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Late Bleeding Episodes Following Intestinal Transplantation: It Is Not Always Rejection or Infection

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Abstract: Ectopic varices have been reported in 5% of children presenting with variceal bleeding and are defined as portosystemic venous collaterals occurring anywhere in the abdomen except in the cardioesophageal region. The liver-intestinal transplant or isolated liver-intestinal transplant patient presenting several years post-transplant with ectopic variceal bleeding as a consequence of portal hypertension is a seldom reported complication. Etiologies such as rejection or infection are a more common source of bleeding, and only after excluding these can differentials such as portal hypertension secondary to a blocked portacaval shunt or native liver disease be considered.

Key Words: gastrointestinal bleeding, intestinal transplant, varices

INTRODUCTION

Ectopic varices may present in the duodenum (17%), jejunum or ileum (18%), colon (14%), rectum (8%), and peritoneal region (9%) (1,2). Reports of ectopic variceal bleeding from portal hypertension as a consequence of portosystemic shunt blockage post pediatric liver-intestinal transplant (Itx) are extremely rare (3–5). The purpose of this case description is to highlight this etiology and other rare causes, such as development of chronic liver disease post isolated Itx in the Itx cohort.

CASE REPORT

Case 1

A 3-year-old girl presented 1-year post liver-Itx for midgut volvulus with stomal bleeding over several months. Upper gastrointestinal endoscopy (UGIE)/ileoscopy showed ulceration in the stomach, duodenum, as well as at the anastomosis between native and graft jejunum. She underwent video capsule endoscopy (VCE) demonstrating ulceration of the mucosa, as previously seen, but the entire length of the bowel could not be visualized due to lack of passage through the anastomosis. Rejection and infection were excluded on the basis of biopsy and culture. A multidisciplinary team meeting was arranged due to persistent bleeding despite acid suppression. She underwent computed tomography (CT) angiogram that demonstrated occlusion of the portacaval shunt. Splenic vein catheterization via direct splenic puncture with a view to unblock the shunt was not successful, and thus, the patient was referred for a double-balloon enteroscopy that revealed 5 ectopic small bowel varices that were banded. The varices were likely a result of neovascularization present due to the portal caval shunt thrombosis. The patients' stomal bleeding continued intermittently for several years with further UGIE revealing esophageal varices and varices at the native to graft jejunal anastomosis that were injected with thrombin on several occasions. Several years later, the patient had a large gastrointestinal (GI) bleed with varices now larger than previously on UGIE. Splenectomy was advised to manage her portal hypertension but the family declined any further therapy, and she has since managed with occasional bleeding from her stoma and intermittent blood transfusions.

Case 2

Eight-year-old boy presented with melena and splenomegaly 4 years following isolated Itx for microvillus inclusion disease. UGIE revealed ulceration and edema at the anastomosis of native jejunum and graft, there was no evidence of infection or rejection. A multidisciplinary team meeting was arranged and second UGIE performed for ongoing bleeding demonstrated varices at this anastomosis (Fig. 1). CT angiogram demonstrated numerous intra-abdominal varices, as well as a small but patent portal vein but an inferior vena cava (IVC) that was occluded distal to the donor superior mesenteric vein. Endoscopic ultrasound was used to treat the anastomotic varices with sclerotherapy. In the context of difficult to treat portal hypertension with evidence of chronic liver disease in his native liver, he was listed for an isolated liver transplant. His liver biopsy 2 years post Itx had demonstrated severe cholestasis and moderate fibrosis. He represented several months later with a further upper GI bleed. UGIE demonstrated distal duodenal bleeding. Endoscopic ultrasound again demonstrated varices at the anastomosis and thrombin was injected. Bleeding persisted and a transjugular intrahepatic portosystemic shunt (TIPPS) was performed with resolution of the bleed. Shortly after this, he developed acute on chronic liver failure, acute kidney injury, hypotension needing inotropic support, and died secondary to Gram-negative septicemia and multiorgan failure.

DISCUSSION

The presence of a blocked portacaval shunt in case 1 leading to varices as a consequence of neovascularization has been infrequently reported. Conventionally the portacaval shunt has been done in liver-Itx by end to side anastomosis of the native portal vein to the native inferior vena cava (6). Gondolesi et al (4) suggested a modification of the conventional technique to an end-to-end anastomosis of native portal vein and donor IVC to mitigate the risks of development of varices. However, despite the adaptation of the technique, there have been case reports of development of thrombosis within the portacaval shunt (5). The portacaval shunt post liver intestinal transplant

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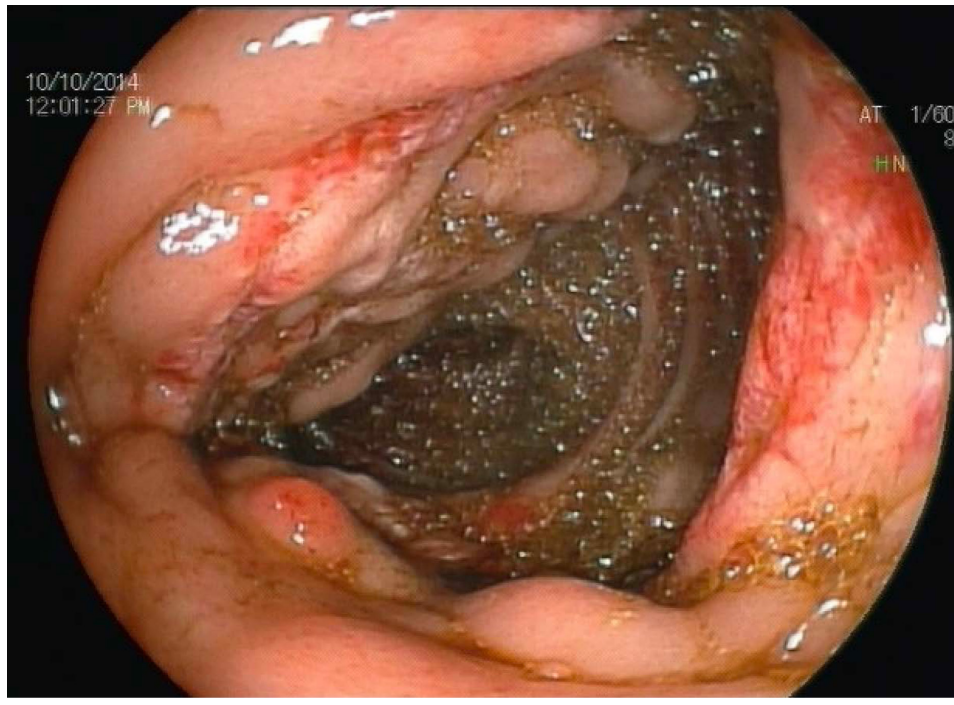

FIGURE 1. Jejunal varices with stigmata of bleeding and mucosal ulceration.

may have higher propensity for thrombosis due to the following reasons: (1) the hyperdynamic circulation present pretransplant in children with intestinal failure liver disease and portal hypertension is changed to a "low flow" system as it only drains part of the stomach, jejunum, and spleen; (2) correction of coagulation with a new functioning liver; and (3) presence of a procoagulant environment in immediate post-transplant period (7). Detection of shunt thrombosis is often a late complication manifesting as signs of portal hypertension such as thrombocytopenia, splenomegaly, and then GI bleeding; thus, the presentation of this patient only at 1-year post-transplant.

A Different Phenomenon Occurred in Case 2

The presence of a progressive familial intrahepatic cholestasis-like phenotype is infrequently associated with microvillus inclusion disease that progressed post isolated Itx (8), along with occlusion of the IVC distal to the donor superior mesenteric vein leading to portal hypertension and variceal bleed. In this instance, the presentation 4 years after transplant was a consequence of the complications of chronic liver disease such as portal hypertension, which can also take some time to manifest.

Technical difficulty in diagnosing and treating the bleed can be added to by the Roux-en-Y jejunojejunostomy between native and graft jejunum, small size, and infrequency of use in children. While the initial approach may include endoscopy and VCE if varices are not initially visualized. However, VCE may not demonstrate the exact site of bleeding, especially in the transplanted bowel, as the capsule may run out of battery life negotiating the Roux-en-Y jejunojejunostomy. Small bowel ectopic varices are inaccessible by endoscopy most of the time, and thus CT angiogram and double-balloon enteroscopy are often needed being both diagnostic and interventional. If this approach does not succeed, nonendoscopic treatment options include the use of interventional radiology procedures such as TIPPS to create a new portosystemic shunt. While the TIPPS was effective in case 2, it could only serve as a bridge to super-urgent liver transplantation. There is scant literature on how to treat ectopic variceal bleeding in those who have undergone Itx. The 3 existing reports on portal hypertensive bleeding in the liver-Itx cohort utilized a balloon dilation of stenosed shunt (5), side-to-side distal splenorenal shunt after unsuccessful balloon dilation of the portacaval anastomosis (3), and an end-to-end anastomosis for portosystemic shunts rather than end to side, potentially creating higher flow (4). Anastomotic technique in the portacaval shunt of case 1 was end to side.

These 2 cases highlight a multidisciplinary approach in thinking outside of common differentials and interventions. The altered anatomy in children who had prior abdominal surgery then Itx defies the management algorithm of variceal bleeding but requires individualized approach depending on the size of the patient, location, and the cause of the varices and the available expertise.

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