Diagnosis and management of ectopic varices

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ABSTRACT

Ectopic varices are large portosystemic collaterals in locations other than the gastroesophageal region. They account for up to 5% of all variceal bleeding; however, hemorrhage can be massive with mortality reaching up to 40%. Given their sporadic nature, literature is limited to case reports, small case series and reviews, without guidelines on management. As the source of bleeding can be obscure, the physician managing such a patient needs to establish diagnosis early. Multislice computed tomography with contrast and reformatted images is a rapid and validated modality in establishing diagnosis. Further management is dictated by location, underlying cause of ectopic varices and available expertise. Therapeutic options may include double balloon enteroscopy, transcatheter embolization or sclerotherapy, with or without portosystemic decompression, i.e., transjugular intrahepatic portosystemic shunts. In this article we review the prevalence, etiopathogenesis, anatomy, presentation, and diagnosis of ectopic varices with emphasis on recent advances in management.

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Introduction

The term “ectopic varices” has historically been used to describe abnormally dilated veins associated with gastrointestinal mucosa with propensity for gastrointestinal hemorrhage, and it has also been loosely used for portosystemic collaterals in the abdominal wall and retroperitoneum. Ectopic varices may be best defined as large pressurized portosystemic venous collaterals occurring anywhere in the abdomen except in the gastroesophageal region.1,2

Ectopic varices account for up to 5% of all variceal bleeding.3 They may be present in duodenum, jejunum, ileum, colon, anorectum, peristomal, biliary, peritoneal, retroperitoneal, umbilical, urinary bladder, uterine, ovaries, and other locations.

Prevalence

In a review of 169 cases of bleeding ectopic varices, 26% bled from peristomal varices, 17% from duodenal, 17% from jejunal and ileal, 14% from colonic, 9% from peritoneal, 8% rectal, and a few from infrequent sites such as the ovary and vagina.1 A study of 37 patients with liver cirrhosis who underwent capsule endoscopy, 8.1% were found to have small bowel varices.4 One 1968 angiographic study of patients with portal hypertension demonstrated an unusually high rate of paraduodenal varices, in 46 out of 106 (40%) patients; this likely described all regional venous collaterals, and not solely submucosal duodenal varices.5 Anorectal varices have been reported in approximately 44% of patients with cirrhosis,6 although only a fraction become symptomatic. Thus, true incidences are likely subject to reporting bias and the modality used for diagnosis and only a fraction of diagnosed ectopic varices are likely to become symptomatic.

Etiology and pathogenesis

Ectopic varices represent natural portosystemic shunts secondary to portal hypertension. These collaterals occur where the portal venous system is in juxtaposition to the systemic venous system. Under normal circumstances the resistance within these collaterals is high, while it is low in the portal venous system. With the development of intrahepatic portal hypertension, these shunts act to divert flow from the increased intrahepatic vascular resistance. Surgical literature and cadaveric studies have shown portosystemic communications via (a) gastroesophageal plexus to azygous-coronary system, (b) hemorrhoidal plexus, (c) recanalized umbilical vein, and (d) pancreatoduodenal venous arcade to inferior vena cava through retroperitoneal veins of Retzius. Most reported cases of hemorrhage from ectopic varices in the West are associated with intrahepatic portal hypertension in contrast to extrahepatic portal hypertension, because of low prevalence of the latter. Prior abdominal surgery predisposes patients with portal hypertension to develop varices in unusual locations, like urinary bladder, ovaries

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and bare area of the liver due to adhesions.\textsuperscript{1,2,7} Finally, ectopic varices can develop in the absence of portal hypertension due to congenital anomalous portosystemic anastomoses,\textsuperscript{8} abnormal vessel structures,\textsuperscript{9} arteriovenous fistulae,\textsuperscript{10} rare familial conditions,\textsuperscript{11} or related to thromboses.\textsuperscript{12}

Wall tension in all varices is a recognized risk factor for rupture. Per LaPlace’s law it is proportional to transmural pressure across the vessel wall and the radius of the vessel. Hence, portal pressure and vessel size are determinants of ectopic variceal hemorrhage.\textsuperscript{13} In our and others’ experience ectopic varices, like gastric varices may bleed at a portosystemic gradient of less than 12 mmHg.\textsuperscript{14,15} emphasizing the need for different transcatheter treatments then those used for bleeding esophageal varices.

\section*{Presentation and diagnosis}

Ectopic varices present in a multitude of ways. For example, duodenal varices may manifest with mild or massive hematemesis or lower gastrointestinal bleeding.\textsuperscript{16} Intestinal varices distal to duodenum, usually present with hematochezia, melena, or intra-peritoneal bleeding.\textsuperscript{17-19} Urinary bladder varices may present with hematuria,\textsuperscript{20} and biliary varices with biliary obstruction,\textsuperscript{21} or rarely hemobilia and gastrointestinal bleeding.\textsuperscript{22} Ruptured varices at the right diaphragm can cause hemothoraces and dyspnea.\textsuperscript{23} Abdominal wall varices (e.g., umbilical) can rupture externally or internally, whereas those located around the falciform ligament, diaphragm, splenic ligament or in the rectovesical region may rupture into the peritoneal cavity, leading to occult, potentially fatal intraperitoneal hemorrhage.\textsuperscript{19,23,24}

Brisk upper gastrointestinal bleeding and hematochezia should be first evaluated with emergency upper gastrointestinal endoscopy. If this fails to define an acute source of hemorrhage, intravenous contrast enhanced computed tomography (CT) may be preferable to colonoscopy (in the unprepped acute setting). Thus, presence of ectopic varices should be strongly considered in patients with known liver disease or stigmata of portal hypertension, particularly when both upper and lower endoscopies fail to identify a source of bleeding.\textsuperscript{2} Elective capsule endoscopy has been successful in detecting jejunal and small bowel varices,\textsuperscript{6,25} although its role in acute bleeding is small. Similarly, double balloon enteroscopy or push enteroscopy has the potential to visualize the greater small bowel and allow intervention.\textsuperscript{3,26} Endoscopic ultrasound has been reported for the hemodynamic assessment of rectal\textsuperscript{27} and biliary varices.\textsuperscript{28}

Color Doppler ultrasound has shown its value in the diagnosis of umbilical (Fig. 1A and D), duodenal,\textsuperscript{29} rectal,\textsuperscript{30} gall bladder,\textsuperscript{21} and choledochal varices.\textsuperscript{31} However, intravenous contrast enhanced multislice CT (Fig. 2A and B), should be considered the primary modality for diagnosis of ectopic varices, given the rapid and ubiquitous availability. CT, CT angiography, and CT enteroclysis have all been used for successful diagnosis of duodenal\textsuperscript{32,33} and colonic varices.\textsuperscript{34} While technetium TC-99m red blood cell scintigraphy has

\begin{figure}[h]
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\caption{A 53-year-old female with history of alcoholic cirrhosis transferred from outside the hospital with external bleeding around the umbilicus from cutaneous varices. (A) Preprocedure color Doppler ultrasound in periumbilical region shows flow in varices (white arrow); (B) digital subtraction image DSA from the transjugular intrahepatic portosystemic shunt (TIPS) procedure during the initial portogram shows the left portal vein (white arrow), with retrograde flow in the recanalized umbilical vein (black arrows), leading to large periumbilical varices (lowest black arrow). Initial portosystemic gradient: 21 mmHg; (C) portogram after TIPS and embolization of umbilical vein varix with liquid embolic agent (Onyx, ev3 Endovascular, Inc. Plymouth, MN, USA), shows antegrade flow without retrograde filling of umbilical vein. Post TIPS portosystemic gradient: 15 mmHg; (D) post-TIPS and embolization ultrasound of periumbilical region shows thrombus in the periumbilical varices (white arrows).}
\end{figure}
been used,\textsuperscript{35} its modern role in this setting is appropriately diminishing. Finally, contrast-enhanced three-dimensional magnetic resonance (MR) angiography\textsuperscript{36} can equally outline unusual portosystemic collaterals, but has little role in the acute setting. Of note, barium studies of the colon or small bowel may misdiagnose ectopic varices as polyps or tumors,\textsuperscript{11} emphasizing the importance of tomographic imaging and clinical suspicion.

**Specific anatomic locations**

**Duodenal varices**

Cirrhosis is the most commonly associated cause of duodenal varices, accounting for 30% of the cases,\textsuperscript{37} but causes vary and include portal venous thrombosis and obstruction of the splenic vein and inferior vena cava.\textsuperscript{38,39} Duodenal varices have also developed after band ligation of esophageal varices, presumably as alternate sites of spontaneous portosystemic shunting.\textsuperscript{40} These varices are formed by the collateral veins originating from the portal vein trunk or superior mesenteric vein draining into the inferior vena cava through retroperitoneal veins of Retzius.\textsuperscript{41} Duodenal variceal rupture can lead to severe hemorrhage, with mortality as high as 40% from initial bleeding.\textsuperscript{42}

**Jejunal, ileal, colonic, and ano rectal varices**

Small bowel varices are commonly seen in patients with intrahepatic portal hypertension who have previously undergone abdominal surgery. Adhesions bring the parietal surface of the viscera in contact with the abdominal wall, and portal hypertension results in formation of varices below the intestinal mucosa.\textsuperscript{7} A triad of portal hypertension, hematochezia without hematemesis and prior abdominal surgery characterize hemorrhage from small intestinal varices.\textsuperscript{43} These varices most commonly flow into systemic circulation through the gonadal veins, and less commonly through branches of the internal iliac veins.

Rectal varices are distinguished from hemorrhoids by their typical presence above the dentate line. The differentiation of hemorrhoids and anorectal varices is an important one. Anal varices collapse with digital pressure, whereas hemorrhoids do not; of note, the prevalence of hemorrhoids in patients with liver disease is not higher than in the general population.\textsuperscript{6} These varices represent a portosystemic collateral pathway between the superior rectal veins of the inferior mesenteric system to the middle and inferior rectal veins of the iliac system (Fig. 3). They can be present with mild or uncontrolled hematochezia.\textsuperscript{44} The most common colonic sites are the cecum (Fig. 2C) and rectum,\textsuperscript{45} although isolated colonic varices, in the authors experience, rank among the rarest.
Stomal varices

Ectopic stomal varices refer to abnormally dilated veins that have developed in the stomal mucosa, often recognized by a purplish hue around the stoma. They are common in patients with intrahepatic portal hypertension secondary to primary sclerosing cholangitis, and are frequently seen in patients with ileostomies after proctocolectomy for inflammatory bowel disease associated with primary sclerosing cholangitis (Fig. 4A). The mechanism of stomal variceal hemorrhage is related to local trauma and variceal erosion. The overall morbidity is high, given the propensity for recurrent bleeding requiring multiple blood transfusions but mortality is low, between 3% and 4% because of the ability to institute local measures such as pressure dressing, epinephrine soaked gauze, gel foam packing, and suture ligation. These therapies are however, not effective in preventing recurrent bleeding. Importantly, stomal varices can be missed by endoscopy, emphasizing the need for clinical suspicion and CT imaging in occult cases.

Biliary tract varices

In extrahepatic portal vein thrombosis, gall bladder and common bile duct varices can occur in as many as 30% of patients. They maybe an incidental finding or present with biliary obstruction secondary to mass effect on extrahepatic bile ducts. The appearance of biliary tree, by direct endoscopic retrograde cholangiopancreatography may mimic that of primary sclerosing cholangitis, and is termed as pseudosclerosing cholangitis. Rarely, biliary varices can lead to hemobilia or even catastrophic hemorrhage.

Vesical varices and other unusual sites

The urinary bladder wall is an unusual collateral route for venous splanchnic blood flow and these varices may develop after abdominal surgery secondary to adhesions. Bleeding from vesical varices is a rare event in patients with portal hypertension and an

Fig. 3. A 49-year-old female with history of primary biliary cirrhosis presented with upper gastrointestinal hemorrhage. Repeated endoscopy and banding was unable to stop hemorrhage. Balloon tamponade was done with an orogastric tube. DSA during the transjugular intrahepatic portosystemic shunt (TIPS) procedure with the catheter in the inferior mesenteric vein (black arrows) shows retrograde flow, with filling of hemorrhoidal plexus and anorectal varices (white arrow). Initial portosystemic gradient: 18 mmHg and post TIPS gradient: 6 mmHg. Post TIPS there was no retrograde flow in inferior mesenteric vein and anorectal varices. The upper gastrointestinal hemorrhage ceased, and the balloon tamponade tube was deflated at end of procedure. The patient was discharged from hospital after 5 days.

Fig. 4. Middle-aged male with uncontrolled bleeding from a recent ileostomy, with no source detected on endoscopy. (A) DSA during the transjugular intrahepatic portosystemic shunt (TIPS) procedure with the catheter in the peripheral superior mesenteric vein shows stomal varices (white arrow), a faint outline of the ileostomy bag is seen (black arrows); (B) post coil embolization (white arrows) of stomal varices, with the catheter in the superior mesenteric vein (black arrows), shows non-filling of stomal varices. The TIPS resulted in cessation of further bleeding from the stoma.
usual cause of hematuria\textsuperscript{20}; however, due to intraperitoneal hemorrhage, this can be catastrophic.\textsuperscript{19}

Other more unusual sites include right diaphragm,\textsuperscript{21} splenorenal ligament,\textsuperscript{24} splenopancreatic,\textsuperscript{49} adnexal,\textsuperscript{50} vaginal,\textsuperscript{51} umbilical (Fig. 1),\textsuperscript{52} and cutaneous varices\textsuperscript{53} leading to unusual manifestations like pleural effusion, dyspnea, hematuria, and percutaneous exsanguination.

Management

There are no randomized trials or set guidelines that dictate the management of bleeding ectopic varices. The management depends upon location of hemorrhage, presentation, local physician expertise, and the underlying causes of portal hypertension. A multidisciplinary approach is in order, with input from intensivists, gastroenterologists, interventional radiologists, and surgeons. The medical management of variceal hemorrhage is discussed in other texts and we will confine our discussion to interventional management.

Endoscopic interventional procedures

Many ectopic varices are within reach of standard endoscopy,\textsuperscript{7} and, with the advent of double balloon or push enteroscopy, the reach has extended even further.\textsuperscript{26} The options include endoscopic band ligation (EBL) and endoscopic injection sclerotherapy (EIS) with different agents including N-butyl-2-cyanoacrylate (NBCA), thrombin or other sclerosants. EBL was found to be superior to EIS for the treatment of esophageal varices, on the basis of lower rebleeding rate, mortality, complications, speed of application, and the need for fewer endoscopic treatments; however, the main disadvantage remains the observed higher rate of variceal recurrence in comparison to sclerotherapy. Sclerotherapy on the other hand may lead to deep ulceration, which can lead to rebleeding, stricture formation, or perforation.\textsuperscript{34,53} Combination of two in the form of endoscopic scleroligation (ESL), has shown to be superior with decreased recurrence rates.\textsuperscript{36} No set protocol exists for the use of above mentioned modalities for the management of ectopic varices and the choice is often situation and expertise dependent.

Endoscopic band ligation and sclerotherapy have been successfully used solo or in combination with each other and other interventional radiological modalities in controlling hemorrhage from duodenal,\textsuperscript{57,58} jejunal,\textsuperscript{59} colonic,\textsuperscript{59} anorectal,\textsuperscript{60} and stomal varices.\textsuperscript{61}

Interventional radiological procedures

Multiple image-guided approaches to management of ectopic varices have been extensively reported. They include direct percutaneous access to varices, antegrade and retrograde sclerotherapy and/or embolotherapy, and portosystemic shunts. Transjugular and transhepatic as well as retrograde transjugular or transmural venous approaches have been proven useful.

Transjugal intrahepatic portosystemic shunts (TIPS)

Many publications have emphasized the role of TIPS in the management of bleeding ectopic varices in cirrhotics caused by intrahepatic portal hypertension.\textsuperscript{16,42,62} TIPS have proven more effective in preventing recurrent esophageal variceal rebleeding than endoscopic therapy.\textsuperscript{53,64} It has been shown that a $>50\%$ reduction in pressure gradient protected patients from rebleeding and even a reduction between 25% and 50% was also effective, with a probability of rebleeding of only 7% and less risk of encephalopathy and liver failure.\textsuperscript{55} The portosystemic gradient thresholds for adequate ectopic varix decompression are not those of above mentioned modalities for the management of ectopic varices and the choice is often situation and expertise dependent.

Balloon occluded retrograde transvenous obliteration (B-RTO)

As opposed to TIPS, which is a shunt creation procedure, B-RTO is a shunt occlusion procedure. Further, it uses a retrograde rather than antegrade approach. This technique has been employed for control of gastric variceal bleeding, with success rates reaching 89%,\textsuperscript{71} without detriment in hepatic function or in hepatic encephalopathy. However, since increased portal pressure is not addressed by this procedure, there is a risk of increased pressure and bleeding from varices that have not been sclerosed and are at other sites, or development of ascites. Aggravation of esophageal varices is recognized after B-RTO of gastric varices.\textsuperscript{72} To forego or salvage bleeding from varices after B-RTO, different procedures have been utilized, including TIPS,\textsuperscript{73} percutaneous obliteration,\textsuperscript{74} and endoscopic interventions.\textsuperscript{57} While largely used for primary prophylaxis of gastric varices in the East, increasing case reports have described its successful role in treatment of varices within the duodenum,\textsuperscript{75} small bowel,\textsuperscript{76} colonic,\textsuperscript{77} stomal,\textsuperscript{78} and mesentery.\textsuperscript{79}

Percutaneous embolization

Percutaneous embolization has been widely reported using a transhepatic approach. While, successful embolization rates reach 80%, up to 65% rebleeding rate within 5 months have been described.\textsuperscript{80} The earlier use of this approach largely predates the routine role of TIPS for other indications. The transhepatic route may provide more rapid access to portal system for less-experienced operators; however, its added risks include transhepatic tract bleeding, recurrent hemorrhage due to lack of secondary portal decompression, and added contraindications in ascites patients. Certainly embolization is important for durable control of varices.\textsuperscript{81} In cases where decompression is contraindicated, a transjugular approach (without shunt creation) can still provide direct access to the varices. In some cases, portal hypertension leading to varices may be wholly due to extrahepatic obstruction, e.g., after Whipple or similar surgeries. Correction of portal vein stenoses or thromboses with stents may provide adequate decompression and restore hepatopetal flow.\textsuperscript{82} Finally, more recent case reports have described direct, ultrasound guided abdominal wall,\textsuperscript{54} or stomal varical,\textsuperscript{83} puncture, and sclerotherapy or coil embolization. Percutaneous embolization by itself or in association with other interventional modalities has been reported for management of hemorrhage from ectopic varices in duodenum,\textsuperscript{84} small bowel,\textsuperscript{25} anorectum,\textsuperscript{85} stomata,\textsuperscript{47,81} mesentery,\textsuperscript{86} umbilicus,\textsuperscript{52} and urinary bladder.\textsuperscript{87}
Surgical interventions

The role of surgery in the modern management of ectopic varices has naturally lessened, as the operative morbidity and mortality in bleeding patients with liver disease is high. Surgery may be considered a salvage option in select patients when endoscopic and interventional radiological procedures have failed. Although distal splenorenal shunts and small diameter portocaval shunts carry less risk of encephalopathy and hepatic failure,88 than mesocaval or portocaval shunts, they are rarely performed in acute settings. Devascularization procedures may have a small role, may not require long segment resections and can be done in patients with portal venous thrombosis, but they still require great expertise and can carry high morbidity and mortality rates.89 Other unusual shunts include long segment resections and can be done in patients with portal portocaval shunts, they are rarely performed in acute settings.

Surgery has been used for dearterialization of bleeding duodenal varices,92 enteroctomy for bleeding ileal varices,93 resection and anastomosis for colorectal varices,94 and stapled anoplasty for anorectal varices.95

Conclusion

No randomized studies exist to guide the best management of ectopic varices; the bulk of knowledge comes from case reports and small retrospective case series. It is clear that many approaches have value in each specific case. Regardless of the approach, it is important to emphasize that complete obliteration and embolization of the target varix (as with BRTO) is preferable for preventing recurrent symptoms over focal embolization of feeding veins, which can allow stent-shunt insertion at a single centre. Euro J Gastroenterol Hepatol. 2004;16; 9–18.


