Duodenal variceal bleeding secondary to idiopathic portal hypertension treated with transjugular intra-hepatic porto-systemic shunt plus embolization: A case report

Bu-Shan Xie, Jia-Wei Zhong, An-Jiang Wang, Zhen-Dong Zhang, Xuan Zhu, Gui-Hai Guo

BACKGROUND
Duodenal varices are a lesser-known complication with non-cirrhotic portal hypertension. We report a circuitous route from missed diagnosis of duodenal varices to correction. An extremely rare case of duodenal variceal bleeding secondary to idiopathic portal hypertension (IPH) is expounded in this study, which was controlled by transjugular intra-hepatic porto-systemic shunt (TIPS) plus embolization.

CASE SUMMARY
A 46-year-old woman with anemia for two years was frequently admitted to the local hospital. Upon examination, anemia was attributed to gastrointestinal tract bleeding, which resulted from duodenal variceal bleeding detected by repeated esophagogastroduodenoscopy. At the end of a complete workup, IPH leading...
to duodenal varices was diagnosed. Portal venography revealed that the remarked duodenal varices originated from the proximal superior mesenteric vein. TIPS plus embolization with coils and Histoacryl was performed to obliterate the rupture of duodenal varices. The anemia resolved, and the duodenal varices completely vanished by 2 mo after the initial operation.

**CASE PRESENTATION**

A 46-year-old woman had symptoms of dizziness and fatigue for two years, during which she suffered from recurrent anemia and frequently required blood transfusions at a local hospital.

**History of present illness**

Hypoferric anemia was found by bone marrow aspiration, and erosive gastritis was observed by an esophagogastroduodenoscopy (EGD) in the local hospital. Due to recurrent anemia, she was initially hospitalized in the Department of Hematology in our hospital.

**History of family and past illness**

Her father died from liver cirrhosis, and she denied a history of viral hepatitis, alcohol use and schistosomiasis.

**Physical examination**

During the physical examination, she was pale, yet remained cardiovascularly stable, with the following vital signs on admission: temperature was 37.1°C, heart rate was 92 beats per minute (bpm), initial blood pressure was 100/60 mmHg, and expiration was 20 bpm. In addition, her lungs and heart were found to be normal by auscultation, and the abdomen was soft and flat.

**Laboratory testing**

Abnormal laboratory data of complete blood count were as follows: RBC 1.64 × 10¹²/L, Hb 32 g/L, HCT 0.125%, MCHC 256 g/L, WBC 2.87 × 10⁹/L, PLT 76 × 10⁹/L, and they progressively decreased in the days after admission. Other abnormal results included the following: Positive fecal occult blood test (FOBT), transferrin 2.99 µg/L, HBsAg 138.5 IU/mL, hepatitis B virus DNA 8.01e + 0.03 IU/mL. In addition, bone marrow aspiration revealed hyperplasia of granulocytes, erythrocytes, and platelets.

**Imaging examination**

Anemia may be attributed to the bleeding of gastro-intestinal tract based on the reduced Hb and RBC count, as well as the positive FOBT. In order to detect the potential cause of hemorrhage, an EGD was performed 5 d after admission to the hospital, and four grade 1 esophageal varices without any evidence of recent bleeding, as illustrated in Figure 1A. Further observation demonstrated the presence of a small amount of fresh blood in the stomach. When reaching the duodenum, the authors observed the occurrence of more fresh blood, as well as evidence of upper gastrointestinal (GI) bleeding, and further detected a large submucosal vermicular mass located in the first

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**Key words:** Idiopathic portal hypertension; Anemia; Duodenal variceal bleeding; Transjugular intra-hepatic porto-systemic shunt; Embolization; Case report

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and second duodenum (Figure 1B and C).

The patient was then transferred to our department to examine the cause of esophageal and duodenal varices associated with portal hypertension, which was followed by the corresponding treatment. In addition to a contrast-enhanced CT scan that demonstrated dilated and tortuous duodenal varix, dilated portal and splenic vein, and splenomegaly, but normal liver, liver function, renal function, coagulation function and liver fibrosis was normal. Serum was negative for anti-hepatitis A, C and E virus antibody, and also negative for autoimmune liver disease and Wilson disease. Moreover, Doppler ultrasound of hepatic vein, portal vein and inferior vena cava was normal.

Pathological evaluation
Histological evaluation of liver biopsy was performed by two pathologists, aiming to determine the unexplained cause of PH. An integrated structure was observed in hepatic lobule, while there was no evidence of pseudolobuli formation based on Hematoxylin & Eosin staining that was used to detect the extreme extension and occlusion of portal branches in portal regions (Figure 1D and E). Furthermore, perportal and perisinusoidal fibrosis was demonstrated through Masson staining (Figure 1F), suggesting that IPH contributed to these manifestations.

Figure 1 Imaging features of endoscopy and hepatic pathology. A: An esophagogastroduodenoscopy (EGD) showed mild varices (white arrow) located in the esophagus without bloody scab; B and C: An EGD displayed a large submucosal verrucular mass (white arrow) located in the first and second duodenum with bloody scab; D and E: Liver samples were observed pathologically with Hematoxylin and Eosin staining. There was an integrated structure in the hepatic lobule with small sporadic necrotic foci, in which hepatic cells were moderately swollen with uneven nuclear size and fibrosis in portal triads. The extreme extension (D) and occlusion (E) of portal branches in portal regions are denoted by the black arrow; F: Perisinusoidal fibrosis (black arrow) was surrounded by hepatic lobule, as shown by Masson staining.

**FINAL DIAGNOSIS**
The patient was eventually diagnosed with IPH.

**TREATMENT**
An emergent transjugular intra-hepatic porto-systemic shunt (TIPS) was successfully performed on the day after the patient was transferred. During the TIPS procedure, portal venography initially displayed a mild coronary vein (black arrow in Figure 2A), while the remarkably dilated duodenal varices (Black arrow in Figure 2B and C) were shown to extend from the proximal superior mesenteric vein (White arrow in Figure 2B) with shunting of flow towards the inferior vena cava (White arrow in Figure 2C), in line with EGD observation, which is mainly due to the acute upper GI bleeding, in contrast to the mild esophageal varices. To control GI bleeding, the duodenal varices were initially embolized with three stainless-steel coils, which were 6 mm in diameter (White arrow in Figure 2D), in combination with Histoacryl. Subsequently, a balloon catheter with a diameter of 8 mm and a length of 8 cm was used to dilate the TIPS tract (White arrow in Figure 2E), then a metallic bare stent with a diameter of 8 mm and a length
of 5 cm (White arrow in Figure 2F) was placed in the tract. Once the TIPS shunt was set up, portal venous pressure significantly decreased from 17.25 mmHg to 10.5 mmHg.

OUTCOME AND FOLLOW-UP

After the TIPS operation, RBC count and Hb markedly increased, and FOBT was negative within 48 h. Anemia was cured 2 mo after TIPS, and there was no sign of varix in the duodenum, as observed by an endoscopy examination.

DISCUSSION

In this study, the authors reported a rare case of a patient that had been referred to a hematologist because of iron deficiency anemia. Further examination was performed, and the cause of iron deficiency anemia was confirmed to be GI bleeding, primarily resulting from duodenal variceal bleeding. It is difficult to detect duodenal varices, likely due to their concealed and occult location in the duodenum. A gastroenterologist will rarely encounter such conditions because they only account for about 0.4% of all variceal bleeding. Through repeated EGD in our department, a large submucosal vermicular mass was located in the first and second duodenum and further confirmed by TIPS venography.

The patient suffered from PH, characterized by splenomegaly, esophageal and duodenal varix, and enlarged portal and splenic vein. Decompensated liver cirrhosis was excluded by further examination. When PH occurs in the absence of decompensated liver cirrhosis, the most common manifestation is extrahepatic portal venous block. Nevertheless, no extrahepatic obstruction was detected by CT and Doppler vascular ultrasound in the portal venous system. Additionally, a number of common causes of portal hypertension, including hepatitis C virus, alcoholic hepatitis, non-alcoholic fatty hepatitis, autoimmune hepatitis, primary biliary cholangitis, Wilson's disease and gallstones, were ruled out. Interestingly, Hepatitis B virus, which is the most common cause of liver cirrhosis in China, was positive. Moreover, the patients had a family history of liver cirrhosis. Thus, a liver biopsy was performed to determine whether the patient suffered from compensated liver cirrhosis associated with PH.
Unexpectedly, the pathological feature of cirrhosis was the integrated structure in the hepatic lobule rather than pseudo-nodular, effectively eliminating liver cirrhosis as a possibility. PH with unexplained causes is relatively uncommon. Therefore, liver pathology was performed to assess if IPH contributed to the patient's PH. As expected, the extreme extension and occlusion of portal branches in portal regions, periporal fibrosis and perisinusoidal fibrosis, as well as the specific pathological characteristics of PH, were detected in liver sections. It has been generally accepted that the pathological entities of IPH are characterized by hepatoportal sclerosis, periporal and perisinusoidal fibrosis, and nodular regenerative hyperplasia[2]. Furthermore, some rare causes of portal hypertension, such as Biliary diseases (e.g., seronegative PBC, small duct PSC, toxic biliary injury), drug/toxin-induced diseases (e.g., amiodarone, methotrexate, vinyl chloride), granulomatous liver lesions (e.g., schistosomiasis, tuberculosis, mineral oil granuloma, sarcoidosis), Zellweger syndrome, amyloid or light-chain deposition in the space of Disse, Gaucher disease, agnogenic myeloid metaplasia, veno occlusive diseases, granulomatous phlebitis or lipogranulomas are further excluded in the case through histopathological findings. By excluding other causes of PH, IPH was diagnosed at the end of a complete diagnostic workup.

IPH is frequently misdiagnosed as liver cirrhosis, even in well-known hepatology centers. Since IPH was first proposed by an Italian pathologist in 1889, there have been sporadic reports of IPH for decades, most of which were carried out in India[3]. It is not easy to diagnose IPH, due to the fact that there are no typical clinical or lab alterations and that it depends on elucidation of the hepatic pathology[3]. Most IPH patients at an early stage also suffer from esophageal variceal bleeding. However, the occurrence of duodenal varices associated with IPH is extremely rare. In 1988, Tanaka et al[6] reported a case of duodenal variceal bleeding associated with IPH in their study, which was successfully controlled by surgery. In this report, we identified an exceedingly rare case of duodenal variceal bleeding secondary to IPH, which was arrested by TIPS and venous embolism. IPH pathophysiology is poorly understood, but it may be due to an increase in portal flow and/or intrahepatic vascular resistance, due in part to an initial injury to the intrahepatic vascular bed[6]. Recent studies report that over-expression of serum anti-endothelial cell antibodies and deletion of ADAMTS13 may be associated with IPH, which causes splenomegaly and portosystemic communications[2,7-9]. Duodenal varices represent an ectopic portosystemic shunt. Almost half of the patients with duodenal varices also had gastroesophageal varices. Intrahepatic PH was the most common identifiable anatomical source of patients with duodenal varices[5,10].

Intervention radiologic treatment and endoscopic operation have been confirmed to arrest duodenal varix[11]. Besides, endoscopic band ligation and endoscopic injection sclerotherapy have been shown to control acute duodenal variceal bleeding[12,13]. Nonetheless, there are some cases of re-bleeding after endoscopic operation. Consequently, TIPS has been performed to obliterate bleeding of duodenal varices as initial treatment or recurrent bleeding as rescue therapy after failure of endoscopic treatment[14,15]. The authors indicated that a duodenal variceal bleeding associated with IPH was successfully performed by emergent TIPS implantation with dual stent plus embolism with coils and Histoacryl. In contrast to TIPS alone, TIPS plus embolization stopped bleeding in all patients except one[16]. Furthermore, an EGD was performed for a follow-up visit after 2 mo, showing that the dilated varix completely disappeared in the duodenum. Therefore, TIPS plus embolization may be more appropriate to control the rupture or reduce the risk of bleeding of the giant duodenal varices.

In conclusion, we report an extremely rare case of duodenal variceal bleeding secondary to IPH that was controlled by TIPS plus embolization. In future clinical use, it is recommended that TIPS plus embolization with coils and Histoacryl is a good option for treating large ectopic varices.

**CONCLUSION**

The duodenum was reported to be normal by the local endoscopist, who missed the diagnosis of duodenal varices, possibly owing to the rare incidence of such disease and the local endoscopist's inexperience. Misdiagnosis in the local hospital led to the initial admission to the Hematology department, and thus resulted in more complex processes for final diagnosis.

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