Gastrointestinal CMV in an Elderly, Immunocompetent Patient

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ABSTRACT
An 83-year-old male with a history of diabetes but with an otherwise intact immune system presented with melena. Upper endoscopy showed gastric and duodenal ulcers. Colonoscopy showed colonic ulcers. Biopsies revealed cytomegalovirus (CMV). Therapy with an antiviral such as ganciclovir should be considered even in an immunocompetent patient if male and over the age of 55, or if they have chronic diseases such as diabetes or chronic kidney disease.

KEYWORDS: CMV, Colitis, Immunocompetent, Ganciclovir

INTRODUCTION
Gastrointestinal Cytomegalovirus (CMV) infection is well-described in patients immunocompromised by HIV and low CD4 counts, chemotherapy, chronic steroids, or immunosuppressive therapy after organ transplantation. However, GI CMV can also represent a very rare yet significant problem in immunocompetent patients. We report an elderly immunocompetent patient with GI CMV disease, and we provide a management algorithm (Table 1) to determine whether or not to treat such a patient with antivirals.

CASE REPORT
An 83-year-old male with a past history of diabetes mellitus presented with melena. EGD showed multiple small antral ulcers, gastritis, and a 1-cm, non-bleeding, duodenal ulcer. One month later a repeat EGD showed persistence of the gastric and duodenal ulcers despite a trial of PPI therapy. Biopsies for H pylori was positive, yet for some reason the patient was not treated.

Over the next four months he had no further bleeding or symptoms. A repeat EGD and colonoscopy demonstrated two 3-cm antral ulcers, a duodenal ulcer, and colitis. Biopsies revealed gastric, duodenal, and colonic CMV. Serum CMV antibody level was elevated, and HIV test was negative. Since he was asymptomatic at this time, CMV therapy was not initiated. The patient was referred to us to evaluate for underlying inflammatory bowel disease and to confirm that the CMV had resolved.

Table 1. Treatment algorithm for Gastrointestinal CMV

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<th>Patient is immunocompetent (No HIV, no steroids, no chemo, and no transplant)</th>
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<td>Male &gt;55 yrs old, pregnant, CRI, DM, or cancer</td>
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<td>Consider treatment with antivirals if potential benefit outweigh risk</td>
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First line: ganciclovir 2.6 mg/kg IV q8 or 5 mg/kg IV q12 x 2-3 wks<br>or 1000 mg PO q8 x 2-3 wks

Second line: foscarnet 60 mg/kg IV q8 or 90 mg/kg IV q12 x 3 wks

Third line: cidofovir 3-5 mg/kg IV x1 or can repeat q 2 wks

Male <55 yrs old, female, or no comorbidities

Consider regular followup and conservative treatment without antivirals
Another EGD showed antral and duodenal ulcers [Image 1]. Colonoscopy revealed scattered colonic ulcers [Image 2]. Antral, duodenal, and colonic biopsies were positive for CMV [Images 3 and 4]. Immunohistochemistry was positive for CMV [Image 5]. Because Helicobacter pylori was positive in the past, he was treated with 2 weeks of triple therapy. One year later, the patient expressed concern about the ulcers, so endoscopies were repeated. Biopsies this time continued to show persistence of the antral, duodenal, and colonic CMV. CMV viral culture was positive, and CMV DNA was positive as well.

Because the patient had been asymptomatic for quite some time, whether or not to treat him was controversial, and a literature review was performed. One large case series suggested treatment for older male patients or patients with any chronic systemic disorder in contrast with observation for younger and healthier patients. Because of the possibility of increased mortality from the patient’s male sex, age, and
diabetes, we decided to treat him with a 21-day course of oral ganciclovir. Post-treatment colonoscopy showed resolution, but EGD showed persistence of the duodenal ulcer and biopsies showed CMV. A second round of treatment was started with intravenous ganciclovir. The EGD after this round of treatment showed a partially healed duodenal ulcer and less CMV on biopsy, but not full resolution. Because the elderly patient had received two attempts at antiviral treatment and was asymptomatic, we decided not to pursue anything further except clinical follow-up. Four years later he remained asymptomatic, and EGD showed no ulcer but continued persistence of the CMV.

**DISCUSSION**

CMV is a double-stranded DNA virus in the Herpes virus family. It is often acquired in infancy or through sexual contacts, and most adults in the United States are colonized with CMV. Initial infection usually causes flu-like symptoms, and most CMV disease is due to reactivation of latent virus. CMV can affect any organ in the body, but it most often causes retinitis, gastrointestinal disease, or encephalitis.1 Most CMV disease occurs in patients immunocompromised by HIV,2,3 organ transplantation,4 chronic steroids, or chemotherapy. One third of AIDS patients have CMV disease, and the greatest risk occurs to HIV patients when the CD4 count falls below 50. Clinical manifestations of GI CMV disease are very rare in immunocompetent people being the subject of only a few case reports.5 The elderly are at particular risk of CMV disease and related mortality because T cell function declines with normal aging.6,7

CMV gastrointestinal disease can affect the gastrointestinal tract from the mouth to the anus,8 and it can also affect the pancreas, liver9 and bile duct. Colitis is the most frequent gastrointestinal manifestation, but often multiple discrete areas of the GI tract can be involved. Gastrointestinal CMV can present in many ways, but most often it presents as diarrhea, abdominal pain, and bleeding. On a cellular level, vascular endothelial cells are damaged leading to erosion and ulceration. Because symptoms of GI CMV are diverse and nonspecific, CMV can often be mistaken for other GI disorders like inflammatory bowel disease (IBD) or ischemic colitis.10 CMV can also be a potential causative factor in exacerbations of IBD (particularly in severe UC not responding to treatment).11

The gold standard for diagnosis is visualization of large cells containing intra-nuclear and intracytoplasmic inclusions surrounded by a clear halo (“Cowdry owl eye”) in tissues samples. Immunohistochemical studies like monoclonal antibodies and in-situ DNA hybridization can be confirmatory tests. Serum antibodies, viral cultures, and stool cultures are generally not useful.

Treatment is usually with either oral or intravenous ganciclovir12 (5 mg/kg twice daily) or foscarnet (90 mg/kg twice daily), both of which are viral DNA polymerase inhibitors. Cidofovir is used less commonly. Immunocompetent patients often do not need treatment with antivirals.

A meta-analysis of cases with CMV colitis in immunocompetent hosts was published in Digestive Diseases and Sciences in 2005.13 Galiatsatos and colleagues found that there was higher mortality rate in patients who were males over the age of 55 and in patients with chronic diseases such as diabetes or chronic kidney disease. Young patients with no co-morbidities had an excellent prognosis without any intervention. Among patients younger than 55 years, 50% of those older than 55 years, only 32% had spontaneous resolution, and survival for their group as only 45%. Eleven of the 14 deaths in their study were directly caused by CMV colitis. Therefore it was suggested that antiviral therapy be used in patients who are males older than 55 years or in patients with chronic diseases that may affect the immune system. A summary of the proposed treatment algorithm is presented in Table 1.

**CONCLUSION**

Our case was a male older than 55 years with diabetes. Since he was at risk for significant mortality based on this meta-analysis, we decided to treat him with antiviral therapy. As of the current time, our patient remains asymptomatic.

There are only a few published case reports of CMV gastrointestinal disease in immunocompetent hosts. Here we presented a case of CMV in an elderly patient with a normal immune system, and we discuss our management based on the literature reviewing when to treat CMV in an immunocompetent host. The decision to use antivirals can be a complex and challenging one, but one with likely benefit when a patient has certain risk factors.

**References**


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