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Review Article

Embolization of procedure-related upper gastrointestinal bleeding

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ABSTRACT

Non-surgical procedure-related, upper gastrointestinal bleeding (UGIB) is considered as one of the rarest of all UGIB causes, although it is a serious complication when it occurs. It presented as hematemesis, melena or hemobilia in which is associated with hepatobiliary intervention. In most patients the bleeding resolves spontaneously and in those in which it does not, the majority respond to conservative management. Endoscopy is the first line of treatment if bleeding does not stop after medical management, although if it failed due to massive bleeding, in hemodynamically unstable patients or in hepatobiliary procedure-related bleeding, endovascular or surgical intervention should be considered. In this manuscript we will discuss the endovascular diagnosis and treatment of non-surgical procedure-related UGIB.

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Keywords: Embolization, therapeutic; Hemorrhage; Upper gastrointestinal tract

Introduction

Upper gastrointestinal bleeding (UGIB) is defined as bleeding originating from the distal esophagus to the duodenum at the level of the ligament of Treitz. Since the first use of angiography in the diagnosis and management of UGIB, it has been considered as the first treatment of choice in acute bleeding which is refractory to endoscopic management. Although non-variceal UGIB results in the hospitalization of 30 to 100 patients per a 100,000 population per year, non-surgical procedure-related bleeding is considered one of the rare causes of UGIB and which represents less than 5% of all causes.^{1,2} There are many published literature reports regarding the angiographic diagnosis and intervention in UGIB due to various causes.^{3,4} However, information regarding the role of this technique in the management of non-surgical procedure-related UGIB has rarely been published.

Upper gastrointestinal (GI) procedures are done either endoscopically or percutaneously. Procedure-related UGIB could present as hematemesis, melena or hemobilia associated with hepatobiliary intervention. In most cases the bleeding resolves spontaneously and of those that do not, the majority respond to medical management with fluid resuscitation, correction of the coagulopathy, and administration of blood products.⁵ Endoscopy may be applied to visualize the bleeding and for targeted treat-

ment if bleeding does not respond to medical treatment.⁶ In failed endoscopic treatment due to massive bleeding or in the case of hemodynamically unstable patients or hepatobiliary procedure-related bleeding, endovascular or surgical intervention should be considered.⁷ Moreover, endovascular embolization represents the most viable treatment option in patients receiving anticoagulation therapy for various diseases.⁸ In this article we will discuss the endovascular management of non-surgical procedure-related UGIB.

Clinical Presentation and General Management

Procedure-related UGIB could present as immediate or delayed bleeding. Immediate bleeding is defined as bleeding that occurs at the time of a procedure, while delayed bleeding is that occurs 0 to 30 days after a procedure. Most intra-procedural bleeding resolves without further intervention. On the other hand, delayed bleeding is usually clinically significant.

Direct clinical evidence of active bleeding may present as persistent melena, hematochezia, hematemesis or hemobilia. The vital signs must be closely monitored for signs of active bleeding that could manifest as tachycardia, hypotension, and potential hypoxemia. Hemodynamic instability despite vigorous resuscitation is the best indicator of active bleeding.

Blood loss of 100 mL per day may be asymptomatic, blood

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loss of 500 mL usually results in systemic abnormalities; i.e., tachycardia and hypotension, and blood loss of 15% of the circulating blood volume results in systemic shock.⁹ Overall, approximately 75% of patients present with asymptomatic or mild systemic symptoms can be treated conservatively, whereas 25% of patients need immediate medical attention and resuscitation.¹⁰

Medical management is the first-line treatment of UGIB. Stabilization of blood pressure and fluid resuscitation are the immediate goals. Blood transfusion should be considered for correction of coagulopathy and which considered an important component of medical management.

Endoscopy is the primary technique for the diagnosis and treatment of UGIB. However, it often fails to depict the exact bleeding focus when massive bleeding (1 mL/min) occurs.⁵ Vreeburg et al¹¹ reported that no diagnosis could be made at the first endoscopy in 24% of patients with acute UGIB. In their study, excessive blood or clots in the gastroduodenal tract impaired the endoscopic view in 15% of the patients. Endoscopic hemostasis can be achieved via thermocoagulation, sclerosant injection or clips/banding. Endoscopic clip placement, even if ineffectual, can assist subsequent endovascular intervention by directing the interventional radiologist to the area of concern.^{12,13} However, there are no endoscopic interventions possible if the hepatobiliary source of hemorrhage is identified. The primary therapeutic option in such cases is endovascular or surgical treatment.

Imaging Modality

If a patient is hemodynamically stable and the exact site of bleeding is obscure, the bleeding site could be evaluated with a radionuclide technetium 99m-tagged red blood cell scan, as the nuclear scintigraphy study can demonstrate active bleeding at rates as low as 0.1 mL/min.^{14,15} A positive scintigram increases the likelihood of a positive angiogram from 22% to 53%.¹⁶ Although the high sensitivity of nuclear scintigraphy study, it is associated with limitations: it cannot precisely locate the bleeding site or even identify its cause in a positive scan because of the poor spatial resolution, or the tendency of tagged blood moving in GI lumen with peristalsis or position changes.¹⁷

A computed tomography angiography (CTA) scan may be useful if a bleeding site cannot be identified endoscopically. CTA has the advantage of greater availability, speed, and noninvasiveness. It also does not suffer from a bowel or respiratory motion artifact. In an animal model, CTA was shown to detect bleeding rates as low as 0.3 mL/min more successfully than conventional angiography.¹⁸ In addition to being able to localize a bleeding site, CTA also has the benefit of providing information regarding the vascular anatomy for pre-interventional planning, as well as identifying extraluminal abnormalities.¹⁹

Indications and Contraindications of Angiography

Angiography is indicated if there is massive bleeding which could not be treated by endoscopy or if a patient is hemodynamically unstable (systolic blood pressure < 100 mmHg and heart rate > 100 beats per minute or clinical shock). Furthermore, it is indicated in patients with hepatobiliary procedure-related bleeding in which endoscopy has no role in the intervention.

In general, it has no absolute contraindications because angiography and embolization are needed as lifesaving procedures. For patients with severe reactions to iodinated contrast media, alternative contrast agents, such as carbon dioxide, can be used. Relative contraindications include renal insufficiency, contrast al-

lergy, and uncorrectable coagulopathy. There is an increased risk of gastric or duodenal infarction after embolization in patients with previous, extensive UGI surgery or radiotherapy.

Technique of Endovascular Management

Diagnostic angiography

Because UGIB is normally intermittent, the successful angiographic demonstration of the source of bleeding depends on the presence of active bleeding at the time of the examination. In literature reports, bleeding rates of 0.5 to 1.0 mL/min have been considered necessary if contrast extravasation is to be angiographically visible.²⁰ Moreover, digital subtraction angiography (DSA) is five to nine times more sensitive than screen-film arteriography for detecting bleeding, and which seems to be equivalent to the detection rates of scintigraphic images.^{21,22}

Although in most procedure-related UGIB it is possible to identify the source of hemorrhage, in some patients it is difficult to localize it because of the intermittent nature of GI bleeding, which can result if the bleeding has temporarily stopped at the time of the contrast injection. In such circumstances, to enhance the detection rate of bleeding, glucagon and Buscopan may be given before the procedure in order to limit peristalsis and respiratory motion artifacts on DSA.²³ Furthermore, longer injection durations of the contrast or the use of carbon dioxide as a contrast medium can also improve the sensitivity for detecting small bleedings.²⁴ Oblique views can provide a clearer view of colic vessels in flexures. In addition, right and left anterior oblique views open up hepatic and splenic flexures, respectively. Endoscopic clips, which are placed around the area of bleeding during pre-embolization endoscopy, can help to accurately localize the bleeding vessels. In such cases, even if no extravasation is seen, the branches terminating at the clip are superselected using microcatheter techniques and are embolized. Administration of vasodilators, anticoagulants, and/or thrombolytics can stimulate bleeding and thus help in detecting the origin of bleeding.²⁵

The vessel selected first should be based on the suspicion of the likely source of bleeding according to the patient's history, clinical signs, as well as localization provided by previous imaging or endoscopy. Generally, in UGIB, the celiac and superior mesenteric arteries (SMAs) are the primary targets. If there is no sign of active bleeding on contrast injection of the main trunks, more selective injection may be needed. For duodenal or gastric fundus bleeding, the gastroduodenal artery (GDA) or left gastric arteries, respectively, should be studied. And if there is hemobilia, hepatic arteries are the most suspected source of bleeding. Obtaining images should be continued until the venous phase has cleared out in order to help distinguish contrast extravasation from persistent venous opacification.

Angiographic findings

The primary angiographic findings of bleeding are visualization of active contrast extravasation and contrast pooling in the venous phase. A review of studies by Loffroy et al²⁶ found that angiographic evidence of active extravasation was seen in 54% of patients. Other indirect signs of bleeding on angiography include a pseudoaneurysm, vessel spasm or cut-off, and early venous filling.

Empirical or blind embolization of the vessels supplying the area of concern can be performed if no arterial abnormality is seen.^{27,28} A review of the published series by Loffroy et al²⁶ dem-

onstrated that blind embolization is performed in 46% of endovascular cases. This technique is feasible due to the rich collateral circulation of the upper GI tract. The left gastric artery supplies the distal esophagus, cardia, and fundus, and there is collateralization with branches of the short gastric and right gastric arteries. The GDA supplies the remainder of the stomach and the duodenum. The SMA also provides a duodenal supply via the pancreaticoduodenal arcades. And there are collateral arterial branches to hepatic arteries from the inferior phrenic, intercostal, left gastric arteries, and omental branches from the GDA. Moreover, in the hepatobiliary bleeding origin, transarterial embolization is considered the first-line treatment due to the dual vascular supply of the liver (75% via the portal vein and 25% via the hepatic artery) which permits embolization of hepatic artery branches without significant concern for infarction.²⁹

No statistical difference in outcomes was shown between patients treated with empirical embolization versus embolization after angiographically demonstrated contrast extravasation.^{27,30} An alternative to blind embolization in cases of negative angiography is to target branches supplying the area of endoscopically placed clips.

Types of embolic agent

The choice of embolic agent depends on a combination of the vascular anatomy, angiographic findings, the achievable catheter position, and the operator's preference. Vessel diameter and the nature of permanent or temporary embolization should be also considered. The most common embolic agents are metallic coils and gelatin sponge particles (GSPs).¹ However, using coils as the only embolic agent is significantly associated with early rebleeding compared with adding polyvinyl alcohol or GSP to coils.^{27,31} The use of N-butyl cyanoacrylate (NBCA) has recently gained acceptance. As it is a liquid embolic material with a non-radiopaque nature, it should, therefore, be mixed with Lipiodol to provide radiopacity and to control the viscosity. The more diluted the NBCA concentration is, the deeper penetration to the distal is achieved. Usually NBCA: lipiodol ranges from 1:1 to 1:4. It is advantageous for massive bleeding that requires urgent hemostasis, especially in patients with coagulopathy caused by rapid polymerization with blood.³²

Types of embolization

Types of embolization depend on the microcatheter superselection accessibility to the bleeding point. There can be localized, proximal or segmental embolizations. In localized embolization,

the microcatheter is superselected at the bleeding point. On the other hand when the bleeding point cannot be superselected, either proximal embolization is done in which the embolization is in its parent artery or segmental embolization in which an adjacent branch artery or arteries are included to be embolized. In cases of proximal embolization, recanalization of the bleeding point can occur due to distal back flow, while in segmental embolization, ischemic complications of the involved bowel can occur.

Upper GI Procedures

Upper GI procedures are done either endoscopically or percutaneously. An upper GI endoscopic diagnostic procedure complicated by bleeding is rare and does not have a clinical significance.³³ On the other hand, endoscopy for therapeutic purposes carries a risk of bleeding which needs further angiographic management in failed endoscopic treatment.³⁴ Endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), as well as endoscopic ultrasound (EUS)-guided procedures are associated with the risk of bleeding that may necessitate endovascular management, as reported in published literature reports.³⁵ Furthermore, percutaneous endoscopic or radiologic gastrostomy (PEG, PRG) related bleeding is rare, but may be catastrophic when it occurs.^{36,37}

EMR and ESD

EMR and ESD are effective and minimally invasive procedures for management of upper GI epithelial and subepithelial lesions. They are useful techniques for treating early gastric cancer without lymph node metastasis or with a lower risk of local recurrence, as well as other polyps or submucosal tumors.^{38,39} These endoscopic techniques enable physicians to confirm the histopathologic diagnosis based on the resected specimens. Although these procedures are effective and safe, they could be accompanied by delayed, life-threatening bleeding which may be the most serious complication.⁴⁰ However, significant bleeding only occurs in approximately 2.8% of esophageal resections and less frequently than in the stomach.⁴¹ A recent meta-analysis found no differences in the bleeding rates with EMR and ESD.

Endovascular embolization is considered the first-choice treatment compared with surgery for uncontrolled medical and endoscopic management (Fig. 1). There is no preferable embolic agent which can be used for the management of bleeding and its choice depends on the operator. Lee et al⁴² used microcoils only and Komatsu et al⁴³ used microcoils with GSP for successful

Fig. 1. Active bleeding after endoscopic submucosal dissection (ESD) for gastric subepithelial tumor. (A) Profuse bleeding was noted on endoscopy. Endoscopic bleeding control was unsuccessful. (B) Left gastric angiogram two hours after ESD shows extravasation of contrast (arrow). (C) After embolization using gelatin sponge particles and coils, spot radiograph shows coils and extravasated contrast into the stomach. (D) Post-embolization, gastroduodenal artery angiogram shows no further bleeding from.

embolization of uncontrolled bleeding during ESD of the stomach. Moreover, Lang et al⁴⁴ proposed prophylactic embolization of the left gastric artery when there is definite prior identification of a lesion in the left gastric artery area or if a patient has a controlled, previous, massive bleeding due to a gastric lesion and the patient is at risk for multi-organ failure if bleeding recurs. Previous reports by Park et al⁴⁵ support the validity of prophylactic transcatheter arterial embolization in UGIB without extravasation seen on an angiogram in patients with gastric intramural hematoma caused by EMR.

Endoscopic ultrasound-guided Intervention

EUS has been a diagnostic procedure concentrating on structural identification and staging of GI cancers. However, with advancement in this technology, EUS has expanded from diagnostic sampling into the field of therapeutic procedures.⁴⁶ Numerous procedures have been increasing associated with an increased risk of complications. The incidence of complication rates varies in each diagnostic and therapeutic technique.⁴⁷ Recently, a systematic review found the overall complication rate and mortality were 0.98% and 0.02%, respectively. The most significant complications were acute pancreatitis (34%), infection (16%), bleeding (13%), and perforation or bile/pancreatic leaks (3%).⁴⁶ Moreover, reports describing the role of arterial embolization in the management of interventional, EUS-related bleeding are limited (Fig. 2, 3). Brandon et al⁴⁸ reported embolization of massive arterial hemorrhage following endoscopic, ultrasonography (US)-guided cystogastrostomy for pancreatic pseudocyst drainage. Right and left gastric arteries were successfully embolized by coils. No rebleeding was detected.

Percutaneous gastrostomy

Percutaneous gastrostomy is a well-established procedure for long-term nutritional support or gastric decompression in patients incapable of oral intake due to various disorders. The incidence of major complications after PRG or PEG has been found to range from 0% to 6%.^{49–51} UGIB complicating enterostomy is rare but it is a serious complication if it occurs.^{52,53} Pseudoaneurysm formation also can occur.⁵⁴ UGIB complication is usually due to direct puncture of blood vessels, traumatic erosion, ulceration, and pressure necrosis of the gastric mucosa which may occur due to excessive tension of the inner bumper.

Although endoscopy is superior in localizing the bleeding site, characterizing the cause of bleeding, and showing the relationship between the bleeding site and the gastrostomy tube,³⁷ it may be limited by several factors including the presence of comorbid illnesses, active bleeding, bleeding vessels larger than 2 mm, and endoscopic blind spots, all of which may increase endoscopic hemostatic failure for UGIB.⁵⁵

There have been a few reports regarding endovascular embolization management for bleeding complications after PEG/PRG (Fig. 4).^{53,54,56} Lewis et al⁵⁶ reported occlusion of both gastroduodenal arteries by selective embolization which successfully stopped bleeding in a patient with an unstable hemodynamic status after PEG/PRG. Seo et al⁵⁴ retrospectively evaluated the incidence and management of bleeding complications in 574 patients who underwent PRG. Only eight patients (1.4%) had symptoms or signs of UGIB after PRG. Five patients underwent angiography because bleeding could not be controlled by conservative management as in the other three patients. In one patient, wedge resection, including the tube insertion site, was performed for hemostasis because

Fig. 2. Active bleeding after endoscopic ultrasound-guided, fine needle aspiration biopsy of a pancreatic lesion. (A) Common hepatic artery angiography shows a pseudoaneurysm from the gastroduodenal artery (arrow). (B) Superior mesenteric artery (SMA) angiogram shows no other bleeding focus. (C, D) Post-embolization SMA angiograms show no further bleeding focus. The distal portion of the pseudoaneurysm was embolized using microcoils (arrows) and the proximal portion was embolized with N-butyl cyanoacrylate (NBCA; NBCA:lipiodol = 1:3) (arrowheads).

Fig. 3. Active bleeding after endoscopic ultrasound-guided hepatoduodenostomy. (A) On endoscopy, bleeding control was impossible. (B) Common hepatic artery angiogram shows a pseudoaneurysm (arrow) at the right main hepatic artery near the proximal stent end. (C) The post-embolization angiogram shows no further bleeding focus with preserved right hepatic flow via intrahepatic collaterals. The proximal portion of the pseudoaneurysm was embolized using microcoils, followed by embolization of the pseudoaneurysm and its proximal part with N-butyl cyanoacrylate (NBCA; NBCA:lipiodol = 1:3).

no bleeding focus was discovered. In three patients, successful hemostasis was achieved by TAE, whereas in the remaining patient failure of embolization was reported because of the difficulty with the microcatheter advancing to the distal part of the bleeding focus, and therefore having persistent bleeding which was managed by surgery. This result supports the concept that if both the proximal and distal parts of the bleeding focus cannot be securely embolized, there is the potential for rebleeding by collaterals.

Hepatobiliary Procedure

Hemobilia is bleeding from the hepatobiliary tract and is considered as one of rare causes of UGIB.^{2,57} It occurs when the arterial bleeding is so rapid that blood is easily dissolved in bile and passes directly into the duodenum, appearing as hematemesis or melena. However, when the hemorrhage occurs more slowly, the blood and bile do not mix easily and clots obstruct the bile ducts and produce colicky pain and jaundice. It is often caused by trauma to the liver and biliary tract, including percutaneous transhepatic cholangiography (PTC) and percutaneous transhepatic biliary drainage (PTBD), biliary drainage during endoscopic retrograde cholangiopancreatography (ERCP), cholecystectomy, TIPS procedure, liver biopsy, and radiofrequency ablation (RFA).⁵⁸ The incidence of hemobilia following RFA and liver biopsy is estimated to be 0%–0.5% and 0.06%–1%, respectively; PTC (up to 4%) and PTBD (2%–10%) have a higher risk because of the use of larger needles and the presence of bile stasis.^{58–60} The mechanism of hemobilia after a liver/biliary tract intervention is not completely understood. An arteriobiliary fistula can occur immediately or may be the result of an erosion and breakthrough of a pseudoaneurysm to a nearby bile duct after days or weeks.⁵⁸ The most frequent cause is a direct trauma associated with the procedure.^{61,62}

Hemobilia from a venous source is rare. It is thought to originate from a source in the liver parenchyma in 50% of patients and from the bile ducts/gallbladder in 45% of them. A pancreatic source has been identified in fewer than 5% of patients.⁶³ The gold standard for diagnosing hemobilia is selective arteriography. In up to 90% of these patients, a vascular abnormality is found. The most common finding is a pseudoaneurysm, followed by an arteriobiliary or an arterioportal fistula.⁶⁴ Arterial embolization remains the treatment of choice. Success rates of 80%–100% have been reported in the published literature.^{65–67} Complications are rare and include hepatic necrosis, abscess formation, gallbladder infarction, non-target embolization, and intimal dissection with arterial thrombosis.⁶⁸ Other endovascular treatment for hemobilia due to pseudoaneurysm include covered stent deployment which has the advantage of maintaining the arterial blood flow, maintaining perfusion of the liver, and minimizing the risk of ischemia seen with embolization. However, using stents is associated with several limitations including the possible challenging navigation of the stent delivery system through the vascular loops, particularly through celiac axis, or SMA, tortuous, and small hepatic artery, and excessive manipulation of the device which may lead to vasospasm, dissection at the ends of the stent, and even vessel rupture.⁶⁹

Fig. 4. Bleeding complication after percutaneous endoscopic gastrostomy. (A) Enhanced abdomen computed tomography scan shows a large amount of hemoperitoneum with pneumoperitoneum. (B, C) Left gastric artery angiograms show contrast extravasation (arrows) from the left gastric artery. (D) The left gastric artery angiogram after embolization with gelatin sponge particles and a microcoil shows disappearance of contrast extravasation.

Fig. 5. Bleeding complication after right percutaneous transhepatic biliary drainage. (A) Enhanced abdomen computed tomography (coronal reconstruction) shows a large hepatic hematoma with active bleeding (arrow). (B) Selective right hepatic artery angiogram shows a pseudoaneurysm (arrow) with extravasation (arrowhead) from the A6 artery. (C, D) After embolization using N-butyl cyanoacrylate (NBCA; NBCA:lipiodol = 1:3), the spot radiograph (C) shows NBCA cast filling the A6 branch and the pseudoaneurysm. Common hepatic artery angiogram (D) shows no further bleeding focus.

Fig. 6. Active bleeding after endoscopic sphincterotomy for stone removal. (A) An endoscopic image eight hours after EST shows active bleeding from the ampulla. A covered stent was inserted to tamponade the bleeding, however, bleeding persisted. (B) The superior mesenteric artery (SMA) angiogram 10 hours after EST shows contrast extravasation (arrows) from the pancreaticoduodenal arcade. (C, D) Post-embolization SMA angiograms show no definite residual bleeding after embolization with N-butyl cyanoacrylate (NBCA; NBCA:lipiodol = 1:3).

PTBD

PTBD is an effective method for primary or palliative treatment of biliary abnormalities. Hemobilia due to hepatic arterial injury is a serious but infrequent complication, occurring in 1.3%–8% of PTBDs.^{66,70} The most common causes of bleeding are arteriobiliary fistula and pseudoaneurysm.²⁹ Left-sided PTBD seems associated with a greater risk of hepatic artery injury due to the anatomic arrangement of the hepatic arteries and bile ducts.

The reported initial technical and clinical success rates of arterial embolization are 100% and 95.8%, respectively.^{29,70,71} Coil as well as NBCA embolization is highly effective in order to control bleeding (Fig. 5). The complication rate following embolization of the hepatic artery is low due to its dual vascular supply through the portal vein and hepatic artery as well as the intrahepatic collateral pathways.

ERCP

ERCP is an efficient and safe invasive procedure that is performed to diagnose and treat pancreatic and biliary disease. However, in a prospective multicenter study, 9.8% of the patients had post-ERCP complications. Pancreatitis (5.4%) and hemorrhage (2%) are considered the most common complications associated with ERCP.⁷² Moreover, the incidence of complications related to therapeutic ERCP procedures was more common than that in diagnostic procedures.⁷³ Bleeding associated with endoscopic sphincterotomy is one of the most frequent complications of ERCP and has been reported in 1%–10% of patients.^{72–74} So et al⁷⁵ reported 10 patients who underwent selective embolization for post-endoscopic sphincterotomy bleeding and found that most of the bleeding branches arose from the posterior pancreaticoduodenal artery. In their study, they could determine the optimal approach to the bleeding branches by celiac and SMA arteriography, and two bleeding branches were found in two patients. Therefore, multiple branches should be considered because there is no anatomic landmark of the avascular zone on duodenal papilla. Coil, NBCA or GSP were proven to be effective for embolization at the bleeding focus (Fig. 6).

Conclusion

Procedure-related bleeding is considered one of rare causes of UGIB. It could present as hematemesis, melena or hemobilia, all of which are associated with hepatobiliary intervention. In most

patients the bleeding resolves spontaneously and in those that do not, the majority respond to medical or endoscopic management. In failed endoscopic treatment due to massive bleeding or in the case of hemodynamically unstable patients or in hepatobiliary procedure-related bleeding, endovascular or surgical intervention should be considered. Endovascular embolization represents the most viable treatment option as it is less invasive and not associated with the complications of general anesthesia.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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All authors have contributed to the paper and have not submitted the manuscript, in whole or in part, to other journals.

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