

Cytomegalovirus Enteritis Causing Ileal Perforation in an Elderly Immunocompetent Individual

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Cytomegalovirus (CMV) infection is usually subclinical in immunocompetent individuals, however it can be life threatening in an elderly immunocompetent individual. We report a case of CMV enteritis causing ileal perforation in a physically active elderly man. An 88-year-old healthy man presented with abdominal pain and diarrhea. After initial conservative treatment, emergency laparotomy was performed for ileal perforation. The diagnosis of CMV enteritis was based on histological findings revealing many large cells with CMV inclusion bodies in the surgical specimen. In elderly individuals, even though they are immunocompetent, CMV enteritis may result in major complications such as bowel perforation, and it should be included in the differential diagnosis of diarrhea if it is resistant to conventional treatment.

Key Words: Cytomegalovirus, enteritis, perforation, immunocompetent, old age

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INTRODUCTION

Cytomegalovirus (CMV) infection can cause organ-specific damage or severe complications such as bowel perforation in immunocompromised patients.¹ On the other hand, CMV infection in an immunocompetent individual is very rare, and only anecdotal reports have described CMV-associated bowel perforation in these patients.^{2,3} In the present report, we describe a healthy human immunodeficiency virus (HIV)-negative elderly man with CMV enteritis resulting in ileal perforation, and have reviewed the relevant English literature with specific reference to different ages at diagnosis.

CASE REPORT

An 88-year-old healthy man was admitted with six days history of diarrhea with diffuse abdominal pain. He had no noteworthy past history or any conditions of immunosuppression, including diabetes. He denied any weight loss or fever at admission. His physical examination revealed mild distension and tenderness in the right lower abdomen without rebound tenderness. Laboratory investigation showed leukocytosis of $14.3 \times 10^6/\mu\text{L}$ (normal range, 4.0-10.0) and elevated C-reactive protein of 26 mg/dL (normal range, 0.0-5.0). Electrolyte disturbances and azotemia were attributed to dehydration and were easily corrected after rehydration. Blood and stool cultures were negative, and *Clostridium difficile* toxin was not detected. Widal test and HIV serology were also negative. Colonoscopy revealed no specific lesions from the rectum to the cecum, but intubation into the

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terminal ileum was failed due to technical difficulty caused by the tortuous course of the colon. The patient began empirical antibiotic therapy for the most probable diagnosis of microbial enteritis. During the first 18 days of hospital stay, his clinical conditions were thought to have improved because his abdominal pain disappeared, white cell count was normalized to $4.7 \times 10^6/\mu\text{L}$ and C-reactive protein level was lowered to 1.9 mg/dL.

On the nineteenth hospital day, his general conditions were suddenly aggravated. He had a newly developed fever (38°C), and appeared to be suffering from localized abdominal pain. Palpation of the abdomen revealed tenderness and muscular spasm in the right lower abdomen. Computed tomography of the abdomen revealed wall thickening of the distal ileum and extraluminal air in the peritoneal cavity (Fig. 1). Emergency laparotomy was performed for the presumed diagnosis of peritonitis due to ileal perforation. A segment of ileum, about 25 cm in size, was hyperemic and edematous. One site of bowel perforation was found at the proximal 15 cm from the ileocecal valve. A segment of the ileum including the perforation site was resected and an anastomosis was performed.

The surgical specimen grossly demonstrated reddish ileal mucosa with ulcerations and perforation (Fig. 2). Histopathological examination revealed ulcerations with acute and chronic inflammatory reactions, transmural inflammation around the perforation site, and large cells containing cytoplasmic and nuclear inclusions in the ulcer bed, suggestive of certain viral infections (Fig. 3A). Immunohistochemical staining for CMV showed a positive reaction to the large cells (Fig. 3B). Serologic studies of the CMV infection were negative for CMV IgM, but CMV IgG was 203 AU/mL (upper normal value, < 6 AU/mL). The diagnosis was confirmed as an ileal perforation due to CMV enteritis. The patient recovered without any complications, even though antiviral drugs were not administered after surgical resection. During 15 months follow-up, he has been well without disease recurrence.

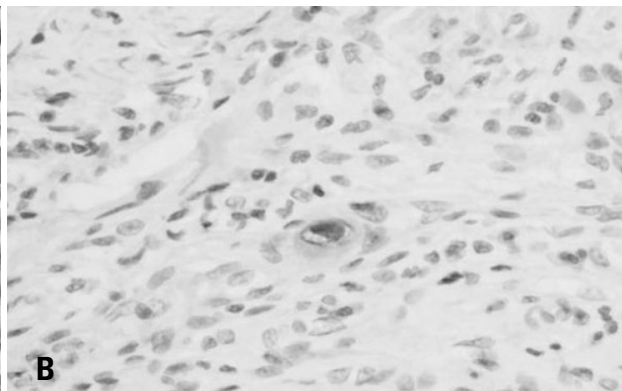
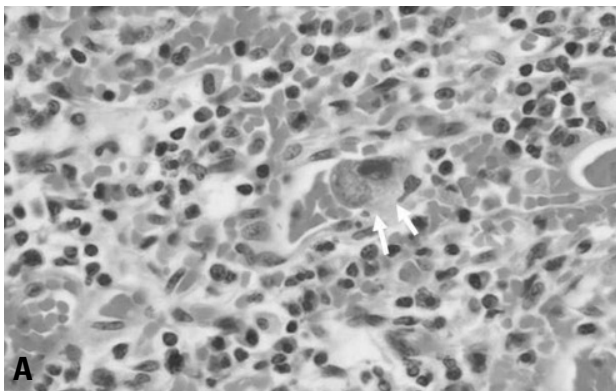


Fig. 3. Histological examination revealed ulcerations with acute and chronic inflammatory reaction, and large cells (white arrows) containing cytoplasmic and nuclear inclusions at the perforation site (H&E stain, $\times 400$) (A). These large cells showed strong immunoreactivity to CMV antibody (B). CMV, Cytomegalovirus.

DISCUSSION

The whole gastrointestinal tract can be affected by CMV, however, small bowel was rarely the only site of disease in all reported cases of CMV infection, therefore, this case is unusual in that there was CMV-associated ileal perforation without evidence of colonic lesions. In contrast to CMV infection in immunocompromised hosts,¹ only a few reports have described clinically evident CMV infection and their prognosis in immunocompetent individuals.

We reviewed reports of CMV enterocolitis in immunocompetent adults, identified using a computerized search

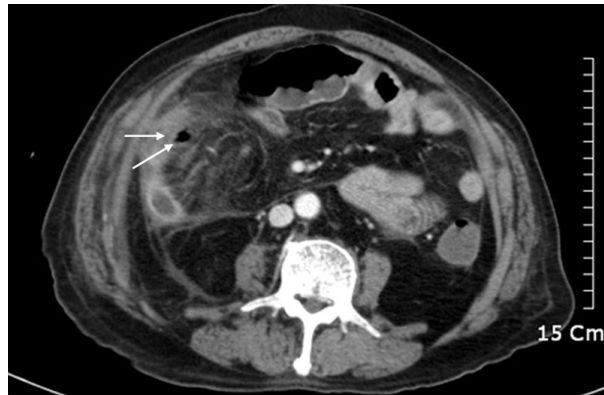


Fig. 1. Abdominal CT scan revealed extraluminal air in the peritoneal cavity (white arrows), reactive fluid collection, and wall thickening of the distal ileum.

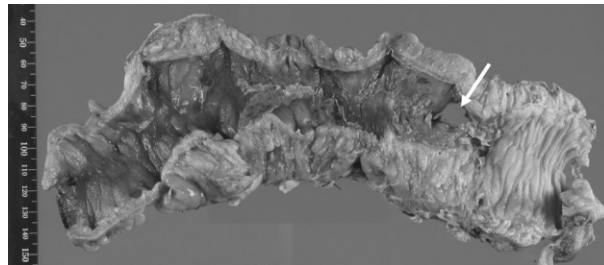


Fig. 2. Grossly, the specimen revealed one site of bowel perforation (white arrow), measuring about 3×2 cm, at the proximal 15 cm from the ileocecal valve.

Table 1. Clinical Characteristics of 27 Cases of CMV Enterocolitis in Immunocompetent Individuals Reported in English Literature

Author	Year of publication	Reference Number	Age / Sex	Clinical feature	Comorbidity	Location	Treatment	Outcome
Less than 70 yrs old								
Maignan	1992	9	36 / M	Fever, diarrhea, hematochezia	None	Rectum-SC	None	Survived
Blair	1992	10	35 / M	Diarrhea, fever, malaise	None	SC - HF	Foscarnet	Survived
Lortholary	1993	7	27 / F	Fever, diarrhea	Ulcerative colitis	Left colon	Ganciclovir	Survived
Orvar	1993	12	33 / F	Abdominal pain, diarrhea, fever	Ulcerative colitis	Pan colon	Ganciclovir	Survived
			35 / M	Fever, diarrhea	Ulcerative colitis	Left colon	Ganciclovir	Survived
Consten	1993	13	22 / F	Fever, vomiting, diarrhea	Pregnancy	SC - DC	Colectomy + ganciclovir	Survived
Loftus	1994	14	39 / M	Diarrhea	Ulcerative colitis	pan colon	Ganciclovir	Survived
Tsai	1996	15	68 / F	Diarrhea, malaise, weight loss	None	SC	Ganciclovir	Survived
Chau	1996	5	62 / F	Bloody diarrhea	Shigellosis	Ileum	None	Survived
Taniwaki	1997	16	68 / F	Diarrhea, perforation	None	Ileum	Enterectomy	Survived
Klauber	1998	18	67 / M	Diarrhea	Parkinson's disease	Rectum - SC	Ganciclovir	Survived
Chamberlain	2000	2	52 / M	Abdominal pain, perforation	Renal failure, MI	Ileum	Enterectomy	Survived
Choi	2001	21	57 / M	Hematochezia	None	Ileum	Enterectomy	Survived
Pfau	2001	8	24 / F	Diarrhea, fever, fatigue	Ulcerative colitis	Pan colon	Ganciclovir	Survived
Sakamoto	2002	19	57 / F	Hematochezia, diarrhea	Uterine myoma	Rectum - TI	None	Survived
Sugisaki	2004	23	22 / M	Fever, diarrhea	DM, rubella	Rectum - SC	None	Survived
Petrogiannopoulos	2004	24	60 / F	Diarrhea, fever, perforation	None	Jejunum	Enterectomy	Survived
Lee	2004	6	29 / M	Diarrhea, fever	Amebiasis	SC-SF	None	Survived
Lookwood	2006	27	64 / F	Diarrhea, nausea	Stroke, pneumonia	Rectum	Ganciclovir + valgancyclovir	Survived
More than 70 yrs old								
Coll	1992	11	81 / F	Delirium, fever, diarrhea	Osteoarthritis	DC	Ganciclovir	Survived
Machens	1996	3	75 / M	Diarrhea, perforation	Multiple trauma	AC	Right hemicolectomy	Died
al Mahdy	1998	17	72 / F	Diarrhea	IHD	SC	None	Survived
Klauber	1998	18	85 / M	Abdominal pain, perforation	Pneumonia	SC	Ganciclovir + colectomy	Died
Grimsehl	1999	20	70 / F	Diarrhea, hematochezia	Multi-organ failure	TC-HF	Colectomy + ganciclovir	Died
Karakozis	2001	22	79 / M	Hematochezia, perforation	None	SC	Colectomy + ganciclovir	Survived
Siegal	2005	25	82 / M	Diarrhea	None	rectum - SC	Ganciclovir	Survived
Carter	2006	26	76 / F	Abdominal pain, diarrhea	DM, hypertension	SC	Ganciclovir + valgancyclovir	Survived
Current case			88 / M	Diarrhea, perforation	None	Ileum	Enterectomy	Survived

M, male; F, female; SC, sigmoid colon; HF, hepatic flexure; DC, descending colon; AC, ascending colon; IHD, ischemic heart disease; TI, terminal ileum; MI, myocardial infarction; TC, transverse colon; HF, hepatic flexure; DM, diabetes mellitus; SF, splenic flexure.

of PubMed database (articles in English between 1992 and 2007) and their references. As there is no consensus on how to define the immunocompetent individuals, the immunocompetence in this analysis was defined with the same definition reported by Galiatsatos, et al.⁴ as the absence of congenital immune deficiency, acquired immune deficiency syndrome (AIDS), transplantation, prior chemotherapy, or immunosuppressive medication (including corticosteroids). Patients with malignancies or chronic renal failure undergoing hemodialysis were also excluded. Under this definition, 27 of the cases identified by the computerized search were reviewed (Table 1).^{2,3,5-27} They are composed of 13 men and 14 women with a median age of 60 years. The clinical spectrum ranged from a mild self-limiting colitis to severe complications and death. Surgery was performed in 9 (33%) of 27 patients, who suffered from severe complications including profuse bleeding,^{19,20} toxic megacolon¹² or perforation.^{2,3,16,18,22,24} Among eight patients more than 70 years old, four (50%) patients underwent laparotomy and 3 (38%) patients were died from severe bacterial sepsis^{18,20} or multiple organ failure.³ In contrast, overall prognosis in 19 patients less than 70 years old was rather good, as only five (26%) of them underwent laparotomy and none of them was died. In this regard, the prognosis of CMV enterocolitis in immunocompetent individuals morer than 70 years old may be worse and depend mainly on their comorbidities.

The diagnosis of CMV infection has been considered probable by histology of biopsies or detection of more than 4-fold increase in anti-CMV antibody titer and/or CMV-specific IgM. In the meta-analysis of CMV colitis in immunocompetent hosts, only 38.6% had supporting serology.⁴ Klauber, et al.¹⁸ also reported that CMV-IgM antibody was detected in 6 of 13 immunocompetent hosts with CMV colitis. In the cases reviewed here, CMV-IgM antibody was not detected in 6 cases including our patient.^{3,16,19-21} Therefore, serology is not sufficient to make a timely diagnosis of CMV infection, and the absence of CMV-IgM antibody may not exclude CMV infection. There is no consensus on the use of antiviral drugs, such as ganciclovir, in the treatment of immunocompetent individuals with CMV infection, and CMV enterocolitis resolves spontaneously after surgical resection without antiviral drugs in some immunocompetent cases.^{2,16,21,24} In this regard, no antiviral drugs were administered to our patient. However, the administration standard requires further discussion in immunocompetent individuals, especially elderly patients.

In elderly individuals, even though they are immunocompetent, CMV enteritis may result in major complications such as bowel perforation, and it should be included in the differential diagnosis of diarrhea if it is resistant to conventional treatment. Serology is not sufficient to make

a timely diagnosis of CMV infection, and the absence of CMV-IgM antibody may not exclude acute CMV infection as in our case.

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