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EDUCATION AND IMAGING

Hepatobiliary and Pancreatic: Hepatic arterioportal fistula: A novel and treatable feature of Alagille syndrome

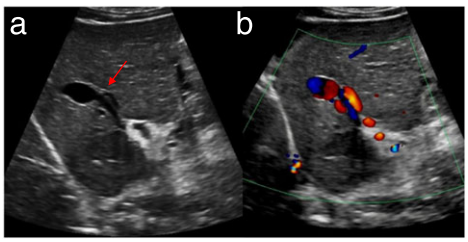

Figure 1 Ultrasound of the liver, showing the arterioportal fistula communicating with a portal venous varix (arrow, a), which is demonstrated on Doppler image (b).

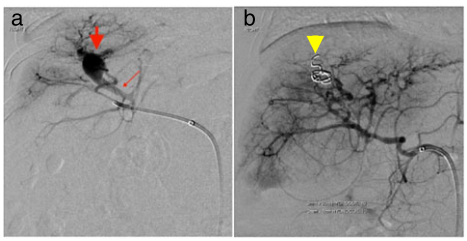

Figure 2 Selective right hepatic arteriogram showing the arterioportal fistula communication with the portal venous varix (solid arrow) and retrograde opacification of the right portal vein (long arrow) (a). The fistula was closed by deploying two coils (arrow head), and the right portal venous varix was no longer opacified (b).

A 1-week-old boy presenting with neonatal jaundice underwent work-up for conjugated hyperbilirubinemia. The child's stools were pigmented but a hepatobiliary scintiscan revealed no extrahepatic biliary excretion of tracer. Further investigations revealed bilateral branch pulmonary artery stenoses, posterior embryotoxon, renal cysts, and multiple butterfly vertebrae. Alagille syndrome was clinically suspected.

Liver histopathology at 3 weeks of age revealed prominent cholestasis, focal bile duct plugging, and bile duct proliferation. There was no paucity of intrahepatic bile ducts that was presumed secondary to the young age (28 days) at biopsy. Subsequent genetic testing confirmed a pathogenic *JAG1* variant confirming the diagnosis of Alagille syndrome. A hepatobiliary scan at 6 weeks of age revealed extrahepatic biliary dilatation.

At 4 months of age, the patient presented with upper gastrointestinal tract bleeding. An upper gastrointestinal endoscopy revealed a grade one varix in the distal esophagus, and an ultrasound scan (Figs 1) showed a large vascular space in the right lobe of the liver that demonstrated mixed arterial and venous flow suggestive of a communication between the hepatic artery and portal vein.

Over the next 3 months, the child developed increasing ascites and splenomegaly. Liver synthetic function remained intact. The AV fistula was suspected and at 8 months of age, hepatic angiography was performed. This demonstrated a branch artery of the right hepatic artery communicating with a portal venous varix via a fistula. On angiography contrast showed early retrograde opacification of the portal vein (Fig. 2a). The fistula was embolized with placement of a 3- and 2-mm Hydrasoft hydrocoils (Terumo Microvention, CA, USA) that resulted in complete occlusion of the fistula (Fig. 2b).

Following this intervention, the patient has progressed well clinically, with good growth, resolution of his ascites, and increase in his platelet count. Follow up ultrasonography has demonstrated normal portal flow with no evidence of AV shunting.

Alagille syndrome is a multisystem, autosomal dominant disorder caused by defects in the Notch signaling pathway. It is associated with liver disease of variable severity, and the main presentation is neonatal cholestasis due to a paucity of intra-hepatic bile ducts. Almost 90% cases are due to mutations in *JAG1* (20p12), 5–7% are due to deletions incorporating *JAG1* and about 1% due to mutations in *NOTCH2* (1p13). A range of vascular anomalies are known to occur in Alagille syndrome. However, to our knowledge, this is the first case of hepatic AV malformation described in Alagille syndrome.

The course of liver disease in Alagille syndrome is variable. The presence of cholestasis in early life, fibrosis on liver biopsy, and xanthomata suggest worse hepatic outcomes. Up to half of children with Alagille syndrome will require liver transplantation with a significant proportion also developing portal hypertension. These features seldom present within the first 12 months of life. Intrahepatic APFs are a rare cause of portal hypertension and gastrointestinal bleeding in children. Less than 10% of them are congenital. APFs are defined as intrahepatic communication between the hepatic artery and the portal system with no connection to the systemic venous circulation. The clinical manifestations of APFs are due to portal hypertension and tend to appear within the first year of life. Doppler ultrasound is a reliable diagnostic modality for intrahepatic APF; however, magnetic resonance imaging or computed tomography is usually required to better elucidate the anatomy. Catheter angiography remains the gold standard modality of imaging to accurately identify the number of feeding vessels and delineate the anatomy of the portal system. Catheter angiography is routinely done as a therapeutic procedure. Endovascular treatment of APFs by interventional radiology has high success rates and is considered the first therapeutic option. There has been no reported case of spontaneous closure of an APF.

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