

# Transcatheter embolization of congenital hepatic arteriovenous malformation using ethylene-vinyl alcohol copolymer (Onyx)

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## ABSTRACT

A male infant with high-output heart failure who had been found to have a hepatic arteriovenous malformation by ultrasound imaging was referred to our center (Department of Diagnostic and Interventional Radiology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Islamic Republic of Iran) for further evaluation. Computed tomography angiography revealed a large hepatic arteriovenous malformation with feeders originating from enlarged hepatic arteries and draining to enlarged hepatic veins. We performed a transcatheter embolization of the anomaly using ethylene vinyl alcohol copolymer (Onyx) during a single session. The cardiac function of the infant rapidly improved after the procedure. Over the 19 months of follow-up, his cardiac output remained stable and within the normal limits, and no complications were detected.

*Key words:* • ethylene-vinyl alcohol copolymer • arteriovenous malformation • embolization

Congenital hepatic arteriovenous malformation (AVM) is a rare anomaly that presents with high-output heart failure at infancy (mean age of 2.2 months). Other presenting features include hepatomegaly, consumptive coagulopathy, portal hypertension, anemia, brisk pulse, hydrops fetalis, and intestinal ischemia secondary to a steal phenomenon (1). Patient management consists of medical treatment for heart failure and definitive elimination of the underlying cause by means of hepatic artery embolization or ligation, partial hepatic resection or liver transplantation. In recent years, endovascular embolization using metallic coils or polyvinyl alcohol (PVA) particles has been pursued. However, the success of these techniques has been hampered by complications including recurrent cardiac failure; pulmonary, portal vein or systemic embolization; fatal liver necrosis; and biliary tract damage (2, 3).

We successfully used ethylene-vinyl alcohol copolymer (Onyx) to embolize the hepatic AVM of a child suffering from high-output heart failure. No complications were noted during the 19 months of follow-up.

## Case report

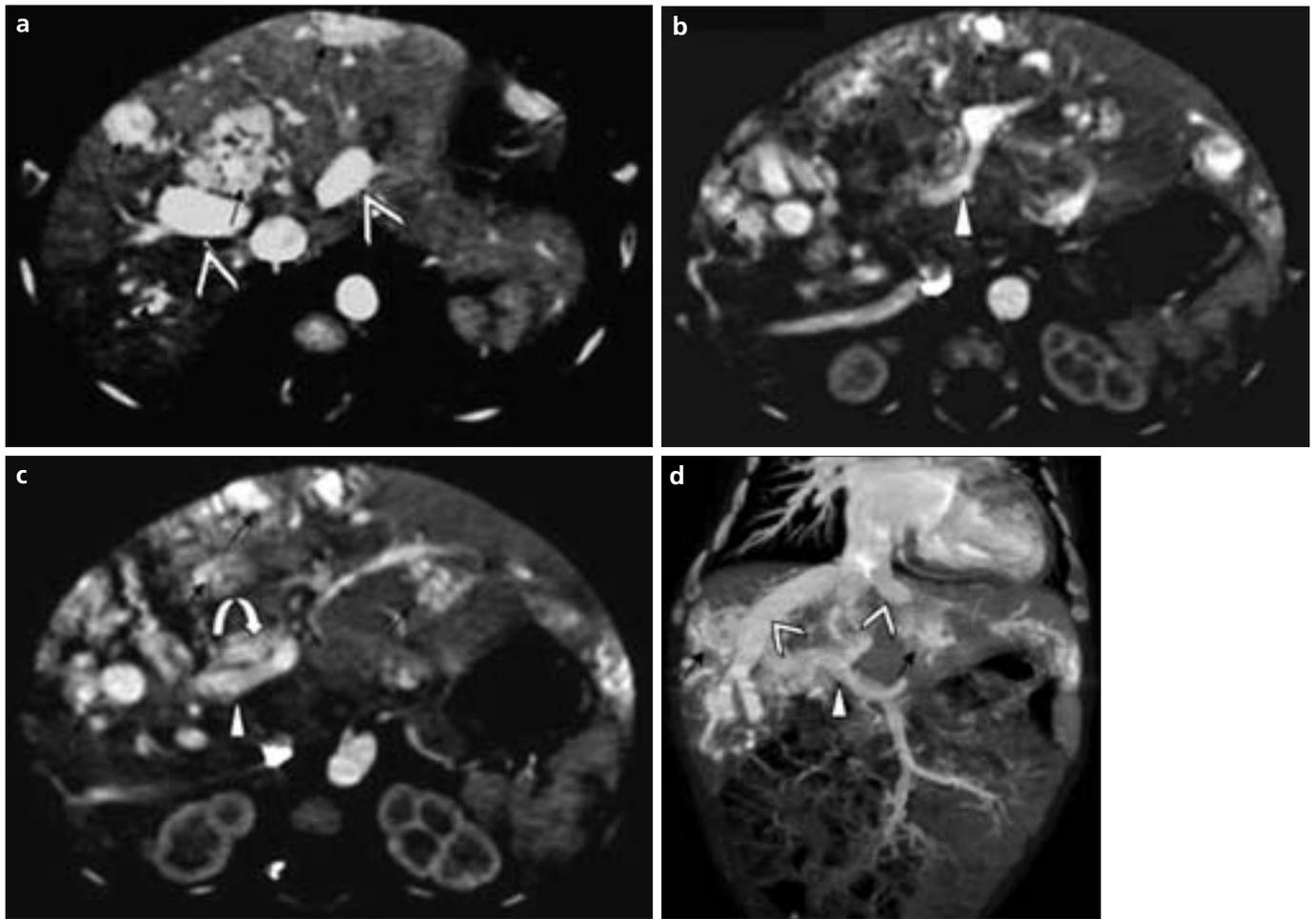
A term male infant was delivered vaginally by a primigravida whose pregnancy had been complicated by gestational diabetes mellitus. The Apgar scores were 6 and 5 at 5 min and 7 min, respectively. Physical examination revealed a holosystolic murmur in the left sternal border, hepatomegaly, and bruits in the right upper quadrant. Developmental retardation was noted with body weight under the 10th percentile for sex and age. The chest radiography and electrocardiography were within the normal limits. Echocardiography (Miramax Ultrasound System, SonoSite Inc., Bothell, Washington, USA) on the second day of life showed a patent ductus arteriosus, which had closed spontaneously by the time of the follow-up visits. During the echocardiography, evaluation of the liver showed multiple abnormal enlarged vessels and enlarged hepatic veins throughout the organ. The patient did not have any skin or mucosal telangiectasis or hemangioma, and the family history of hereditary hemorrhagic telangiectasia (HHT) was negative.

Ultrasonography showed hepatomegaly and a large intrahepatic arteriovenous malformation with severe dilatation, tortuosity of the hepatic veins, and a normal diameter of the portal vein. A multislice computed tomography (CT) scan (Lightspeed VCT, 64-slice MDCT, GE Healthcare, Waukesha, Wisconsin, USA) revealed multiple abnormal tortuous vessels throughout both liver lobes in the arterial phase without any accompanying soft tissue masses. Large feeders from enlarged hepatic and inferior phrenic arteries and draining veins mainly to enlarged hepatic veins. The portal vein diameter was normal. A reduced aortic diameter below the enlarged celiac trunk, mild cardiomegaly, and a small arteriovenous

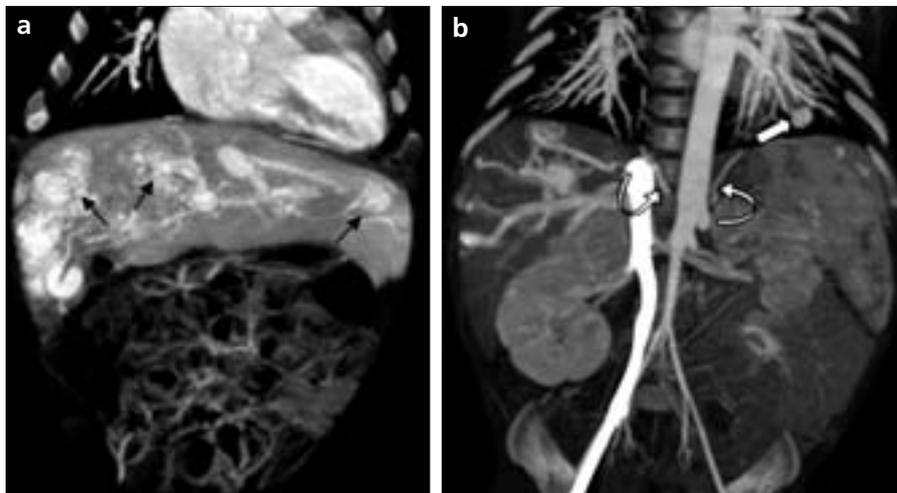
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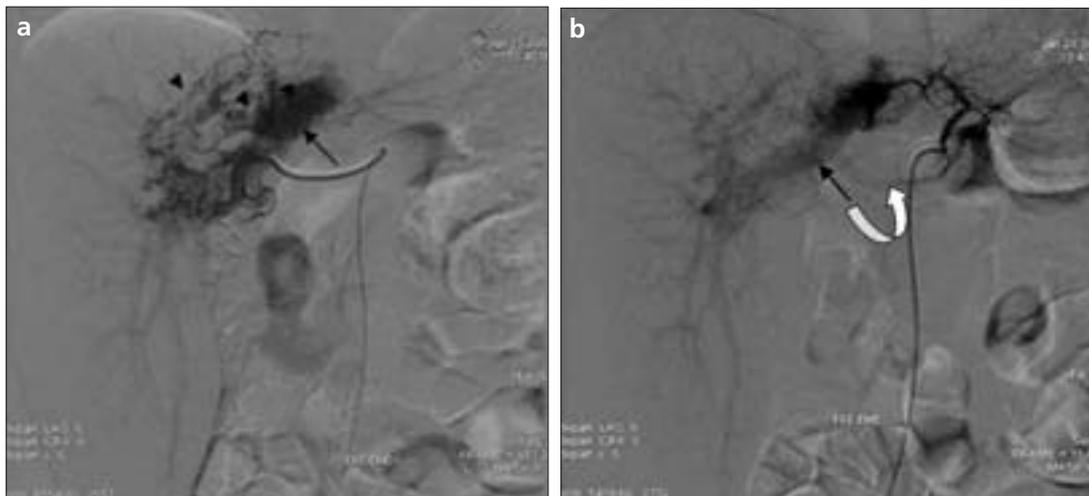
**Figure 1. a–d.** CT angiogram shows multiple abnormally dilated vessels (**a**, *black arrows*) and enlarged hepatic veins (**a**, *white arrowheads*); abnormal tortuous vessels without any accompanying mass (**b**, *black arrows*) and a normal-diameter portal vein (**b**, *solid white arrowhead*); multiple abnormal dilated vessels (**c**, *black arrows*), an enlarged hepatic artery (**c**, *curved arrow*), and a normal-diameter portal vein (**c**, *solid white arrowhead*); and coronal reconstructed images showing similar findings (**d**, *black arrows and white arrowheads*).



**Figure 2. a, b.** A coronal, reconstructed, arteriportal-phase CT scan showing multiple abnormal tortuous vessels without any accompanying mass (**a**, *black arrows*) and obvious reduction in the diameter of the aorta below the celiac trunk (**b**). *Curved arrows* show enlarged inferior phrenic arteries, and the *solid white arrow* shows an incidental small pulmonary arteriovenous fistula (**b**).

fistula in the lower lobe of the left lung were also noted. No signs of cirrhosis or portal hypertension were observed (Figs. 1 and 2). The cardiac output (CO) of the patient was controlled using Digoxin (Novartis Corporation, New York City, New York, USA) until he was 18 months old. Echocardiography at this age showed a CO of 6.6 L/min (cardiac index [CI], 15.7 L/min/m<sup>2</sup>).

At 19 months of age, we embolized the hepatic AVM using Onyx. Informed consent was obtained from the parents of the patient. Under general anesthesia and angiographic imaging (Innova 4100, GE Healthcare, Waukesha, Wisconsin, USA), a hydrophilic 4 F cobra II catheter (0.038" lumen) (Terumo, Saint-Quentin en Yvelines Cedex, France) over a hydrophilic guide wire was inserted into the celiac trunk and after that, into the common hepatic artery. A large AVM with multiple feeders originating from both hepatic arteries, the left gastric



**Figure 3. a, b.** Right hepatic artery angiogram (a) showing multiple dilated and tortuous feeders of the AVM nidus (arrowheads) and rapid filling of the hepatic vein (arrow). Left gastric artery angiogram showing feeders of the AVM (b, arrow). Some reflux to the hepatic artery is noted (b, curved arrow). The main portal vein is not opacified.



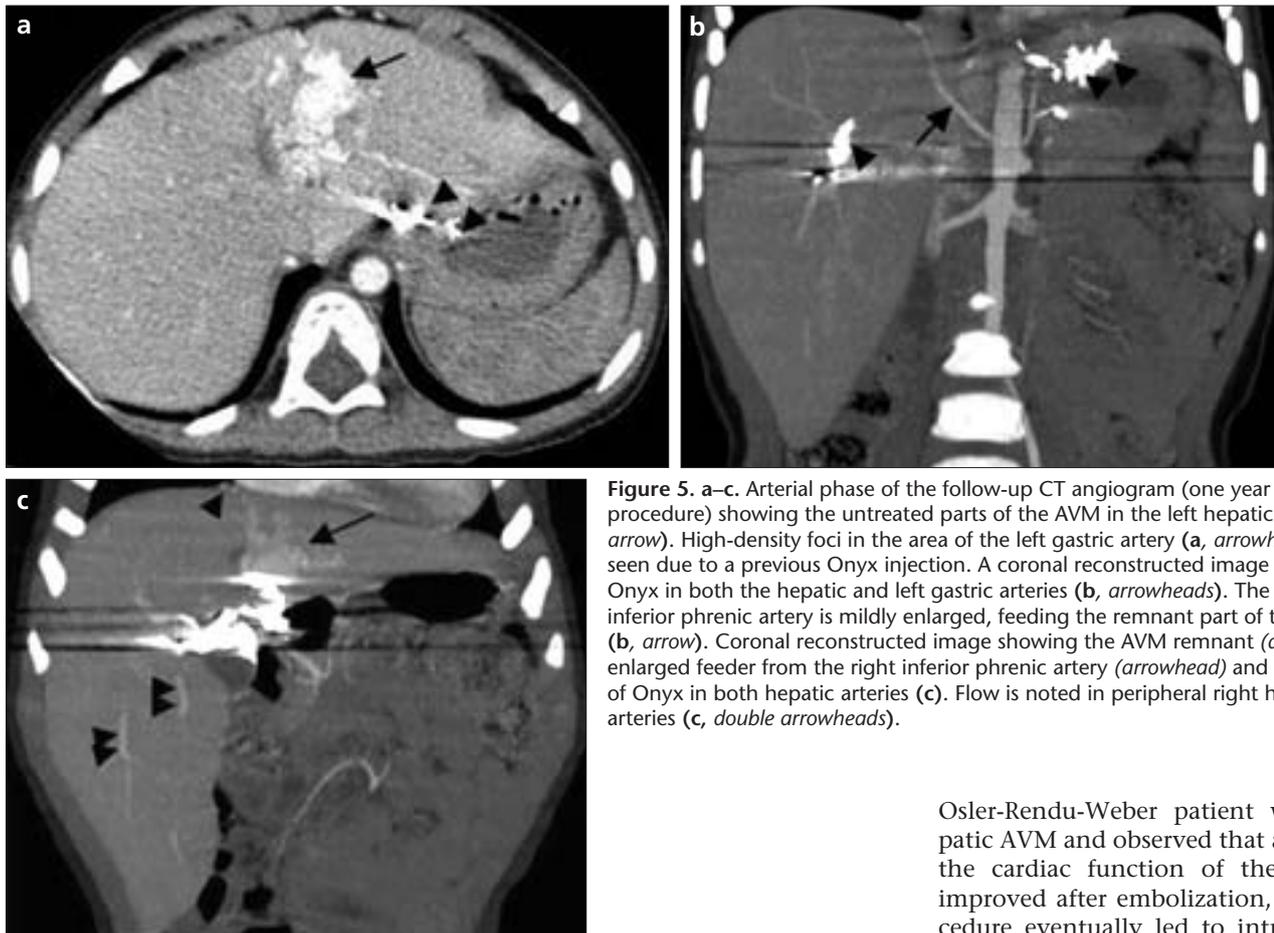
**Figure 4. a–c.** Gastroduodenal artery angiogram showing reflux to the proper hepatic artery after embolization of the right hepatic artery (a). Arterial branches originating from the left hepatic artery (a, arrow) and gastroduodenal branches (a, arrowheads) are seen. Late arterial phase showing prominent early venous filling of the AVM (b). Angiography after occlusion of the left gastric artery branches to the AVM (arrow) and both hepatic arteries, showing some small

non-occluded feeders originating from the gastroduodenal artery (c). Some small, inadvertent reflux of onyx into the proximal part of the gastroduodenal artery is also evident (c, arrowhead).

using a technique that has been commonly described for the interventional management of cerebral AVM (4). Multiple back washes were noted, and the nidus could not be penetrated with Onyx. Therefore, we occluded both hepatic arteries and the common hepatic and left gastric branches using 5 mL of Onyx-18. Although the proximal part of the gastroduodenal artery was inadvertently partially embolized due to Onyx backflow, some small feeders of the hepatic AVM originating from the gastroduodenal artery and the inferior phrenic artery remained patent and could not be embolized due to either their acute angle with the gastroduodenal artery or their small diameter. After successful embolization, the flow of the hepatic veins was dramatically reduced (Fig. 4). The control echocardiography showed a CO of 3.1 L/min (CI, 7.38 L/min/m<sup>2</sup>)

artery, the inferior phrenic artery, and the gastroduodenal branches, which drained mainly to the right hepatic veins, was noted (Fig. 3). Coaxial to the cobra II catheter, a Rebar-18 microcatheter (ev3 Endovascular Inc., Plymouth, Minnesota, USA) was inserted first into the right hepatic artery branches, then

into the left hepatic artery and finally into the left gastric branches. However, gaining access to the nidus of the malformation was impossible due to the small and tortuous vessels. Thus, Onyx-18 (ev3 Endovascular, Inc.) was injected into the branches proximal to the nidus. The injections were performed



**Figure 5.** a–c. Arterial phase of the follow-up CT angiogram (one year after the procedure) showing the untreated parts of the AVM in the left hepatic lobe (a, arrow). High-density foci in the area of the left gastric artery (a, arrowheads) are seen due to a previous Onyx injection. A coronal reconstructed image shows Onyx in both the hepatic and left gastric arteries (b, arrowheads). The right inferior phrenic artery is mildly enlarged, feeding the remnant part of the AVM (b, arrow). Coronal reconstructed image showing the AVM remnant (arrow), enlarged feeder from the right inferior phrenic artery (arrowhead) and presence of Onyx in both hepatic arteries (c). Flow is noted in peripheral right hepatic arteries (c, double arrowheads).

immediately following the procedure. Liver function tests showed a mild elevation in serum alkaline phosphatase (up to 1.5 times higher than the upper normal limit), which returned to normal limits in the second week. No signs of cholangitis or intrahepatic bile duct dilatation were observed in follow-up visits or further abdominal ultrasound imaging. Follow-up echocardiography at 6, 12, and 19 months after the procedure showed a CO of 2.54 L/min with a CI of 5.08 L/min/m<sup>2</sup> (body weight, 12 kg), a CO of 2.4 L/min with a CI of 4 L/min/m<sup>2</sup> (body weight, 14 kg), and a CO of 1.95 L/min/m<sup>2</sup> with a CI of 2.97 (body weight, 15 kg), respectively. A follow-up CT angiography (BrightSpeed Elite, 16-slice MDCT, GE Healthcare, Waukesha, Minnesota, USA) showed some remnant patent feeders originating from the left inferior phrenic and gastroduodenal arteries (Fig. 5). Over the 19 months of follow-up, the CO remained favorably stable and within the normal limits, and no signs of cholangitis or hepatic insufficiency were observed.

#### Discussion

In the late 1970s, the treatment of choice for hepatic AVM was surgical arterial ligation (5). Since the 1980s, embolization of the hepatic artery with metallic coils, gelatin sponges or polymer particles has been pursued. However, legitimate concerns about the success rate of these materials have been reported by numerous studies (2, 6, 7). For example, a transarterial coil embolization was unsuccessful in a study performed by Zentler-Munro et al. (8) due to the development of collateral circulation. Caselitz et al. (6) reported one patient death due to variceal bleeding and one case of cholangitis after performing three to five sessions of embolization with PVA and steel coils on five Osler-Rendu-Weber patients with hepatic AVM. Chavan et al. (7) investigated the same method in five patients with HHT and observed one case of ischemic cholangitis and one patient death due to postoperative sepsis. In another study, Hisamatsu et al. (5) performed arterial coil embolization of the hepatic artery in an

Osler-Rendu-Weber patient with hepatic AVM and observed that although the cardiac function of the patient improved after embolization, the procedure eventually led to intrahepatic cholangitis and hepatic insufficiency. They concluded that the principle leading causes of this complication were stagnation of the bile ducts and reduction of portal venous flow to the parenchyma due to the pressure effect of re-shaped tortuous metallic coils in the nearby hepatic arteries.

Onyx is a biocompatible polymer, which is an ethylene vinyl alcohol copolymer (EVOH) that is dissolved in an organic solvent, dimethylsulfoxide (DMSO). It becomes radiopaque by mixing with micronized tantalum powder. When Onyx is injected into the vessels, the DMSO rapidly diffuses, and EVOH solidifies at the tip of the catheter in a shape that conforms to the target area. Unlike other liquid embolic agents, Onyx does not adhere to the endothelial wall and catheter tip (9–11). The application of EVOH in the endovascular treatment of intracranial AVMs was first described by Taki et al. (12) and Terada et al. (13) in the early 1990s. Since that time, Onyx has been used for the treatment of cerebral aneurysms and cerebral AVMs; however, few studies have examined its use in other organs (14, 15). Recently,

Golewale et al. (16) reported three cases of Down syndrome that were complicated by portal vascular anomalies. This group used Onyx and a complex arterioportal shunt to occlude hepatic artery feeders in one of these patients. Although the arterioportal shunting was decreased after embolization, the patient expired due to major congenital cardiac defects. For the present case, we used Onyx because it has several advantages compared to other materials. First, Onyx probably does not reshape due to pressure from coils on the bile ducts and the hepatic artery. Second, using Onyx allowed us more control over the embolization. Finally, pulmonary, portal or systemic embolization would be less likely.

To the best of our knowledge, there are limited studies reporting the successful embolization of a hepatic AVM with Onyx without a subsequent procedure. Although we could not attain our primary goal of accessing the nidus of the malformation due to small and tortuous feeders and although follow-up CT angiography revealed that some parts of the AVM remained untreated, the outcome was considered favorable, and no complications were detected after embolizing the hepatic artery in one session. The significant side effects reported in previous studies, including ischemic cholangitis and cholecystitis, were not observed during the follow-up visits.

Onyx has some limitations for use in interventional radiology, including its higher cost compared to other commonly used materials and its propensity for leaving artifacts on CT images due to high radiopacity and severe vasospasm, which is most likely to occur in the early phase of the procedure. The final limitation may

be avoided by using no more than 0.2 mL of DMSO in the first min of injection (17).

In conclusion, we successfully performed a transcatheter embolization of a congenital hepatic AVM in an infant suffering from high CO heart failure using Onyx without the need for any subsequent procedures. Further studies with a larger number of cases would be beneficial for achieving a more thorough evaluation of this technique.

#### Conflict of interest disclosure

The authors declared no conflicts of interest.

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