technical issues, as there was specifically a twisted portion of the artery that was left rather long. When patients do not comply with OLT criteria, resection with an intent to cure should be performed. Furthermore, the use of preoperative chemoembolisation for tumour downsizing¹² and the use of trans-arterial radioembolisation has also been described.¹⁴ For one of our patients, not complying with OLT criteria due to tumour mass size and a favourable tumour localisation with ‘exophytic’ characteristics a left hemihepatectomy was performed, R0 resection margins were archived and after 8 years of follow-up, no signs of local or systemic recurrence was found.

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ORCID iD

Manuel Jaklitsch <http://orcid.org/0000-0003-3459-4612>

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