Mycophenolate Mofetil (MMF) Induced Hemorrhagic Colitis with Safe Reintroduction of Alternative Low Dose Enteric-Coated Mycophenolate Sodium (EC-MPS)

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Introduction

Mycophenolate mofetil (MMF) is a common immunosuppressant used in patients with solid organ transplant. MMF is associated with gastrointestinal toxicities such as diarrhea, nausea, and vomiting. MMF induced colitis is a rare but serious morbidity which often presents with diarrhea, pain, and hematochezia. It is characterized by endoscopic and histologic changes resembling inflammatory bowel disease, self-limited colitis, and graft-versus-host disease. There are no specific treatment guidelines for MMF-induced colitis, but generally symptoms resolve following discontinuation of MMF. It is unclear if colitis would recur with the use of alternative enteric-coated mycophenolate sodium (EC-MPS).

Case Background

A 36 y/o M with kidney transplant in 2015 on tacrolimus, prednisone and MMF 500 mg PO twice a day presented with hematochezia, loose stools, and abdominal discomfort. Patient was hemodynamically stable and anemic (Hgb of 12.4 g/dL). Hepatitis B serology, stool culture, ova and parasite, herpes II IgG, QuantiFERON gold, C.Diff, and tissue transglutaminase IgA were negative. Cytomegalovirus (CMV) IgG and herpes I IgG were positive. Fecal calprotectin (FCP) and CRP were elevated to 3250 mcg/g and 45.9 mg/L respectively. Colonoscopy revealed diffuse eroded mucosa with spontaneous hemorrhage. Biopsies showed active colitis without chronic changes or evidence of CMV. Patient was diagnosed with MMF induced hemorrhagic colitis. MMF was discontinued in favor of Azathioprine (AZA) 100 mg daily. Symptoms completely resolved. Follow-up routine screening donor-specific antibody (DSA) screen revealed strong de-novo DSA and biopsy reviewed antibody mediated rejection. For this, he received high dose IV methylprednisolone and IVIG, and plasmapheresis. AZA was replaced by enteric coated EC-MPS 360 mg PO daily. Flexible sigmoidoscopy two months later revealed normal mucosa without any histologic changes suggesting recurrent colitis. Repeat FCP and CRP were 27 mcg/g and 12.4 mg/L respectively.

Imaging

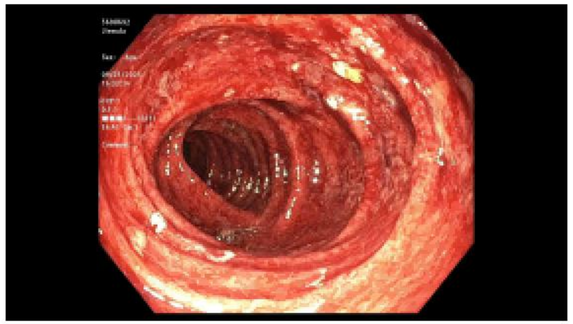


Figure 1: Endoscopic view of severely altered, vascular, friable (with spontaneous bleeding), erythematous, and eroded mucosa of transverse colon on 9/21/21.

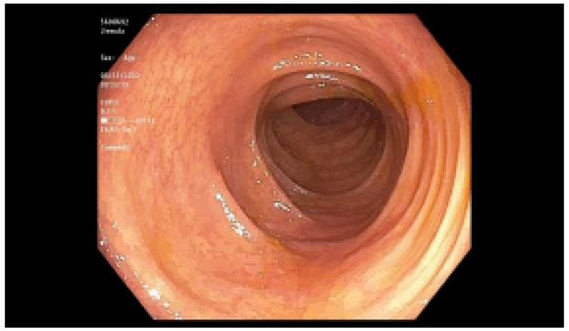
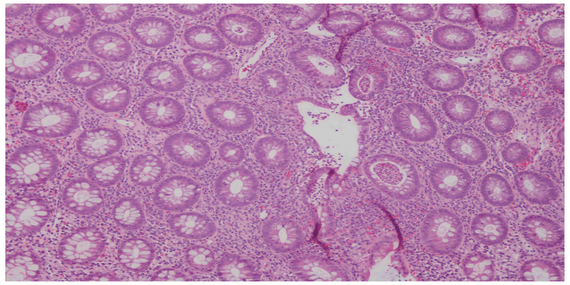


Figure 2: Endoscopic view of resolved colitis and normal transverse colonic mucosa on flexible sigmoidoscopy performed on 5/31/22 post-transition to EC-MPS



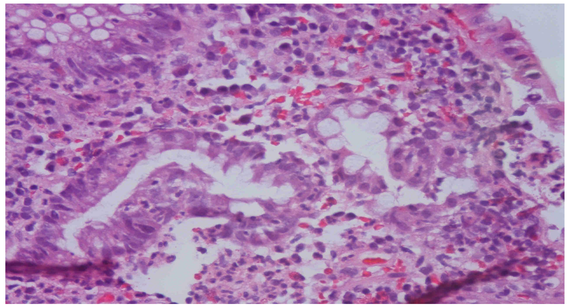
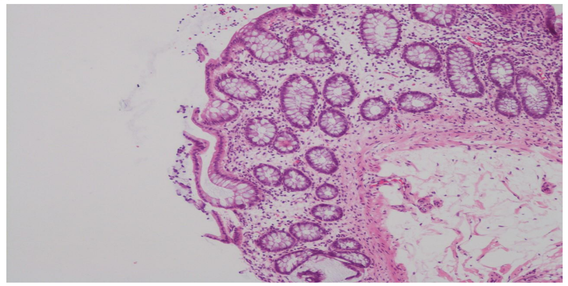


Figure 3: Abnormal colonic mucosa with high degree of active inflammation from pathology specimen on 9/21/21



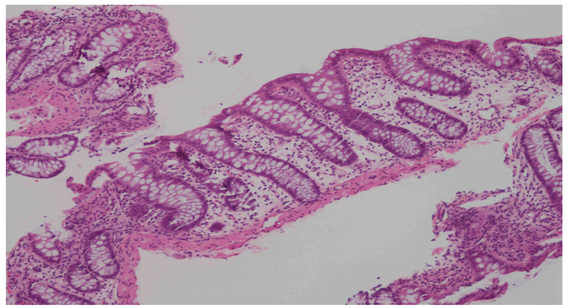


Figure 4: Chronic inflammatory changes with resolved colitis post-transition to EC-MPS from pathology specimen of colonic mucosa on 5/31/22

Discussion

MMF induced hemorrhagic colitis can be observed in post-transplant patients on MMF. Risk for MMF induced colitis is difficult to predict yet most patients respond rapidly to discontinuation of MMF. Still, this may lead to acute graft rejection as seen in our case. Our case suggests that EC-MPS may be a safe alternative in instances of MMF-induced colitis given the reduced association with GI related toxicities.

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