

Case of cytomegalovirus colitis in an immunocompetent patient: a rare cause of abdominal pain and diarrhea in the elderly

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Abstract: Cytomegalovirus (CMV) colitis usually occurs in immunocompromised patients after undergoing organ transplantation or chemotherapy. We report the case of a 60-year-old immunocompetent Japanese woman who presented with abdominal pain and bloody diarrhea. She was initially diagnosed as having ischemic colitis with pseudomembranous colitis on the basis of her symptoms, *Clostridium difficile* antigen positivity, and colonoscopic findings, which showed ulcer formation from the sigmoid colon to rectum. In spite of bowel rest and administration of metronidazole, her symptoms did not improve. On follow-up colonoscopy, ulcerations remained unchanged. Biopsy of the ulceration revealed CMV-infected cells leading to a diagnosis of CMV colitis. CMV colitis is a rare but possible differential diagnosis in immunocompetent patients. We recommend endoscopic biopsy in a case of refractory abdominal pain and bloody diarrhea.

Keywords: cytomegalovirus, colitis, immunocompetent, enterocolitis

Introduction

Cytomegalovirus (CMV) is classified as a herpes virus. The proportion of humans with evidence of prior CMV infection varies throughout the world, with seroprevalence rates ranging between 40% and 100% of the adult population. CMV infection in immunocompetent hosts is generally asymptomatic or may present as a mononucleosis syndrome. Gastrointestinal involvement with CMV is uncommon in immunocompetent hosts, but can cause significant morbidity and mortality. Symptomatic CMV colitis is a well known entity in immunocompromised patients undergoing immunosuppressive chemotherapy, those with human immunodeficiency virus (HIV), and transplant recipients. While CMV colitis is almost always secondary to reactivation of latent infection in immunosuppressed patients, CMV colitis in the immunocompetent host can occur in the setting of primary infection. We report a case of CMV colitis in an immunocompetent Japanese woman with no history of HIV infection, organ transplant, or malignancy.

Case report

A 60-year-old Japanese woman presented with watery diarrhea. She denied nausea, vomiting, or abdominal pain. She noted a 4-week history of extremity weakness. Her past medical history involved schizophrenia, treated with paliperidone 6 mg and flunitrazepam 2 mg per day. She had no history of diabetes, malignancy, or steroid use. On admission, her physical findings included a masked face and slight rigidity. No electrolyte abnormalities were detected and magnetic resonance imaging showed no abnormal findings.

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Her cerebrospinal fluid revealed no inflammatory changes and albuminocytologic dissociation was not detected. Her family doctor had increased her dose of paliperidone 1 month prior. We suspected her weakness might be caused by drug-induced parkinsonism. On admission, her white blood cell count was $22,500/\text{mm}^3$ and C-reactive protein was 1.91mg/dL . Aspartate transaminase was slightly elevated (66 U/L ; normal reference $9\text{--}32\text{ U/L}$), compared with normal alanine transaminase (28 U/L ; normal reference $3\text{--}38\text{ U/L}$). Urine white blood cells and nitrites were positive. We suspected concomitant urinary tract infection and administered cefotaxime. Nine days after admission, her weakness improved gradually, but she developed abdominal pain and bloody diarrhea. She had no fever, nausea, or vomiting. On abdominal computed tomography, bowel wall thickening, and nonspecific inflammatory changes of surrounding fat tissue were seen from the sigmoid colon to rectum. Firstly, we suspected ischemic colitis and treated her with bowel rest. Four days after bowel rest, her symptoms did not improve. We performed colonoscopy, which revealed mucosal erosion and ulceration from the sigmoid colon to rectum (Figure 1A). *Clostridium difficile* was detected from culture of bowel lavage. We suspected pseudomembrane colitis and treated her with a 10-day course of metronidazole 250 mg four times daily. After treatment, her symptoms persisted and

we performed follow-up colonoscopy, which showed only minimally improved ulceration (Figure 1B). Hematoxylin-eosin stained biopsy specimens of ulceration showed no inclusion bodies (Figure 2A), but immunostained specimens revealed CMV-infected cells (Figure 2B). Laboratory findings showed elevated CMV-immunoglobulin M (0.87 ; normal reference $0.00\text{--}0.79$). We made a diagnosis of CMV colitis. HIV serology was negative and upper gastrointestinal endoscopic examination revealed that she had no malignancy, in addition to the result of the colonoscopy described above. She was considered as immunocompetent. By the time of diagnosis, her symptoms had substantially improved. Two months later, we performed follow-up colonoscopy, which showed complete resolution of ulceration (Figure 1C); biopsy demonstrated no CMV-infected cells.

Discussion

We found 12 case reports involving CMV colitis in an immunocompetent host over the past 16 years^{1–10} (Table 1). The age of onset ranged from 29 to 85 years. Presenting symptoms included fever, diarrhea, gastrointestinal bleeding, and abdominal pain. Patel et al¹¹ reported frequent involvement of the sigmoid colon and rectum in CMV colitis occurring in immunocompetent patients.

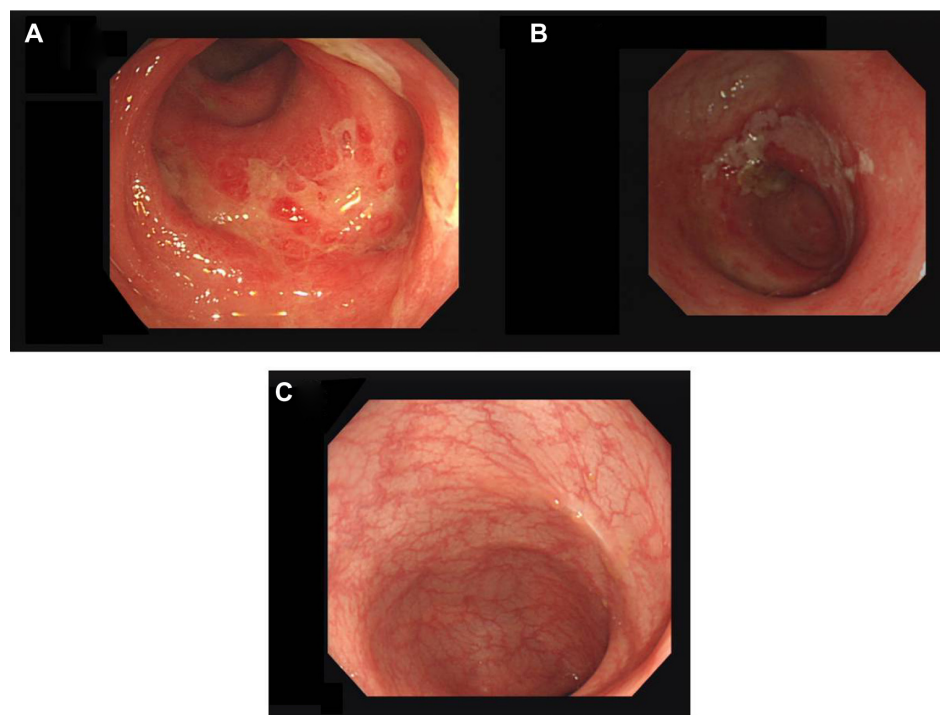


Figure 1 Endoscopic findings.

Notes: (A) Mucosal erosion and ulceration in rectum. (B) The lesion got little improvement after 10-day course of metronidazole. (C) The lesion showed complete recovery of the ulceration.

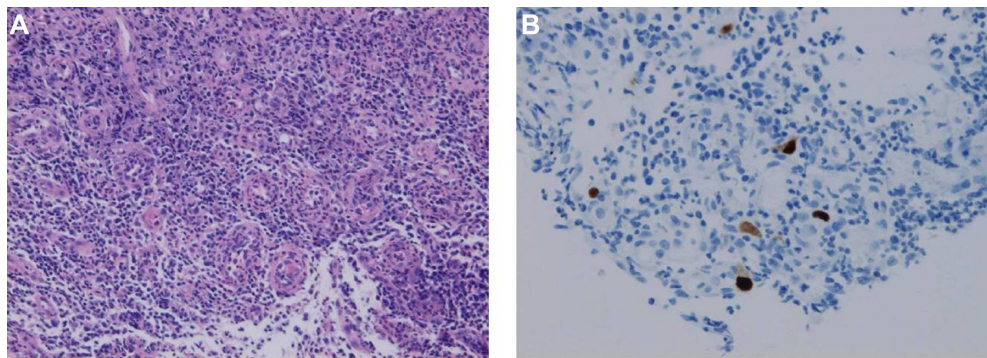


Figure 2 Histopathological findings. (A) Hematoxylin-eosin stained, 100×. (B) Immunohistochemistry for cytomegalovirus, 200×.

Endoscopic findings often show ulceration. Occasionally pseudomembrane and pseudopolyps may be detected, findings which can be pitfalls in the misdiagnosis of CMV colitis as pseudomembranous colitis. In this case, we used antibiotics to treat urinary tract infection, leaving the patient at risk for pseudomembranous colitis. Coinfection of CMV and *C. difficile* sometimes occurs in immunocompromised hosts such as post-transplant recipients and patients undergoing immunosuppressive chemotherapy.^{12,13} With regards to immunocompetent patients, the concomitant infection is rare. We found one case report of coinfection in an immunocompetent patient over the past 10 years.¹⁴ However, bloody diarrhea and a poor response to metronidazole is not characteristic of pseudomembranous colitis. Additionally, the poor response to bowel rest is not typical in the time course of ischemic colitis. CMV colitis, a rare but possible disease in immunocompetent hosts, may cause bowel perforation, leading to a poor prognosis. We recommend endoscopic biopsy and measurement of CMV immunoglobulin M antibody level in cases of refractory abdominal pain and bloody

diarrhea, in consideration of CMV colitis. In immunocompromised patients, a viral antibody test is usually insufficient to diagnosis CMV colitis, because their ability to produce antibodies is often suppressed. In such cases, detection of the antigen DNA and RNA is helpful for correct diagnosis of CMV colitis. However, in immunocompetent patients, such advanced tests are not always necessary, considering their costs.

Galiatsatos et al¹⁵ performed a meta-analysis of CMV colitis in immunocompromised hosts, reporting that advancing age (>55 years), male sex, and immunomodulating conditions (pregnancy, chronic renal failure, untreated nonhematological malignancy, and diabetes) may adversely influence survival, and patients with such risk factors should be treated with antiviral therapy. Our case had the poor prognostic factor of advanced age. Nonetheless, the colon ulceration and erosions improved and CMV was eradicated without use of antiviral drugs. Indication for antiviral drugs warrants further discussion.

Table 1 Case reports on cytomegalovirus colitis in immunocompetent hosts

Age	Sex	Comorbidity	Initial presentation	Treatment	Reference
75	F	Achalasia, gallstone	Fever, watery diarrhea	Gancyclovir	1
61	F	None	Abdominal pain, fever	Supportive	2
29	M	Unknown	Altered mental status	Gancyclovir	2
56	M	CRF, DM	Abdominal pain, watery diarrhea	Gancyclovir	3
33	M	None	Fever, bloody stool	Supportive	4
78	F	None	Abdominal pain, bloody stool	Colectomy	5
76	F	DM, HTN	Abdominal pain, watery diarrhea	Gancyclovir	6
64	M	Cerebral infarction	Nausea, diarrhea	Gancyclovir	7
82	M	None	Epigastric pain, diarrhea	Gancyclovir	8
60	F	None	Fever, abdominal pain, bloody stool	Enterectomy	9
85	M	Pneumonia	Abdominal pain, diarrhea	Colectomy	10
76	M	Parkinson's disease, peptic ulcer	Diarrhea	Gancyclovir	10

Abbreviations: CRF, chronic renal failure; DM, diabetes mellitus; HTN, hypertension.

Disclosure

The authors report no conflicts of interest in this work.

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