

## Case Report

# Cytomegalovirus involving gastric antrum in immunocompromised hosts: a report of 5 cases

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Cytomegalovirus infection, which is common in immunosuppressed patients, only rarely affects the stomach, especially the gastric antrum. We report five patients with cytomegalovirus infection of the stomach with antral involvement. Of these, four had undergone renal transplant and one had HIV infection. All patients presented with upper gastrointestinal symptoms that did not respond to proton pump inhibitors and prokinetic drugs. In addition, all had systemic symptoms. Diagnosis was made at upper GI endoscopy and biopsy, and ganciclovir treatment led to improvement. [*Indian J Gastroenterol* 2005;24:258-260]

Opportunistic infections are common in patients who have undergone renal transplant and are receiving immunosuppressants,<sup>1</sup> and those with HIV/AIDS.<sup>2</sup> Cytomegalovirus (CMV) is one such pathogen. Although affliction of the entire gastrointestinal tract with CMV has been described, localization to the stomach, especially gastric antrum, is rare.<sup>3</sup> We report five patients who had CMV infection of the stomach and were treated successfully, seen over the past four years.

### Case Reports

*Case 1:* A 53-year-old woman, who underwent live-related renal transplant and was receiving induction immunosuppression with cyclosporine, prednisolone and mycophenolate, was admitted 3 months later with dull aching epigastric pain, post-prandial abdominal bloating, nausea, and high-grade fever of 5-day duration. Investigations for cause of fever were inconclusive. IgG anti-CMV was positive (161.7 AU/mL; positive >14.45), whereas IgM anti-CMV was negative. Upper GI endoscopy revealed target lesions in the antrum and fundus. Biopsy showed eosinophilic intranuclear inclusion bodies characteristic of CMV infection in many glandular epithelial cells. She was treated with ganciclovir (5 mg/Kg) twice daily for 21 days followed by maintenance therapy for 3 months. She was asymptomatic 6 months later.

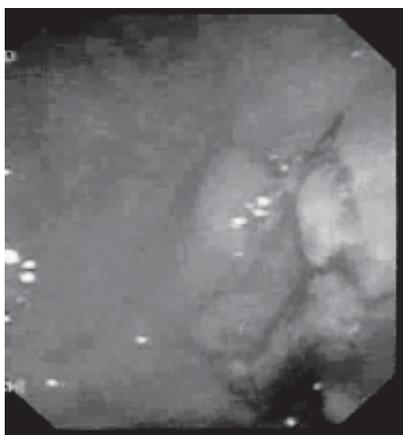
*Case 2:* A 66-year-old man, who received renal transplant was admitted 2 months later with fever

and epigastric discomfort of one-month duration, along with constipation of 4-day duration. IgM anti-CMV was positive (0.655 AU/mL; positive >0.500). Upper GI endoscopy showed multiple creamy white plaques in the lower third of the esophagus and antral gastritis. Antral biopsy revealed intranuclear inclusion bodies. Esophageal biopsy revealed submucosal blood vessels laden with degenerated eosinophilic cells and intranuclear inclusions, highly suggestive of CMV infection. Treatment with ganciclovir (5 mg/Kg) led to transient improvement. He however died of nosocomial pneumonia and septic shock.

*Case 3:* A 58-year-old woman with hypertension, hypothyroidism, sleep apnea and pulmonary hypertension underwent cadaveric renal transplant, following which she received triple immunosuppression. Six months later, she was admitted with fever, cough, breathlessness and post-prandial abdominal pain not responding to pantoprazole. Endoscopy showed a small hiatus hernia with multiple antral ulcers with surrounding erythema. Biopsy showed an ulcerated area with neutrophilic exudate with large number of intranuclear inclusion bodies. Test for CMV antigen in blood (CMV-PP65) was positive. IgM anti-CMV was also positive (0.70 AU/mL). Pain disappeared with ganciclovir treatment, which was continued for 6 months. She is well since for a year.

*Case 4:* A 38-year-old woman underwent cadaveric renal transplant, and was receiving prednisolone, mycophenolate mofetil, and cyclosporine. She was admitted 3 months later with anorexia, fever, post-prandial abdominal pain and dry cough. Investigations for cause of fever were inconclusive. Two days later, she had hematochezia, requiring transfusion of 6 units of blood. Colonoscopy showed a large ulcer at the ileocecal junction. Upper GI endoscopy revealed duodenitis and antral gastritis. CMV-PP65 was negative. Biopsy from gastric and ileocecal lesions showed epithelial cells with large intranuclear CMV inclusions. Following ganciclovir treatment, she is asymptomatic 8 months later.

*Case 5:* A 40-year-old man was detected to have

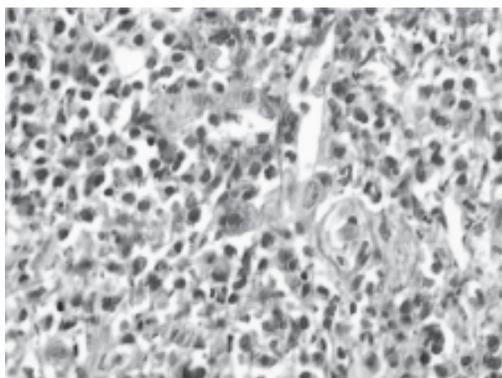


**Fig 1: Endoscopic photograph showing frond ulcers and inflammation in antrum (Case 5)**

HIV infection 2 years ago, when he had presented with fever and weight loss. He was on triple-drug HAART, which he had stopped on his own since 4 months. Following this, fever and significant weight loss recurred. He also had post-prandial abdominal pain, with occasional radiation to the back, for 2 months, which did not respond to anti-acid treatment. Serum amylase and lipase levels were normal. CD4 count was  $5/\mu\text{L}$ , and HIV viral load was 59,500 copies/mL. Upper GI endoscopy revealed extensive antral ulceration and surrounding erythema (Fig 1). Gastric biopsies showed negative rapid urease test for *Helicobacter pylori*, and inflammation and eosinophilic intranuclear inclusion bodies suggestive of CMV infection (Fig 2). CMV-PP65 in blood was positive. Symptoms and endoscopy findings improved after ganciclovir treatment. Currently he is well at 2 months' follow up on maintenance ganciclovir.

### Discussion

CMV infection develops in 70%-90% of transplant patients.<sup>3</sup> One of the important sites of latent infection is the GI tract.<sup>3</sup> Most CMV infections follow-



**Fig 2: Microphotograph (Case 5) of CMV inclusion body (H&E, 40X)**

ing renal transplant surgery occur via allograft transmission. Less commonly they occur from infection by a new strain or endogenous reactivation of latent infection. All our live donors and recipients were CMV IgG +ve and IgM -ve at the time of transplant. The CMV status of cadaveric donors was not known. All patients in this study had received mycophenolate, which is an independent risk factor for CMV infection.<sup>4</sup>

CMV is one of the pathogens that cause the most serious opportunistic viral infections in HIV-positive patients and is one of the most common causes of AIDS-related gastritis.<sup>5</sup> CD4 counts are invariably less than  $100/\mu\text{L}$  when there is CMV gastric infection.<sup>6</sup> CMV has been found at autopsy in more than 90% of AIDS patients, with GI involvement in 15% to 43% of these patients.<sup>1</sup>

Though the rate of GI affliction by CMV is high, localization to the gastric antrum is not common.<sup>7</sup> Gastric CMV infections are usually located in the fundus with occasional contiguous involvement of the gastro-esophageal junction. All our patients had lesions in the antrum, and one of them had gastro-esophageal involvement. The mechanism of injury in CMV infection is believed to be due to infection of the endothelial cells, causing small-vessel vasculitis, thereby leading to ischemic necrosis.<sup>1</sup>

The endoscopic appearance of CMV gastric infection is highly variable and includes normal mucosa, superficial or deep ulcers (isolated giant ulcers being typical), mucosal erythema, and a discrete antral mass. H & E staining reveals "owl's-eye" cytoplasmic and intranuclear inclusion bodies.<sup>1</sup> The ulcer base is the site of most intense inflammation. These histologic changes may be patchy; hence 8-10 biopsies of suspicious lesions are recommended. The diagnosis of CMV infection can also be made by antigen detection, the sensitivity and specificity of which are 95% and 91%, respectively.<sup>8</sup>

The treatment of CMV stomach is the same in both the above settings, as is for any systemic infection by CMV. All our patients, except one, had complete recovery following ganciclovir therapy. However, in view of the possibility of reactivation, long-term maintenance therapy is mandatory. Valganciclovir is now being favored for CMV prophylaxis because its oral bioavailability is similar to that of intravenous ganciclovir and also long-term intravascular access may be detrimental in these immunosuppressed individuals.<sup>9</sup>

In summary, CMV infections of the stomach should be suspected if upper GI symptoms occur in the first 3 months after organ transplantation or in a patient with advanced HIV infection if upper GI symptoms do not respond to standard therapy with antisecretory and prokinetic agents, and particularly if systemic symptoms are present. In these patients, upper GI endoscopy should be considered to diagnose CMV infection early in the course to prevent morbidity and mortality.

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