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ORIGINAL ARTICLE

Surgical intervention for patent ductus venosus

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Abstract Patent ductus venosus (PDV) is a rare condition, which usually presents secondary to hepatic atrophy and hepatic failure. We have treated eight cases of PDV, all with hypergalactosemia and hyperbilirubinemia. Ultrasonography and three-dimensional computed tomography demonstrated communication between the portal vein and the inferior vena cava. Of the eight PDV cases, three from the older age group (ages 9, 11, and 14 years) had high-density lesions in their brain nucleus, and one case (age 19 years) had undergone prior Kasai portoenterostomy for biliary atresia. Six PDV patients underwent ligation of PDV and the remaining two cases underwent partial banding of PDV with intraoperative monitoring to maintain portal vein pressure (PVP) under 30 cm H_2O. Improvement of the intrahepatic portal vein flow was achieved by ligation or banding of PDV. Postoperatively, serum galactose and bilirubin fell to normal ranges, but portal thrombus occurred postoperatively in the first case. We subsequently administered postoperative anticoagulation in the remaining cases and experienced no major complications. These results suggest that PDV ligation and banding are effective surgical approaches for patients with PDV. Close postoperative monitoring to avoid portal thrombus is imperative in these cases.

Keywords Patent ductus venosus · Surgery · Ligation · Banding · Portal thrombosis

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Introduction

Patent ductus venosus (PDV) is a rare form of congenital portosystemic shunt (PSS). Clinical symptoms and complications from PSS have not been clarified, and the natural course of this disease remains unclear [1]. Surgical treatments for PDV include ligation, banding, coiling, or stenting of the PDV, as well as liver transplantation, but there is no standard operation for symptomatic PDV [1–3]. We recently performed surgical treatment for eight cases with PDV. In this paper, we analyze these cases and show the clinical, radiological, and surgical findings in PDV cases.

Patients and methods

Eight children with a PDV underwent surgery at the Department of Pediatric Surgery in Hiroshima University Hospital during the study period of 1998–2009. All patients, except for one patient with biliary atresia, had undergone a clinical assessment and detailed biochemical investigations in the department of pediatrics. In each patient, radiological examinations included a combination of ultrasonography, computerized tomography (CT), magnetic resonance imaging, angiography, and echocardiography. We analyzed the clinical examinations, radiologic images, operative findings, including the pressure of portal

vein (PPV), and outcomes. In all patients, we analyzed their postoperative course, including hepatic hemodynamics and perioperative complications. Two patients had been followed more than 5 years before surgical consultation in the department of pediatrics, so we also investigated their change in clinical data and portal vein hemodynamics in their follow-up periods.

Results

The clinical and radiological findings for all eight patients are summarized in Tables 1 and 2. All cases except case 6 had been followed up for hypergalactosemia detected by neonatal screening. In case 6, PDV was detected by CT scan in the follow-up period for biliary atresia. This patient had undergone Kasai portoenterostomy at 3 months of age and had no evidence of portal hypertension or splenomegaly. However, progressive liver atrophy was identified at age 19 years and CT scan revealed PDV. The representative CT and angiography for cases 1 and 2 are shown in Figs. 1 and 2, respectively. As shown in Fig. 2a, CT angiography was used to reconstruct intraabdominal vessels in 3D, which was useful for evaluating PDV.

Preoperatively, hemodynamic analysis was performed in all cases, especially in cases 1, 4 and 6 (Table 2). In these three cases, the venous phase of superior mesenteric angiography revealed a PDV measuring 11, 25, and 18 mm in diameter, respectively. In these cases, portal vein and hepatic vein were atrophic when compared to the diameter of PDV (Figs. 1, 3). In the remaining five cases, CT angiography showed apparent portal and hepatic veins to have sufficient blood supply to the liver (Fig. 2). Atrophy of portal vein was defined when the diameter of the portal vein was smaller than half of the PDV diameter. In our series, the cases 1, 4, and 6 showed atrophic portal vein. In case 4, the atrophic portal vein was too small to perform selective portal venography through the vena cava (Fig. 3). Portal venography was performed during PDV occlusion using a balloon catheter introduced via the superior vena cava. We visualized the extrahepatic portal vein or the main portal vein as a fine line, <1.0 mm in diameter,

Table 1 Clinical and radiological findings

Case	Age at diagnosis	Age at surgery (y)	Symptoms	Primary disease	Serum			Radiological findings by CT and angiography			
					Galactose	Bile acid	NH_3	Liver atrophy	High-density area in brain	Portal vein atrophy	Hepatic vein atrophy
1	5 y	11	–	–	High	High	High	+	+a	+	+
2	1 m	1	–	–	High	High	High	–	–	–	–
3	1 m	9	–	Hemangioma	High	High	High	–	+a	–	–
4	4 y	14	–	–	High	High	High	+	+a	++	+
5	1 m	6	–	–	High	High	High	–	–	–	–
6	19 y	21	General tiredness	Biliary atresia	High	High	High	+	–	+	+
7	1 m	1	–	–	High	High	High	–	–	–	–
8	1 m	1	–	–	High	High	High	–	–	–	–

y year, *m* month, *a* high-density area in basal ganglia

Table 2 Operative findings of PDV cases

Case	Age at surgery (years)	PVP at laparotomy (cmH_2O)	Diameter of PDV (mm)	PVP at PDV occlusion (cmH_2O)	Liver atrophy	Regenerative nodule	Surgical procedure	PVP after surgery (cmH_2O)	Complication
1	11	6	11	19	+	+	Ligation	18	+a
2	1	9	10	17	–	–	Ligation	15	–
3	9	8	5	22	–	–	Ligation	23	+b
4	14	7	25	45	+	–	Banding	25	–
5	6	8	15	28	–	–	Ligation	28	–
6	21	6	18	40	++	–	Banding	30	–
7	1	5	6	16	–	–	Ligation	17	–
8	1	7	7	19	–	–	Ligation	16	–

y year, *PVP* portal vein pressure, *PDV* patent ductus venosus, *a* portal thrombosis, *b* hydrocele of testis

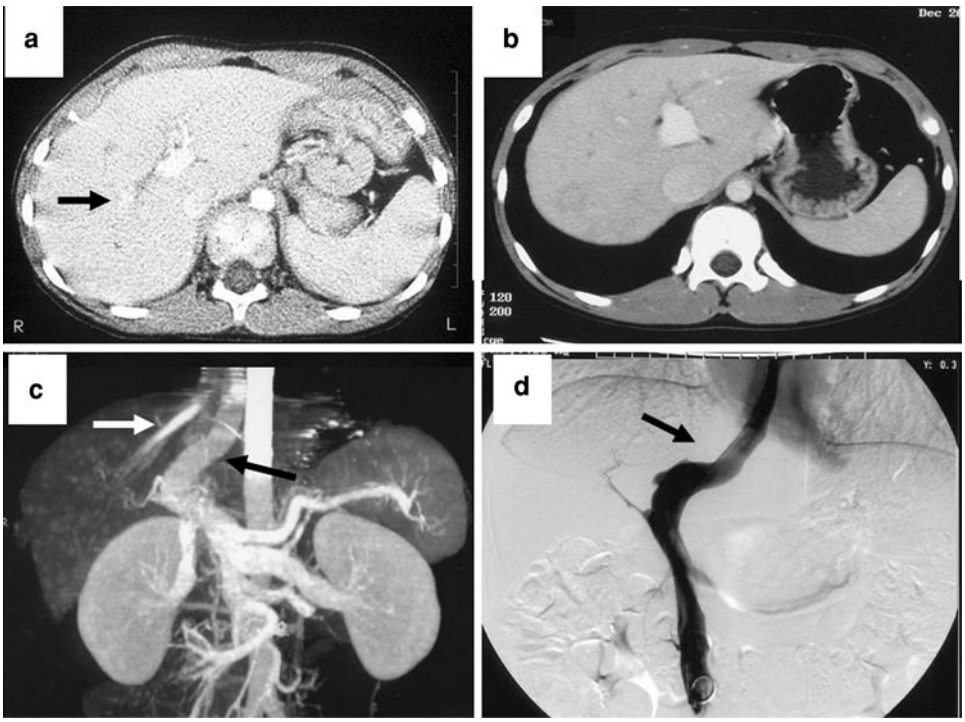

Fig. 1 Radiographic findings in case 1. Apparent intrahepatic portal vein flow (*arrow*) was detected in CT scan at age 5 years (**a**). CT angiography (**b**, **c**) and portal venography via the superior vena cava (**d**) at age 13 years revealed a large patent ductus venosus (*black arrow*) and hypoplastic portal vein. These findings suggested that hepatic atrophy had progressed in these 8 years. However, the hepatic vein (*white arrow*) was also detectable at that time

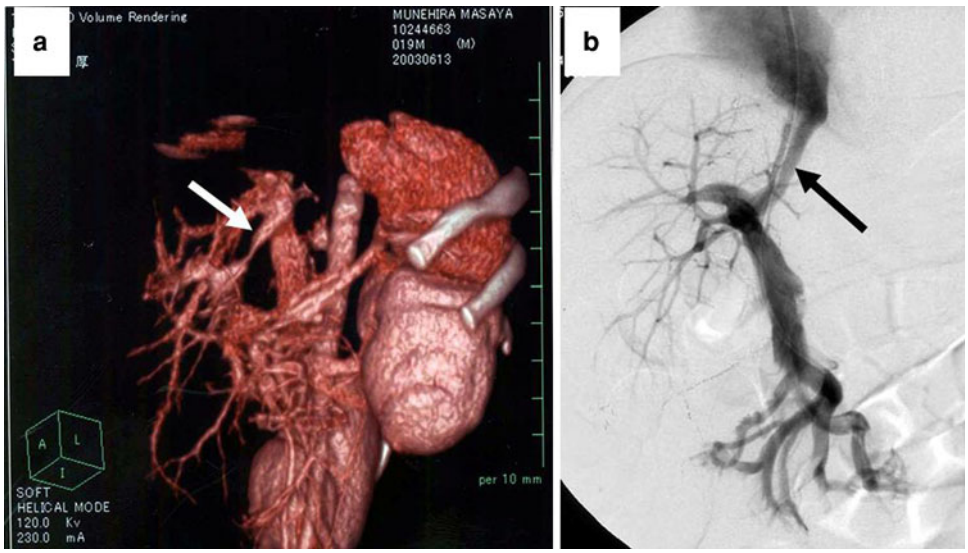

Fig. 2 CT angiography with 3D reconstruction in case 2 (1-year-old boy) with clearly visible patent ductus venosus (**a**). This is a similar grade as portal venography via the superior vena cava (**b**)

suggesting severe portal vein atrophy. Complete occlusion test of the PDV with the balloon catheter for 5 min resulted in elevation of the portal vein pressure (PVP) from 8 up to 45 cm H_2O. In cases 1 and 6, whose angiographic findings also revealed portal and hepatic vein atrophy, complete occlusion test of the PDV resulted in elevation of the PVP from 6 up to 29 cm H_2O and from 6 up to 34 cm H_2O, respectively.

Open laparotomy revealed liver atrophy in cases 1, 4, and 6 and a hepatic nodule was detected in case 1 (Fig. 4). To measure PVP, we introduced a catheter (Nipro, Osaka, Japan) from the peripheral inferior mesenteric vein to the portal vein. After manipulation of the left hepatic lobe, we detected PDV and encircled it with vessel tape. Test clamping of the PDV increased the PVP from 5–9 to 16–45 cm H_2O (Table 2). However, PVPs after occlusion were under 30 cm H_2O in cases with detectable apparent portal and hepatic veins in preoperative CT (Fig. 1). In cases 4 and 6, PVPs after temporary occlusion were >30 cm H_2O. Thus, we performed partial banding of PDV under intraoperative PVP monitoring. In fact, Teflon tape (Kono, Chiba, Japan) was banded surrounding the ductus

venosus. Banding size was controlled by the moving of the cuff using the remaining tape. It was then fixed with a 3-0 prolene suture (Fig. 3b, c) resulting in a PVP of 25–30 cm H_2O. In other cases, temporary occlusion for 20 min showed PVP of <30 cm H_2O and ligation of PDV was performed using double or triple ligation with prolene. Immediately following banding or ligation of PDV, slight intestinal congestion was observed in some cases, but no hepatic congestion or intestinal edema was noted 30 min after PDV occlusion. Biopsy was performed of normal liver in all cases and from the tumor in case 1. The abdomen was then closed in standard multilayer fashion. Microscopic examination of liver biopsy specimens did not reveal any specific findings. The tumor of case 1 was diagnosed as nodular regenerative hyperplasia.

Minor postoperative intestinal congestion was observed in all cases, which caused a hydrocele testis in case 3, but no patients had a postoperative ileus longer than 3 days after surgery. Laboratory data, including serum levels of ALT, AST, galactose, bilirubin, and ammonia, returned to normal within 7 days after surgery. However, case 1 was complicated by postoperative portal thrombosis (Fig. 4d, e). We treated this patient with heparin anticoagulation and his thrombosis resolved within 1 month after surgery. After this complication, the following seven cases underwent anticoagulation therapy for 2–3 weeks after surgery. Postoperative ultrasonography and CT scanning revealed no revascularization of ductus venosus in the cases that underwent ligation. In case 4, the shunt ratio of PDV was <10%, 1 year after surgery. Interestingly, in case 6, the PDV blood flow became undetectable 6 months after banding. The CT findings in cases 1, 4, and 6 revealed that their hepatic volume gradually enlarged after surgery.

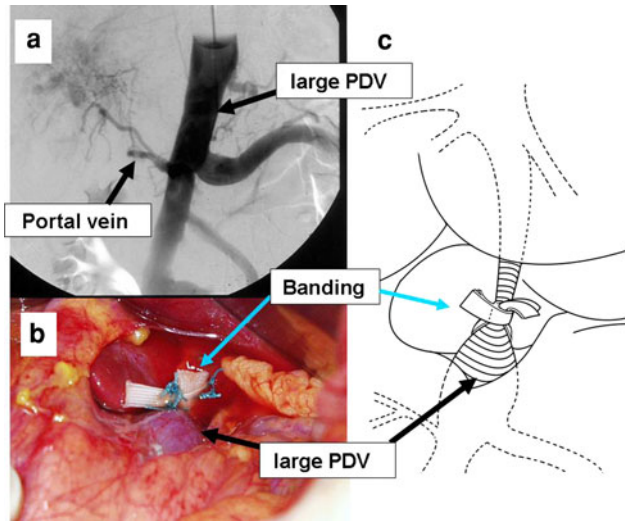

Fig. 3 Portal venography and intraoperative findings in case 4 (14-year-old girl). Portal venography via the superior vena cava (**a**) showed large patent ductus venosus and hypoplastic portal vein (*arrow*). The occlusion test for 5 min showed remarkable increase in portal vein pressure (45 cm H_2O). Therefore, banding of PDV by Teflon cuff was performed by laparotomy (**b**)

Discussion

Congenital PSS may be more common in Japan, but it is possible that these shunts are simply detected more readily because of routine newborn screening for hypergalactosemia [4, 5]. Continuous galactosemia in the absence of

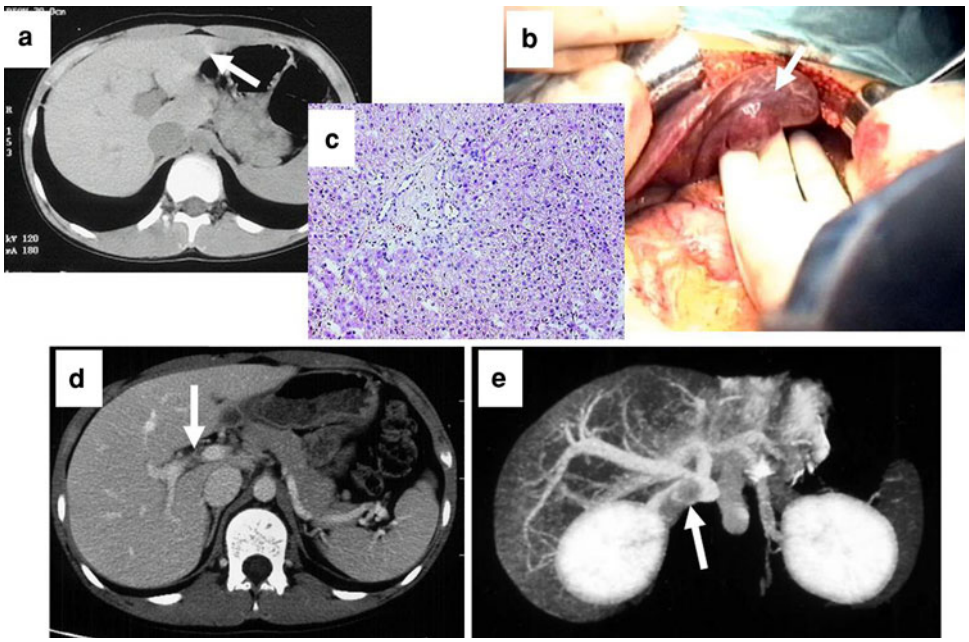

Fig. 4 Hepatic tumor and postoperative portal thrombosis in case 1. In case 1, hepatic tumor (*arrow*) was detected on CT scan (**a**) and at intraoperative findings (**b**). Histologic examination revealed a hyperplastic regenerative nodule (**c**). In this case, postoperative CT (**d**, **e**) showed intraportal thrombosis (*arrow*). This thrombosis was diminished following therapeutic anticoagulation

enzyme deficiency sometimes indicates the existence of PSS, and possibly PDV. As described by our series, PDV presents hypergalactosemia, hyperammonemia, and hyperbilirubinemia, and cases 2, 3, 5, and 7 were detected in infancy. However, before 2000, the relationship between hypergalactosemia and PDV had been unclear [6]. In cases 1, 3, and 4 born before 1999, PDV was difficult to diagnose in infancy. Thus, these cases were considered as late-phase patients with PDV.

CT angiography with 3D reconstruction is very useful for evaluating PDV. Spontaneous closure of the ductus venosus begins immediately after birth and complete functional closure usually occurs by about 17 days of age [7, 8]. Closure may be delayed temporarily in the presence of congenital heart disease, presumably as a result of elevated venous pressure, but spontaneous closure has not been reported in older patients. Of associated congenital malformations reported, cardiovascular anomalies are the most frequent [3, 4]. Biliary atresia has also been reported in several cases [9, 10]. In our series, case 6 had biliary atresia, but her PDV was not detected at the initial portoenterostomy procedure and a large one was first detected as an adolescent. These findings suggest the possibility that PDV might develop secondary to biliary atresia, resulting in atrophy of the liver.

Patients with either type of congenital PSS, including PDV, may be asymptomatic but they are prone to two specific complications: development of intrahepatic tumors and hepatic encephalopathy. PDV was previously reported to coexist with hypoplasia of the intrahepatic portal venous system [2, 11]. This is likely a consequence of PDV for two reasons. First, hypoplasia is not found in all cases; and second, the shunt can be successfully ligated without the development of portal hypertension [2, 12]. In our series, atrophy of the intrahepatic portal venous system was not found in infants. However, three older cases showed atrophy of the liver at laparotomy. In case 1, CT scan at age 5 years showed apparent portal vein flow, but CT at age 13 years showed atrophy of the intrahepatic portal vein and the liver. These findings also suggest that portal and hepatic vein flow gradually decreased in cases with PDV, resulting in apparent liver atrophy in adolescents. Thus, ligation of PDV should be performed in the early childhood period. Hepatic encephalopathy due to cerebral effects of circulating toxins, which normally undergo first pass metabolism in the liver, is another critical problem in patients with PSS. The age of onset of encephalopathy is variable and partially related to the volume and duration of the shunt [5], but hepatic encephalopathy has been diagnosed in children as young as 3 years [12]. The evidence for gradual increase in the PDV flow and progressive age-related liver atrophy may complicate hepatic encephalopathy, indicating that early surgical closure of PDV is preferable for children. In fact, cases 1 and 4 showed abnormal high-density loci on cerebral CT. Although they are currently asymptomatic, we believe these cases should be carefully followed.

Benign hepatic lesions including fatty infiltration, nodular regenerative hyperplasia, adenoma, focal nodular hyperplasia [3, 11–14, 20], and malignant liver tumors [15, 16] have been reported in PDV cases. Regression of benign tumors was reported because tumor development may be a consequence of excessive arterialization of the liver, lack of portal blood flow, and increased circulating levels of hepatic growth factors [17]. Rats with congenital portocaval shunt may also develop liver atrophy and hyperplastic nodules [18, 19]. These lesions correlate with abnormal blood circulation in the liver, and might be the cause of liver dysfunction.

For closure of PDV, potential therapeutic options include surgical ligation or radiological occlusion of the shunt. In some reports, radiologic embolization might be possible, and some patients with a shunt size of <5 mm have been successfully treated by interventional embolization [4, 21]. Occlusion of the shunt may cause portal hypertension if the native intrahepatic portal venous system becomes atrophic. Therefore, we have not attempted this procedure, because we cannot completely exclude the need to revascularize the shunt in the patient who develops intestinal congestion after occlusion or banding. Thus, surgical ligation or banding is our preferred approach if the PVP increases after test clamping of the PDV. If the patients have life-threatening complications, such as massive intestinal congestion, reoperation may be performed to release the ligation or bandings. To avoid such complications, we must assess whether PDV closure can safely accommodate the increased portal venous inflow without severe intestinal congestion from portal hypertension. CT angiography is most effective to evaluate intrahepatic portal veins and hepatic veins, as well as PDV anatomy. Portal venography during PDV occlusion with a balloon catheter introduced via the superior vena cava in cases 1 and 4 demonstrated severe atrophy of the extrahepatic and intrahepatic portal veins (Figs. 1b–d, 3a). Functionally, complete occlusion of the PDV with the balloon catheter for 5 min resulted in elevation of the portal vein pressure (PVP) from 8 up to 45 cm H_2O in case 4. Thus, in this case, we chose the banding procedure to narrow the ductus venosus instead of ligation. This radiological occlusion test is one of the useful methods for choosing surgical treatments including liver transplantation in cases with large PDV. Furthermore, surgical procedures under intraoperative PVP monitoring are safe and effective. Our series suggest that intraoperative PVP monitoring is most beneficial in the surgical decision-making process for PDV. After intraoperative testing of PDV occlusion, the patients

whose PVP did not overcome 30 cm H_2O underwent complete ligation and showed no life-threatening complications. Therefore, the critical PVP after PDV ligation is probably about 30 cm H_2O. Thus, ligation under PVP monitoring could be an appropriate and effective treatment, even if the shunt is very large. In some cases, a staged procedure with preliminary narrowing of the shunt before final occlusion is more appropriate [4]. We attempted this procedure in the two cases. Interestingly, the flow of PDV diminished in one case and decreased markedly in the remaining case, indicating that banding method for narrowing PDV might be one of the most effective and safe procedures in cases with large PDV. Fortunately, there were no cases that suffered life-threatening complications and required liver transplantation. For the cases with severely hypoplastic portal vein and liver, liver transplantation may be the only available definitive treatment [9, 10, 22]. In case 1, we detected postoperative portal venous thrombosis. After PDV ligation or banding, portal hemostasis occurred in all cases to varying degrees. Thus, we should pay careful attention to hepatic inflow and outflow as well as intestinal congestion after surgery.

We concluded that the surgical ligation or banding of PDV should be preformed in patients who have hyperammonemia, hypergalactosemia, and hyperbilirubinemia at age <3 years. In older patients, progression of portal vein hypoplasia, liver atrophy with tumor formation, and intrapulmonary shunting result in hepatic dysfunction and encephalopathy. In some of these advanced patients, the only effective surgical procedure may be liver transplantation instead of surgical ligation or banding of PDV.

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