

Cytomegalovirus Colitis in an Immunocompetent Patient with Amebiasis:

Case Report and Review of the Literature

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Abstract

Most cases of cytomegalovirus colitis occur in adults with severe immune deficiency. Only a few cases involving immunocompetent patients have been reported. We describe the first case reported in English, of cytomegalovirus colitis in an immunocompetent patient with preceding amebiasis. Eight previous cases have been reported of cytomegalovirus colitis occurring after colonic mucosal injury in immunocompetent patients. Similar to our case, all eight of these cases resolved without the use of antiviral therapy. This suggests that disruption of colonic mucosa may predispose immunocompetent patients to cytomegalovirus colitis, and that the colitis may become self-limited once the preceding intestinal damage resolves.

Key Words: Cytomegalovirus, colitis, amebiasis, immunocompetent.

Introduction

CYTOMEGALOVIRUS (CMV) is a common human viral infection, occurring in 40–100% of the adult population (1). Most primary CMV infections are asymptomatic (2). However, CMV can cause a variety of illnesses, including gastrointestinal illness. The colon is one of the organs most commonly involved. CMV usually affects immunocompromised subjects, including patients taking immunosuppressant medications and those with acquired immune deficiency syndrome (AIDS), organ transplants, or cancer (3). It has rarely been reported in immunocompetent subjects (4–17). Many of these cases were preceded by some form of mucosal injury (7–12). This report describes the first case reported in English, of CMV colitis in an immunocompe-

tent patient with preceding amebiasis. It then discusses CMV colitis in the immunocompetent host, with speculation on the importance of preceding colonic mucosal injury.

Case Report

A 29-year-old, previously healthy white male noted diarrhea two weeks after a four-day vacation in Cozumel, Mexico. He reported that he had up to six watery, non-bloody bowel movements per day, which became bloody after two days. He also had fevers to 38.9°C, fatigue, chills, “sweats,” and anorexia, with three kilograms of weight loss. He denied any abdominal pain, nausea, vomiting or jaundice. The patient was evaluated by his primary care physician, who prescribed oral levofloxacin 500 mg once per day for presumed traveler’s diarrhea. The patient had persistent fevers and bloody diarrhea after four days on levofloxacin and was subsequently admitted to the hospital.

The patient reported that in Mexico he had consumed fresh fruits, vegetables, dairy products, and local tap water. He denied any previous travel outside the United States. The patient had no significant medical history, and specifically no previous sexually transmitted diseases or parasitic infections. He had taken no medication other than levofloxacin. He did report occasional alcohol intake and a history of promis-

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cuous, unprotected sexual activity. The patient denied any intravenous drug abuse, tattoos, tobacco use, or sex with men.

Initial examination was notable for a temperature of 37.7°C, pulse of 113 beats/min, respiratory rate of 20/min, and blood pressure of 135/82 mm Hg. He appeared well developed, well nourished, and in no apparent distress. Head and neck examination revealed oropharyngeal erythema without exudate, sub-centimeter, scattered cervical adenopathy, and no scleral icterus. His abdomen was soft and nontender without organomegaly. Rectal examination was normal and without any bright red blood or melena.

Admission laboratory studies were significant for alanine aminotransferase of 224 U/L (normal, 24–63 U/L) and aspartate aminotransferase of 143 U/L (normal, 12–37 U/L). Lactate dehydrogenase was 423 U/L (normal, 100–190 U/L). White blood cell count was $7.9 \times 10^3/\text{mm}^3$, with a differential count of 42% neutrophils, 45% lymphocytes (with many atypical lymphocytes), and 13% monocytes. Serum electrolytes, hemoglobin, hematocrit, total bilirubin, and alkaline phosphatase were all normal.

CMV IgG and IgM antibody titers were obtained because there was a clinical suspicion of CMV, since the patient had pharyngitis, cervical adenopathy, elevated aminotransferases and atypical lymphocytes. CMV IgM antibody was positive at 9.84 index (<0.9 is negative), while CMV IgG antibody was negative at 1.23 AU/mL (<15 AU/mL is negative). Serologies also showed an elevated *Entamoeba histolytica* titer of 70 AU/mL (>50 AU/mL is indicative of current or recent invasive amebiasis as per Epidemiology Division, Brooks Air Force Base, TX) (18). Human immunodeficiency virus (HIV) serology, HIV RNA by polymerase chain reaction, blood cultures, monospot test, hepatitis A IgM, hepatitis B surface antigen and core IgM, hepatitis C antibody, and malaria smears were all negative. Stool studies during the patient's hospitalization were positive for occult blood, and negative for *Clostridium difficile*, ova and parasites (including *Cryptosporidium*), fecal leukocytes and enteric bacterial pathogens.

Chest and abdominal x-rays were within normal limits. Right upper quadrant ultrasonography did not reveal any focal mass lesions or abscess formation. Contrast-enhanced abdominal computed tomography revealed splenic enlargement with a craniocaudal span of 15 cm, and a normal liver without evidence of abscess formation.

Colonoscopy was performed on the third hospital day. The distal sigmoid colon had mild,

patchy inflammation. In the proximal descending colon and at the splenic flexure, there was severe inflammation with bowel wall edema and multiple shallow, serpiginous ulcerations. The colonoscope was not advanced beyond the splenic flexure because of the risk of perforation, given the severe inflammation. On biopsy, a moderately dense inflammatory cell infiltrate was present in the lamina propria of the colonic mucosa. Neutrophils were seen in clusters around blood vessels with dilated endothelial cells. Some cells had intranuclear basophilic inclusions set off from the nuclear membrane by a clear halo, consistent with CMV. These findings were confirmed with immunohistochemical studies, which showed a significant number of immunoreactive CMV cells in the stroma.

The patient was treated for amebic colitis with oral metronidazole 750 mg three times per day for ten days, along with oral paromomycin 1000 mg three times per day for seven days. His symptoms completely resolved over a three-week period without the administration of any antiviral agents. The patient has remained healthy without recurrent symptoms during 16 months of follow-up.

Discussion

CMV colitis usually affects immunosuppressed patients, including those having organ transplantation, hematological malignancies, or AIDS. It is uncommon in immunocompetent subjects (4–17). The most common presenting manifestations of CMV colitis in immunocompetent patients are diarrhea, fever, gastrointestinal bleeding and abdominal pain (14–16). Endoscopy most often shows erosive colitis with multiple ulcers (14, 16). Complications include massive hemorrhage, toxic megacolon, perforation, and protracted inflammatory bowel disease (14). In immunosuppressed patients, CMV colitis almost always occurs secondary to reactivation of latent CMV infection. However, in the immunocompetent patient, it often accompanies primary CMV infection (14).

It is unclear why some immunocompetent individuals develop CMV colitis. One possibility is that disruption of the colonic mucosa can predispose patients to colonic CMV disease (8, 11, 12). Vogel demonstrated *in vivo* and *in vitro* that CMV has a propensity to infect proliferating endothelial cells in inflamed, damaged tissue (19). Levine and co-workers initially described CMV colitis as a superinfection of another intestinal disorder (20). In a study by Hinnant and colleagues, 79% of AIDS patients with CMV colitis

had coexistent gastrointestinal infections (21). It is not known how preceding colonic injury may predispose patients to CMV colitis. One possibility is that the presence of colonic mucosal injury and inflammation may promote migration of CMV-infected macrophages to the colon.

Of the small number of CMV colitis cases with immunocompetent hosts, eight occurred after a preceding local colonic insult (Table) (7–12). Two cases occurred after *Shigella* dysentery (7, 8). Three cases of CMV colitis occurred less than one week after traumatic receptive anal intercourse (9, 10). Two cases presented less than two weeks after mucosal damage caused by ischemia (7, 11). One case occurred in an infant who had enterocolitis from bovine milk allergy (12). CMV colitis was confirmed by endoscopic biopsy in all cases. None of the patients had any evidence of immunodeficiency at the time of symptoms or during follow-up.

Our patient was judged to be immunocompetent from his negative tests for HIV antibody and HIV RNA, his normal leukocyte count, and the absence of prior infections or illnesses in his medical history. He probably became predisposed to develop CMV colitis secondary to the damage

caused by the colonic amebiasis that he contracted while he was in Mexico. Although the stool studies and the colonic biopsies did not show evidence of amebic cysts or trophozoites, organisms may have been excreted in an acyclic manner and may have been unevenly distributed in the colon, causing falsely negative samples (22). Approximately 5–15% of amebiasis may be missed despite examination of three stool specimens (22), and the detection rate of trophozoites by histopathologic examination of colonic biopsy specimens is highly variable (23). Misdiagnosis may be even higher in laboratories that are not accustomed to detecting amebic trophozoites (24).

The diagnosis of amebiasis in our patient is based on the clinical history, the response to anti-amebic therapy, and the positive serology. The positive serology is specific for recent amebiasis infection in this patient, because he had never previously traveled to an endemic region. Moreover, he did not have any risk factors for previous amebiasis exposure, such as homosexuality, recent immigration, or residence in a chronic psychiatric care facility.

Our case is similar to the previous cases in terms of patient presentation, treatment and out-

TABLE
Summary of Reported Cases of CMV Colitis in Immunocompetent Patients with Preceding Colonic Injury

Case (reference)	Age, years /Sex	Preceding Insult	Symptoms	Treatment	Outcome
1 (7)	71/female	<i>Shigella</i> dysentery	Bloody diarrhea, fever, constipation	Supportive	Resolution in 3 weeks
2 (8)	62/female	<i>Shigella</i> dysentery	Bloody diarrhea	ofloxacin	Resolution in 4 weeks
3 (9)	37/female	Anal intercourse	Hematochezia, rectal pain	Antibiotics	Resolution in 2 weeks
4 (9)	25/male	Anal intercourse	Constipation, hematochezia, fever, headache	Antibiotics	Resolution in 4 weeks
5 (10)	38/female	Anal intercourse	Constipation, fever, anorexia, rectal bleeding, rectal pain, tenesmus	Supportive	Resolution in 2 weeks
6 (7)	59/female	Cardiogenic shock	Bloody diarrhea	Supportive	Resolution in 20 days
7 (11)	72/female	Perioperative hypotension	Bloody diarrhea, fever	salazopyrine, metronidazole	Resolution in 4 weeks
8 (12)	<1/male	Allergic colitis	Rectal bleeding	Supportive	Resolution
9 (current case)	29/male	Amebiasis	Bloody diarrhea, anorexia, fever	metronidazole, paromomycin	Resolution in 3 weeks

come. Each of the patients had preceding disruption of the colonic mucosa prior to the development of CMV colitis. None of the patients received specific antiviral therapy for CMV colitis. The main treatments these patients received were supportive measures, along with treatment of the underlying cause of the initial colonic insult. All nine cases of CMV colitis resolved without major complications. It appears that CMV colitis becomes self-limited as the initial colonic injury resolves.

In contrast to patients with preceding injury of the colonic mucosa, those immunocompetent patients without a previous insult may not have a favorable prognosis. In one review, only 3 of 15 patients without previous colonic insults had self-limited disease (14). Five patients required either partial or total colectomy, and four patients died. Perhaps patients without prior mucosal injury have an unappreciated mild immunodeficiency, or they require a higher viral exposure, which lead to more severe systemic disease.

With regard to treatment, the role of antiviral agents or surgery for CMV colitis in immunocompetent patients is not clear. In a comprehensive review of CMV colitis in immunocompetent patients (15), the overall mortality rate was 32% (13/38). Mortality was 25% (5/20) in patients who received supportive therapy alone, 25% (2/8) in patients who received antiviral therapy alone, 40% (2/5) in patients who had surgery and antiviral therapy, and 80% (4/5) in patients who had surgery alone (15). In light of the high morbidity and mortality documented in previous reviews, several authors have recommended antiviral agents for the treatment of CMV colitis in immunocompetent patients (14, 15). Based on the favorable outcome of the patient described in our report, we feel that specific antiviral agents are not always necessary in the treatment of CMV colitis in immunocompetent patients who have a preceding colonic insult that is treatable or self-limited.

This case adds to a small body of literature on CMV colitis in immunocompetent patients. Based on this limited experience, we feel that preceding disruption of the colonic mucosa probably represents a risk factor for CMV colitis in immunocompetent patients. When a preceding, reversible colonic insult is present in these patients, specific antiviral agents to treat the CMV colitis may not be necessary.

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