# CASE REPORTS

# ILEAL PERFORATION DUE TO CYTOMEGALOVIRUS INFECTION

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**This article reports a case of cytomegalovirus (CMV) ileitis with perforation in a woman with transfusion-acquired human immunodeficiency virus (HIV) infection. The clinical problem of small bowel perforation due to CMV disease in association with HIV infection is emphasized. Typically, a patient with a history of chronic diarrhea, fever, and abdominal pain develops the superimposed picture of an acute abdomen and has pneumoperitonium on radiograph. The prognosis is poor. (*J Natl Med Assoc.* 1994;86:145-148.)**

**Key words** • ileal perforation • cytomegalovirus • acquired immunodeficiency syndrome • human immunodeficency virus

Cytomegalovirus (CMV) is a well-known pathogen in patients with acquired immunodeficiency syndrome (AIDS).[1-12] Cytomegalovirus is the cause of a wide variety of lesions in AIDS. In the gastrointestinal tract, it can produce stomatitis, esophagitis, gastritis, duodenitis, and ulceration of the esophagus, stomach, duodenum, ileum, and colon[1,12]; bleeding and perforation can occur at these sites. Pathologically, acute and chronic inflammation occurs along with vasculitis and large basophilic intranuclear and intracytoplasmic inclusion bodies within macrophages and endothelial cells.[13] Intestinal perforation due to CMV occurs mainly in the colon, ileum, and appendix.[10]

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Since the first report in 1984 by Frank and Raicht,[3] there have been several reports of small-intestinal perforation in patients with AIDS who were infected with CMV.[3-11] This article describes a case of small intestinal perforation associated with CMV in a heterosexual woman with human immunodeficiency virus (HIV) infection and reviews other reported cases of ileal perforation.

## CASE REPORT

A 52-year-old Hispanic woman with a history of HIV infection was admitted to Thomason Hospital with 3 days of progressive diffuse abdominal pain superimposed on chronic abdominal pain of several months' duration. The recent worsening of symptoms was associated with nausea, vomiting, fever, and chills. She was known to be seropositive for HIV for a year prior to admission; the presumed source was a blood transfusion after a cholecystectomy performed in Mexico 3 years prior to admission. She had complained of fever, diarrhea, and abdominal discomfort for several months and had been seen in an outpatient clinic. Blood cultures and stool examinations for ova, parasites, and enteric pathogens were negative. She had been treated empirically with metronidazole. The patient was not receiving antiretroviral therapy.

On physical examination, her blood pressure was 110/70 mm Hg, her pulse was 140 beats/minute, and her temperature was 98°F. The abdomen was mildly distended with diffuse tenderness, guarding, rigidity, and absent bowel sounds. Her CD4 count at the time of admission was 6 cells/mm$^3$, and the CD4:CD8 ratio was 0.04. Her hemoglobin was 8 g/dL, and her hematocrit was 24%. Her white blood cell count was 2300 cells/mm$^3$ with 35% band forms. Flat and upright plates of the abdomen showed the presence of free air in the abdomen. An exploratory laparotomy was performed

**TABLE. SMALL INTESTINE PERFORATIONS ASSOCIATED WITH CYTOMEGALOVIRUS INFECTIONS IN PATIENTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)***

| Ref | Age/Sex | Clinical Presentation | Surgical Procedure & Findings | Pathology Report & Outcome |
|---|---|---|---|---|
| 3† | 45/M | 6 months of abdominal pain, nonbloody diarrhea, & fever | Small bowel resection; 3-mm perforation found in terminal ileum | Acute inflammation, intranuclear inclusion bodies; patient died 7 days postsurgery |
| 4† | 35/M | Severe periumbilical pain, nausea, & vomiting | Ileocolonic resection; ileal perforation found 50 cm from ileocecal valve | Compatible with CMV infection; patient died, undetermined time |
| 5† | 22/M | 6-month history of diarrhea with fever & abdominal pain | Laparotomy, resection of ileal segment; 4 ulcers & 1 perforation found on small bowel | Inflammation & vasculitis; intranuclear inclusions in macrophages, endothelial & smooth muscle cells; numerous viral capsids in macrophage nuclei; patient died 1 week postsurgery |
| 6† | 40/M | Sudden onset of abdominal pain & fever | Small bowel resection; 3-mm terminal ileum perforation & Kaposi's sarcoma nodules found | CMV inclusions; patient died 3 weeks after |
| 7† | 28/M | Chronic diarrhea, fever, & abdominal pain | Small bowel resection, jejunostomy, & mucus fistula; ileal & jejunal perforations found | CMV inclusions; patient died 1 month postsurgery |
| 8 | 40/M | Shock & diffuse peritonitis | Localized resection with end ileostomy & mucous fistula of the right colon; distal ileal perforation found | Compatible with CMV; patient died 24 hours postsurgery |
| 9 | 40/M | 24-hour history of lower abdominal pain with fever | 60-cm jejunum resection with enteroenterostomy; 3 perforations found in the jejunum | Chronic active inflammatory infiltrate, CMV inclusion bodies in all bowel layers; 110-nm virion with envelope particle ranging from 180 nm to 250 nm; patient discharged after the 21st postoperative day on DHPG |
| 10 | 32/M | 2-day history of rectal bleeding & hematemesis | Small bowel resection; terminal ileum perforation | Chronic inflammation & full thickness necrosis secondary to CMV infection; patient died 1st postoperative day |
| Present case | 52/F | Chronic diarrhea, abdominal pain, & fever | Ileocecal resection with ileocolonic anastomosis; ileum perforation found | Multiple cytomegalic inclusion bodies; patient died 7 days postsurgery |

Abbreviations: Ref = reference, CMV = cytomegalovirus, KS = Kaposi's sarcoma, and DHPG = 9-(1,3-dihydroxi-2-propoxymethyl) guanine.
*Reference 15 was not used due to lack of specific patient information.
†Pneumoperitoneum.

with an ileocecal resection and ileocolonic anastomosis. The patient could not be weaned off the ventilator postoperatively and developed multi-organ failure. She died 7 days after surgery. An autopsy was declined by the family.

Pathological examination of the resected distal 25 cm of ileum showed multiple areas of mucosal ulceration with diameters ranging from 2 cm to 5.5 cm. A 0.3 cm perforation was also seen in the distal ileum. Microscopic examination showed areas of mucosal ulceration with granulation tissue formation and acute and chronic inflammatory cell infiltration. The classic owl's eye (intranuclear) inclusion bodies were seen. Also seen were slightly enlarged elongated cells with tapering cytoplasm and indistinct hematoxyphilic smudged nuclei, as described by Francis et al.[12] There were

multiple cytomegalic viral inclusions present, mainly in the vascular endothelium. Some of the blood vessels showed endothelial proliferation, and a few of them were occluded by fibrin thrombi. The inflammatory process involved the muscularis as well as the serosa. Some ganglion cells also contained intranuclear inclusions. The number of infected cells is said to be associated with severity of disease[12]; by these criteria, the patient had severe infection. Special stains for fungi and mycobacteria were negative. No evidence of malignancy was noted in the specimen.

## DISCUSSION

Cytomegalovirus is a common infection in patients with AIDS.[1,2,14] In the homosexual population with AIDS, seropositivity for CMV approaches 100%. Several cases of gastrointestinal involvement with CMV and subsequent bowel perforation have been reported in this patient population.[3-11,15-17] The frequent seropositivity of AIDS patients for CMV and the frequent culture of this organism in asymptomatic persons has made it difficult to ascribe causality in all instances. Although adenovirus may mimic the histopathologic appearance of CMV,[18] Francis et al,[12] in a study where a positive adenovirus culture was noted in the stool of a few patients with a histological picture "typical" of cytomegalovirus colitis, confirmed the presence of CMV in tissue by immunohistochemical studies. Other studies also have supported this finding.[19,20] Our patient's histopathology was typical of that due to CMV, and infection caused the perforation.

The Table summarizes cases of small bowel perforation associated with CMV infection reported in AIDS patients. Ulceration and perforation occurred in the context of pathologic and ultramicroscopic findings compatible with CMV, namely, CMV intranuclear and intracytoplasmic inclusion bodies and significant inflammatory changes including areas of focal necrosis that seemed to be the cause of perforation. Our case is different from those described in that the patient was female and presumed to have acquired her HIV infection by blood transfusion.

Of the nine reported cases of small bowel perforation associated with CMV infection (including ours), the average age was 37 years (range: 22 to 52 years). The most common presenting complaint was abdominal pain in eight of the nine cases (88%), followed by fever in five patients (55%), and diarrhea in four (44%). There was one case in which the initial presentation was gastrointestinal bleeding with no other associated symptoms.[10] Lymphocyte studies were reported in only four patients (44%), with CD4 counts ranging from 6 to 395 cells/mm$^3$ and CD4:CD8 ratios from 0.04 to 0.23. Pathological findings included CMV intranuclear inclusions in all nine cases; in two patients,[7,9] ultramicroscopy was performed showing the presence of viral particles in the tissue. Therapy included supportive measures and surgical resection. One patient received antiviral therapy with ganciclovir. The outcomes were poor with patients dying in the hospital. The only patient discharged home was the patient on ganciclovir.[9] Ganciclovir has been shown to be of benefit in gastrointestinal CMV infections,[21] and therapy with ganciclovir in patients with suspected bowel perforation probably should be started preoperatively.

Increased survival of AIDS patients as a result of prophylaxis and treatment of other infections may result in more patients presenting with CMV disease involving the gastrointestinal tract. The clinical entity of small bowel perforation due to CMV infection needs to be recognized and may be associated with the development of acute abdominal pain in the setting of longstanding pain, chronic diarrhea, and fever. Whether earlier recognition and treatment of CMV gastrointestinal disease can prevent the disastrous complication of perforation can be answered only through careful clinical trials.

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