Portal hypertension induced by congenital hepatic arterioportal fistula: Report of four clinical cases and review of the literature

Dan-Ying Zhang, Shu-Qiang Weng, Ling Dong, Xi-Zhong Shen, Xu-Dong Qu

Abstract
Intrahepatic arterioportal fistula (IAPF) can be caused by many secondary factors. We report four cases of portal hypertension that were eventually determined to be caused by congenital hepatic arterioportal fistula. The clinical manifestations included ascites, variceal hemorrhage and hepatic encephalopathy. Computed tomography scans from all of the patients revealed the early enhancement of the portal branches in the hepatic arterial phase. All patients were diagnosed using digital subtraction angiography (DSA). DSA before embolization revealed an arteriovenous fistula with immediate filling of the portal venous radicles. All four patients were treated with interventional embolization. The four patients remained in good condition throughout follow-up and at the time of publication. IAPF is frequently misdiagnosed due to its rarity; therefore, clinicians should consider IAPF as a potential cause of non-cirrhotic portal hypertension.

Key words: Intrahepatic arterioportal fistula; Portal hypertension; Ascites

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: In Western countries, less than 10% of portal hypertension cases are caused by non-cirrhotic portal hypertension, including intrahepatic arterioportal fistula (IAPF). IAPF is a condition characterized by abnormal communication between the portal vein and the hepatic artery that most often occurs secondary to surgery, trauma, transhepatic intervention or biopsy. Currently, only 35 cases of congenital IAPF have been reported. To better understand the clinicopathological presentation of this
type of portal hypertension, IAPF-induced PH confirmed by angiography was studied in four patients. Because congenital hepatic arteriportal fistulae are rare, they are often misdiagnosed.

Zhan DY, Weng SQ, Dong L, Shen XZ, Qu XD. Portal hypertension induced by congenital hepatic arteriportal fistula: Report of four clinical cases and review of the literature. World J Gastroenterol 2015; 21(7): 2229-2235 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i7/2229.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i7.2229

INTRODUCTION

Portal hypertension is the result of resistance to portal blood flow. This resistance occurs most frequently within the liver (as in the case of cirrhosis) and can be caused by prehepatic and posthepatic factors\(^5\). In Western countries, less than 10% of portal hypertension cases are caused by non-cirrhotic portal hypertension\(^5\). We can easily diagnose portal hypertension if the risk factors are known; however, in some cases, the diagnosis may be challenging\(^5\). The causes of non-cirrhotic portal hypertension include schistosomiasis\(^6\), portal vein thrombosis and primary myelofibrosis, among others. Intrahepatic arteriportal fistula (IAPF), a rare cause of portal hypertension, is a condition characterized by abnormal communication between the portal vein and hepatic artery that most often occurs secondary to surgery\(^6\), trauma\(^7\)\(^9\), transhepatic intervention\(^10\) or biopsy\(^11\)\(^12\), or ruptured hepatic artery aneurysms\(^13\). If the diagnosis is in doubt, digital subtraction angiography (DSA) can be performed to help confirm the diagnosis\(^14\). To date, only 35 cases of congenital IAPF have been reported in the literature. IAPF can lead to portal hypertension (PH), which can pose a diagnostic challenge. To better understand the clinicopathological presentation of this type of portal hypertension, IAPF-induced PH confirmed by angiography was studied in four patients. The patients ranged in age from 33 to 74 years, with a mean age of 53.75 years; all of the patients received embolization therapy (Table 1).

CASE REPORT

Case 1

A 65-year-old woman was admitted to our hospital complaining of abdominal distension and oliguria of 3 months duration. Three months prior to presentation, the patient visited a local hospital for an abdominal ultrasound examination because of increased abdominal girth and decreased urine output. The examination revealed a large volume of ascites fluid and an increased flow rate in the portal vein with phasic flow reversal. A subsequent CT revealed the early enhancement of the portal branches in the hepatic arterial phase (Figure 1A).

No family history of chronic hepatic disease was elicited.

A physical examination upon presentation to our institution revealed the presence of ascites. A liver function test produced the following results: alanine aminotransferase (ALT), 23 U/L; aspartate transaminase, 34 U/L; total bilirubin (TB), 5.6 \(\mu\)mol/L; and conjugated bilirubin (CB), 2.2 \(\mu\)mol/L. All viral markers for hepatitis were negative. To ascertain the cause of ascites for the sake of diagnosis and treatment, diagnostic paracentesis was performed. The serum ascites albumin gradient was > 11 g/L, indicating that the ascites was due to portal hypertension. Hepatic angiography was performed, raising the suspicion of IAPF (Figure 1B and C). The patient was treated with interventional embolization. Figure 1D depicts the fistula reduction after the embolization. Anti-infectious therapies were instituted after the embolization. The patient’s ascites gradually resolved. Six months after the first embolization, the patient underwent a second embolization and recovered well.

Case 2

A 33-year-old woman with no previous history of viral hepatitis, hepatoma or other liver diseases was admitted with recurrent variceal bleeding despite repeated endoscopic therapy. The patient had no history of trauma or liver biopsy. The patient was confirmed to have severe esophageal and gastric fundal varices by endoscopy.

The patient had been admitted to the hospital twice prior to the current admission for fatigue and weakness. A hepatic ultrasonography revealed an intrahepatic portal vein 15 mm in diameter with tortuous branches. The patient had previously undergone two episodes of percutaneous transarterial embolization. On admission, liver function tests produced the following results: ALT, 16 U/L; AST, 18 U/L; TB, 19 \(\mu\)mol/L; and CB, 10 \(\mu\)mol/L. The abdominal color Doppler ultrasound revealed a diffuse aneurysmal portal vein fed by a large arterial branch with reversed blood flow in the portal vein. Gadolinium-enhanced magnetic resonance angiography (MRA) confirmed the diagnosis of multiple IAPF connecting the hepatic artery and the portal vein branch. No other vascular or parenchymal anomalies were detected. An endovascular procedure was performed to embolize the hepatic artery branch contributing to the fistula.

Table 1: Tabulation of the patient characteristics, treatments, results and follow-up

| Age/gender (mo) | Clinical presentation | Imaging | Treatment | Result |
|---------------|-----------------------|--------|----------|--------|
| 65/female 18  | Ascites               | CT/DSA | Embolization | Successful |
| 33/female 33  | Variceal bleeding     | Ultrasound/MRA | Embolization | Successful |
| 43/5/male 15  | Melaena               | MRA    | Laparotomy | Embolization Successful |
| 74/male 16    | Hepatic encephalopathy| CT/DSA | DSA | Embolization Successful |

Zhang DY, Weng SQ, Dong L, Shen XZ, Qu XD. Portal hypertension induced by congenital hepatic arteriportal fistula: Report of four clinical cases and review of the literature. World J Gastroenterol 2015; 21(7): 2229-2235 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i7/2229.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i7.2229
2 presents the arteriovenous fistula with the immediate filling of the portal venous radicles. The patient suffered no bleeding during the following 3 years. The patient was subjected to DSA 1 year after her initial presentation, which revealed that the fistula had significantly decreased in size. The patient underwent a second embolization treatment.

Case 3
A 43-year-old male patient with a history of severe melena was admitted on July 9, 2012. Eight years prior to admission, the patient had undergone a medical checkup at a referring hospital and was found to have a mass in his liver. The patient received an exploratory laparotomy, during which the diagnosis of IAPF was confirmed. Ligation of the hepatic artery was performed. The patient continued to be followed by imaging after discharge. Four years prior to admission at our hospital, the patient suffered from melena and an endoscopy revealed esophageal varices. A Doppler ultrasonography revealed a patent portal vein with reversed flow and a compensatory increase in the hepatic arterial signal. A CT scan (Figure 3) revealed the synchronous filling of the portal vein and hepatic artery in the arterial phase. The CT finding was sufficiently characteristic to justify this diagnosis and thus curtail any additional investigation. The fistula in this patient was occluded successfully by embolization. Further portography

Figure 1  Contrast-enhanced computed tomography revealed an earlier enhancement of the portal vein compared with the superior mesenteric vein during the arterial phase. Digital subtraction angiography indicated that there was rapid filling through the fistula into the portal vein. A: Early enhancement of the portal branches in hepatic arterial-phase; B, C: The hepatic angiography; D: The fistula reduction after embolization.

Figure 2  Digital subtraction angiography before embolization revealed the arteriovenous fistula with the immediate filling of the portal venous radicles.
confirmed the restoration of normal portal blood flow. The patient recovered well and continues to be followed by imaging.

Case 4
A 74-year-old male patient was admitted because of an altered mental status and dysarthria for three months. The patient was unable to respond appropriately to questions, was disoriented and exhibited a decreased ability to perform calculations. Thus, the patient was sent to the referral hospital. No family history of chronic hepatic disease was elicited. The patient’s ammonia level was increased to 144 μmol/L. The values of other biochemical tests were within the normal ranges. All viral markers for hepatitis, including hepatitis A-E viruses, auto-antibodies (antinuclear, anti-mitochondrial, anti-smooth muscle, anti-soluble liver antigen and anti-mitochondrial antibody), were also negative. His serum alpha fetoprotein level was 10 μg/L. An ultrasound revealed an enlargement of the portal vein, high flow in the hepatic artery and reversed flow in the portal venous system. Selective DSA of the hepatic artery revealed a diffuse arterioportal fistula (Figure 4). The patient was treated with a low-protein diet, bowel cleansing with lactulose, antibiotic treatment and parenteral nutrition via an IV line. Five days later, the patient gradually became conscious and responded appropriately to questions and commands. However, 10 months after admission, the patient suffered recurrent hepatic encephalopathy. An embolization was performed in August 2013 to correct the precipitating causes. By follow-up in March 2014, the patient had recovered well. The short-term prognosis of embolization is quite good but the long-term effect is still unknown. Liver transplantation should potentially be considered.

DISCUSSION
The portal venous system has a large volume capacity and low resistance. PH occurs when the portal flow or vascular resistance is increased. Based on the anatomical location, PH is classified as prehepatic, intrahepatic or posthepatic. Intrahepatic PH is further histologically classified as presinusoidal, sinusoidal and postsinusoidal[15]. IAPF was first reported approximately 40 years ago[16] and is now defined as an intrahepatic communication between the hepatic artery and the portal venous system. IAPF is an uncommon cause of presinusoidal PH and is believed to be the result of increased blood flow in the portal system.

IAPF was first reported approximately 40 years ago by Gryboski et al.[16] but its etiology remains unclear. IAPF often occurs secondary to fine needle liver biopsy[11,12], interventional radiology, blunt[17] or penetrating liver trauma[9,10], hepatectomy[6], liver cancer[17,18], hepatic artery aneurysms or hemangioma[13], percutaneous transhepatic biliary drainage[10,20], radiofrequency ablation...
or transhepatic portosystemic stent shunts. In 1997, Vauthey et al. analyzed 88 cases of IAPF and found that spontaneous arteriportal fistula may be caused by hepatic diseases such cirrhosis, adenoma, hepatocellular carcinoma (HCC) and cavernous hemangioma. The authors also found that fewer than 10% of IAPF cases were congenital. Congenital IAPF is a rare entity and is always diffuse or multiple, whereas a solitary fistula is always acquired. To date, only 35 cases of congenital IAPF have been reported in the literature, mostly occurring in infants.

The symptomatology of IAPF can include hepatomegaly, ascites, bleeding episodes and splenomegaly. Small IAPF can be asymptomatic. These clinical presentations occur as consequences of imbalances in Starling’s law such that the force keeping fluid in the vascular space is not as strong as the force moving fluid out of the vascular space.

IAPF is usually divided into three classes: (1) small peripheral intrahepatic (type 1); (2) large central IAPF (type 2); and (3) diffuse congenital intrahepatic (type 3). Norton et al. classified IAPF according to the supplying afferent vessels. A unilateral IAPF is supplied by only one of the right, left or main hepatic arteries (type 1). Bilateral lesions include a supply from both hepatic arteries or their branches (type 2). Type 3 consists of complex lesions.

Ultrasonography is now widely used to investigate IAPF because it is convenient, reliable, economical and noninvasive in detecting blood flow from small targets in all directions in the liver. Even some small asymptomatic arteriportal fistulas that are easily overlooked can be detected by ultrasound. Ultrasonography can also be used to determine hepatic hemodynamics, especially in patients with cirrhosis. In our four cases, ultrason demonstrated reverse pulsatile flow in the portal vein, thus helping establish the diagnosis. CT and MRI are also helpful for the accurate diagnosis of IAPF because fistula vessels can be easily identified in the early arterial phase. Contrast-enhanced CT findings of IAPF typically include the following: (1) earlier enhancement of the affected portal vein compared with the superior mesenteric or splenic vein during the early arterial phase; and (2) earlier enhancement of the portal vein branches compared with the main portal vein. The MRI pattern of IAPF is similar to that of a CT. Contrast-enhanced MRA can provide both an accurate depiction of portal vascular anatomy and a measurement of portal hemodynamics. DSA is an important diagnostic and therapeutic procedure in cases of unexplained PH. Haruki et al. reported an IAPF mimicking a metastatic liver tumor, indicating that the selection of an appropriate diagnostic modality is important for careful diagnosis.

The differential diagnosis of IAPF is very important. IAPF can be misinterpreted for HCC, metastatic liver tumors or hemangioma. For example, the key characteristics of HCC on CT are hypervascularity in the arterial phase and washout or de-enhancement in the portal and delayed phases. Generally, metastatic liver tumors are seen as a ring-enhancement on enhanced CT and they usually exhibit an increased high signal intensity on DWI with low apparent diffusion coefficient values. In contrast, IAPF is visualized as a low intensity on DWI. DSA should be performed to make the final diagnosis and to exclude hepatic sinusoidal obstruction syndrome (SOS) and Budd-Chiari syndrome. These two diseases can also be characterized by hepatomegaly, ascites and right upper quadrant pain. Most cases of SOS are diagnosed clinically. SOS typically occurs in the context of hematopoietic cell transplantation and can also be induced by the ingestion of pyrrolizidine alkaloids. The diagnosis of hepatic SOS relies heavily on clinical diagnostic criteria. A liver biopsy can be diagnostic of SOS. Budd-Chiari syndrome is defined as hepatic venous outflow tract obstruction. Ascites and lower extremity edema may occur because of chronic occlusion of the hepatic veins. A CT or MRI can be performed to confirm the diagnosis. Venography can be used to make the diagnosis if the noninvasive tests are negative.

The treatment of IAPF includes a percutaneous transarterial embolization, surgical ligation of the implicated hepatic artery, partial hepatectomy and liver transplantation. Interventional radiological treatment is considered the preferred procedure. However, whether this treatment is effective long-term remains unknown.

There is a wide range of embolic agents and devices available, including ethanol, Gelfoam, steel coils and detachable balloons. The combination of microcoils and N-butyl Z-cyanoacrylate is reportedly an effective method of embolization. Chen et al. reported the successful treatment of complex high-flow IAPF cases with a Guglielmi Detachable Coil in combination with NBCA injection. Studies have also reported that end-to-site portocaval shunting can reduce portal pressure effectively and preserve vascular anatomy to facilitate liver transplantation.

Embolization is advantageous in that it can decrease pain, lower morbidity and shorten the length of hospital stay. The main risks of embolization are as follows: (1) the material could move from the original site to the portal system because of the high flow in the fistula; and (2) the material used could float to an incorrect site. Surgery is indicated only when the embolization fails.

In conclusion, we diagnosed four cases of congenital IAPF using multiple imaging modalities, including angiography. Angiography is useful to distinguish IAPF from malignant liver tumors. Embolization plays an important role in the treatment of IAPF.

**COMMENTS**

**Case characteristics**

The 4 cases presented with complications of portal hypertension (ascites, variceal bleeding, liver mass and altered MS).

**Clinical diagnosis**

The disease exhibits the characteristics of portal hypertension, including hepatomegaly, ascites, bleeding episodes and splenomegaly.

---

**ZhanDYet al. Congenital hepatic arteriportal fistula**
Related reports

Very few cases of congenital intrahepatic arterioportal fistula (IAPF) have been reported in the literature. Embolization is considered the preferred procedure but whether it is effective in the long run remains unknown.

Term explanation

SOS: Hepatic sinusoidal obstruction syndrome, also called veno-occlusive disease. Long-standing congestion can cause centrilobular fibrosis, leading to cirrhosis.

Experiences and lessons

The case report presents the clinical characteristics of congenital IAPF and discusses the treatment of IAPF. Because congenital hepatic arterioportal fistula is rare, it is often misdiagnosed. Therefore, clinicians should consider IAPF as a potential cause of non-cirrhotic portal hypertension.

Peer-review

The authors have described four cases of congenital IAPF. The article highlights the clinical characteristics of this disease and provides insights into the therapeutic implications.

REFERENCES

1. Ikawari Y. Pathophysiology of portal hypertension. Clin Liver Dis 2014; 18: 281-291 [PMID: 24679494 DOI: 10.1016/j.cld.2013.12.001]
2. Kim MY, Jeong WK, Baik SK. Invasive and non-invasive diagnosis of cirrhosis and portal hypertension. World J Gastroenterol 2014; 20: 4300-4315 [PMID: 24766467 DOI: 10.3748/wjg.v20.i15.4300]
3. Garcia-Pagán JC, Gracia-Sancho J, Co J, Bosch J. Functional aspects on the pathophysiology of portal hypertension in cirrhosis. J Hepatol 2012; 57: 458-461 [PMID: 22504334 DOI: 10.1016/j.jhep.2012.03.007]
4. Berzigotti A, Seijo S, Reverter E, Bosch J. Assessing portal hypertension in liver diseases. Expert Rev Gastroenterol Hepatol 2013; 7: 141-155 [PMID: 23363263 DOI: 10.1586/egh.12.83]
5. Khanna R, Sarin SK. Non-cirrhotic portal hypertension - diagnosis and management. J Hepatol 2014; 60: 421-441 [PMID: 23978714 DOI: 10.1016/j.jhep.2013.08.013]
6. Davenport M, Redkar R, Howard ER, Karani J. Arterioportal hypertension: a rare complication of partial hepectectomy. Pediatr Surg Int 1999; 15: 543-545 [PMID: 10631729]
7. Tanaka H, Iwai A, Sugimoto H, Yoshio T, Sugimoto T. Intrahepatic arterioportal fistula after blunt hepatic trauma: case reports. J Trauma 1993; 34: 143-146 [PMID: 1986122]
8. Eastridge BJ, Minei JP. Intrahepatic arterioportal fistula after hepatic gunshot wound: a case report and review of the literature. J Trauma 1997; 43: 523-526 [PMID: 9314320]
9. English WP, Johnson MB, Borman KR, Turner WW. Mesenteric ischemia: an unusual presentation of traumatic intrahepatic arterioportal fistula. Am Surg 2001; 67: 865-867 [PMID: 11565765]
10. Kim TK, Choi BI, Han JY, Chung JW, Park JH, Han MC. Nontumorous arterioportal shunt mimicking hypertensive tumor in cirrhotic liver: two-phase spiral CT findings. Radiology 1998; 208: 597-603 [PMID: 9722834]
11. Okuda K, Musha H, Nakajima Y, Takayasu K, Suzuki Y, Morita M, Yamasaki T. Frequency of intrahepatic arteriovenous fistula as a sequela to percutaneous needle puncture of the liver. Gastroenterology 1978; 74: 1204-1207 [PMID: 648810]
Choi BI, Lee KH, Han JK, Lee JM. Hepatic arterioportal shunts: dynamic CT and MR features. *Korean J Radiol* 2002; 3: 1-15 [PMID: 11919473]

Sharpley J, Thode H, Sestina L, Park R, Monnet E, Kraft SL. Distal abdominal aortic thrombosis diagnosed by three-dimensional contrast-enhanced magnetic resonance angiography. *Vet Radiol Ultrasound* 2009; 50: 370-375 [PMID: 19697601]

Mai W. Multiphase time-resolved contrast-enhanced portal MRA in normal dogs. *Vet Radiol Ultrasound* 2009; 50: 52-57 [PMID: 19241754]

Haruki K, Wakiyama S, Shiba H, Ishida Y, Yanaga K. Intrahepatic arterioportal shunt mimicking a metastatic liver tumor: report of a case. *Surg Today* 2012; 42: 391-394 [PMID: 22143359]

Chen Q, Tack C, Morcos M, Ruggiero M, Schlossberg P, Fogel J, Weng LJ, Farkas J. Embolotherapy of an arterioporal fistula. *Cardiovasc Intervent Radiol* 2007; 30: 1047-1051 [PMID: 17497067]

Sutcliffe R, Mieli-Vergani G, Dhawan A, Corbally M, Karani J, Heaton N. A novel treatment of congenital hepatoporal arteriovenous fistula. *J Pediatr Surg* 2008; 43: 571-573 [PMID: 18358306 DOI: 10.1016/j.jpedsurg.2005.07.005]

Tannuri AC, Tannuri U, Lima FR, Ricardi LR, Leal AJ, da Silva MM. Congenital intrahepatic arterioportal fistula presenting as severe undernutrition and chronic watery diarrhea in a 2-year-old girl. *J Pediatr Surg* 2009; 44: e19-e22 [PMID: 19853734 DOI: 10.1016/j.jpedsurg.2009.07.027]

Heaton ND, Davenport M, Karani J, Mowat AP, Howard ER. Congenital hepatoporal arteriovenous fistula. *Surgery* 1995; 117: 170-174 [PMID: 7846621]

Kumar A, Ahuja CK, Vyas S, Kaira N, Khandelwal N, Chawla Y, Dhiman RK. Hepatic arteriovenous fistulae: role of interventional radiology. *Dig Dis Sci* 2012; 57: 2703-2712 [PMID: 22875308]

Srivastava DN, Sharma S, Pal S, Thulikar S, Seith A, Bandhu S, Pande GK, Sahni P. Transcatheter arterial embolization in the management of hemobilia. *Abdom Imaging* 2006; 31: 439-448 [PMID: 16447087]

Tasar M, Gulce B, Bozlar U, Saglam M, Ugurel MS, Ucoz T. Intrahepatic arterioportal fistula and its treatment with detachable balloon and transcatheter embolization with coils and microspheres. *Clin Imaging* 2005; 29: 325-330 [PMID: 16153538]

Flum AS, Geiger JD, Gemmete JJ, Williams DM, Teitelbaum DH. Management of a traumatic hepatic artery pseudoaneurysm and arterioporal fistula with a combination of a stent graft and coil embolization using flow control with balloon remodeling. *J Pediatr Surg* 2009; 44: e31-e36 [PMID: 19853737 DOI: 10.1016/j.jpedsurg.2009.07.036]

Botelberge T, Van Vlierberghhe H, Voet D, Defreyne L. Detachable balloon embolization of an arterioporal fistula following liver biopsy in a liver transplant recipient: a case report and review of literature. *Cardiovasc Intervent Radiol* 2005; 28: 832-835 [PMID: 15889440]

Cil RE. Transhepatic embolization of a recanalized congenital hepatic arterioportal fistula with NBCA and coils. *Cardiovasc Intervent Radiol* 2004; 27: 172-174 [PMID: 15259817]

Dumortier J, Pilleul F, Adham M, Vochelle V, Hervieu V, Bouffard Y, Valette PJ, Scoalze JY, Boilot O. Severe portal hypertension secondary to arterio-portal fistula: salvage surgical treatment. *Liver Int* 2007; 27: 865-868 [PMID: 17617130]

---

**P-Reviewer:** Garcia-Martinez B, Liang XS, Penkova-Radicheva MP, Wang GY  
**S-Editor:** Qi Y  
**L-Editor:** Roemmele A  
**E-Editor:** Liu XM
