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Lymphatic Leakage in Pediatric Heart Transplantation

Early Recognition and Timely Management with Interventional Radiologic and Endoscopic Therapy

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Abstract: Protein-losing enteropathy (PLE) is a severe complication of the Fontan procedure that leads to systemic complications owing to enteric protein loss. Hepatoduodenal lymphatic leakage resulting from increased lymphatic pressure is one such complication. We present the case of a pediatric heart transplant patient who experienced refractory PLE symptoms requiring serial albumin infusions and exhibited lymphatic leakage into the duodenum. Using diagnostic lymphangiography and endoscopy, we identified the affected area and treated it successfully with endoscopic sclerotherapy using ethanolamine injection. This treatment allowed for the cessation of lymphatic fluid and may serve as a potential intervention for PLE-associated hepatoduodenal lymphatic leakage. The present case highlights the importance of early recognition and timely intervention with radiology and endoscopic therapy to manage PLE and its associated complications.

Key Words: protein-losing enteropathy, sclerotherapy, ethanolamine, lymphatic leakage, duodenum, heart transplantation

INTRODUCTION

Protein-losing enteropathy (PLE) in the gastrointestinal tract is a condition characterized by the loss of proteins through the intestinal epithelium that can result in peripheral edema, bleeding, and immunodeficiency (1). Lymphatic leakage is associated with PLE and is caused by increased lymph production due to an elevated systemic venous pressure causing leakage through dilated lymphatic connections, which can be identified on lymphangiography (2). Although rare, lymphatic leak many years after a heart transplant may occur due to elevated central venous pressure above the thoracic duct pressure secondary to chronic graft rejection, cardiac allograft vasculopathy, or related to post-transplant lymphoproliferative disease (PTLD), surgical complications, trauma, infections, or chronic inflammation (3).

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Optimal treatment requires a combination of identifying the leaking vessels using imaging guidance and occluding those dilated leaking lymphatics under real-time imaging (3). Injection of dyes such as isosulfan blue can be used to diagnose a lymphatic leak along the gastrointestinal tract upon escape into the lumen after direct injection into a nearby lymph node. When the blue dye mixes with yellow bile within the lumen, it transitions from a blue hue to a greenish appearance (4).

CASE REPORT

The patient, a 15-year-old male, underwent orthotopic heart transplantation at 3 years of age after a failed Fontan operation for hypoplastic left heart syndrome with a history of PLE previously treated with budesonide. The transplant was complicated by acute early rejection and pulmonary B-cell PTLD, which were successfully treated with pulse steroids and rituximab, respectively. The patient was monitored by the transplant cardiology service for ongoing diarrhea, poor appetite, ascites, and weight loss, with a work-up notable for hypoalbuminemia (2.4 g/dL) managed by infusions and an elevated stool alpha-1-antitrypsin (125 mg/dL). Upon follow-up, he had worsening edema, sudden 4 kg weight gain within a 1-week period, and abdominal distention, warranting admission to the Cardiovascular Intensive Care Unit for concern of PLE. There, multiple cardiac procedures were performed, including a cardiac catheterization, which demonstrated normal cardiac filling pressures, cardiac output and pulmonary vascular resistance, and a coronary angiography without evidence of cardiac allograft vasculopathy. Despite the history of PTLD, there was no evidence of recurrence.

Initial testing revealed hypoalbuminemia (2 g/dL), indicating worsening PLE. Interventional radiology was consulted to investigate the suspected PLE using magnetic resonance (MR) lymphangiogram (Fig. 1A). The hepatic, mesenteric, and groin lymphatics were accessed using fluoroscopic and ultrasound-guided placement. While in MR, 3 cc gadolinium contrast diluted 50% with sterile saline was injected into each site. The MR lymphangiogram showed no leak from the hepatic or mesenteric sites, but a large leak from the groin retroperitoneal lymphatics into the second portion of the duodenum (Fig. 1B, C). Therefore, a combined radiologic-endoscopic therapeutic intervention was scheduled. Using ultrasound guidance, the left groin lymph node was accessed using a 27-gauge needle, and 5 cc of isosulfan blue contrast was injected into the lymphatics while the endoscope was monitored for duodenal leakage.

The duodenum showed an irregular mucosal appearance on endoscopy (Fig. 2A). Narrowband imaging revealed focal blue discoloration of the villi, indicating dilated lymphatics in the first and second portions of the duodenum. (Fig. 2B, C). Injected isosulfan blue dye was observed to slowly accumulate between 2 circular duodenal folds (plicae circulares), but not at the tip of the folds, in a focal area just distal to the ampulla of Vater (Fig. 3A). Once the main lymphatic leak was identified, ethanolamine (50 mg/mL) was injected directly into the affected area using a 25-gauge, 4 mm long injection

needle. Seven ethanolamine injections (0.5 mL aliquots of 25 mg each)—3 injections into each circular duodenal fold on either side of the accumulated blue dye for a total of 6 injections, and 1 injection in the duodenal bulb (Fig. 2C)—were given for a total ethanolamine dose of 175 mg. The overflowing blue dye slowly turned green when mixed with yellow bile in the duodenum over time (Fig. 3B). Three days after the procedure, the diarrheal frequency reduced from 4–6 stools per day to 1–2 stools, and the albumin improved from 2.0 (g/dL) to 4.0 (g/dL). The patient was discharged the following day. Four months later, diarrhea resolved, the patient's albumin stabilized between 4.5 (g/dL) and 5.0 (g/dL) without infusions, and no further fecal alpha-1-antitrypsin levels were ordered.

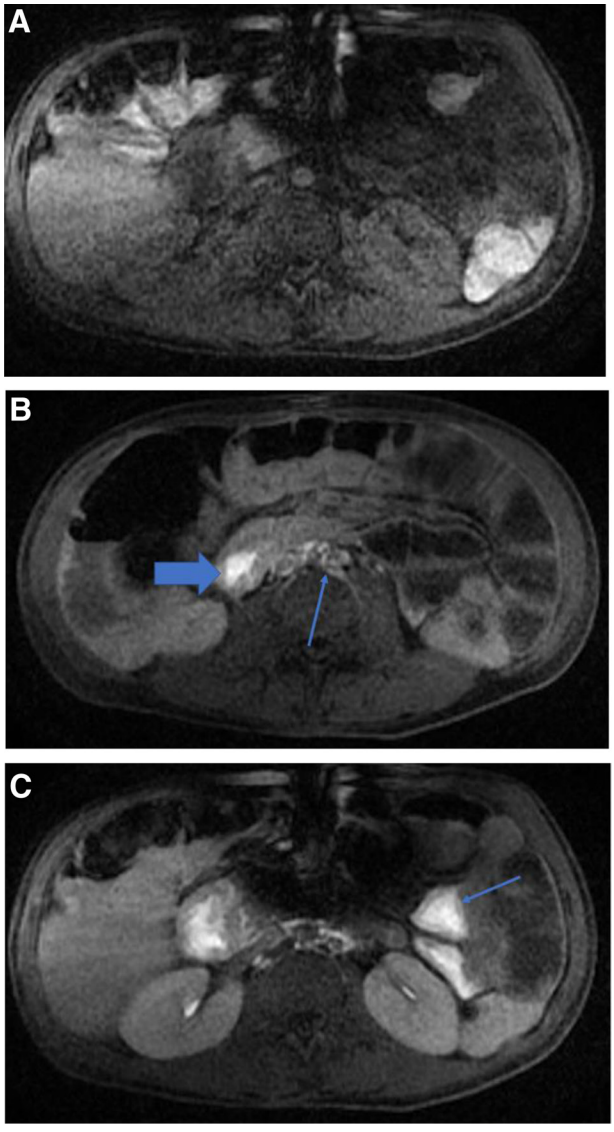

FIGURE 1. A) Precontrast axial liver acceleration volume acquisition (LAVA) MRI before gadolinium contrast injection. B) Axial LAVA after inguinal intranodal gadolinium injection showing retroperitoneal lymphatics (thin arrow) and early extravasation of contrast into the duodenum (thick arrow). C) Delayed postcontrast axial LAVA demonstrates accumulation of duodenal contrast and flow of contrast into the jejunum (arrow).

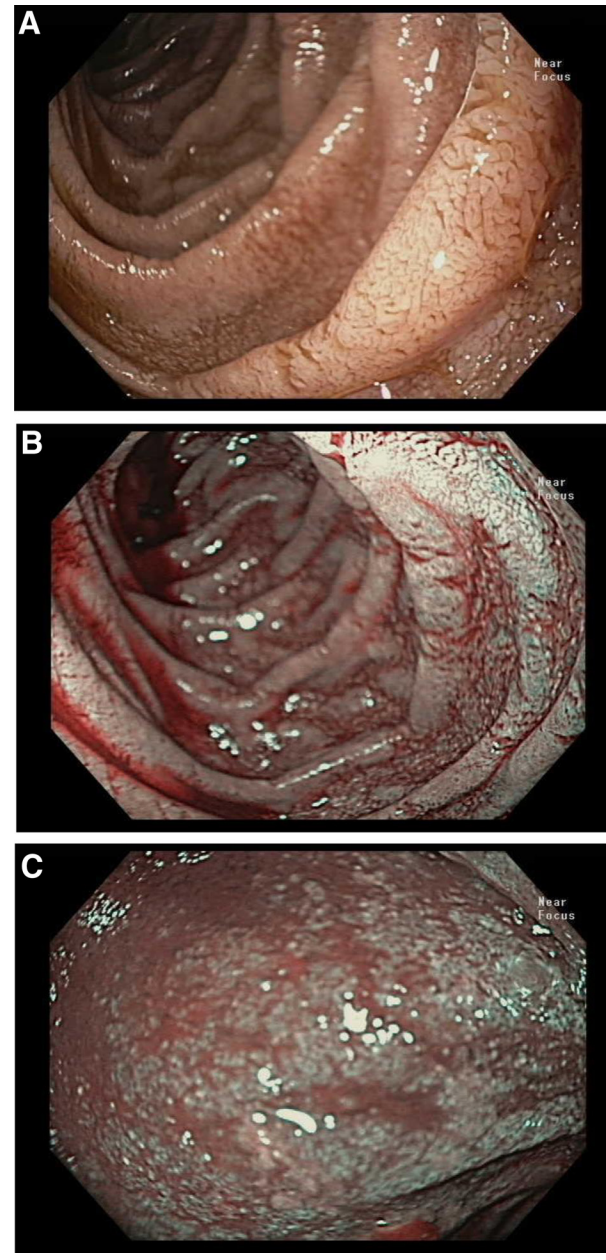

FIGURE 2. A) Irregular mucosal appearance of the duodenum visualized during endoscopy. B) Narrow band imaging (NBI) identifying dilated lacteals (focal blue discoloration) in the villi of the 2nd portion of the duodenum. The blue color indicates increased vascularity or lymphatic vessels in the area, which can be a sign of lymphatic dilation or abnormality. C) Focal coalescence of dilated lymphatics (blue) identified in the duodenal bulb on NBI.

DISCUSSION

Endoscopic sclerotherapy using ethanolamine injection combined with interventional radiology localization of PLE can successfully treat duodenal lymphatic leakage. Early reports used isosulfan blue dye injected into liver lymphatics and endoscopic injection of lipidiol mixed with adhesive poly n-butyl cyanoacrylate to embolize dilated hepatoduodenal lymphatics and treat duodenal leaks

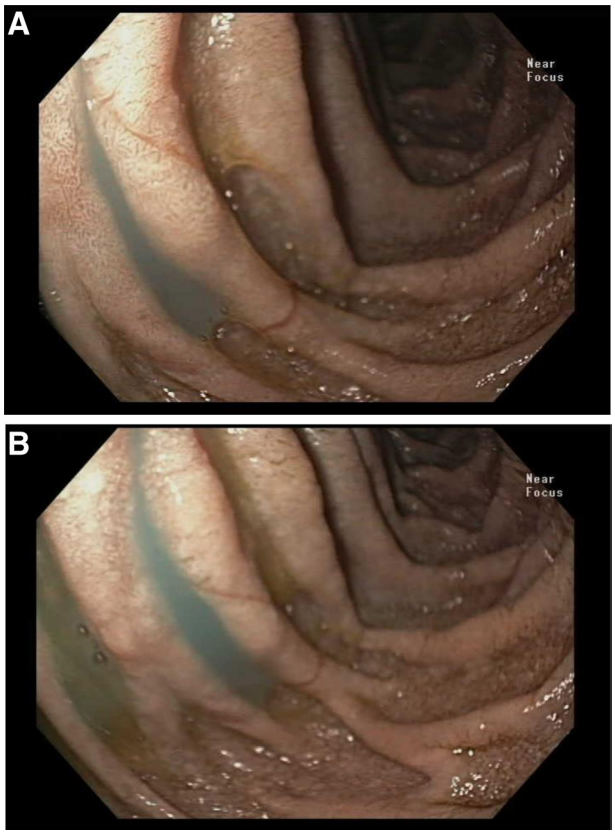

FIGURE 3. A) Isosulfan blue injected into the lymphatics seen to slowly emerge between 2 circular folds of the duodenum. B) The overflowing blue dye slowly turned green when mixed with yellow bile in the duodenum over time.

(3). Current techniques include accessing the lymphatics under fluoroscopy, injecting gadolinium into hepatic lymphatics, superior mesenteric vein lymphatics, and both groin lymph nodes, using MR lymphography to locate the duodenal leak after gadolinium injection, and returning to fluoroscopy for needle embolization of the leaking site with n-butyl cyanoacrylate glue. Alternatives to MR lymphography to evaluate lymphatic pathologies include computed tomography lymphangiography, lymphangioscintigraphy, and invasive lymphangiography (4). Complications, such as nontarget embolization, venous migration, microcatheter blockage, and catheter retention, can occur because of the unpredictable nature of glue deposition (5).

Ethanolamine was previously used to treat vascular anomalies such as esophageal varices, duodenal varices, and lymphatic malformations of the head and neck (6–10). It functions by causing scarring of the tissue to seal off lymphatic leaks (3). Other sclerosing agents include ethanol, picibanil (OK-432), sodium tetradecyl sulfate, doxycycline, and bleomycin, sometimes with adjunctive adhesive polymers (3). Ethanolamine is preferred in esophageal and duodenal varices over ethanol because ethanol can be caustic if it leaks out of the intended area. To prevent potential adverse effects, ethanolamine is diluted when used for sclerotherapy (7).

The case report highlights the importance of early recognition and collaborative management in pediatric heart transplant patients with lymphatic leakage and PLE. Regular surveillance, diagnostic imaging, and a multidisciplinary team approach are crucial for timely detection and targeted treatment. Endoscopic sclerotherapy using ethanolamine injection emerges as a viable therapeutic option for lymphatic leaks. Optimizing immunosuppression and maintaining long-term follow-up are essential to enhance patient outcomes.

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