Esophageal Stricture Secondary to Mycophenolate Mofetil Induced Injury

Nicole L. Miler, MD, Brian Frank, MD, John Jacobs, MD
Division of Digestive Disease and Nutrition, University of South Florida Morsani College of Medicine

Introduction

- The incidence of mycophenolate mofetil (MMF) induced injury to the GI tract occurs in up to 40-85% of patients on long standing MMF therapy
- Mycophenolate is primarily absorbed in the stomach and small intestine. MMF toxicity of the GI tract is likely associated to the production of downstream metabolites which is thought to cause irritation and inflammation of the mucosal lining [3]
- This toxicity most commonly manifests clinically as diarrhea, nausea, abdominal pain, vomiting, bleeding, and dyspepsia

Case Report

This is a 40-year-old man with type I diabetes mellitus complicated by renal/pancreatic transplant in 2016 on MMF, prednisone, and tacrolimus for immunosuppression who originally presented to his gastroenterologist in March 2018 with progressively worsening nausea, vomiting, and hematemesis.

- EGD/treatment at OSH: EGD revealing focal acute ulcerative esophagitis, negative stains; started on PPI for presumed reflux esophagitis
- Early 2021: progressive dysphagia to solids and liquids with 30 pound weight loss; specifically complained of progressive difficulty with swallowing the MMF pill
- EGD 2021: severe distal esophageal stricture non-transversable, biopsies revealed acute erosive esophagitis, IHC staining negative for HSV and CMV
- Next following months: non-improving dysphagia, underwent four subsequent EGDs with persistent severe distal stricture, s/p dilation to 33 Fr
- Patient switched from tablets to esomeprazole granules 40 mg twice daily and referred to our institution
- Our initial EGD 2022: 3 cm severely ulcerated distal esophageal stricture [Figure 1], traversed with the XP endoscope
- Suspicion for MMF-induced esophageal injury was high for which PO tablet was changed to liquid formulation and patient continued on PPI granules twice daily
- Underwent serial endoscopies with dilation every 2 weeks for 2 months [Figure 2]
- After transitioning to liquid formulation, each subsequent EGD with improvement in the ulcerated stricture s/p dilation to 45 Fr [Figure 3]
- Ultimate resolution of his dysphagia with liquid formulation of MMF

Endoscopy Images

Figure 1

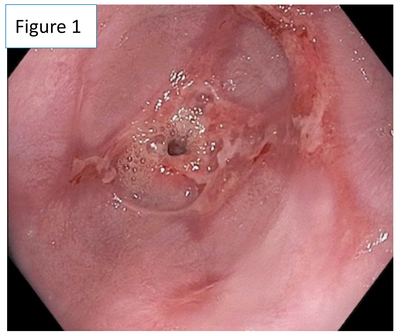

Figure 1

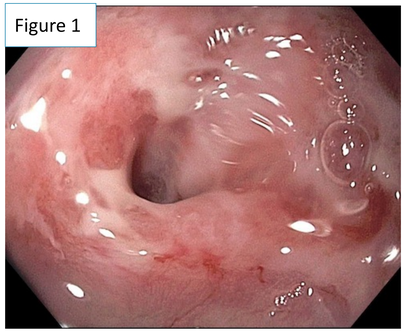

Figure 2

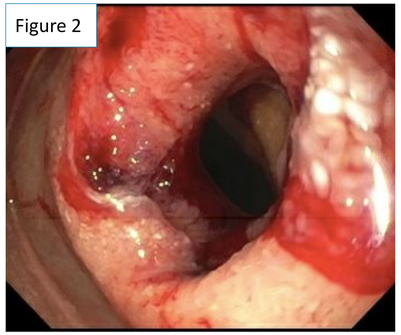

Figure 2

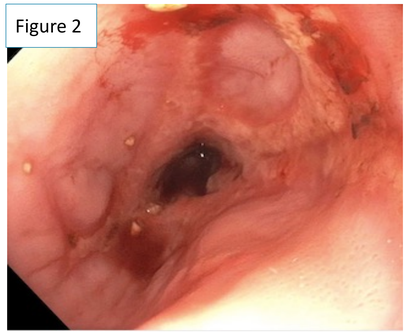

Figure 3

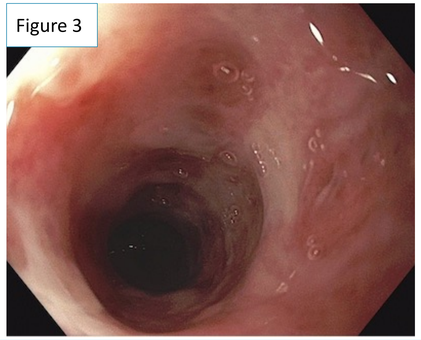

Figure Legend

- Figure 1: Initial non-transversable esophageal stricture
- Figure 2: Esophageal stricture status post multiple dilations
- Figure 3: Improving ulcerative stricture after switching to liquid formulation of MMF and multiple dilations

Discussion

- Medication induced esophagitis is a common phenomenon however few case reports discuss esophageal strictures from MMF induced injury
- MMF toxicity has been attributed to 1)metabolites produced from the digestion of mycophenolate, which induce direct toxic effect on the GI luminal wall [3]; 2) mycophenolate metabolites induce hypersensitivity reactions and elicit features of graft versus host disease throughout the GI tract [2]; 3) nonspecific acute and chronic inflammation with reactive epithelial changes and active erosive and ulcerative esophagitis [4]
- Suspicions for this process should be high in patients on immunosuppressant therapy with mycophenolate who present with dysphagia and stricture formation not explained by infections, neoplasms or other medication induced processes
- Surveillance of these specific patients is needed for prevention of refractory esophageal stricture complications caused by MMF

Conclusions

- This case demonstrates a patient who developed a severe esophageal stricture from MMF induced injury with resolution of symptoms after multiple dilations and transition to a liquid formulation of mycophenolate
- Though the exact physiologic mechanisms of the esophageal injury are not well understood, gastroenterologists should be suspicious in patients on MMF who present with dysphagia and stricture that is not explained by infection, malignancy, reflux, or other medications

Contact

Nicole Miller, MD
Internal Medicine, PGY-2
miller399@usf.edu
(941)662-7623

References

1) Telkes G, Peter A, Tulassay Z, Asderakis A. High frequency of ulcers, not associated with Helicobacter pylori, in the stomach in the first year after kidney transplantation. Nephrol Dial Transplant. 2011 Feb;26(2):727-32. doi: 10.1093/ndt/gfq401. Epub 2010 Jul 4. PMID: 20603242.

2) Nguyen, Thong DO; Park, Jason Y. MD, PhD; Scudiere, Jennifer R. MD; Montgomery, Elizabeth MD. Mycophenolic Acid (Cellcept and Myofortic) Induced Injury of the Upper GI Tract, The American Journal of Surgical Pathology: September 2009 - Volume 33 - Issue 9 - p 1355-1363 doi: 10.1097/PAS.0b013e3181a755bd

3) Arns W. Noninfectious gastrointestinal (GI) complications of mycophenolic acid therapy: a consequence of local GI toxicity? Transplant Proc. 2007 Jan-Feb;39(1):88-93. doi: 10.1016/j.transproceed.2006.10.189. PMID: 17275481.

4) Kim, Joyce J et al. "Recalcitrant Esophageal Stricture Secondary to Mycophenolate Mofetil." Case reports in gastrointestinal medicine vol. 2020 8817801. 23 Nov. 2020, doi:10.1155/2020/8817801