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Case report

Embolization for acute gastrointestinal hemorrhage secondary to post-transplant lymphoproliferative disorder

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ABSTRACT

Gastrointestinal manifestations of post-transplant lymphoproliferative disorder (GI-PTLD) encompasses a spectrum of mucosal inflammation and ulceration that can present as severe acute gastrointestinal bleed. This case report describes a case of GI-PTLD in a 19-year-old female status postcardiac transplant. This patient presented with extensive gastrointestinal hemorrhage secondary to PTLD involving the duodenum. The patient was treated with extensive embolization of the gastroduodenal artery and the pancreaticoduodenal arcades. Embolization was used to mitigate gastrointestinal bleeding, thus preventing the need for surgical resection and extensive reconstruction. This case report demonstrates the utility of embolization as potential therapeutic option in the setting of GI-PTLD in addition to medical and endoscopic therapy.

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Introduction

Post-transplant lymphoproliferative disorder (PTLD) results from uncontrolled B cell proliferation in patients after solid organ or bone marrow transplant. Two forms have been described. The early form occurring within the first year is most common and is usually mediated by Epstein-Barr virus (EBV). The other form of PTLD presents greater than 5 years, is usually EBV-negative. This later form accounts for about 20% of PTLD and is not well understood. It is hypothesized to result possibly from a different viral

factor, long-standing immunodeficiency, or due to replacement of EBV genes with other oncogenes. [1,2] Most patients present with fever, weight loss, and lymphadenopathy, but PTLD can affect any organ system. It is commonly seen in the gastrointestinal (GI) system in both pediatric and adult patients. [3] The variation in severity of PTLD is likely related to a number of factors, but namely the degree of immunosuppression and the host immune response against the aberrant B cell production.

The mainstay of treatment is to reduce EBV burden and also targeting the unabated cellular proliferation. First, by decreasing T-cell immune suppression, EBV-specific

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Fig. 1 – (A) Initial run of the gastroduodenal artery (GDA) demonstrated hemorrhage into the stomach and duodenum. (B) Postembolization of the GDA, anterior superior pancreaticoduodenal artery (ASPD), posterior superior pancreaticoduodenal artery (PSPDA), and the retroduodenal artery (RDA) demonstrated no further bleeding.

T-lymphocytes can proliferate and curtail the runaway B cell proliferation. In addition, rituximab and other therapies targeted at CD-20+ cells are routinely used. Chemotherapy is mainly used in refractory cases. Additionally, there are ongoing trials evaluating more novel EBV-specific cytotoxic T-lymphocytes and new agents. However, these treatments can take time and must be carefully balanced with side effects and the risks of rejection and graft vs host disease. In the setting of EBV negative disease, the main target is reducing the lymphoproliferative processes through reducing immunosuppression and chemotherapeutic agents [1,2]. Since the treatment of PTLD can several weeks or more, patients often require symptom-specific treatment and temporizing measures while addressing the underlying proliferative process [4]. Here, we present a case of PTLD in a patient after cardiac transplant with upper GI involvement and severe GI bleeding (GIB) treated with endovascular embolization.

Case description

This report is exempt from IRB review per institutional guidelines. The patient is a 19-year-old female with a history of cardiac transplant approximately 2.5 years. Recently diagnosed with PTLD complicated by superimposed EBV infection on combination therapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. She also had superimposed cytomegalovirus infection, which was concomitantly treated with Ganciclovir. She presented to the emergency department with fever and melanic stools concerning for GIB. Initial endoscopic evaluation revealed multiple antral-pyloric gastric ulcers and duodenal ulcers, but no focal area of bleeding. The patient was initially managed with a pantoprazole drip, Carafate, and transfusions, but bleeding secondary to her ulcers worsened, requiring 4 units of packed red blood cell transfusions per day prior to angiography. The patient underwent conventional angiography, 12 days after presentation, which demonstrated active extravasation

into the stomach and duodenum. Coil embolization of the gastroduodenal artery (GDA) and the anterior superior pancreaticoduodenal arteries (SPDA) and posterior SPDA was performed (Fig. 1). The patient's symptoms abated for several days after embolization. Day 4 after this embolization she began having worsening GIB requiring transfusions. An Esophagogastroduodenoscopy (EGD) was performed which demonstrated multiple bleeding gastroduodenal ulcers, which were treated with Hemospray (Cook Medical, Winston-Salem, NC). The patient's GIB continued and slowly increased in severity, requiring up to 4 units packed red blood cell transfusions in a 24-hour period. A CTA performed did not identify a focus of hemorrhage. Repeat angiography was performed. This was 10 days after the first embolization, 21 days after initial presentation. This demonstrated numerous punctate petechial hemorrhages in the pancreaticoduodenal distribution. Coil embolization of the retroduodenal artery, the origin of the right gastroepiploic artery and the inferior pancreaticoduodenal artery was performed (Fig. 2). After embolization, there was persistent but significantly decreased blood loss requiring one unit of packed red blood cells every 3-4 days. Two weeks after the second embolization, endoscopy performed for biopsy demonstrated improvement in ulcers and no signs of active bleeding. Patient required no further intervention for bleeding in the 6 weeks following embolization. Patient was ultimately transferred to another care center for specialized experimental trials regarding her PTLD 45 days after the second embolization, approximately 66 days after initial presentation.

Discussion

Early PTLD is an aggressive lymphoma occurring within the first year after transplant precipitated by EBV. This contrasts, the less common, late presentations of PTLD, which are EBV negative. There are varying estimates of PTLD, depending on the type of transplant, age, EBV status, etc. However, as in our case about, 5% of pediatric heart transplant patients develop

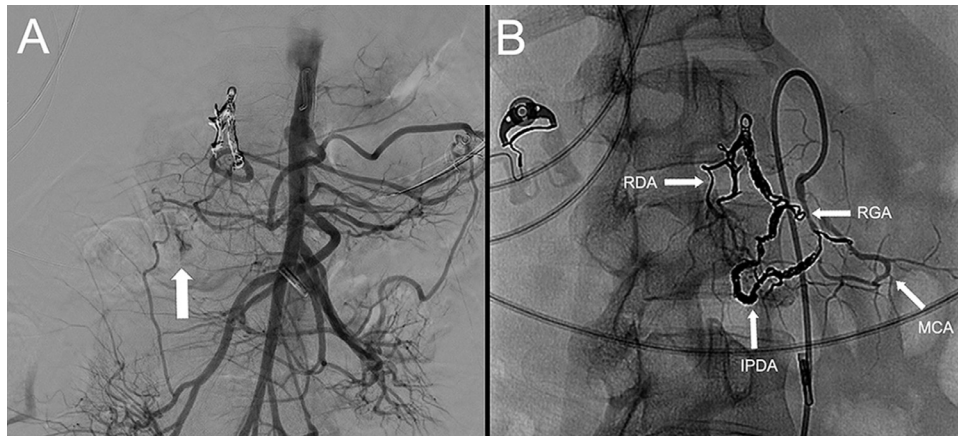


Fig. 2 – (A) Initial run of the SMA demonstrated multiple petechial hemorrhages involving the inferior pancreaticoduodenal distribution. (The white arrows show several.) (B) Postsubsequent embolization of the retroduodenal artery (RDA), the take-off of the right gastroepiploic artery (RGA), and inferior pancreaticoduodenal artery (IPDA). Contrast run through the superior mesenteric artery demonstrates reflux into the middle colic artery (MCA) and jejunal branches without evidence of active hemorrhage.

PTLD. [5] Treatment of PTLD is associated with several complications, namely side effects from chemotherapy and allograft failures. One-year survival in pediatric heart transplant patient is 83%; this survival rate decreases to 68% at 3 years. [5]

PTLD has been shown to involve the GI system, 17%-30% percent of the time. It can present anywhere along the GI tract. The severity ranges from ulcerative nodular lesions resulting in recurrent GI bleeding to obstruction and even perforation due to transmural involvement. [3,6] Initial management is supportive medical care with antiulcer medications including proton pump inhibitors and transfusions as needed. Endoscopic treatment with clips and hemostatic agents are used in concert. Despite this many patients go on to require surgical resection of the afflicted organ(s) due to complications. Overall there is little data on surgical management of hemorrhage in this setting. In a review of 34 pediatric patients with GI-PTLD, 41% required surgical intervention, only 1 due to hemorrhage [6]. Embolization provides another option which can be used in tandem with medical and endoscopic therapy.

There are several important factors to consider when treating PTLD patients and performing embolization. First, there are the inherent risks of embolization, which apply in all cases. Before embolization, one must consider the collateral blood supply, both to ensure adequate embolization and to prevent ischemia. In this case, the vascular supply of the stomach and duodenum is well collateralized. The lesser curve of the stomach is supplied by the left gastric artery, which most commonly arises from the celiac. This anastomosis with the right gastric artery originating from the hepatic artery or GDA. The left gastric also collateralizes with the short gastric arising from the splenic. The other large vessel in consideration is the GDA, which arises from the common hepatic artery. This branches into the right gastroepiploic and the SPDA. This latter branch forms anterior and posterior portions which course along the head of the pancreas supplying the duodenum. These form a loop inferiorly joining at the inferior

pancreaticoduodenal artery, supplied by the superior mesenteric artery. There are several smaller pancreaticoduodenal arcades, which form from the pancreaticoduodenal arteries off the GDA and superior mesenteric artery. [7] Given this extensive collateral system, embolization in this region should be extensive as bleeding can continue from remodeling of the arterial collateral network.

In our patient, initial embolization was performed of the GDA and SPDA. This was expected to reduce the overall bleeding and has been shown to be effective, and there is limited risk of ischemia given the aforementioned collaterals [8,9]. Given that the patient continued to bleed and failed endoscopic treatment, a decision was made to repeat angiography. During this second attempt, further embolization was performed of the inferior pancreaticoduodenal artery. This effectively reduced most of the blood supply to the duodenum and to a lesser degree the stomach, which effectively controlled the gastroduodenal bleeding.

There is a paucity of data on embolization in the setting of PTLD. A small series evaluating GI-PTLD found no difference in outcomes between patients required surgical intervention vs those that did not. [6] However, GI-PTLD patients are prone to perforations. While this presentation is likely secondary to transmural involvement of PTLD, it may be exacerbated by ischemia inducing endovascular treatment. As a result, embolization in cases of tenuous or terminal vascular supply should be performed with caution or in tandem with planned resection, that is, small bowel. In our case, the patient did not have any complications despite the extensive embolization.

Overall, this case demonstrates the utility of embolization for GIB in cases of refractory GI-PTLD. Embolization should be considered in patients with GI-PTLD with extensive bleeding, as this may spare patients from undergoing bowel resection, especially in the proximal duodenum, where extensive reconstruction such as pancreaticoduodenectomy may be required.

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