Chapter 8
Diagnosis and Hemodynamics of Ectopic Varices

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Abstract Varices may form in any part of the gastrointestinal tract from the esophagus to the colon, when portal pressure increases. The most common site of ectopic varices is the rectum followed by the duodenum. Other sites of varices are the small intestine, colon, gall bladder, anastomotic site, and stoma. The incidence of rectal varices has been increasing in recent years. Patients have to be monitored for possible rectal varices especially after the treatment of esophageal and gastric varices. While cirrhosis is the most frequent underlying disorder in Japan, extrahepatic portal obstruction associated with thrombosis, tumor, or pancreatitis is common in the USA and Europe. Endoscopy to directly observe the variceal lesion is most frequently used for diagnosis. Computed tomography and magnetic resonance imaging are required for understanding the hemodynamic profiles of ectopic varices regardless of their sites. Ectopic varices may be fatal once bleeding occurs because of the high blood flow rate and volume. However, bleeding is considered infrequent in general. Ectopic varices are an important clinical issue in portal hypertension, and the incidence is expected to increase. The pathophysiology of ectopic varices needs to be elucidated to establish the diagnosis and treatment.

Keywords Ectopic varices · Diagnosis · Endoscopy · Diagnostic imaging
Collateral hemodynamics

8.1 Introduction

Portal pressure elevates due to the increase in vascular resistance of the intrahepatic portal veins and blood volume flowing into the liver [1, 2]. When portal pressure exceeds 200 mmH_2O, a variety of collateral vessels such as esophageal and

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gastric varices, epigastric vein, splenorenal shunt, and gastrorenal shunt develop. Varices may form in any part of the gastrointestinal tract when portal pressure increases since the portal system is fed by venous blood flow in the gastrointestinal tract, from the stomach to the colon, and other abdominal organs. Although so-called ectopic varices other than esophageal and gastric varices are considered a relatively rare disorder, approximately 5% of all varices associated with gastrointestinal bleeding are identified as ectopic varices in the USA and European countries [3, 4]. The frequency and the site of ectopic varices are yet to be understood.

Endoscopic treatment for esophageal and gastric varices, i.e., endoscopic injection sclerotherapy (EIS) and endoscopic variceal ligation (EVL), has become established as the standard treatment in Japan over the past 20 years. Although treatment guidelines for esophageal and gastric varices have mostly been established [5], no consensus has been reached about the treatment of ectopic varices. With the advancement of diagnostic imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) in recent years, a variety of ectopic varices have been reported. This chapter outlines the diagnosis and the hemodynamics of ectopic varices, focusing on relatively frequent duodenal and rectal varices, in addition to the current status of ectopic varices in Japan.

8.2 Site of Varices

According to the Japanese nationwide survey in 1990, the frequency of ectopic varices was extremely low: 129 of 18,540 cases (0.7%) of all types of varices. Ectopic varices develop in a variety of organs, mainly in the gastrointestinal tract such as the duodenum, small intestine, colon, rectum, and gall bladder [6]. The survey in 2005 reported 57 of 173 cases (32.9%) of all ectopic varices were duodenal varices. There were two cases of duodenal varices in the duodenal bulb, 47 cases in the descending part and eight cases in the transverse part. Most of the duodenal varices were found in the descending to transverse part [7]. Small intestinal varices were reported in 11 cases: jejunal varices in seven cases, ileal varices in two cases, and varices in unknown sites in two cases. Colonic varices were reported in six cases. Rectal varices were the most common ectopic varices reported in 77 cases (44.5%), showing a significant increase from 20.2% reported 10 years earlier. Other reported sites of varices included the biliary tract in eight cases, anastomotic site in ten cases, stoma in three cases, and diaphragm in one case (Fig. 8.1). Lebrec et al. reported bleeding from ectopic varices in 1–3% of patients with portal hypertension, and 40% of the ectopic varices were found in the colon [8].

Duodenal varices were first reported by Alberti in 1931 [9]. The sites of duodenal varices are different between Japan and other countries because the hemodynamic profiles vary depending on the underlying disease. While the duodenal bulb is the most common site in the USA and Europe, varices are likely to develop in the descending or horizontal part of the duodenum in Japanese patients. Thirty-three

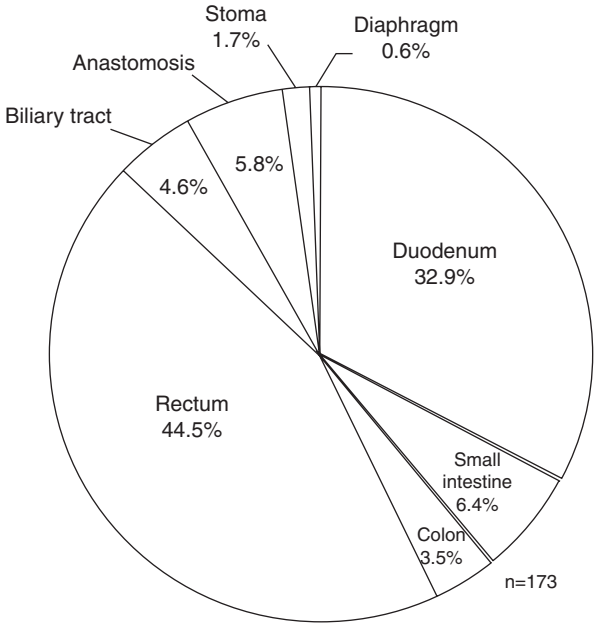

Fig. 8.1 Site of ectopic varices. Rectal varices are the most common ectopic varices (44.5%) followed by duodenal varices (32.9%). Other common sites of ectopic varices include the small intestine, colon, biliary tract, anastomosis, stoma, and diaphragm

cases of rectal varices were first reported in 1954 [10]. The frequency of rectal varices in patients with portal hypertension is roughly 10% or lower [11, 12]. On the other hand, Chawla et al. reported rectal varices in 78% of patients with portal hypertension. The incidence was 56% in patients with cirrhosis and as high as 89% in those with a non-cirrhotic liver [13].

8.3 Underlying Diseases

The most common disease underlying ectopic varices in Japan is cirrhosis, and it is found in approximately 80% of the patients. The causes of cirrhosis include hepatitis B virus, hepatitis C virus, alcohol, primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC). Type C cirrhosis takes up about a half of the diseases underlying ectopic varices. Non-cirrhotic diseases underlying ectopic varices include idiopathic portal hypertension (IPH) and extrahepatic portal vein obstruction (EHO) [7]. Although no apparent association is generally noted between the site of ectopic varices and the underlying disease, the majority of ectopic varices in patients with alcoholic cirrhosis are duodenal varices, and biliary varices are most common in patients with EHO. It has been reported that the site of duodenal varices may be associated with the underlying disease. While cirrhosis is the most common disease underlying duodenal varices in Japan, cirrhosis causes only about 30% of duodenal varices in other countries. EHO such as occlusion of the splenic vein or

superior mesenteric vein due to thrombosis, tumor, or pancreatitis is the common underlying disease reported overseas [9]. In duodenal varices, the difference in reported underlying disease between Japan and the USA and Europe may be associated with the site of varices.

Ectopic varices are accompanied by esophageal and gastric varices in 78.0% of patients overall. A strong association is suggested between ectopic varices and esophageal/gastric varices based on the high percentage of patients with esophageal varices recognized in their past history (76.9%) and those who have been treated (57.9%). Notably, a past history of esophageal varices was recognized in 73 (94.8%) of 77 cases of rectal varices. The percentage is apparently higher especially in patients with rectal varices compared with those with varices in other organs. The findings indicated that rectal varices were noted among patients having been treated for esophageal varices. Rectal varices should be anticipated after the treatment of esophageal varices [7]. Since the inferior mesenteric vein and the superior rectal vein are frequent as afferent vessels of rectal varices, descending collateral vessels are likely to develop after the treatment of esophageal and gastric varices that scleroses the ascending left, posterior, and short gastric veins, allowing rectal varices to form [14, 15]. Periodic rectal endoscopy should be required after the treatment of esophageal and gastric varices based on the high incidence of rectal varices after treatment.

8.4 Diagnostic Methods

8.4.1 Endoscopy

Endoscopy to directly observe the lesion is indispensable for diagnosing ectopic varices. Endoscopy is the most frequently used method of diagnosing ectopic varices. Upper gastrointestinal endoscopy is performed in approximately 90% of patients with duodenal varices. All rectal varices are diagnosed using lower gastrointestinal endoscopy. Double-balloon endoscopy and capsule endoscopy are now used to diagnose small intestinal varices. Medium and larger varices, i.e., form (F) 2 or greater varices according to the general rules for recording the endoscopic findings of esophageal varices [16], are frequently found in ectopic varices. There is no difference among the various ectopic varices with respect to the degree of color or form in endoscopic findings, while F2 or greater variceal lesions constituted more than 70% of the lesions in the duodenum, colon, and rectum. Varices positive for red color (RC) sign are found in 24% of duodenal cases and in 40% of rectal cases. Duodenal varices and rectal varices may exist extramurally and be generally less likely to bleed, but any enlarged or RC sign-positive rectal varices should be treated [11]. Matsui et al. pointed out that the F factor bears greater importance than RC sign-positive varices as a risk factor for bleeding from duodenal varices [17]. The propriety of prophylactic treatment for ectopic varices should be subject to further discussion because neither findings to predict hemorrhage nor any guidelines for treatment has been established.

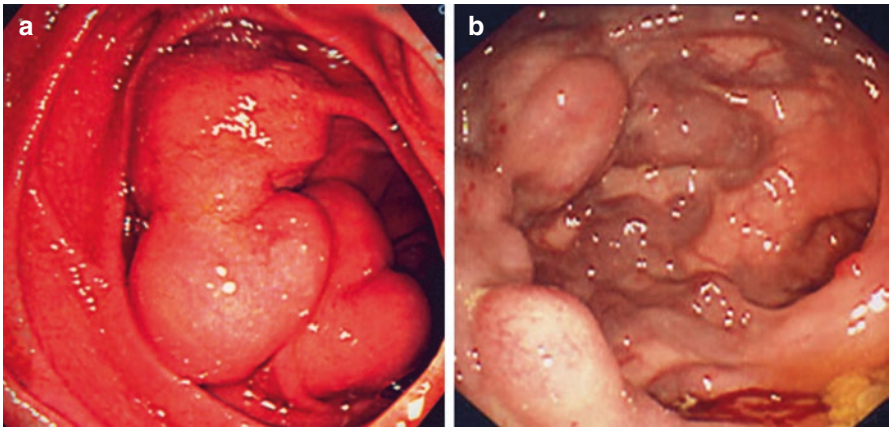

Fig. 8.2 Endoscopic findings of ectopic varices. (**a**). Duodenal varices, (**b**) Rectal varices. Both duodenal and rectal varices are recognized as elevated tumorous or tortuous submucosal lesions

Duodenal varices are often diagnosed with upper gastrointestinal endoscopy since most reported cases are hemorrhagic. Hemorrhagic varices are difficult to diagnose because of blood accumulation. They are usually protruded lesions with erosion and gushing blood. Duodenal varices were recognized as elevated tumorous or tortuous submucosal lesions (Fig. 8.2a). They may be difficult to differentiate from submucosal tumor. Only 44% of duodenal varices are accurately diagnosed with endoscopy [18]. It is important to exclude duodenal varices, nevertheless, in cases of upper gastrointestinal tract bleeding in liver cirrhosis. Varices are formed more frequently in the descending or transverse parts of the duodenum in Japan; thus the upper gastrointestinal tract must be explored down to deep parts in the duodenum.

Direct observation with an endoscope is the most useful diagnostic method for rectal varices. Colonic varices are usually localized in the rectum but may be found anywhere in the colon. The endoscopic findings are mostly the same as those of duodenal varices: elevated tumorous or tortuous submucosal lesions (Fig. 8.2b). Endoscopic ultrasonography (EUS) is a useful examination for diagnosing rectal varices and defining the hemodynamics. The variceal visualization rate of EUS is significantly higher compared with that with the regular endoscopy. The submucosal layer, the penetrating branches, and the extramural varix can be visualized [19]. In colonic varices, blue veins and arborescent vascular dilatation are visualized other than the varices.

8.4.2 MRI and CT Scan

Rapidly progressing in recent years, CT and MRI are used for diagnosing ectopic varices and understanding the hemodynamic profiles irrespective of the site of varices. With the emergence of magnetic resonance angiography (MRA), the portal veins are now noninvasively and easily visualized. MRA is an excellent tool for

defining collateral hemodynamics in portal hypertension. It is an important means of examination to evaluate the hemodynamics before and after the treatment of varices and to determine the indication and the efficacy of interventional radiology (IVR) [20]. In addition, MRA can visualize the entire portal vein system in the abdomen, and it is excellent in identifying ectopic varices such as duodenal and rectal varices and defining hemodynamics of the collateral vessels (Fig. 8.3).

CT angiography (CTA) with multidetector-row CT (MDCT) produces very high-quality images and reconstructs images in all sections including cross, sagittal, and coronal sections. With a higher resolution performance compared with MRA, CTA is excellent in visualizing small vessels and can take images in the arterial, portal, and venous phases (Fig. 8.4). The stereoscopic relationship between the collateral

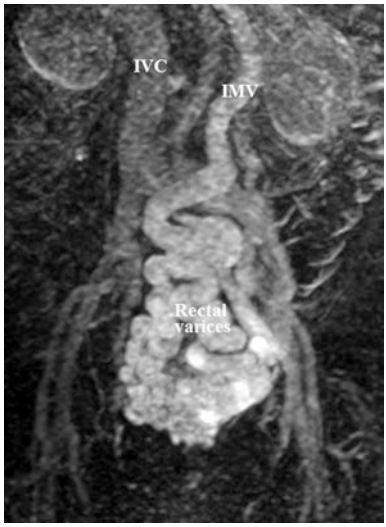

Fig. 8.3 MRA image of rectal varices. In rectal varices, the superior rectal vein branching out of the inferior mesenteric vein (IMV) serves as an afferent vessel. After rectal varices form, the blood flows into the inferior vena cava (IVC) through the internal iliac vein

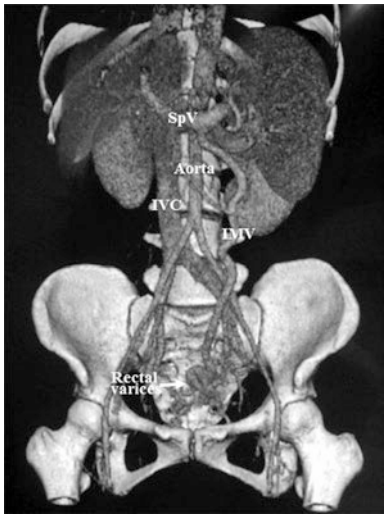

Fig. 8.4 CTA image of rectal varices. With a higher resolution performance, CTA visualizes three-dimensional images to clearly show the stereoscopic relationship of the varices, the afferent vessel (inferior mesenteric vein; IMV), and the efferent vessel. *IVC* inferior vena cava, *SpV* splenic vein

vessels and the varices is clearly visualized in three-dimensional images [21, 22]. The use of CTA is expected to increase to identify ectopic varices and understand the hemodynamic profiles.

8.4.3 Angiography

Collateral vessels should be thoroughly understood before treating ectopic varices since the hemodynamics are complicated in ectopic varices unlike in esophageal and gastric varices. Venous phase imaging of celiac and superior mesenteric artery or percutaneous transhepatic portography (PTP) has been used to visualize the portal veins. In portal hypertension, an increase in portal pressure is noted by measuring the hepatic venous pressure gradient (HVPG) [23], which is the difference between the wedge hepatic venous pressure (WHVP) and the free hepatic venous pressure (FHVP). Portal hypertension is clinically defined as HVPG 10 mmHg or higher. The portal hypertension is considered severe when the HVPG is 12 mmHg [24]. Now that collateral hemodynamics are easily identified by MRA or CTA, abdominal angiography is commonly performed for not only diagnosis but also IVR. Various types of IVR including percutaneous transhepatic obliteration (PTO), balloon-occluded retrograde transvenous obliteration (B-RTO), and transjugular intrahepatic portosystemic shunt (TIPS) are performed for the treatment of ectopic varices [25–28]. An appropriate IVR is selected based on the hemodynamics recognized in each patient.

8.5 Hemodynamic Profiles

In portal hypertension, a variety of collateral vessels such as esophageal and gastric varices, epigastric veins, splenorenal shunt, and gastrorenal shunt develop. Gastric varices are fed by the left, short, and posterior gastric veins. The blood then flows into the left renal vein through the gastrorenal shunt. Identifying the efferent and afferent vessels of ectopic varices is very important to understand the pathophysiology and determine a treatment strategy. The hemodynamics in duodenal and rectal varices, which are relatively frequent ectopic varices, are described here (Fig. 8.5).

The most common afferent vessels of duodenal varices are the inferior pancreaticoduodenal vein (IPDV) followed by the superior mesenteric vein (SMV) (10.2%), other duodenal veins (DV), and superior pancreaticoduodenal vein (SPDV). The gonadal vein is the efferent vessels in the majority of cases. The hemodynamics in duodenal varices vary depending on the underlying disease of portal hypertension. In cirrhosis or posthepatic portal hypertension, the branches of SMV including IPDV, SPDV, and DV develop as hepatofugal routes and often form varices in the descending or horizontal limb of duodenum. In extrahepatic portal vein obstruction, collateral vessels such as the pancreaticoduodenal vein develop to form varices in the duodenal bulb region and then ascend hepatopetally into the liver [29].

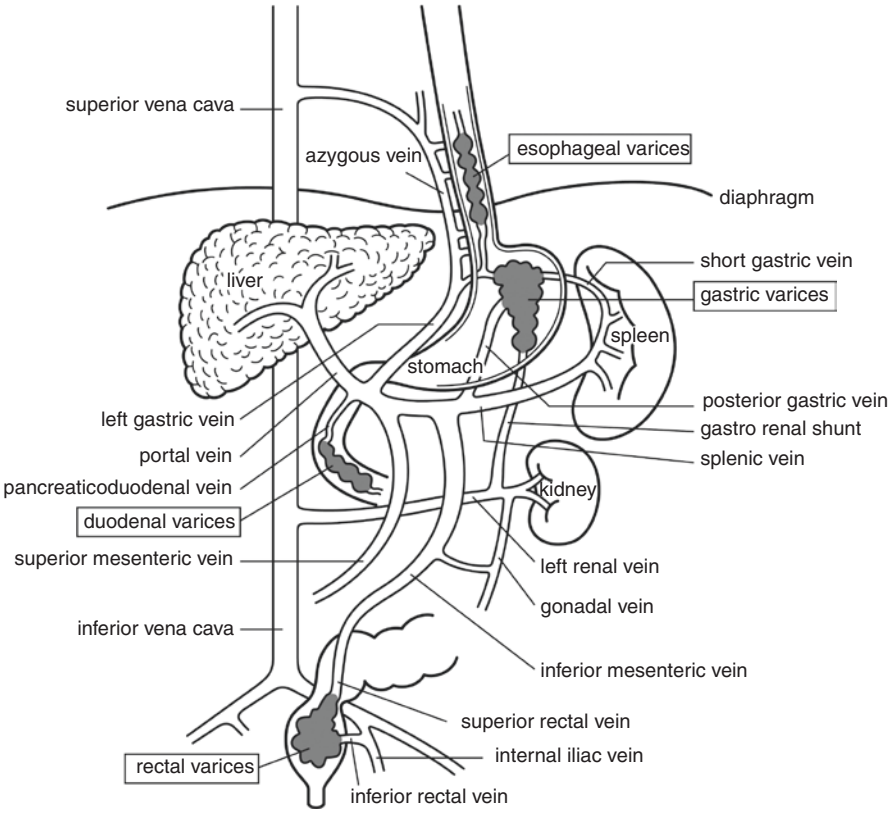

Fig. 8.5 Schema of gastrointestinal varices and collateral hemodynamics in portal hypertension. Gastric varices are fed by the left, short, and posterior gastric vein. The blood then flows into the gastrorenal shunt. Duodenal varices are fed by the superior and inferior pancreaticoduodenal veins. The blood then flows into the left renal vein or IVC through the gonadal vein. Rectal varices form in the superior rectal vein, a branch of IMV. The blood flows from rectal varices into the inferior rectal vein and the internal iliac vein

The hemodynamics are unknown in about a half of rectal varices. In general, the superior rectal vein branching out of the inferior mesenteric vein serves as the feeding vessel to rectal varices. After a rectal varix forms, the blood flows into the internal iliac vein through the middle and inferior rectal veins.

8.6 Bleeding

Once bleeding starts in an ectopic varix, it is often fatal because the blood flow rate and volume are high. Ectopic varices are generally found after gastrointestinal bleeding. Forty-five percent of ectopic varices are hemorrhagic [7]. While bleeding

is most frequent in rectal and duodenal varices, the rate of bleeding is the highest in small intestinal varices followed by duodenal and rectal varices. Bleeding recurs in ectopic varices in colonic stoma. The rate of bleeding is from 3 to 5% [30]. In Japan, the reported rate of bleeding is over 30% in rectal varices [11]. However, the frequency of bleeding is low in other countries: four of 112 patients (3.6%) according to McCormack et al. and two of 100 patients (2%) according to Hosking et al. [31, 32]. Frequent bleeding is therefore considered unlikely.

8.7 Conclusion

Ectopic varices have been the main topic at a number of gastroenterological conferences and remain an important subject associated with portal hypertension. As the treatment of esophageal and gastric varices is standardized, ectopic varices may further increase with their spread. The pathophysiology of ectopic varices should be elucidated to establish a means of diagnosis and treatment.

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