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Colon Cytomegalovirus Infection：A Case Report with Rare Endoscopic Presentations

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Abstract

Cytomegalovirus (CMV) infection can occur in severely immunocompromised populations, such as people suffering from acquired immunodeficiency syndrome (AIDS), patients receiving immunosuppressive therapy after transplantation or undergoing chemotherapy for malignanies, and long-term corticosteroid users. CMV frequently occurs in the gastrointestinal tract of such immunocompromised individuals, but only a few of them develop clinically apparent CMV disease. The gold standard of diagnosis for CMV infection is the presence of viral inclusion bodies in infected cells, after the exclusion of other viral, fungal, parasitic, and bacterial infections. CMV colitis results in lesions varying from segmental to extensive mucosal ulcerations. We report a rare endoscopic feature of severe and extensive colitis, resembling pseudo-polyp lesions, observed in a 72-year-old woman with myelomatosis who had suffered from progressive bloody diarrhea and abdominal pain for one month. Histological examination of biopsies from the ulcer bases, stained with hematoxylin and eosin (H&E) and an immunohistochemical stain for anti-CMV monoclonal antibody confirmed the presence of CMV inclusion bodies. The patient expired despite treatment with ganciclovir. (J Intern Med Taiwan 2008; 19: 67- 71)

Key Words：Cytomegalovirus (CMV), Severe gastrointestinal tract infection, Pseudopolyp colonic lesions

Introduction

Infection with cytomegalovirus (CMV) has been reported in immunocompromised patients with acquired immunodeficiency syndrome (AIDS), solid organ transplant recipients on immunosuppressive therapy, and cancer patients receiving chemotherapy [1, 2]. Although CMV can be detected in the gastrointestinal tracts of 30-43 % of the immonocompromised patients, only about 7 % of them develop clinically apparent CMV disease [1]. Early detection of CMV antigen in infected cells by means of monoclonal an-

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tibody E13 provides a sensitive, specific, and rapid test for CMV infections, but this means may not be available in many hospitals [3]. Therefore, a diagnosis of gastrointestinal CMV disease can be confirmed by the presence of the cytomegalic inclusion bodies with immunohistochemical staining [4]. We report a case of pathologically proven CMV colitis in a multiple myeloma patient with symptoms of progressive bloody stool and abdominal pain, and a rare endoscopic feature of severe and extensive colitis resembling pseudo-polyp lesions.

Case Report

This 72-year-old female had a 20 year history of hypertension well-controlled with regular medication. She presented with general bone pain in June 2000, but did not pay it any further attention after symptomatic relief was provided by a non-steroidal anti-inflammatory agent. In February 2001, she began to suffer from chest tightness, shortness of breath, fever and abdominal pain, and was referred from a local hospital in southern Taiwan. Upon entering our hospital, the patient was initially diagnosed with right lower lobe pneumonia and advanced multiple myeloma, stage IIIA (IgG, lambda) light chain. Hematochezia and diffuse abdominal pain occurred 10 days after admission, but the patient was reluctant to undergo colonscopic examination. However, due to intermittent episodes of bloody stool, she finally agreed to a lower gastrointestinal tract (LGI) series examination, which revealed severe irregularity and rigidity of mucosa over the right side and the transverse colon, especially the hepatic flexure (Figure 1). The patient was persuaded to undergo colonscopy, which revelaed nodular, erythematous, and edematous mucosa with mild oozing extending from the prececal area to the splenic flexure, which was compatible with the LGI findings. A rare endoscopic feature of severe and extensive colitis, resembling pseudo-polyp lesions was, observed at the site of the hepatic flexure of the colonic mucosa (Figure 2). Multiple

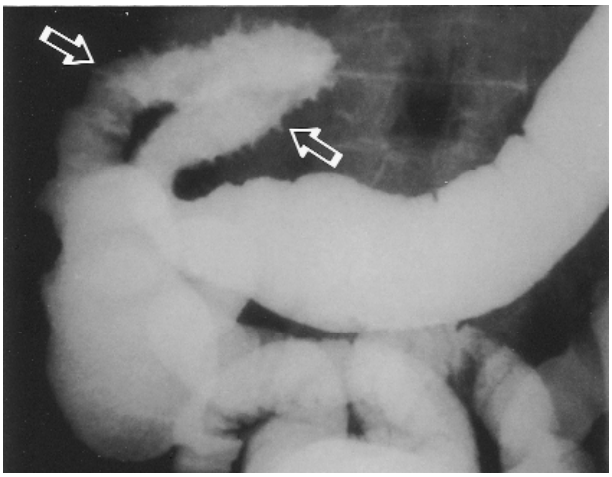

Fig.1. LGI series showing severe irregularity and rigidity of mucosa over the right side and transverse colon, especially in the hepatic flexure (arrowed).

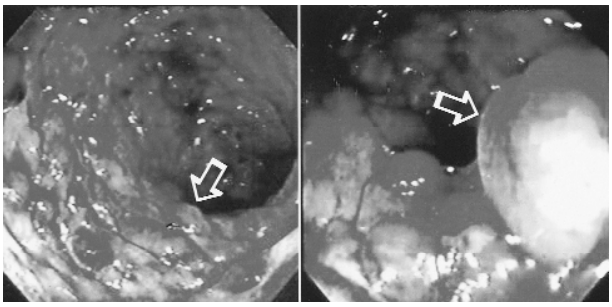

Fig.2. Severe infection of the colon, with extensive nodular surfaces and ulcerations throughout the involved segments resembling an exacerbation of ulcerative colitis, and with rare presentations of pseudo-polyps formation at the hepatic flexure site (arrowed).

biopsies were taken from nodular mucosa to provide sufficient tissue for diagnosis. H&E staining of biopsies revealed the presence of cytomegalic inclusion bodies (Figure 3), and CMV was confirmed by immunohistochemical staining (Figure 4) after exclusion of herpes simplex or other viral, fungal, parasitic, and bacterial infections. A complete blood count showed hemoglobin at 8.4 g/dl, hematocrit at 25.9 %, platelets at 126000/cmm and white blood cells at 5000/cmm (neutrophils, 76.2 %; lymphocytes, 14.5%; monocytes, 7.5 %; basophils, 1.2% and eosinophils, 0.6%). Blood urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, sodium and potassium levels were within normal limits.

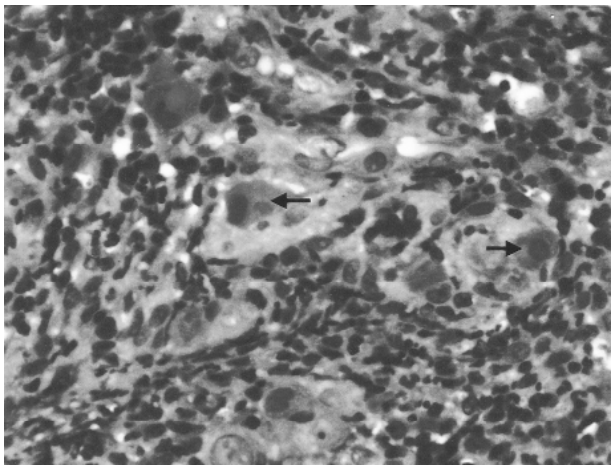

Fig.3. Biopsies from the colonic lesions reveal cytomegalovirus inclusion body, H&E stained (arrowed, original magnification, × 400).

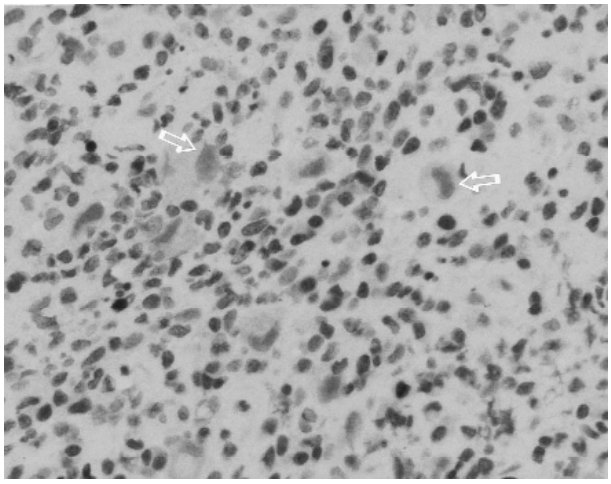

Fig.4. Intra-nuclear inclusion body of CMV in gastrointestinal tract, immunohistochemical staining by anti-CMV monoclonal antibody (arrowed, original magnification, × 400).

The patient received 250 mg ganciclovir intravenously twice daily immediately after diagnosis of CMV infection was confirmed, but the treatment was unfortunately too late. Her condition deteriorated and she expired 2 weeks after beginning treatment.

Discussion

Gastrointestinal CMV infections in Taiwan occur most often among HIV patients[5-7]. However, patients receiving immunosuppressive therapy after transplantation or chemotherapy for malignancies, and long-term corticosteroid users are also at high risk. CMV is a member of the herpes virus family[8]. In immunosuppressed adults, CMV infection can affect the lungs, adrenal glands, liver, and to a lesser extent, the gastrointestinal tract[1]. CMV infection may arise from reactivation of latent infection, or from a new infection in an immunocompromised host[1].

The colon is the most commonly affected region of the gastrointestinal tract, but CMV can involve other regions, such as the esophagus or stomach[8]. The endoscopic morphology of our patient showed extensive nodular surfaces, ulcerations throughout the involved segments resembling an exacerbation of ulcerative colitis, and a presentation of pseudo-polyps formation at the hepatic flexure site (Figure 1). The most commonly encountered colonoscopic features of CMV colitis are multiple ulcers with persistent inflammation and fibrotic changes followed by large, deep ulcers in the colon resulting in lumen stricture. However, presentations of pseudo-polyp formations are rarely mentioned in the literature. Such morphologic presentations suggest imply the severity of the infection producing such peculiar colonic mucosal damage[9,10].

In the American population, the majority of adults have evidence of previous CMV infection, with 53-79 % positive for IgG antibodies[11]. However, IgM antibodies, indicating active CMV infection, are uncommon. The only reliable marker of CMV infection in AIDS patients is the presence of typical viral inclusion bodies, although they may be few in number and atypical in appearance[8]. Among immunocompromised patients who present with gastrointestinal symptoms, CMV disease must be suspected for a successful early diagnosis. Multiple biopsies are necessary to assist in making the pathologic diagnosis. Cytomegalic inclusion bodies may be detected with H&E stain, and confirmed by an immunohistochemical stain, after the exclusion of other viral, fungal, bacterial and parasitic infections.

For immunocompromised individuals, ganciclovir is the choice of treatment for CMV disease,

with a response rate of up to 83 % in gastrointestinal CMV infections [12]. Our patient's poor response to intravenous ganciclovir therapy was probably due to the delayed diagnosis and the severity of the disease. Foscarnet, a virostatic agent reported to advance a rapid resolution of symptoms and healing of ulcers in esophageal disease, is also an effective therapy for CMV disease of the gastrointestinal tract[13]. Reactivation of CMV can occur after a course of treatment, so maintenance therapy is recommended in cases of rapid relapse of CMV esophageal ulceration after the initial treatment [13].

A high level of suspicion for the presence of CMV disease is required when diagnosing immunocompromised patients with gastrointestinal symptoms, and endoscopic biopsies must be taken from all gastrointestinal tract lesions to detect CMV inclusion bodies.

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重度大腸道巨細胞病毒感染：一例罕見之內視鏡所見報告

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摘　要

巨細胞病毒（CMV）感染常發生在嚴重免疫能力缺損的病人。那些後天免疫不全症候群、移植手術後接受免疫抑制治療或惡性腫瘤接受化學治療和長期使用類固醇的病人，皆爲高危險群。巨細胞病毒感染可能存在於病人的胃腸道內，但祇有少數病人會發生臨床上明顯的症狀。感染巨細胞病毒最重要的診斷標準在於排除其它的感染病原如黴菌、其它病毒、寄生蟲和細菌感染後，並在被感染細胞中可發現病毒的包涵體(inclusion body)。我們在此報導了一個72歲的女性多發性骨髓瘤病人，因大量血便，而接受大腸內視鏡檢查，內視鏡發現因爲嚴重大腸發炎而導致彌漫性潰瘍和罕見的僞息肉病灶。從大腸病灶部位取得切片檢體，並以hematoxylin&eosion stain染色和針對巨細胞病毒單株抗體(anti-CMV monoclonal antibody)特別免疫組織化學染色，可以發現巨細胞病毒的包涵體。雖立即於診斷後以ganciclovir治療，但病患臨床症狀仍持續惡化而死亡。