

Cytomegalovirus Colitis in an Older Woman, Successfully Treated with Ganciclovir

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Cytomegalovirus (CMV) infections are usually found in immunocompromised persons and rarely present in those who are immunocompetent. We report a case of CMV colitis in an elderly woman presenting with delirium, prolonged fever, and diarrhea. Treatment with ganciclovir, an antiviral agent, resulted in resolution of the colitis within 3 weeks without noticeable side ef-

fects. Older adults may be more susceptible to CMV infection by virtue of age-related changes in immune function. The possibility of CMV colitis should be considered in an elderly person with persistent fever, diarrhea, and negative stool cultures.

Key words. Cytomegaloviruses; antiviral agents; immunocompetence. *J Fam Pract* 1992; 34:772-775.

Cytomegalovirus (CMV) infections occur almost exclusively in immunocompromised hosts. The most commonly affected group is persons with acquired immunodeficiency syndrome (AIDS).^{1,2} On rare occasions, however, CMV infections have been seen in apparently immunocompetent persons.³⁻⁶ We report an 81-year-old woman presenting with delirium, fever, and diarrhea who was found to have CMV colitis. She was not identified as having an immunological disorder, and her colitis responded to treatment with ganciclovir, a new antiviral agent.

sinophils; alkaline phosphatase, 117 IU/L (normal range 43 to 122 IU/L), aspartate aminotransferase (AST), 166 IU/L (normal 7 to 37 IU/L); and alanine aminotransferase (ALT), 95 IU/L (normal 3 to 36 IU/L).

Initial management included upper gastrointestinal endoscopy, which revealed a large bleeding gastric ulcer. Biopsies of the ulcer showed evidence of acute and chronic inflammation; no cancer was evident. Ranitidine was prescribed. The patient's delirium persisted, and during the day following admission, she developed a low-grade fever, with a maximum temperature of 38.2°C (100.8°F). Urine and blood cultures obtained at that time were negative. Her cerebrospinal fluid was normal with a negative culture. She continued to have occasional loose heme-positive stools. One week after admission, liver function tests returned to normal (alkaline phosphatase, 95 IU/L; AST, 25 IU/L; and ALT, 29 IU/L).

Fever and delirium persisted for 2 weeks, with her temperature becoming progressively more elevated. No source for the fever could be identified in spite of repeated urine, blood, and stool cultures. Several radiologic examinations of her chest were performed, all of which were unremarkable. Because of persistent diarrhea and heme-positive stools, a sigmoidoscopy was performed, and it showed severe segmental colitis 30 to 60 cm from the anus. Mucosal biopsies from the involved area revealed occasional markedly enlarged endothelial cells characterized by intranuclear inclusions, clear halos surrounding the inclusions, and cytoplasmic granules (Figure 1). These findings are characteristic of CMV infection. Ganciclovir, 125 mg intravenously every 12 hours (5 mg/kg/day), was prescribed. An immunologic

Case Report

An 81-year-old woman was admitted to an acute care hospital following a fall at home. Before admission, she lived alone; she was reported to be independent in all her activities of daily living. She had a history of osteoarthritis for which she was taking a nonsteroidal anti-inflammatory agent intermittently. She presented after passing loose melantotic stools. Although she was delirious, she was afebrile at the time of admission. Admission laboratory test results were as follows: hemoglobin, 168 g/L (16.8 g/dL); white blood count (WBC) $14.6 \times 10^9/L$ ($14,600/mm^3$); WBC differential, 62% neutrophils; 10% bands; 12% lymphocytes; 12% monocytes; and 4% co-

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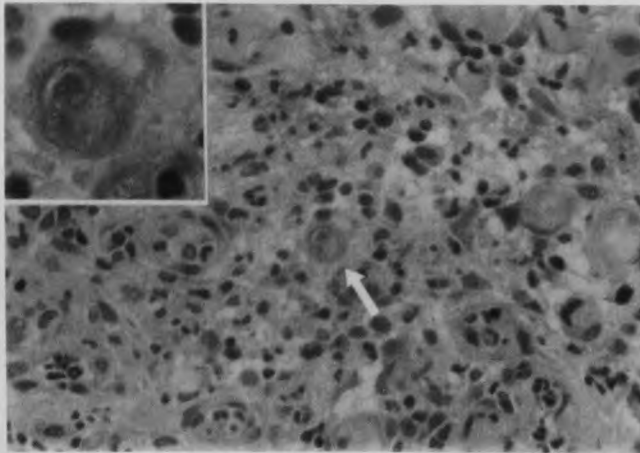


Figure 1. Colonic mucosal biopsy showing subacute colitis with a typical cytomegalic cell (arrow and inset). The cytomegalic cell exhibits a large intranuclear inclusion and cytoplasmic granulation. (hematoxylin-eosin, $\times 200$, inset $\times 1000$)

workup, including human immunodeficiency virus (HIV) serology, bone marrow examination, and serum protein electrophoresis, revealed no abnormalities. The gastric mucosal biopsies were reviewed again, but no evidence of CMV was detected histologically.

The patient's fever began to subside 3 days after initiation of antiviral therapy. She was completely afebrile after the 11th day of treatment with ganciclovir. Her mental status also improved, and for the first time in 3 weeks, she was able to take some nutrition orally. No adverse effects of the ganciclovir treatment were noted. Two weeks following the initiation of antiviral therapy, a repeat sigmoidoscopy was performed, which confirmed that the colitis was resolving. Subsequent biopsies did not reveal evidence of CMV. Administration of ganciclovir was continued for 3 weeks, by which time the patient had recovered completely. Thirteen months following discharge from the hospital, she remained free of diarrhea and infection.

Discussion

CMV colitis is known to occur as part of a systemic infection.⁷ It can result in severe bowel hemorrhage⁸ or colonic perforation.⁹ CMV colitis can occur in association with ulcerative colitis, causing exacerbation of the disease and a poor prognosis. In three cases of CMV colitis described in patients over 70 years of age, two patients died as a direct result of their colitis,^{3,10} while in the third case, the colitis resolved spontaneously without treatment.⁴

Table 1 shows the conditions commonly associated with CMV infection, all of which suggest alteration of normal immune function. It has been suggested that declines in immune function caused by aging could pre-

Table 1. Conditions Commonly Associated with CMV Infection

• Acquired immunodeficiency syndrome (AIDS)
• Post-transplant
Bone marrow
Kidney
Liver
Heart
• Neoplasia
Lymphoma
Leukemia
Disseminated malignancy
• Ulcerative colitis

dispose elderly persons to CMV infection.³ Humoral immunity is impaired in older persons because of alterations in T helper cells. Cell-mediated immunity is also decreased with age. In the case described, we could not identify a specific immunologic disorder, but the patient had a concurrent severe illness: a bleeding gastric ulcer. Although CMV can lead to gastric ulceration, we would surmise that the ulcer was caused by the patient's use of nonsteroidal anti-inflammatory agents since no histologic evidence of CMV was seen on gastric biopsy. Perhaps the stress of the gastric ulcer weakened the patient's immune system, resulting in overt CMV infection. Serology can be used to document CMV infection but was not obtained in this case, as the diagnosis was confirmed by colonic biopsy pathology. The patient's mental status changes were apparently due to the CMV infection, as her delirium did not clear until her colitis resolved. Although we cannot state with certainty that ganciclovir was the causative agent in curing this patient's illness, her fever and diarrhea diminished and her mental status and ability to take oral nutrition improved only after antiviral therapy was started. Resolution of CMV colitis without antiviral therapy has been reported to occur at any time from 2 weeks to several months following the onset of symptoms.⁴

Ganciclovir (dihydroxy-propoxymethyl guanine) is a newly available derivative of acyclovir. In vitro it has been shown to be considerably more effective against CMV than acyclovir.¹¹ There have been several uncontrolled trials reported on the efficacy of ganciclovir for CMV infections.^{12,13} In these studies ganciclovir was used to treat CMV infections of various body sites in AIDS patients. Initial responses were good, but recurrence of the infection after discontinuation of the medication occurred in most of the cases. A recent randomized case control study examining ganciclovir use in bone marrow recipients with CMV gastroenteritis failed to show any benefits when compared with supportive care.¹⁴ Gan-

ciclovir may cause a dose-related granulocytopenia, which usually reverses after discontinuation of the medication. Mental confusion caused by the medication has also been reported.¹⁵ It can only be administered intravenously, and the dose may need to be reduced if impaired renal function is suspected. The usual recommended dose of ganciclovir is 5 mg/kg every 12 hours for 14 to 21 days.

This case illustrates how CMV colitis may present in an older patient who does not have an identifiable immunological disorder. The occurrence of diarrhea in the presence of fever and negative stool cultures should heighten diagnostic suspicion of CMV. In the case reported, treatment of CMV colitis with ganciclovir was effective in an older patient and had no significant side effects.

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