CLINICAL VIGNETTE

Cytomegalovirus Associated Pouchitis

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History of Present Illness

A 55-year-old woman with remote diagnosis of ulcerative colitis (UC) presented for evaluation of profuse, watery diarrhea. She had undergone a total colectomy with ileal pouch-anal anastomosis (IPAA) and J pouch reservoir 26 years previously due to poorly controlled ulcerative colitis. The patient did well after surgery, subsequently averaging 3-4 loose bowel movements per day. She experienced episodes of mild intermittent pouchitis after her J pouch surgery, treated with steroid enemas by her prior gastroenterologist. Before current presentation, she had felt well for the last 5 years and had not seen a gastroenterologist in that time.

During her office visit, she reported diffuse body aches and 8-10 non-bloody, watery bowel movements daily for the last week. She also noted fever to 101.7F about a week ago, with persistent intermittent fevers since that time. Her outside primary care physician started oral methylprednisolone, with some subsequent improvement in her symptoms. Her only other medications were levothyroxine for hypothyroidism and duloxetine for her fibromyalgia. She denied recent use of non-steroidal anti-inflammatory medications. Her exam included temperature of 97.6, blood pressure of 105/63, and pulse of 102. Her abdomen was soft and non-tender with no hepatosplenomegaly. There was no lymphadenopathy. Laboratory studies were remarkable for ALT 68 U/L (NL: 6-29), AST 48 U/L (NL: 10-35), alk phos 398 U/L (NL: 33-130), and GGT 170 U/L (NL: 3-70 U/L). CBC included normal white blood cell count, hemoglobin of 11.5 g/dL and platelet count of 283,000/ul. Stool culture and Clostridium difficile toxin stool assay were negative. Prior testing for viral infection, included cytomegalovirus (CMV) serologies which returned positive, with IgM index of 173 AU/mL (< 30) and IgG 1.8 U/mL (< 0.6).

Clinical Course

As she was maintaining good hydration, she was managed as an outpatient. Endoscopy of the pouch revealed erythematous mucosa with multiple areas of ulceration (Figure 1). The ileum proximal to the pouch appeared normal (Figure 2). She was treated with oral ciprofloxacin 500 mg twice daily for empiric treatment of idiopathic pouchitis and methylprednisolone was stopped.

Histology of the pouch biopsies revealed CMV-associated pouchitis with moderate to severe activity (Figure 3). Histology of the small bowel biopsies proximal to the pouch demonstrated CMV associated ileitis with mild activity. A serum CMV PCR test revealed a CMV DNA level of 413 IU/mL. Based on these findings, ciprofloxacin was suspended, and under the direction of an infectious disease specialist, valganciclovir 900 mg by mouth twice daily was prescribed to the patient for a 14-day course. The patient did not note clinical benefit from the Ciprofloxacin, but after completing valganciclovir therapy, her fever resolved and her stool output returned to baseline. Unfortunately, the patient was lost to follow-up.

Discussion

Pouchitis is the most common long-term complication of IPAA in patients with UC, with a prevalence of up to 50%.[1] Symptoms of pouchitis include increased bowel movement frequency, urgency, nocturnal incontinence, pelvic discomfort and abdominal cramping. Endoscopic evaluation reveals inflammation of the pouch, including erythema and friability.

Patients with pouchitis generally respond well to antibiotics, as most cases of pouchitis are thought to stem from altered microflora of the pouch. This dysbiosis is referred to as an idiopathic pouchitis. But in 20-30% of pouchitis cases, an alternative, secondary cause is identified, such as CMV, Candida, Clostridium difficile infection, ischemia, concurrent autoimmune disorders, or the use of non-steroidal anti-inflammatory drugs.[1] These alternative causes of pouchitis should be considered when a patient fails to respond to antibiotic treatment.

CMV pouchitis was first documented in 1998, with only scattered case reports and case series published subsequently.[2] Primary infection from CMV often occurs in childhood, and it is followed by a period of dormancy in endothelial cells, fibroblasts, and members of the myeloid cell lineage.[3] CMV disease can manifest years later. One case series of patients with CMV pouchitis, found median interval between IPAA construction and CMV pouchitis diagnosis was 9 years.[3] The symptom presentation and endoscopic appearance of CMV pouchitis is similar to that of idiopathic pouchitis. However, fever can be a differentiating feature. Fever is common in CMV pouchitis but rare in idiopathic pouchitis.[4]

There is wide heterogeneity in how CMV infection and CMV intestinal disease are defined.[5] Diagnosis of CMV infection from tissue biopsies carries specificity near 100% but has low sensitivity. Indeed – the mere presence of CMV inclusions in

pouch biopsies does not necessarily represent CMV as the primary cause of pouchitis, particularly when the CMV inclusions are rare.[6] CMV PCR testing in the blood is a helpful adjunct to diagnose CMV disease; however, there is no finite DNA level above which CMV disease is classified. Notably, higher viral loads do seem to correlate with symptomatic disease.[1]

CMV pouchitis tends to respond with complete symptom resolution to treatment with either intravenous ganciclovir or oral valganciclovir.[3] Repeat endoscopic examination should be performed after antiviral treatment to document endoscopic healing and exclude Crohn disease.[4]

Conclusion

CMV pouchitis should be considered in UC patients with IPAA who present with diarrhea, fever, and abdominal pain who do not respond to conventional antibiotic treatment. Resolution of signs and symptoms can be achieved with appropriate anti-viral medication.

Figures

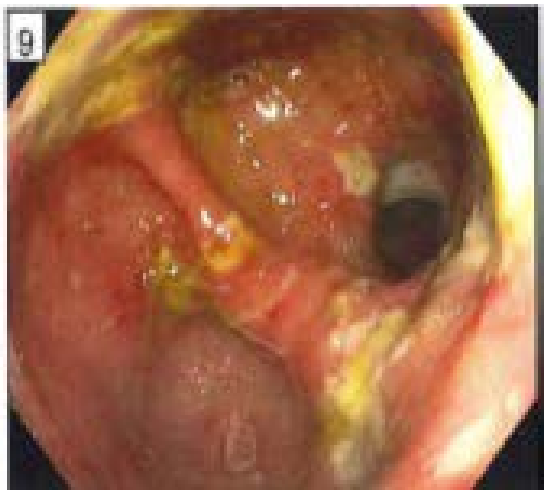

Figure 1.

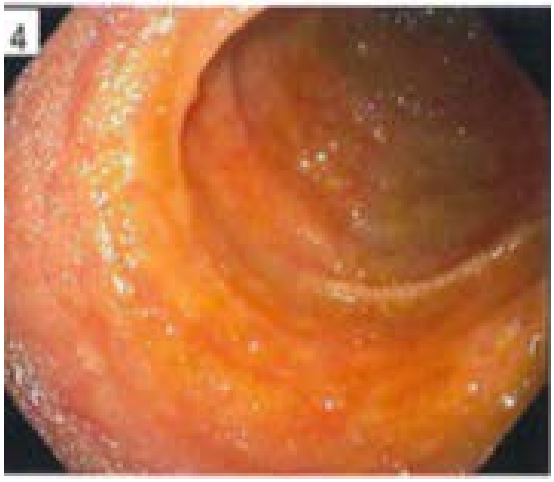

Figure 2.

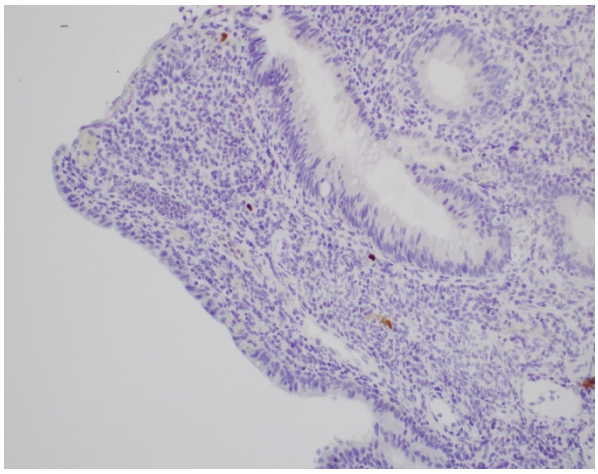

Figure 3.

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