Transarterial and Transhepatic Endovascular Intervention to Alleviate Portal Hypertension Secondary to Arterioportal Fistula in a Trisomy 21 Infant

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Abstract

Individuals with trisomy 21 have an 80% risk reduction of vascular anomalies compared with general population. However, an association of trisomy 21 and portal vascular and arteriovenous anomalies has been defined in the literature. The primary hemodynamic abnormality in portal hypertension is increased resistance to portal blood flow. In various case reports in adults and pediatric age group patients, transarterial coil embolization of hepatoportal fistula was described. One of the authors of this article has previously reported successful treatment of congenital arterioportal fistula (APF) with percutaneous transhepatic liquid embolization in a patient who previously had transarterial coil embolization. To date, eight patients with trisomy 21 (Down syndrome) and congenital portosystemic shunts were reported of which four were treated with embolization. Here, we describe a 3-month-old infant with trisomy 21 and intrahepatic APF associated with extrahepatic portal hypertension and massive ascites. In the current report, a rare case of a patient with a diagnosis of trisomy 21 is discussed who was attempted to be treated with transarterial coil embolization and percutaneous transhepatic liquid embolization of the congenital APF in a single session.

Keywords

- portal hypertension
- arterioportal fistula
- trisomy 21

Introduction

In general, patients with trisomy 21 have a reduced risk of vascular anomalies compared with the general population.¹ It has been thought to be related to increased antiangiogenic factors in trisomy 21. However, arteriovenous and arterioportal anomalies were defined in patients with trisomy 21.^{1–3} Portal hypertension is defined as an elevation of portal venous pressure >10 to 12 mm Hg. The primary hemody-

namic abnormality in portal hypertension is increased resistance to portal blood flow.⁴ There are many causes of portal hypertension including a heterogeneous group of diseases due to intrahepatic or extrahepatic etiologies.⁵ Some extrahepatic causes of portal hypertension are portal vein agenesis, atresia, stenosis, thrombosis, splenic vein thrombosis, increased portal flow, and arteriovenous fistula.

The liver has a special dual blood supply, with a compensatory relationship existing between the arterial and the

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portal venous flow. Intrahepatic vascular shunts consist of abnormal communications between the hepatic arteries, portal veins, and hepatic or systemic veins.⁶ Three different types of hepatic vascular anomalies (short circuits or “shunts”) are defined: from hepatic artery to hepatic vein, from portal vein to hepatic vein and from hepatic artery to a portal vein. The most common type is hepatic artery to hepatic vein shunt. Arterioportal fistula (APF) may be intra- or extrahepatic and acquired or congenital. The most common causes of acquired APF are cirrhosis and hepatic neoplasms, blunt or penetrating trauma, percutaneous liver biopsy, transhepatic cholangiography, gastrectomy, and biliary surgery. Congenital APF is a rare cause of portal hypertension. Although in most case reports they are not associated with any other disease, they can be associated with hereditary hemorrhagic telangiectasia, Ehlers-Danlos syndrome, and biliary atresia.^{7,8} Intrahepatic arterioportal 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 like partial hepatectomy,^{9,10} trauma like blunt hepatic trauma,¹¹ percutaneous liver biopsy¹² or ruptured hepatic artery aneurysms.¹³ Hepatic artery to portal vein fistulae is relatively uncommon lesions with variable clinical presentations, such as variceal bleeding, ascites, splenomegaly, diarrhea or heart failure.

Transarterial coil embolization of hepatoportal fistula has been described in the literature in adult, and pediatric patients in various case reports.^{14–17} Additionally, one of the authors of this manuscript has previously reported successful treatment of congenital APF with percutaneous transhepatic liquid embolization in a patient who previously had transarterial coil embolization.¹⁸ Till date, eight patients with trisomy 21 and congenital portosystemic shunts were reported of which four were treated with embolization.^{2,19–23}

Patients with trisomy 21 are at a reduced risk of developing vascular anomalies compared with the general population.¹ Although, vascular anomalies such as lymphatic malformations and shunts (of arteriovenous, arterioportal, and portosystemic venous types) have been described in patients with trisomy 21, an arteriovenous fistula between a hepatic artery and portal vein are rarely reported.^{1,19,20} Congenital APF was rarely reported in the literature. IAPF, a rare cause of portal hypertension, is a condition characterized by an abnormal communication between the portal vein and hepatic artery. To date, only 35 cases of congenital IAPF have been reported in the literature.²⁴ To the best of our knowledge, 8 out of 35 were diagnosed with trisomy 21. In 1992 and 2004, the first two cases of trisomy 21 patients who had a congenital portosystemic shunt were reported.^{19,20} The other six out of these eight trisomy 21 patients were treated with embolization. In 2007, Landau et al reported a boy with trisomy 21 with a fistula between a superior mesenteric artery and portal vein which was treated with embolization and biological glue.²¹ Golewale et al reported three cases of portal vascular anomalies in trisomy 21, two of which were treated with embolization and one patient was

treated conservatively.² Bogert et al reported a 79-day-old trisomy 21 boy with a diagnosis of arterioportal shunt successfully treated with embolization.²²

We describe a 3-month-old infant with trisomy 21 (Down syndrome) and intrahepatic APF associated with extrahepatic portal hypertension and massive ascites. Here, we report a rare case of a patient with a diagnosis of trisomy 21 who was attempted to be treated with transarterial coil embolization and percutaneous transhepatic liquid embolization of the congenital APF in a single session. In the current case, the APF in between right-left hepatic artery and the left portal vein is reported.

Case Report

A 3-month-old boy weighing 3 kg, with trisomy 21 and congenital heart disease (perimembranous ventricular septal defect, atrial septal defect) and severe portal hypertension was referred to our hospital for coil embolization.

At physical examination, the patient was found to have growth retardation (weight: 3 kg < 3p, height: 65 cm < 3p), characteristic dysmorphic features of trisomy 21 and hepatomegaly, splenomegaly, massive ascites, increased abdominal venous markings, a 2/6 systolic heart murmur, subcostal retractions, prolonged expiration, and bilateral rales.

Laboratory findings were as follows: hemoglobin: 9.6 g/dL (range: 13.6–17.2), activated partial thromboplastin time: 44 (range: 27.9–38.1) seconds, international normalized ratio (INR): 1.8 (range: 0.86–1.20), serum albumin: 2.3 g/dL (range: 3.8–5.4), B-type natriuretic peptide: 2,137 pg/mL (range: 0–100), liver, and kidney function tests and serum electrolytes were at normal range. Low albumin and prolonged INR suggested liver dysfunction.

Sonographic examination of the upper abdomen showed severe ascites and hepatosplenomegaly. Multiple countless aneurysmal arteriovenous fistulae between the second and third branching regions of right and left hepatic artery, gastroduodenal artery, and left portal vein were demonstrated by portal Doppler sonography. He had no previous interventions to the liver, such as liver biopsy or trauma, which might cause APF. Therefore, he was diagnosed as congenital APF. Under general anesthesia by right femoral arterial puncture, celiac arteriography was performed for further evaluation and coil embolization which demonstrated diffuse connections between the left portal vein and main hepatic artery, gastroduodenal artery, second and third branches of right and left hepatic artery (→ **Fig. 1A, B**). Right, and main hepatic arteries were embolized with multiple metallic coils. Detectable metallic coils 0.014 in were used. In addition to transarterial endovascular coil embolization, percutaneous transhepatic access to the left portal vein was performed. Left portal vein fistulae to left hepatic artery were embolized from the portal venous side with 20% diluted n-butyl-2-cyanoacrylate. Following the embolization procedure, celiac arteriography revealed only a partial occlusion of APF due to diffuse involvement (→ **Fig. 2**). Right hepatic artery and main hepatic artery were embolized with multiple metallic coils by

Fig. 1 (A) Common hepatic artery injection shows multiple connections between hepatic artery branches and the left portal vein. Black and white arrow demonstrates right and left hepatic artery, respectively. (B) Late phase image shows aneurysmal dilatation of the left portal vein secondary to the fistulae.

microcatheterization technique (Transcend microcatheter [Boston Scientific]). During the same session, transarterial metallic and percutaneous transhepatic liquid embolization procedure was performed. In control celiac arteriography, 60 to 70% of the widespread fistulas were occluded and especially from peripancreatic collaterals fistula was continuing to fill. Due to the technical impossibility of total embolization, the procedure was finished. Clinical features of portal hypertension including ascites persisted after embolization. Before embolization, we performed paracentesis on

a daily basis. However, after embolization, the paracentesis intervals were decreased to weekly basis. The current case was benefited from interventional embolization therapy. The patient received antibiotic therapy for the nosocomial infections after long intensive care unit hospitalization. Portal hypertension including ascites persisted, and therefore spironolactone therapy was continued. The follow-up of the patient was done by Doppler ultrasonography at 3-month intervals until 2 years from the procedure. During follow-up course, the signs and symptoms of portal hypertension did not worsen.

Fig. 2 Postembolization contrast injection shows occlusion of the hepatic artery. However, left portal vein still fills via small arterial branches from the proximal part of the common hepatic artery.

Discussion

Arteriovenous malformations are defects of the circulatory system that are generally believed to arise during embryonic or fetal development or soon after birth and can develop in any part of the body. The absence of capillaries—small blood vessels that connect arteries to veins—creates a short-cut for blood to pass directly from arteries to veins. The association of arterioportal malformations with extrahepatic portal hypertension is rare, and these findings are even rarer in trisomy 21. Intrahepatic APFs are defined as connections between the systemic arterial system and portal venous system, without any connection with systemic venous circulation. Increased portal blood flow which develops due to this connection leads to presinusoidal portal hypertension.²⁵ Most of the symptoms of hepatic APF are related to portal hypertension. Hepatic APF is a rare,¹⁰ but treatable cause of portal hypertension and may lead to severe gastrointestinal bleeding (66% of cases),²⁶ ascites, splenomegaly, failure to thrive (50%), chronic diarrhea, or steatorrhea (50%). At least 20% of these patients need hospitalization for the symptoms related to hypoalbuminemia and fat malabsorption as part of

protein-losing enteropathy. Physical examination usually reveals signs of portal hypertension. Marked splenomegaly (63% of cases), hepatomegaly (41% of cases), ascites or edema (47% of cases), and prominent abdominal distension (41% of cases).²⁷ As hepatic hemangioma or hemangioendothelioma cannot easily be distinguished from arterioportal malformations, radiological examination plays a critical role in the diagnosis of APF. Doppler ultrasound is one of the acceptable ways for making the decisive diagnosis and is helpful in the subsequent evaluation of these patients.²⁸ In recent years cross-sectional imaging methods (magnetic resonance) are also used for diagnosis. Hepatic angiography is the second step for diagnosis and also a way of confirming the diagnosis, but ultrasonography is preeminent in some points as it is noninvasive, rapid, and inexpensive.^{8,29} Selective arteriography of hepatic arteries provides an opportunity to make definitive diagnosis and planning of treatment, either surgery or embolization.

Clinical features of APF are mostly dependent on the fistula location and shunt size.³⁰ The volume of the shunted blood is proportional to the symptomatology of patient.³¹ Some of the symptoms occur due to mesenteric vascular congestion such as chronic malabsorption, diarrhea, and abdominal pain.³¹

The most common causes of APF are trauma, iatrogenic damage, and congenital vascular malformations or ruptured hepatic artery aneurysms.³² Secondary causes of hepatic APF are well defined which include major blunt or major penetrating abdominal trauma, surgical procedures, such as segmental liver transplantation, liver biopsy or Kasai operation.³³ Dispersed, or multiple APF are generally congenital in origin.³⁴ Congenital APF is initially due to direct arterial pressure being transmitted to the portal vein; later periportal fibrosis, vascular occlusive changes follow. Congenital APF is a rare condition in childhood. To date, only 35 cases of congenital intrahepatic APF have been reported. According to Norton-Jacobson's angiographic classification, congenital intrahepatic APFs are divided into three classes due to their afferent supply: type 1 (unilateral), type 2 (bilateral), and type 3 (complex).³⁵ Preferred treatment modalities are transarterial embolization for types 1 and 2, and ligation or surgery for type 3 APF. Liver function tests are usually normal in these patients like in our patient. Hepatic angiography is considered the gold standard to confirm the diagnosis and to demonstrate the vascular anatomy.³⁶

Trisomy 21 has been associated with more than 80 anomalies, and any organ can be potentially affected with these. Patients with trisomy 21 have reduced the risk of solid tumors and elevated levels of circulating antiangiogenic proteins. These elevated antiangiogenic factors might protect trisomy 21 patients from vascular malformations. Greene et al have shown that vascular anomalies are less common in patients with trisomy 21 compared with general population.¹ There is a case report which describes a boy with trisomy 21 and a novel combination of multiple vascular anomalies: extrahepatic portal hypertension, an arteriovenous malformation at the ileocecal junction, and caval/iliac vein anomalies.³⁷ Among vascular abnormalities of hepatic portal system in trisomy 21

patients, those involving umbilical vein, splenic vein, hepatic vein, and mesenteric superior vein are reported rarely.³⁸ However, our case had trisomy 21 along with a rare vascular malformation APF. It is important to note that a congenital APF might not be related to trisomy 21. Further studies are needed to evaluate the relationship between trisomy 21 and APF.

The aim of treatment of APF is a reduction of blood flow within the portal venous system.²⁴ Also, spontaneous closure/resolution of APFs has been reported in several cases. APF can be closed by angiographic and surgical approaches. Angiographic closure of the shunt consists of occluding the feeding artery, the draining vein, the arterioportal shunt itself, or any combination of these. Surgical options include hepatic resection, hepatic artery ligation, and reconstruction of the involved vessels.¹⁰ Mortality and morbidity of surgical treatment are higher than the angiographic treatment which is more effective and safe. None of these surgical techniques appeared feasible in our patient because of the complex nature of the fistulae. Some of the complex congenital APFs have a tendency to recur after the radiological intervention. By performing coil and liquid embolization in the same session most of the diffuse fistulae were occluded. Our patient was partially treated with the radiological method, and he was followed up at 3-month intervals by Doppler ultrasonography without recurrence until 2 years from radiological intervention procedure. Our patient showed clinical improvement after embolization with a decrease in paracentesis intervals. However, probably because of multiple fistulae, portal hypertension did not resolve completely.

Duration of long-term follow-up in previously reported cases of trisomy 21 with APF who were treated with embolization has not been reported in the literature. Most of the patients become asymptomatic shortly after treatment. Most patients' hepatic functions are preserved. Awareness of this condition in children with symptoms such as ascites, upper gastrointestinal bleeding or splenomegaly will avoid irreversible portal hypertension. In patients with missed or delayed diagnosis, significant morbidity is reported.³⁷

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