

Rare Co-occurrence of Eosinophilic Esophagitis and Type 2B von Willebrand Disease: Implications for Endoscopic Surveillance and Esophageal Dilatation

S. Ryanne Corder, BS¹, Brent W. Weston, MD², and Evan S. Dellon, MD, MPH¹

¹*Division of Gastroenterology and Hepatology, Department of Medicine, Center for Esophageal Diseases and Swallowing, and Center for Gastrointestinal Biology and Disease, Chapel Hill, NC*

²*Division of Hematology and Oncology, Department of Pediatrics, University of North Carolina School of Medicine, Chapel Hill, NC*

ABSTRACT

Eosinophilic esophagitis (EoE) and type 2B von Willebrand disease (vWD) are both rare diseases, and the co-occurrence is unlikely. Patients with EoE often need recurrent endoscopic dilations and esophageal biopsies, and the safety of these procedures in the setting of bleeding disorders is not well described in the literature. We describe successful management strategies in a patient with co-existing EoE and type 2B vWD who required multiple dilations and biopsies. This approach might be used for patients with other esophageal disorders and type 2B vWD as well.

INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic allergen-mediated disorder characterized by an esophageal eosinophilic infiltrate with >15 eosinophils per high power field (eos/hpf) and symptoms of esophageal dysfunction.¹⁻³ Because of the progression from inflammation to fibrosis in this condition, patients frequently need endoscopic dilations for symptom relief and esophageal biopsies to guide disease management.^{2,4} The presence of concomitant bleeding disorders could substantially complicate endoscopic monitoring and treatment of EoE, but there is little literature on this topic. We present a patient with a rare co-occurrence of EoE and type 2B von Willebrand disease (vWD) to demonstrate a successful management strategy. This is important because type 2B vWD itself can be associated with thrombocytopenia, thus limiting the use of desmopressin which is frequently used in the common forms of vWD. Furthermore, given the potential for thromboembolism related to factor replacement, ongoing preprocedure hematologic consultation is necessary.

CASE REPORT

A 20-year-old woman with type 2B vWD presented to a gastrointestinal clinic in 2016 with an 8-year history of solid food dysphagia. She had no concomitant atopic conditions or other medical problems. In 2005, she was diagnosed with type 2B vWD from a de novo mutation (c.3946G>A [p.V1316M]) after developing an epidural hematoma from mild head trauma. She had previous bleeding ranging from recurrent epistaxis, easy bruising, gum bleeding, and prolonged menses, to 2 severe episodes of hemoperitoneum secondary to a ruptured ovarian cyst requiring hospitalization. Her treatment for type 2B vWD was human plasma-derived von Willebrand factor (HP-vWF-FVIII) concentrate prophylaxis, 4,000 units twice weekly. Factor replacement was used instead of desmopressin, and this treatment choice is elaborated on in the discussion.

Because endoscopy with biopsies was planned to evaluate dysphagia, her hematologist felt preprocedure prophylaxis with 1 dose of HP-vWF-FVIII concentrate one hour before the procedure would not be sufficient. Therefore, she was prescribed 2 doses of concentrate one hour preprocedure, with repeat doses postprocedure every 12 hours for 2 days and then daily for 3 days, before

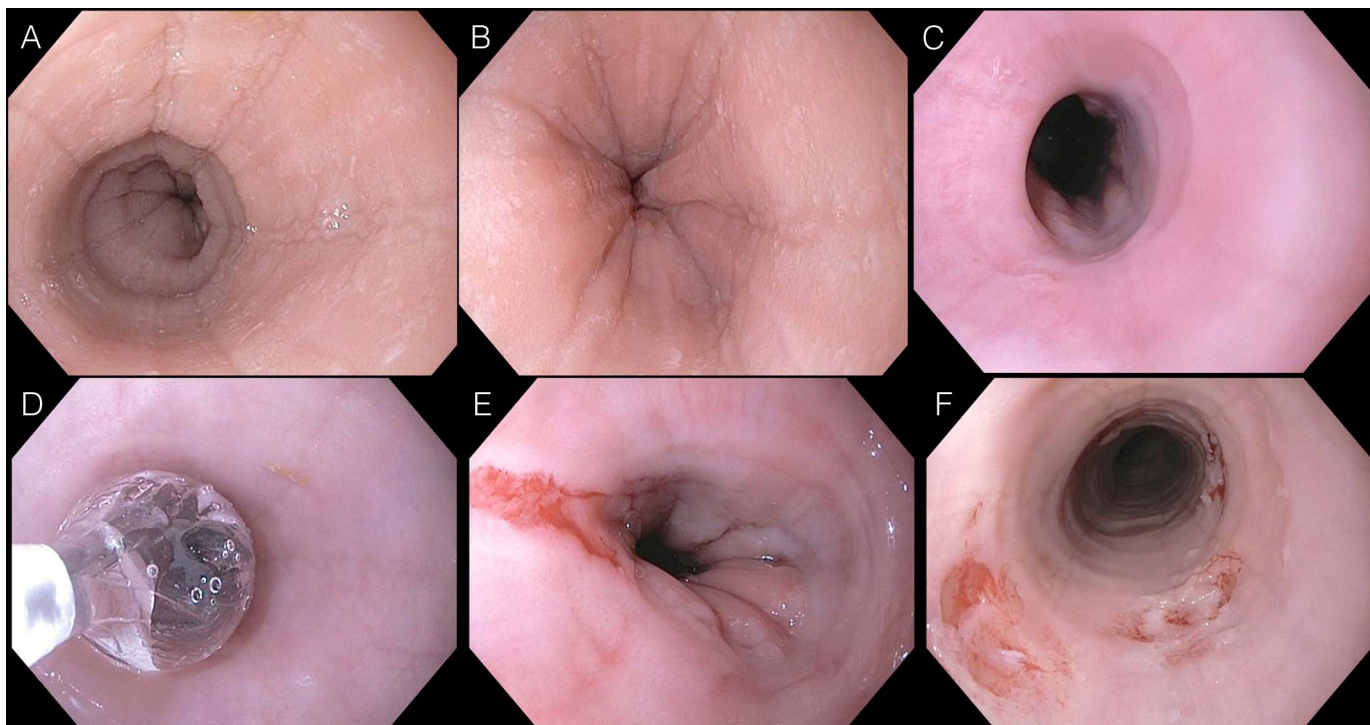


Figure 1. (A) Initial endoscopic findings of longitudinal furrows, white plaques, and edema, with (B) a severe focal stricture at the gastroesophageal junction. (C) Follow-up endoscopy again showing a gastroesophageal junction stricture for which (D) balloon dilation is performed. (E) After dilation, a mucosal disruption reflective of adequate “dilation effect” is noted with no bleeding. (F) After multiple esophageal biopsies, in this view seen in the proximal esophagus, there is also no bleeding.

resuming her typical biweekly administration. She was also instructed to take aminocaproic acid the night before the procedure (50 mg/kg) and every 6 hours for 10 additional days postprocedure.

The initial endoscopy revealed longitudinal furrows, white plaques, and edema throughout the esophagus, with a severe focal stricture at the gastroesophageal junction (Figure 1). Balloon dilation to 13.5 mm was performed, with a good dilation effect, but no immediate bleeding. Esophageal biopsies were also obtained without any bleeding and revealed increased eosinophils in both the proximal (60 eos/hpf) and distal esophagus (80 eos/hpf).

After this procedure, there were no signs of bleeding, and she had an excellent symptom response to dilation. Several months later, she presented to an outside emergency department with hematemesis from a transient food impaction. Two months later, she had a repeat endoscopy using the same periprocedural bleeding prophylaxis strategy as previously mentioned. The gastroesophageal junction stricture persisted and was dilated to 15 mm with the balloon; there was no postdilation bleeding. Biopsies from the proximal and distal esophagus were also obtained without bleeding (Figure 1). When she followed up for repeat endoscopy 2 months later, the stricture remained at a diameter of 15 mm, and this was balloon dilated to 18 mm. There was no bleeding during or after this third endoscopy.

DISCUSSION

Because there have been no previous reports of overlap of type 2B vWD and EoE, the safety of esophageal biopsies and dilation, as well as risk of bleeding complications, are unknown. This unique case provides several instructive points. In EoE, esophageal biopsies are critical for establishing the diagnosis and monitoring disease, and because of the patchy nature of the eosinophilic infiltrate, multiple biopsies from several esophageal locations are required.^{2,5} Esophageal dilation is also a common treatment for EoE complicated by esophageal strictures or narrowing, and although generally safe, complications can include chest pain, perforation, hemorrhage, and hospitalizations.^{6,7} When performing esophageal dilation, the goal is a mucosal rent, or “dilation effect,” and although some minimal bleeding can be noted after dilation, major bleeding issues requiring endoscopic intervention or transfusion are very rare (<1 per 1,000 dilations).^{7,8} However, bleeding complications could be more common in patients with bleeding disorders.

vWD is divided into different subtypes and variants. This patient had type 2B vWD. Type 2B vWD is characterized by qualitative defects in vWF structure or function. This contrasts with the more common type 1 vWD which has a quantitative defect in vWF. The 2B subtype accounts for ~5% of patients with vWD and is characterized by a gain of function mutation that has spontaneous binding of vWF to GPIb α

receptors on platelets which allows for increased clearance of the larger von Willebrand multimers and platelets leading to resulting thrombocytopenia.⁹ Thrombocytopenia is an independent risk factor for bleeding, and should be considered in the management of patients with this subtype of vWD.

The favored therapy for type 2B vWD is with FVIII/vWF concentrates because therapy with desmopressin has classically been relatively contraindicated.⁹ Desmopressin can lead to transient thrombocytopenia and can increase the risk of bleeding, although this is controversial, and a decision to use this should be made in conjunction with a hematologist.^{10,11} Our patient was treated prophylactically with HP-vWF-FVIII concentrates and aminocaproic acid. With this, she had no significant bleeding issues related to the endoscopy, biopsies, or dilation. With type 2B vWD, our patient's platelet counts were lower than normal, so desmopressin was avoided, and her platelet values remained $100 \times 10^9/L$ to $130 \times 10^9/L$ on her treatment regimen. HP-vWF-FVIII is generally considered efficacious and safe; however, rare instances of thromboembolic events have been reported, but this is more likely in patients with risk factors for thromboembolism.¹² Our patient did not have any thromboembolic complications.

In vWD, a bleeding score, a clinical tool that calculates the type and severity of past bleeding events, has been shown to be a predictor of future adverse bleeding events.^{13,14} This could be taken into consideration when evaluating the risk of procedure for specific patients. However, this is not always calculated in practice because it does not always change the treatment or prophylaxis but can be an indicator of the risk of future bleeding events. This was not calculated for our patient. Preprocedure and postprocedure prophylaxis may also be necessary in other upper gastrointestinal conditions where there could be a higher risk of bleeding events, such as erosive esophagitis. A recent cohort study has also shown that endoscopy poses a low risk and can be performed safely in patients with bleeding disorders if prophylactic treatment is initiated. However, this study did not look specifically at the risk of dilation in these patients.¹⁵ Other case reports and studies have reported reassuring outcomes using an organized approach to determine and administer prophylactic therapies for patients with vWD undergoing surgery.^{16–19} Thus, we recommend the following when preparing for endoscopy for a patient with vWD. First, evaluate the subtype of vWD. Then, in conjunction with a hematologist, determine the optimal treatment and prophylactic strategy that will be used. Finally, ensure appropriate monitoring for any postprocedural bleeding and survey for "iatrogenic" thromboembolism as related to higher dosage of replacement factor(s). This strategy was effectively used on 3 separate occasions.

When evaluating the management of bleeding risk in patients with bleeding disorders, concomitant diagnoses and treatment of these diagnoses should be considered. Overall, this case demonstrates successful treatment of a patient with concomitant EoE

and type 2B vWD, in a setting where multiple endoscopies, biopsies, and esophageal dilations were required. Although the conclusions drawn from this one case are by necessity limited, the prophylactic strategy here could be considered for patients with EoE with type 2B vWD and other patients with vWD who require diagnostic and therapeutic endoscopies.

DISCLOSURES

Author contributions: SR Corder collected the data, drafted the manuscript, and revised and approved the manuscript. BW Weston revised and approved the manuscript. ES Dellon conceptualized the project, collected the data, and revised, supervised, approved the manuscript, and is the article guarantor.

Financial disclosure: This study was funded in part by NIH award T35 DK007634 (SR Corder).

Informed consent was obtained for this case report.

Received October 19, 2018; Accepted February 27, 2019

REFERENCES

- Dellon ES, Hirano I. Epidemiology and natural history of eosinophilic esophagitis. *Gastroenterology*. 2018;154:319–32.e3.
- Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: Evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). *Am J Gastroenterol*. 2013;108:679–92; quiz 93.
- Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: Proceedings of the AGREE conference. *Gastroenterology*. 2018;155:1022–33.
- Koutlas NT, Dellon ES. Progression from an inflammatory to a fibrostenotic phenotype in eosinophilic esophagitis. *Case Rep Gastroenterol*. 2017;11:382–8.
- Dellon ES, Speck O, Woodward K, et al. Distribution and variability of esophageal eosinophilia in patients undergoing upper endoscopy. *Mod Pathol*. 2015;28:383–90.
- Runge TM, Eluri S, Cotton CC, et al. Outcomes of esophageal dilation in eosinophilic esophagitis: Safety, efficacy, and persistence of the fibrostenotic phenotype. *Am J Gastroenterol*. 2016;111:206–13.
- Dougherty M, Runge TM, Eluri S, Dellon ES. Esophageal dilation with either bougie or balloon technique as a treatment for eosinophilic esophagitis: A systematic review and meta-analysis. *Gastrointest Endosc*. 2017;86:581–91.e3.
- Dellon ES, Gibbs WB, Rubinas TC, et al. Esophageal dilation in eosinophilic esophagitis: Safety and predictors of clinical response and complications. *Gastrointest Endosc*. 2010;71:706–12.
- Mikhail S, Aldin ES, Streiff M, Zeidan A. An update on type 2B von Willebrand disease. *Expert Rev Hematol*. 2014;7:217–31.
- Casonato A, Pontara E, Dannhauser D, Bertomoro A, Sartori MT, Girolami A. A new variant of von Willebrand's disease (type I Padua): Doublet-organized plasma von Willebrand factor oligomers in the presence of all size multimers. *Haematologia (Budap)*. 1994;26:97–109.
- Fowler WE, Berkowitz LR, Roberts HR. DDAVP for type IIB von Willebrand disease. *Blood*. 1989;74:1859–60.
- Mannucci PM, Franchini M. Laboratory monitoring of replacement therapy for major surgery in von Willebrand disease. *Haemophilia*. 2017;23:182–7.
- Tosetto A, Castaman G. How I treat type 2 variant forms of von Willebrand disease. *Blood*. 2015;125:907–14.
- Federici AB, Bucciarelli P, Castaman G, et al. The bleeding score predicts clinical outcomes and replacement therapy in adults with von Willebrand disease. *Blood*. 2014;123:4037–44.

15. Tomaszewski M, Marc B, Kherad O, et al. A209 endoscopy bleeding risk in patients with inherited coagulation disorders, a retrospective study. *J Can Assoc Gastroenterol.* 2018;1:310.
16. Smilowitz NR, Gupta N, Guo Y, Bangalore S, Berger JS. Perioperative bleeding and thrombotic risks in patients with Von Willebrand disease. *J Thromb Thrombolysis.* 2017;44:67–70.
17. Zulfikar B, Koc B, Ak G, et al. Surgery in patients with von Willebrand disease. *Blood Coagul Fibrinolysis.* 2016;27:812–6.
18. Watterson C, Beacher N. Preventing perioperative bleeding in patients with inherited bleeding disorders. *Evid Based Dent.* 2017;18: 28–9.
19. Sato K, Kuroda S, Kobayashi T, et al. A case report on the successful perioperative management of hepatectomy for hepatocellular carcinoma in a patient with von Willebrand disease. *Int J Surg Case Rep.* 2018;44: 131–4.

Copyright: © 2019 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The American College of Gastroenterology. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.