Portal hypertension after combined liver and intestinal Transplantation, a diagnostic and therapeutic challenge ?

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Abbreviations (in the order of their mention in the paper):

e-PTFE	expandable poly-tetra-fluoro-ethylene
GI	gastrointestinal
TIPS	transjugular intrahepatic portosystemic shunt
TPN	total parenteral nutrition

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Abstract

A widely accepted technique to transplant the liver-bowel bloc is first to perform a piggyback anastomosis of the donor suprahepatic vena cava to the recipient vena cava; second to restore the arterial blood supply through an aortic interposition graft; and third to insure venous drainage of the native foregut. The venous drainage of the native foregut can be restored through an end-to-end portocaval anastomosis between the donor infrahepatic vena cava and the recipient portal vein. Stenosis of this anastomosis can lead to portal hypertension presenting with upper gastrointestinal congestion, bleeding and hypersplenism. We report the successful treatment of this complication using an expanded poly-tetra-fluoro-ethylene-covered stent inserted following balloon angioplasty.

Introduction

Combined liver and intestinal transplantation is considered a valuable treatment option for patients suffering from both irreversible intestinal and liver failure (1). Over the last years, survival after combined liver and intestinal transplantation has substantially improved due to standardization of the surgical technique and the postoperative care. However, the surgical procedure remains challenging and consists of an en bloc transplantation of a liver-pancreas-duodenal-intestinal graft (2). As illustrated in figure 1, the transplanted organs and the liver in particular are transplanted en bloc onto the recipient inferior vena cava which is left intact (piggyback technique). The arterial blood supply is restored through an aortic interposition graft between the recipient suprarenal aorta and the donor aortic patch including the origin of the superior mesenteric artery and celiac trunk. An end-to-end anastomosis between the donor infrahepatic vena cava and the recipient portal vein can then be created to allow adequate portal drainage of the recipient native foregut (including spleen, pancreas).
Here, we describe the case of an 11-year-old girl who successfully received a combined liver intestinal graft using the aforementioned technique. Despite the presence of an end-to-end drainage of her native foregut to the donor infrahepatic vena cava, she gradually developed congestion of her native foregut (including the proximal duodenojejunal anastomosis) with recurrent episodes of upper gastrointestinal bleeding, persisting hypersplenism and thrombocytopenia.

Case report

Our patient is an 11-year-old girl who suffered from a neonatal volvulus at the age of 32 weeks. Complete necrosis of the whole small bowel and colon ascendens eventually required a total intestinal resection leaving her with an ultrashort bowel and a jejunostomy. The remaining colon was resected later (age of 6) due to a refractory diversion colitis following an unsuccessful restoration of the bowel continuity between the remaining jejunum and the colon. Eventually, she was left with a duodenostomy. Due to the short bowel syndrome, she was completely dependent on total parenteral nutrition (TPN) and gradually developed a biopsy-proven liver cirrhosis with portal hypertension including episodes of hemorrhagic/congestive gastro- and duodenopathy at the age of 7.

Eventually, at the age of 9, she was transplanted with an en bloc liver-pancreas-small and large intestinal graft implanted according to Sudan et al (2). The liver part of the graft was piggyback implanted and an arterial reconstruction done using an arterial conduit onto the infrarenal aorta as illustrated in Figure 1 . Because of the en bloc nature of the graft, no biliary nor portal construction was necessary. Adequate drainage of the native foregut (pancreas, stomach and spleen) was achieved through an end-to-end anastomosis between the native portal vein and the transplant infrahepatic inferior vena cava as advocated by Gondolesi et al (3).

Her immunosuppression consisted of Tacrolimus (levels ~5 pg/ml), Azathioprine (1 mg/kg) and methylprednisolone (4). At 3, 6 and 13 months post-transplant, recurrent upper gastrointestinal (GI) bleeding episodes required readmissions and urgent blood transfusion. Additionally, intermittent red blood loss *per stoma* remained present. Biochemical analysis consistently revealed normal coagulation parameters except for a progressive thrombocytopenia. Upper GI endoscopy repeatedly revealed diffuse and ulcerative bleeding sites at the level of the proximal anastomosis between the native stomach and the transplant jejunum which prompted a surgical intervention. At the level of the duodenojejunostomy, congestion was observed and a new anastomosis was created. The resection specimen showed mucosal erosions and submucosal vascular congestive or thrombosed blood vessels compatible with angiodysplasia (Figure 2). There were no signs of bowel rejection. After surgery she continued to present episodes of upper GI bleedings. In addition, hypersplenism (splenic diameter of 17 cm) accompanied by an aggravating thrombocytopenia (which was not present before the

transplantation) was observed. Thrombosis of the native portal vein was repeatedly excluded by ultrasound. Finally, 37 months after the transplantation, an angio-CT scan revealed the presence of a filiform aspect of the intrahepatic transplant vena cava distal to a narrowed portocaval anastomosis (Figure 3).

Subsequently, the patient was referred for percutaneous, transcatheter management of the thight portocaval anastomosis. Under general anesthesia, a large collateral located close to the chronically thrombosed right internal jugular vein was punctured. Using conventional catheter and guide-wire techniques, the portocaval anastomosis and native splenic vein were catheterised. Pressure measurements distally and proximally to the anastomosis were respectively 17 mmHg and 8 mmHg resulting in a pressure gradient of 9 mmHg. Contrast injection through the catheter in the splenic vein confirmed the high grade focal stenosis of the portocaval anastomosis and a filiform aspect of the donor intrahepatic vena cava. In addition, multiple collaterals draining into the donor portal vein were seen (Figure 4). These collaterals were located around the surgical duodenojejunal anastomosis. The portocaval stenosis was first predilated with a 3 x 40 mm angioplasty balloon (Wanda, Boston Scientific, Natick, MA, USA); subsequently, an expandable poly-tetra-fluoro-ethylene (e-PTFE) covered stent (Viabahn, W.L. Gore and Associates, Flagstaff, A, USA) with a diameter of 8 mm and a length of 5 cm was inserted over the stenosis and post-dilated with an 8 mm diameter angioplasty balloon (Boston Scientific). Completion angiography showed a restored patency of the intrahepatic vena cava and the portocaval anastomosis and disappearance of the splenic venous collaterals draining into the donor portal vein (Figure 5). Pressure measurements proximally and distally to the covered stent were respectively 9 and 11 mmHg, resulting in a residual pressure gradient of 2 mmHg. The post-interventional course was uneventful; several control duplex-ultrasound evaluations demonstrated a fully patent covered stent (Figure 6) with progressive decrease of the craniocaudal splenic diameter up to 15 cm and clinically no recurrent gastrointestinal bleeding was noted over the next 12 months after the procedure. Finally, laboratory analysis revealed a progressive rise of the thrombocyte count up to 174,000/l (compared to <50,000/l prior to the e-PTFE insertion).

Discussion

Combined intestinal and liver transplantation has become a life-saving procedure for patients suffering from irreversible intestinal and liver failure. Over the last decades, outcome has improved due to substantial improvement in immunosuppression, standardization of the surgical procedure and the post-transplant care. Outcome is nowadays favorable with patient 5 years survival around 55-60% (5). In addition, combined liver and intestinal transplantation offers surviving recipients an improved quality of life with resumption of oral nutrition and freedom from TPN. However, the postoperative recovery often remains challenging for the transplant physicians taking care of these patients.

This case describes the occurrence of post-transplant hypersplenism and congestive coagulopathy leading to upper GI bleeding episodes due to the progressive stenosis of the intrahepatic vena cava of the liver component of the graft.

In combined intestinal and liver transplantation, venous drainage of the native foregut and upper visceral organs can be done either through an end-to-side anastomosis between the native portal vein and the native vena cava or through an end-to-side anastomosis between the native portal vein and the donor vena cava (3). End-to-end anastomoses may have less risk of late development of anastomotic strictures in comparison to end-to-side anastomoses (3). However, this report confirms previous observations describing the late development of an end-to-end portocaval anastomotic stenosis in combined liver/intestinal transplant recipients (6). As in the presented case, symptomatic intermittent bleeding at the duodenojejunal anastomosis and progressive hypersplenism were present. Medical management including the administration of beta-adrenergic blockade, endoscopic banding or sclerotherapy were ineffective. Surgical management by creating a central shunt or a distal side-to-side splenorenal shunt has been described by Gondolesi et al (3). However in the case presented, this was regarded a too high risk procedure in the light of the numerous collaterals between the native splenic vein and the transplant portal venous system. Alternatively, a minimally invasive treatment option could have been a balloon angioplasty of the portocaval stenosis as described by Fishbein et al (6). However in the latter case, this intervention was unsuccessful, potentially due to elastic recoil of

the dilated vessel. For this reason we decided to insert an e-PTFE-covered stent instead of performing a balloon angioplasty alone or insertion of a conventional, bare vascular stent. In fact, the created surgical portocaval shunt resembles an intrahepatic portosystemic shunt. In analogy to the current standard for transjugular intrahepatic portosystemic shunt (TIPS) creation, an e-PTFE-covered stent-graft was used (7), starting within the proximal splenic vein and ending at the confluence of the piggyback anastomosis of the recipient vena cava. As clearly demonstrated in TIPS-procedures, e-PTFE-covered stents are associated with better long-term patency compared to bare, vascular stents (8).

In summary, a symptomatic, anastomotic portocaval stenosis developing after combined liver and intestinal transplantation can be managed safely and effectively by insertion of an e-PTFE-covered stent. This minimally invasive approach may represent the treatment of choice for this complication.

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Figure legends

Figure 1: Schematic overview of the en bloc liver/ intestinal transplantation (donor organs depicted in bright colours, recipient organs depicted in pale colours) as performed in the case presented. First, a piggyback anastomosis of the donor suprahepatic vena cava (DSVC) to the recipient suprahepatic vena cava (RSVC) is performed *(anastomosis 1)*. Secondly, the arterial blood supply is restored through an aortic interposition graft (AIG) between the recipient infrarenal aorta (RAO) and donor aortic patch (DAP) including the origin of the superior mesenteric artery and celiac trunk *(anastomosis 2)*. Thirdly, an end-to-end anastomosis between the donor infrahepatic vena cava (DIVC) and the recipient portal vein (RPV) was created to allow adequate portal drainage of the recipient native foregut (including spleen, pancreas) *(anastomosis 3)*. Continuity of the gastrointestinal tract is restored by an anastomosis between the donor jejunum and the recipient duodenum *(anastomosis 4)*.

Figure. 2: Histologically, very large sized and congested vessels responsible for the recurrent upper GI bleeding are present in the mucosa (Figure 2A) and the submucosa (Figure 2B).

Figure 3: A. Axial CT-image depicts hypertrophied venous structures around the duodenojejunal anastomosis; B. Coronal reconstructed CT-image clearly demonstrates, besides hypersplenism, the filiform aspect of the intrahepatic vena cava distal to a filiform aspect of the intrahepatic vena cava distal of a narrowed portocaval anastomosis (arrows).

Figure 4: Digital substraction angiography with the tip of the catheter placed in the native splenic vein. A. Early phase images confirm the tight stenosis of the portocaval anastomosis (white arrows); B. Mid phase images show multiple, large collaterals draining into the transplant superior mesenteric vein and branches (black arrows); C. Late phase images clearly depict the main transplant portal vein and its intrahepatic terminal branches (white arrowheads).

Figure 5: Digital substraction angiography after insertion of the e-PTFE-covered stent-graft (arrows) shows fully patent intrahepatic transplant vena cava and portocaval shunt together with the disappearance of the aforementioned collateral network between the native splenic vein and the transplant portal venous system.

Figure 6: A. Control gray-scale ultrasound 8 months after the interventional procedure shows the fully expanded stent-graft; B. Corresponding color-coded ultrasound confirms a fully patent stented portocaval shunt.

Figure 1

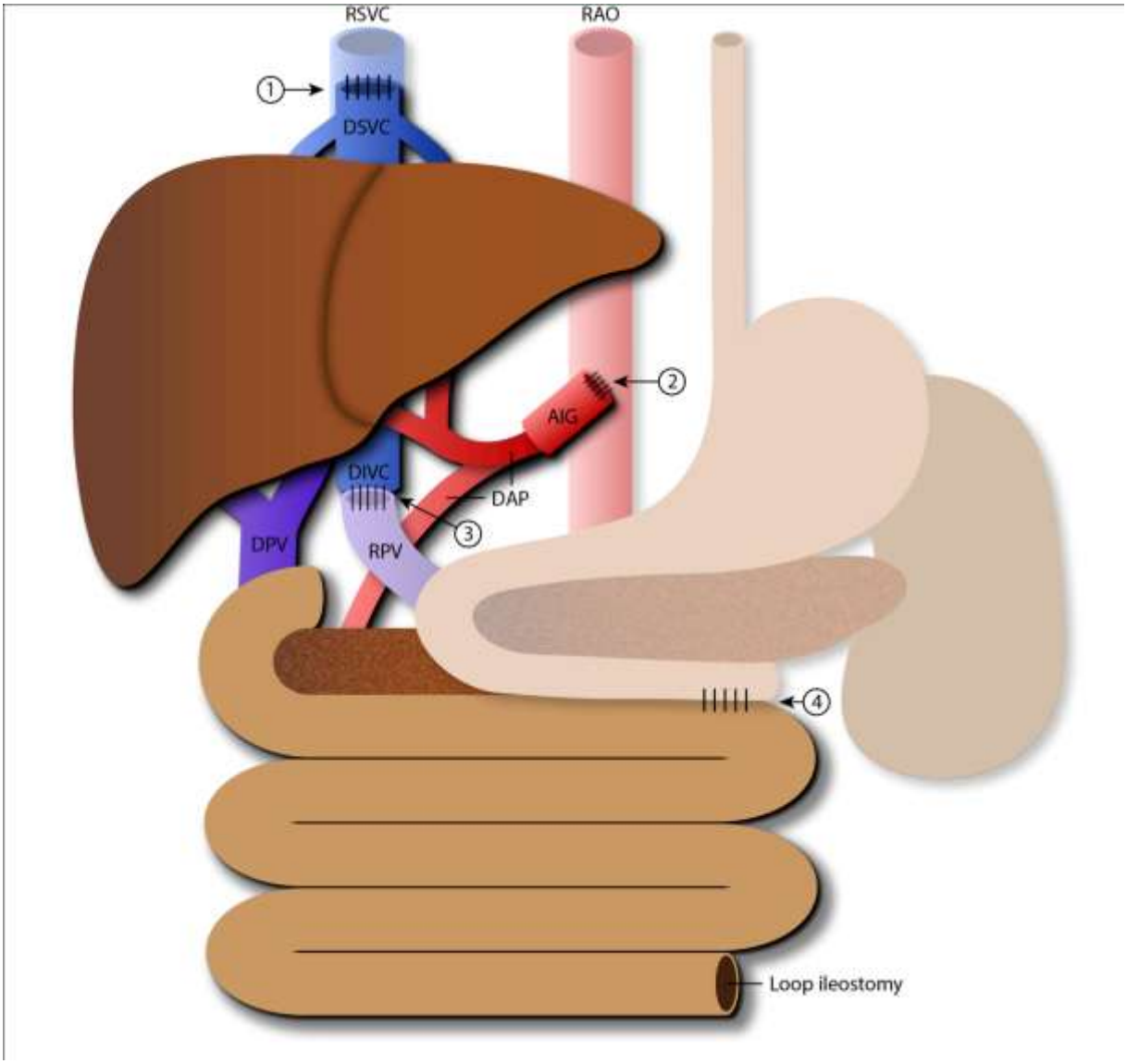

Figure 2.

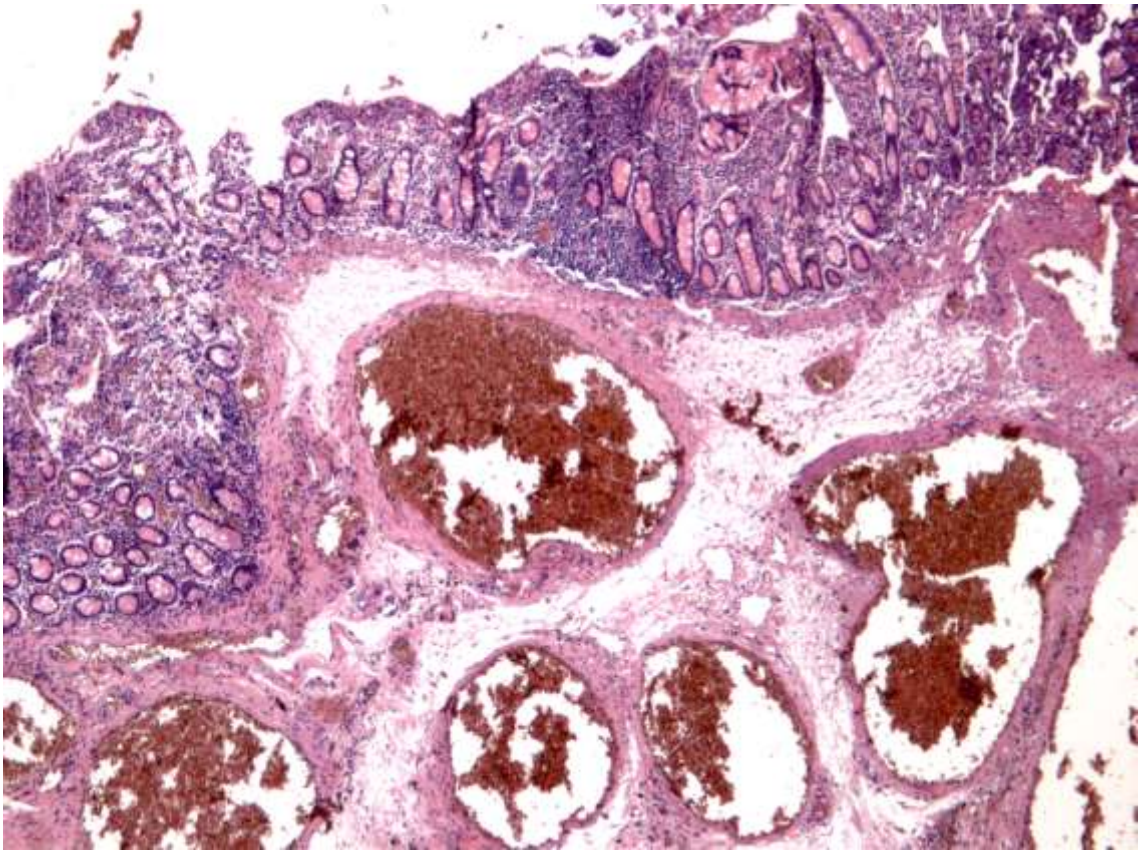

Figure 3.

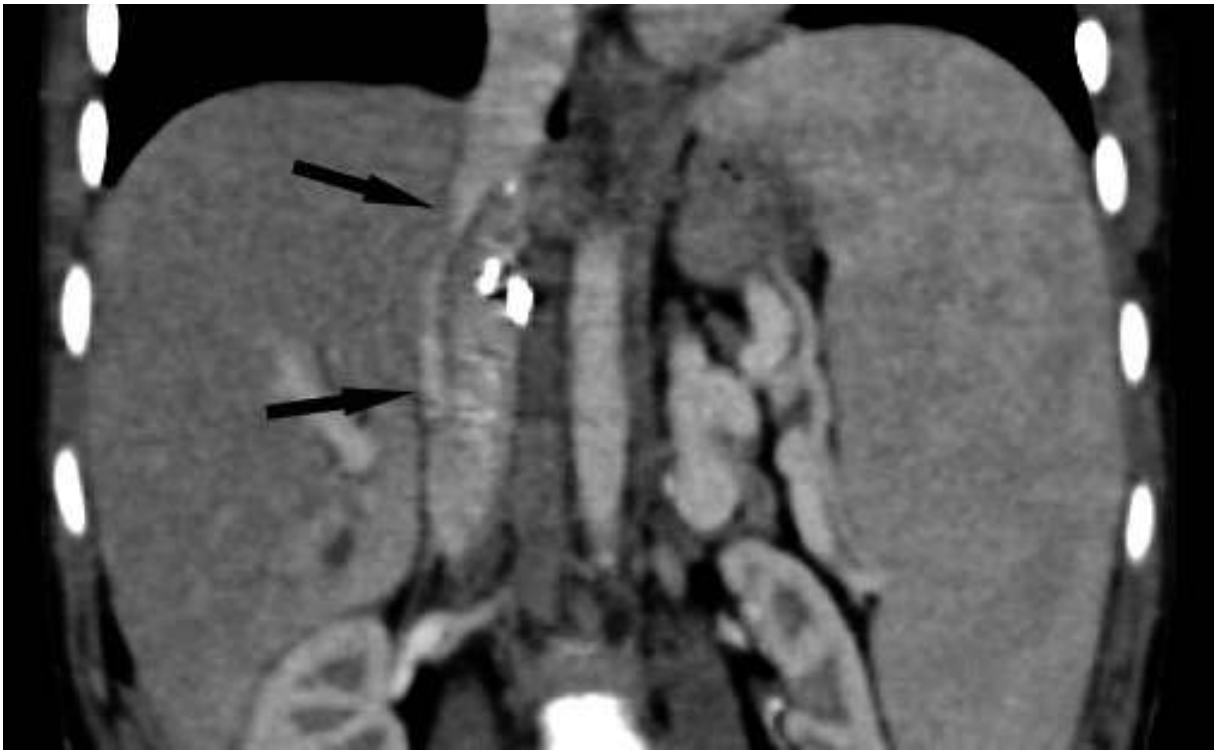

Figure 4A.

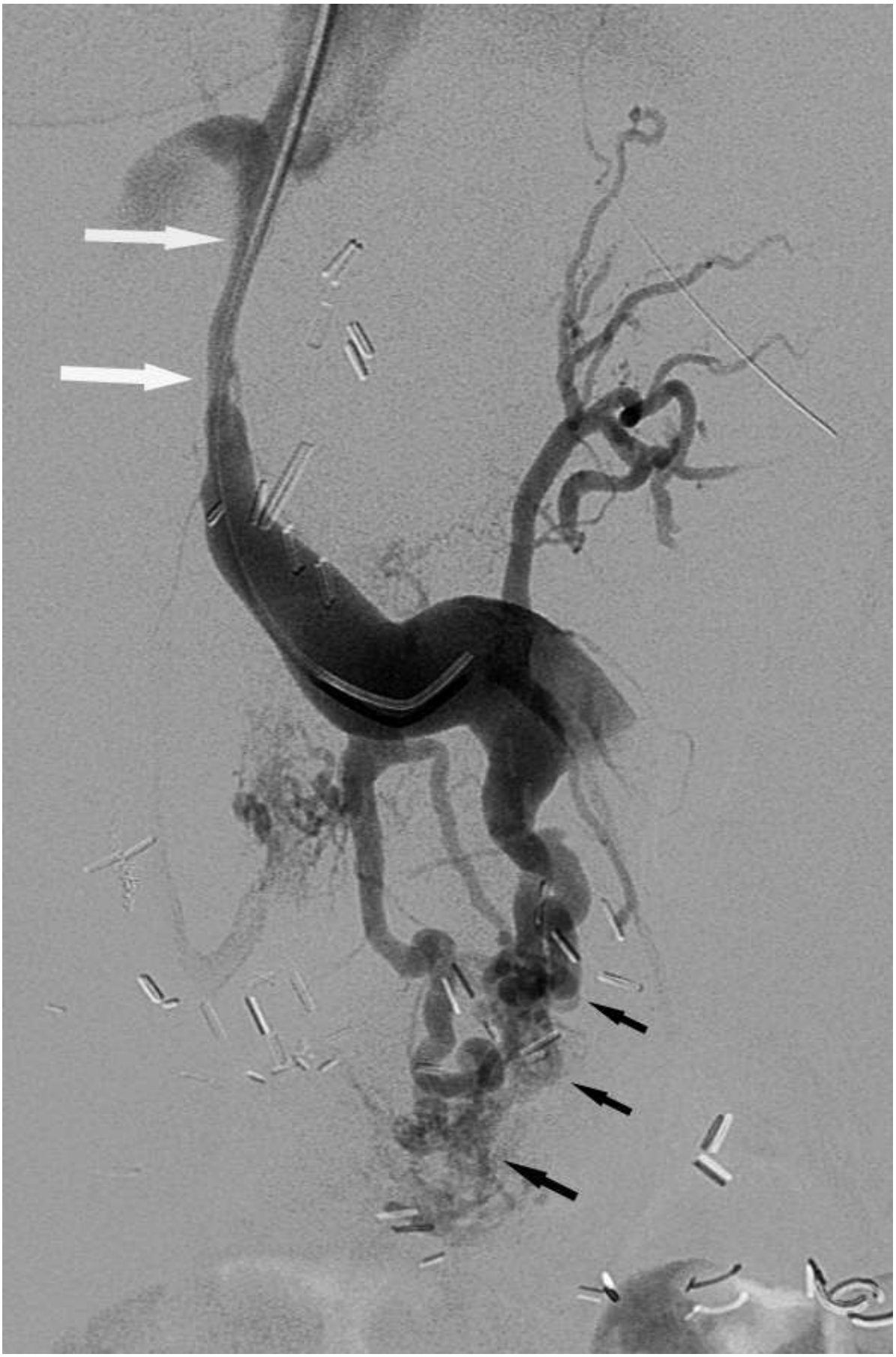

Figure 4B.

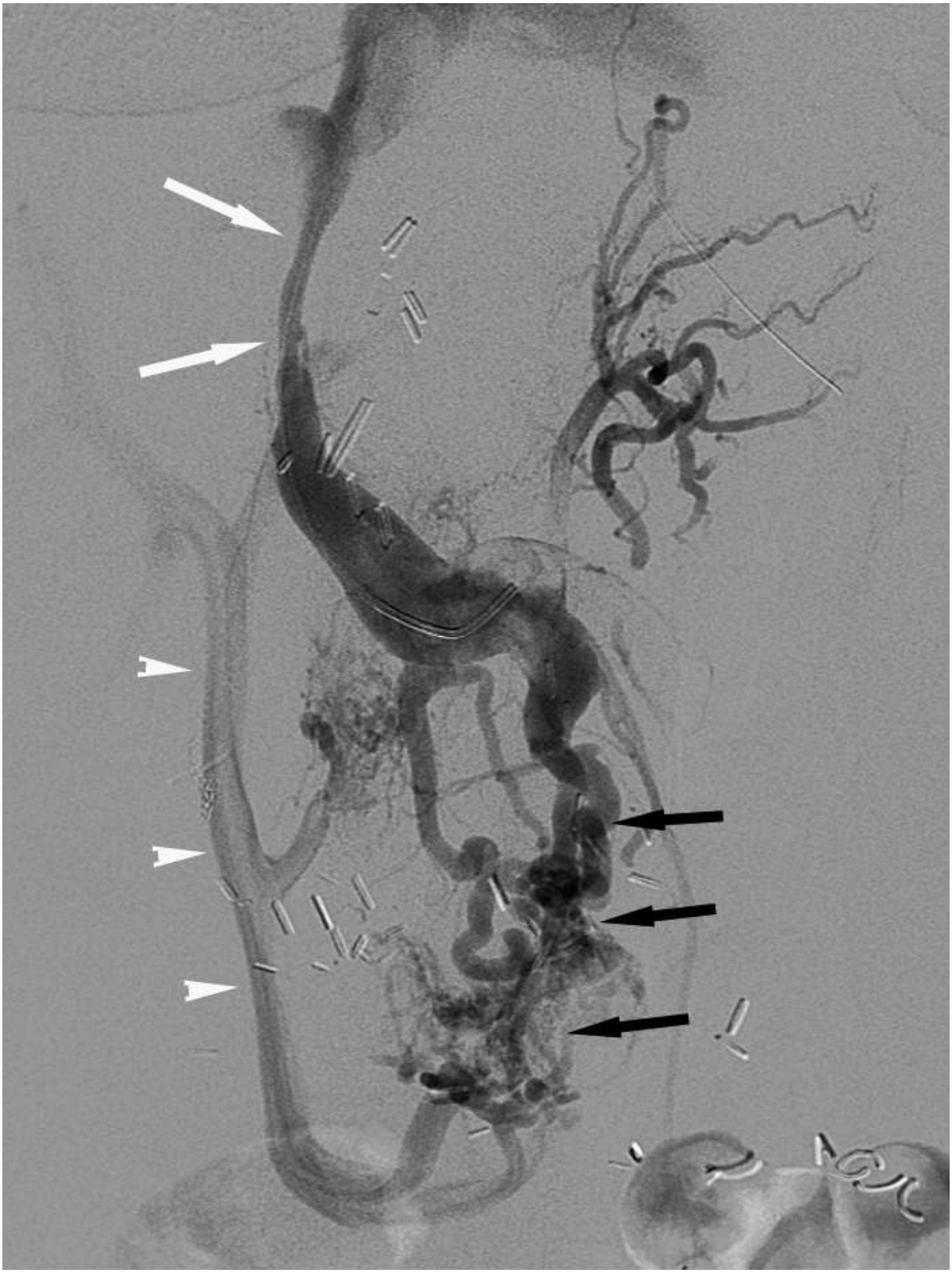

Figure 4C.

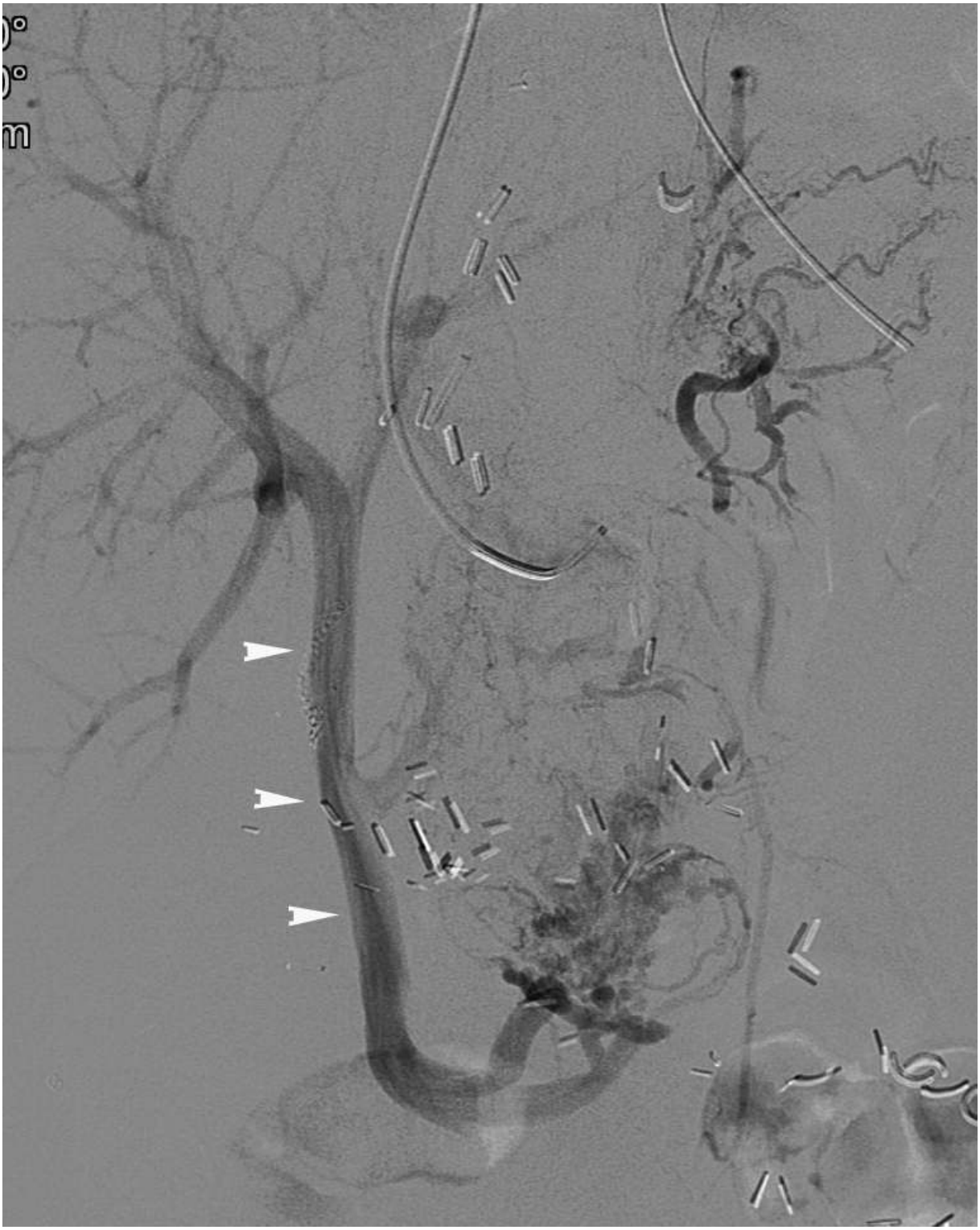

Figure 5.

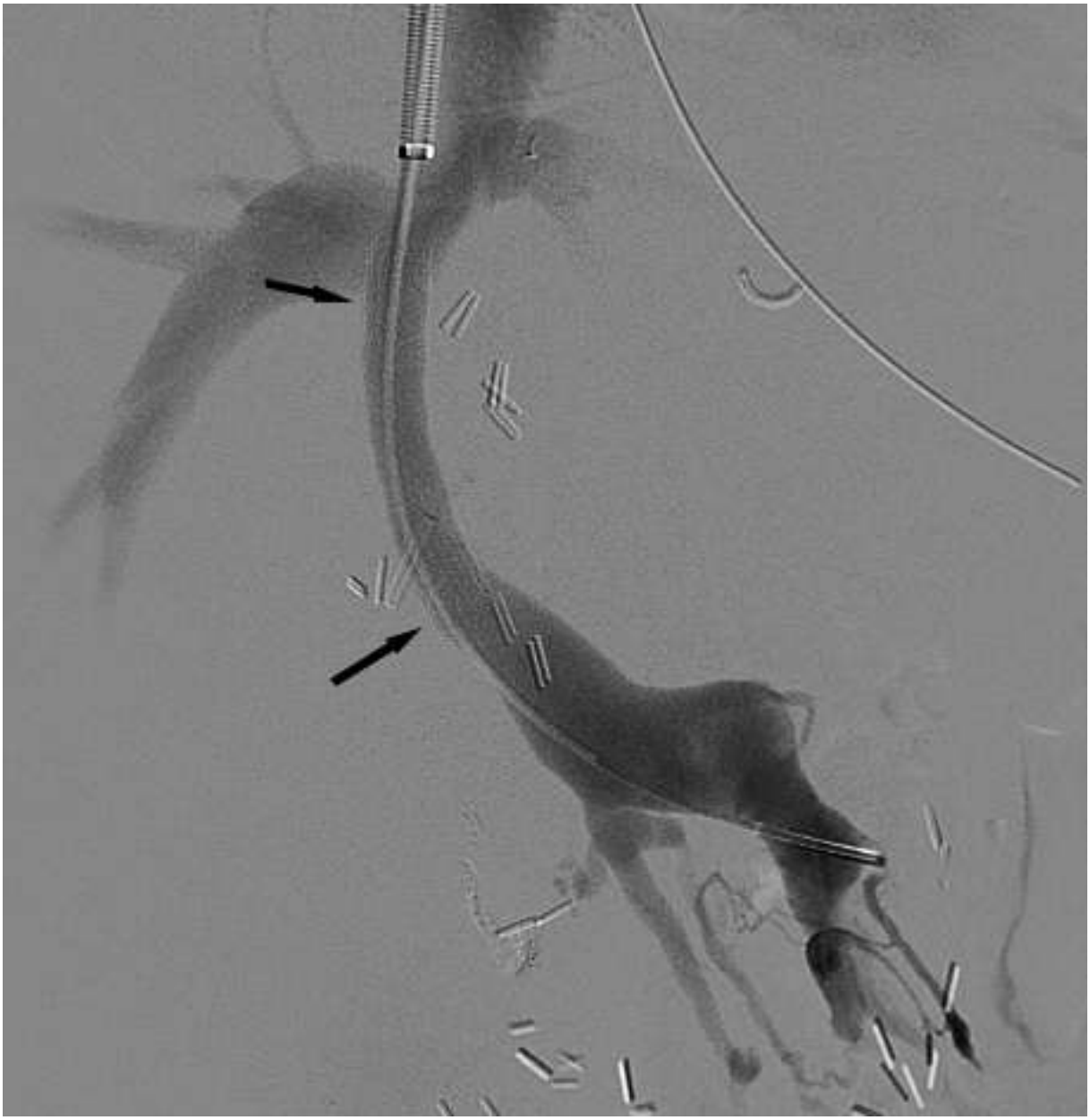

Figure 6A.

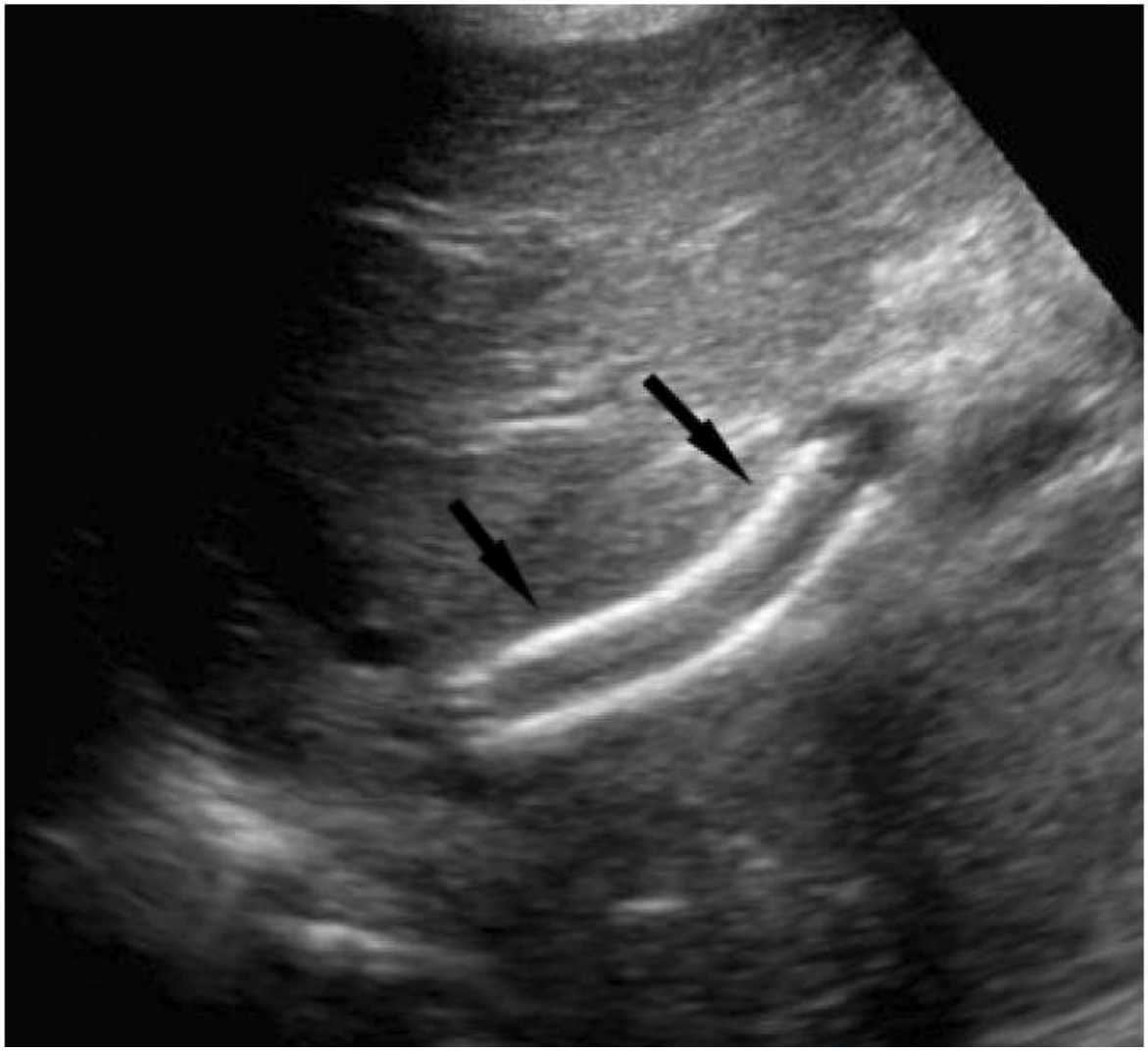

Figure 6B.