

Diverticular colonic perforation in patient on Mycophenolate Mofetil and Prednisolone: a case report and literature review

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We describe the occurrence of a diverticular colonic perforation in a patient with glomerulonephritis 4 weeks after initiating MMF and high dose oral Prednisolone. It is a recognised complication of immunosuppression, carries a higher morbidity and mortality, and is not always so apparent clinically – prednisolone often masking the presenting symptoms.

Clinical Literature Review:

Colonic diverticulosis (the presence of multiple inflamed diverticulae in the bowel, especially the sigmoid colon) is usually asymptomatic, but may cause symptoms ranging from mild discomfort to severe peritonitis. It is present in up to 38% of the general population.

Gastro-intestinal toxicity is a recognised complication of MMF, affecting both the upper and lower intestine, often occurring in the first 6 -12 months of treatment. Symptoms include nausea, vomiting, ulceration, gastritis, diarrhoea and abdominal pain, often in a dose dependent fashion. Dose reduction, or discontinuation usually resolves the symptoms. Oesophageal ulceration, reactive gastropathy and GVHD-like features have been reported in intestinal biopsies, as well as colitis, especially in solid organ transplant recipients.

Endoscopic examination in the subgroup of colitis sufferers can demonstrate erythema (33%), erosions and ulcerations (19%), but also what looks like normal appearances in 47%. There is usually rectal sparing. Histological analysis however often reveals pathological changes including a distinct MMF related colitis, inflammatory bowel disease appearance, ischaemia and GVHD like features. Histological evidence of colitis was seen in 83% of MMF patients undergoing colonoscopy for diarrhoea. Patients with renal transplants may be at particular risk, compared to other solid organ transplant recipients, possibly related to higher doses used, or increase in the free fraction of MPA in the context of transient renal impairment.

There is some evidence that MMF alters the composition of the gut microbiota, selecting for bacteria expressing the enzyme B-glucuronidase (GUS) and leading to up regulation of GUS activity in the gut of mice and symptomatic humans. In the mouse, the administration of vancomycin eliminated GUS expressing bacteria and prevented MMF induced weight loss and colonic inflammation.

Corticosteroids are also recognised to cause both spontaneous diverticular perforation (impairing the ability to contain the perforation in the early stages) and mask the symptoms, leading to diagnostic challenge.

Conclusions:

It is important to consider the role of immunosuppressive medication in all patients presenting with unexplained abdominal symptoms.

There may be a role for prophylactic sigmoid resection in patients with a history of previous diverticulitis in whom immunosuppressive drugs are being considered, for example patients with CKD on the transplant waiting list, but the timing of this surgery remains unclear.