Use of Non-Selective Beta-Blocker for Refractory Stomal Variceal Hemorrhage

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Abstract
Bleeding stomal varices are often difficult to manage given the comorbidities that are associated with their presentation. Here, we report a case of a 62-year-old female with stomal variceal hemorrhage in the setting of chronic portal vein thrombosis who was ineligible for transhepatic intrajugular portosystemic shunt or surgery as a result of her challenging anatomy and peri-operative risks. Despite coil embolization, this patient experienced refractory bleeds which ceased following the initiation of a non-selective beta-blocker (NSBB). This case provides further evidence for the expanding role of NSBBs as an important therapeutic agent for complicated ectopic varices.

Introduction
Stomal varices are a rare complication of portal hypertension in the setting of bowel resection and are associated with substantially higher risks of bleeding relative to esophageal varices [1, 2]. Although there is no standardized therapy, treatment typically involves surgical or image-guided interventions for both acute control of bleeding and decompression of portal systems [3]. Here, we present a case of in-operable stomal varices with acute hemorrhage.
refractory to coil embolization that was successfully managed conservatively with non-selective beta-blockade.

**Case Presentation**

Mrs. X is a 62-year-old female with an ileostomy from prior hemicolectomy secondary to ischemic bowel who presented to our institution with an abrupt episode of painless bright red blood per ostomy. This patient has an extensive medical profile including a history of spontaneous portal vein thrombosis (PVT) that was complicated by splenic rupture and subsequent splenectomy as well as chronic portal hypertension, leading to cavernous transformation of stomal and abdominal wall varices. However, the patient was not treated with anticoagulation at the time of PVT diagnosis due to concurrent hemorrhagic stroke in the setting of suspected thrombocytopenic thrombotic purpura (TTP). She has had extensive investigations in the past regarding suspected autoimmunity, but no unifying diagnosis could be made.

On initial assessment, her hemoglobin (Hb) had dropped to 82 from a baseline of 110. The patient was transfused with 2 units of packed red blood cells (pRBCs) and her Hb improved subsequently to 104. Soon after, her bleeding ceased spontaneously, and she was admitted to the internal medicine service for further workup.

Once admitted, the patient underwent urgent endoscopic investigations which revealed scarring of esophageal varices that had been previously treated with sclerotherapy. The source of her hemorrhage was attributed to tortuous and dilated varices found on computed tomography (CT) imaging which extended throughout the ostomy defect and into the ostomy site (Fig. 1). Shortly after, the patient experienced another episode of substantial hemorrhage through her ostomy and underwent emergent coil embolization to several branches of her stomal varices, achieving temporary hemostasis.

The patient experienced two recurrent episodes of major bleed in the days following embolization that required urgent transfusions before spontaneous hemostasis. Throughout her admission, the patient was assessed and closely followed by our general surgery team. However, after extensive discussions among experts, it was deemed that the peri-operative risks of surgical interventions were too great to warrant any elective procedure. This decision was made in context of a prior elective ileostomy reversal that was abandoned intra-operatively due to excessive bleeding. Our experts from vascular surgery, interventional radiology (IR), and gastroenterology also conducted independent assessments on the patient but unfortunately, no further surgical, radiological, or endoscopic interventions were deemed feasible for the correction of her stomal varices.

Given the lack of therapeutic options, we initiated the use of non-selective beta-blockade after reviewing case reports of its potential efficacy for minimizing recurrent stomal variceal hemorrhage in those with non-cirrhotic portal hypertension [3, 4]. Nadolol was started at a reduced dose due to patient’s low baseline portal pressure and titrated to 40 mg oral daily as tolerated; reaching the targeted 25% decrease in heart rate. The patient was monitored closely over the next 2 weeks, while her diet was slowly advanced from nil per os (NPO) to diet as tolerated. She did not have any further hemorrhage through her ostomy and was discharged home with a safety plan in place. On follow-up, 3-month post-discharge, the patient reported no recurrent bleeds and her Hb was stable at her previous baseline.
Discussion

NSBBs have been well-described as a frontline therapy for primary and secondary prophylaxis of esophageal variceal hemorrhage among cirrhotic patients [5]. Physiologically, NSBBs reduce portal hypertension primarily through β-2 antagonism which leads to splanchnic vasoconstriction by unopposed α-adrenergic activity [6]. However, the clinical response to NSBBs can vary, as only 38% of patients may have significant reductions in their portal pressures [7]. Furthermore, the benefits of NSBBs have not been well-characterized for ectopic varices where locoregional features play a significant role in their pathogenesis [1]. Therefore, the management of ectopic varices should be individualized based on the distinct anatomy and clinical context of each patient.

Stomal varices are a rare form of ectopic varices that carry a high propensity for hemorrhage [8]. They are most commonly seen among ileostomized patients with inflammatory bowel disease (IBD) and associated primary sclerosing cholangitis (PSC) but may develop in any setting of chronic portal hypertension following bowel resection [4, 8]. Various treatments including surgical revision of ostomy, variceal ligation, sclerotherapy, variceal embolization, and transelective intrajugular portosystemic shunt (TIPS) have been used for management of stomal varices [3]. The latter – TIPS – has been cited as the preferred modality of portal decompression in most cases with consideration for surgical shunting should TIPS fail [3]. Although extensive PVT is not an absolute contraindication for TIPS, the presence of chronic PVT with cavernous transformation, as in the case of our patient, substantially increased the difficulty of TIPS creation and is associated with a high failure rate [9, 10]. Even following successful TIPS, rebleeding rates may be as high as 25% [11]. As a result, some have proposed for concurrent embolization at the time of TIPS insertion whenever possible to further reduce rebleeding risks [11, 12].

Our patient presented us with a challenging clinical scenario. Given her high surgical risks and the lack of therapeutic options from an endoscopic and IR perspective, her refractory stomal variceal hemorrhage following coil embolization prompted us to explore any potential therapies that may minimize her risks of recurrent bleeds. Interestingly, pharmacological therapies have seldomly been explored in the setting of stomal variceal hemorrhage and specifically, the use of NSBBs has only been described in case studies [3, 4, 13]. While the efficacy of NSBBs in this setting has been questioned [3, 14], there have been some reports of its success in preventing stomal variceal rebleeds in the absence of TIPS or embolization [4]. However, it is important to mention that among those treated with NSBB monotherapy as secondary prophylaxis, subsequent rebleeds did occur in most instances [3].

On average, NSBBs roughly lower hepatic venous portal gradient (HVPG) – a measure of portal pressures – by 15% [15]. To put this into perspective, HVPG needs to be reduced to <12 mm Hg or by ≥20% from baseline in order have substantial benefit as secondary prophylaxis for esophageal variceal bleeds [15]. Given that ectopic varices have high propensity to bleed even with HVPG <12 mm Hg [8], NSBB therapy alone is unlikely to be sufficient in the prevention of recurrent stomal variceal hemorrhage. However, when used in combination with interventional therapy, NSBBs may reduce the portal pressures enough such that it is below the threshold for which rebleeds occur. We suspect this to be the case with our patient who showed clinically improvement only after the initiation of NSBB following emergent coil embolization.

In conclusion, stomal variceal hemorrhage is an uncommon presentation among ostomized patients that presents unique clinical challenges for physicians. Although
interventional therapies have been the primary treatment options [3], our case highlights an increasing role that NSBBs may play as secondary prophylaxis against stomal variceal hemorrhage. In the setting of bleeding stomal varices, clinicians should consider the early initiation of NSBBs and its adjunctive use with other invasive interventions.

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Statement of Ethics

This case is reported in compliance with ethical standards described in the 1964 Declaration of Helsinki and its later amendments. Written informed consent for publication of the clinical details and clinical images was obtained from the patient.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

X. Mu contributed to the design, drafting, and revision of the case report. J. Trahey and W. Winsor contributed to the revision of the manuscript. All authors read and approved the final version of the manuscript.

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Fig. 1. Contrast enhanced axial CT image demonstrates multiple dilated varices surrounding and extending through the ostomy site (see arrowhead).