Case Report

Cytomegalovirus Jejunitis with Jejunal Perforation in Immunocompetent Host

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ABSTRACT

Cytomegalovirus (CMV) infection of the gastrointestinal tract in an immunocompetent host is an uncommon condition. It can involve any part of the intestinal tract, but more commonly at the colon. Extensive small bowel involvement is rather uncommon. We report a case of jejunal perforation due to spontaneous reactivation of latent CMV infection in an immunocompetent host. He was a 75-year-old healthy male presented with chronic abdominal pain for 2 months which physical examination revealed signs of localized peritonitis at upper abdomen. After surgical laparotomy, resection of perforated jejunal segment was performed. Histologic study and anti-CMV IgG were in consistent with the diagnosis of CMV jejunitis. He was subsequently treated successfully with a 2-weeks course of intravenous ganciclovir. After 6 months of follow-up period, he was relatively fit and uneventful.

Key words : Cytomegalovirus, Jejunitis, Perforation, Immunocompetent host

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INTRODUCTION

Cytomegalovirus (CMV) is a double-stranded DNA virus belonging to the herpes virus family (International Committee on Taxonomy of Viruses; ICTV name Human herpesvirus-5). The principle routes of transmission is oral and genital secretion with a seroprevalence of about 40-95%.(1) Transmission of CMV infection can occurs, more commonly, via vertical transmission at birth or after the transfer of seropositive donor organs, bone marrow, or blood products to seronegative recipients.(2) Typical manifestations are due to the result of acute mucosal inflammation caused by CMV infection of the intestine. It disrupts nutrient absorption, leading to diarrhea, bleeding, and abdominal pain. In severe cases, transmural involvement of bowel wall can result in perforation. Colonic perforation is the most common complication and usually occurs in patients with underlying ulcerative colitis.

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CMV infection of the gastrointestinal tract is commonly seen in patients with acquired immunodeficiency syndrome (AIDS) or other immunocompromised conditions and is relatively uncommon in immunocompetent host. This report presents a case of an elderly immunocompetent male patient with extensive involvement of CMV jejunitis, without obvious colonic lesion, causing perforation of the small bowel.

CASE REPORT

In August 2005, a 75-year-old Thai male who was previously healthy, with unremarkable medical history, was admitted to Siriraj Hospital with history of chronic upper abdominal pain, diarrhea or vomiting without fever for 2 months. On physical examination, vital signs appeared normal, abdominal examination was notable for the presence of localized guarding and rebound tenderness at upper and mid abdomen. Initial laboratory investigation was unremarkable. He was diagnosed as "localized peritonitis of unknown etiology" and underwent exploratory laparotomy which revealed adhesion of jejunal loops with omental wall-off, after lysis of adhesion, perforation of the jejunum was seen at the level one foot from ligament of Trize, and therefore, resection of perforated jejunal segment with primary anastomosis was performed. After surgery, he gradually recovered uneventfully and abdominal pain disappeared, fever was absent and no other gastrointestinal symptoms were observed. Surgical wound healed without fistula or abscess. The 57 cm long jejunal loop with attached mesentery was covered by yellow suppurative exudates and fibrosis on serosal surface. The mucosa showed a large deep ulcer measuring 15 cm in length with perforation into mesentery. No tumor mass was noted. The remaining mucosa revealed edematous change. Microscopic examination demonstrated mucosal necrosis and ulcer involving submucosa and muscular propria. Acute suppurative inflammation with granulation tissue was found at base of ulcer. The non-ulcerated mucosa was also infiltrated by acute inflammatory cells. (Figure 1) Endothelial cells in the area of ulcer revealed cytomegalic change with large eosinophilic intranuclear inclusion. These cells were stained positive for CMV antibody by immunoperoxidase. (Figure 2A-B).

After CMV jejunitis was confirmed, intravenous ganciclovir was given for 14 days. No post-operative nor post-treatment complications were observed. The patient had no history of prior blood transfusion and

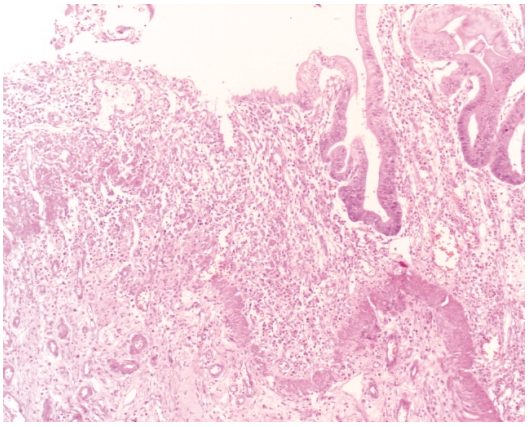

Figure 1 Mucosal necrosis was infiltrated with acute suppurative inflammation.

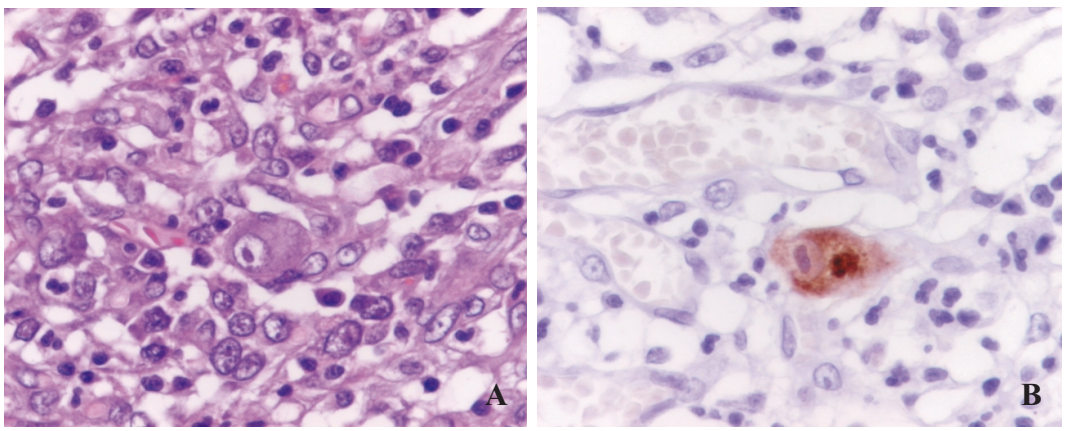

Figure 2 A Endothelial cells have shown cytomegalic change with eosinophilic intranuclear inclusion.
B Immunoperoxidase staining was positive for CMV antibody.

subsequent serologic study was positive for anti-CMV IgG, negative for anti-CMV IgM, negative for anti-HIV, while complete blood count, fasting blood sugar and lipid profiles were also normal. Immunological assessment for determination of CD_4 and CD_8 lymphocytes were also found to be normal. At 6 months post-treatment follow-up, the patient was well and had no other gastrointestinal symptoms suggestive of recurrence of CMV infection.

Discussion and Overview of Gastrointestinal CMV Infection

The patient's presenting complaint was chronic abdominal pain and considered to have probable reactivation of CMV latent infection due to detection of anti-CMV IgG antibody and undetectable of anti-CMV IgM antibody. Diagnosis of CMV jejunitis according to the presence of typical CMV inclusions in endothelial cells from routine histologic examination and subsequently confirmed by immunoperoxidase staining for CMV antigen.

CMV infection of gastrointestinal tract is a well known entity in immunocompromised patients and can cause pathology anywhere starting from esophagus to colon.[3,4] More than 50% of the adult population has acquired CMV antibodies by the fourth decade of life.[5] However, CMV infection in immunocompetent patients may be responsible for significant morbidity and mortality in these individuals. CMV infection of the intestine is most often seen in patients with acquired immunodeficiency syndrome (AIDS), inflammatory bowel disease or those receiving immunosuppressive therapy. Either primary or secondary infection with CMV can occur in an individual, and it is often clinically difficult to differentiate between them. Primary CMV infection is usually asymptomatic or can produce nonspecific symptoms similar to many acute viral illness resembling Epstein-Barr virus mononucleosis syndrome and generally occurs in younger patients who have never been infected with CMV.[1] Primary CMV infection should be consider when a high titer of IgM CMV antibody was detected with an undetectable or low titer IgG of CMV antibody.[6,7] Secondary infection represents an activation of a latent infection or re-infection in a seropositive immuned person and is thought to occur more frequently in elderly persons. CMV can persist indefinitely in host tissue after the first infection and if the patient's immune system subsequently becomes compromised, latent virus can reactivate and cause a variety of syndromes.[6,8] CMV colitis or esophagitis are the second most common sites of infection in immunocompromised patients with AIDS while CMV retinitis is the first most common in these patients.[4,8] In immunocompetent patients, the colon or rectum are the most common sites of infection. CMV jejunitis, as report in this article, is rather rare or uncommon in immunocompetent patients. Perforation of jejunal CMV infection is an even more uncommon condition immunocompetent host.

Gastrointestinal CMV disease should be suspected when gastrointestinal symptoms are suggestive or patients are in the high risk of enteritis (as shown in Table 1).

Diagnostic tests for CMV disease have been reviewed and various methods were suggested. The best method is the direct or indirect demonstration of CMV in pathologic tissue. List of various diagnostic methods are shown in Table 2.

The "gold standard" or definition for establishing the diagnosis of CMV gastrointestinal ùdiseaseû (not for CMV infection only) is the presence of an erosive or ulcerative or tissue with invasive process or inflammatory response in the gut tissue together with the presence of CMV antigens or inclusions shown by means of histologic examination, culture, or antigen

Table 1 Features suggesting possible gastrointestinal CMV disease (Adapted from Goodgame RW)[9]

High-risk patients group
- AIDS patients
- Transplant recipients
- Patients on steroid or other immunosuppressive therapy
- Cancer patients or patients on chemotherapy
- Critically ill and/or elderly patients
Gastrointestinal symptoms
- Odynophagia or dysphagia
- Nausea and vomiting
- Abdominal pain or acute abdomen
- Bloody diarrhea or colitis
- Watery diarrhea
Gastrointestinal lesions
- All ulcerative lesions
- Single or multiple lesions
- Focal or diffuse colitis

Table 2 Methods used to diagnose of gastrointestinal cytomegalovirus disease (Adapted from Goodgame RW)[9]

Acceptable methods
- Histology of pathologic specimen stained with
Hematoxylin and eosin for cytomegalic cells
Immunoperoxidase for CMV antigen
In-situ DNA probe for CMV-DNA
Uncertain methods
- Viral culture from lesions
- Polymerase chain reaction on tissue from lesions
- Culture of blood, urine, stool or oropharynx
- Serum anti-CMV antibody

or DNA detection, in a patient whom other explanations for the lesion have been excluded.

The presence of CMV inclusion bodies indicates active viral replication leading to pathologic lesions. Typical CMV inclusions have "owl's eye" nuclear inclusions and eosinophilic inclusions in the cytoplasm of enlarged cells. Endothelial cells and stromal cells were most commonly infected cell types. (Hence, biopsy should be taken from both the ulcer floor and edge.) It has been suggested that vascular occlusion from the infection of endothelial cells may play a role in the pathogenesis of ulceration, which is frequently associated with CMV infection.[8]

Small bowel involvement by CMV was found at a much lesser extent (about 4%) than the other sites of the gastrointestinal tract.[2] Regardless of the site of involvement, gastrointestinal bleeding, fever, abdominal pain, weight loss, and diarrhea are the common presenting symptoms. CMV enteritis or colitis tends to involve only a single region of the intestine, rather than causing a pan-enteric infectious process (multiple sites of involvement were found in 28-37%).[2,6] In AIDS patients with CMV involvement of small bowel, the most common presenting complaints are abdominal pain (88%), fever (55%), watery diarrhea (44%) and ileum is the most common site of perforation (80%) while the jejunum perforation was found to be less common (20%).[10]

Bowel perforation due to CMV enteritis is a rare event. Up to now, only few cases of CMV-associated ileal perforation in immunocompetent host were reported. This report represents the case of CMV-associated jejunal perforation in immunocompetent host.

The patient presented here is an uncommon case of secondary CMV infection in previously healthy host without any evidence of immunodeficiency conditions. In this case, clearly shown benefit from surgical correction of jejunal perforation but there was still questionable for substantially benefit of antiviral therapy because of rather long duration of 3 weeks delayed in initiation of ganciclovir treatment after surgery. Although antiviral therapy was delayed but this patient still healthy after a long period of follow up for 6 months and neither sign nor symptom of disease recurrence was detected.

CONCLUSION

In conclusion, this illustrative case presents an immunocompetent patient who presented with CMV enterocolitis, although rare in immunocompetent hosts but usually this infection has a good prognosis and should be consider in the differential diagnosis of acute or chronic severe enterocolitis when other causes fail to explain the course of disease.

REFERENCES

1. Cohen J, Powderly WG, (editors). Infectious diseases. 2nd ed. Spain: Elsevier; 2004. p. 2021-41.
2. Chamberlain RS, Atkins S, Saini N, *et al*. Ileal perforation caused by cytomegalovirus infection in a critically ill adult. J Clin Gastroenterol 2000; 30: 432-5.
3. Petrogiannopoulos CL, Kalogeropoulos SG, Dandakis DC, *et al*. Cytomegalovirus enteritis in an immunocompetent host. Chemotherapy 2004; 50: 276-8.
4. Siegel DS, Hamid N, Cunha BA, *et al*. Cytomegalovirus coltitis mimicking ischemic colitis in an immunocompetent host. Heart Lung 2005; 34: 291-4.
5. Eddleston M, Peacock S, Juniper M, *et al*. Severe cytomegalovirus infection in immunocompetent patients. Clin Infect Dis 1997; 24: 52-6.
6. Klauber E, Briski LE, Khatib R, *et al*. Cytomegalovirus colitis in the immunocompetent host: an overview. Scand J Infect Dis 1998; 30: 559-64.
7. Kanno A, Izuma M, Yamada M, *et al*. Cytomegalovirus-induced gastrointestinal disease in previously healthy adult. Dig Dis Sci 1998; 43: 746-8.
8. Patra S, Samal SC, Chacko A, *et al*. Cytomegalovirus infection of the human gastrointestinal tract. J Gastroenterol Hepatol 1999; 14: 973-6.
9. Goodgame RW. Gastrointestinal cytomegalovirus disease. Ann Intern Med 1993; 119: 924-35.
10. Meza AD, Bin-Saagheer S, Zuckerman MJ, *et al*. Ileal perforation due to cytomegalovirus infection. J Natl Med Assoc 1994; 88: 145-8.