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LETTER TO THE EDITOR

Cytomegalovirus-related neutropenic enterocolitis with negative CMV antigenemia as the initial presentation in an acute myeloid leukemia patient

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Dear Editor,

A 35-year-old gentleman, with the past history of diabetes mellitus for 2 years, was transferred to our hospital in 2007 because of cecal enterocolitis with septic shock and pancytopenia. Fever and right lower quadrant (RLQ) abdominal pain without nausea, vomiting, or diarrhea developed 8 days before admission, and he visited another hospital 3 days after onset of symptoms. Pancytopenia with absolute neutrophil count of 250/mL was detected at that time, and abdominal computed tomography (CT) scan revealed prominent wall thickening with submucosal edematous change in cecum and ascending colon. Although broad-spectrum antibiotics were used for several days, abdominal pain and pancytopenia persisted. So, he was transferred to our hospital.

On admission, the patient was mildly febrile (37.8°C); physical examination showed distended abdomen with a tenderness over RLQ. Laboratory findings disclosed: white blood cell count, 5.0×10^9/l (absolute neutrophil count 300/mL, segment 3%, band 3%, blast 15%, atypical lymphocyte 74%), hemoglobin, 11.5 g/dl; platelet, 44×10^9/l; C-reactive protein, 156.7 mg/l. After bone marrow exam, acute monocytic leukemia (M5b) was diagnosed. Cefepime, metronidazole, and IV fluid support for bowel rest were given for his neutropenic enterocolitis. He received induction chemotherapy with the regimen, idarubicin 12 mg/m^2/day for 3 days, and cytarabine 100 mg m^{-2} day^{-1} for 7 days. However, fever, abdominal pain, and RLQ tenderness with abdominal fullness persisted even after white blood cell count recovered from nadir. There was no diarrhea or bloody stool during the course. Blood cultures, urinalysis, and stool cultures all yielded negative results. Serology test was negative for anti-HIV. Abdominal CT scan was repeated and revealed thickening of cecal wall with peri-colic inflammation. Because typhlitis with ileus persisted under conservative treatment, he underwent right hemicolectomy. Histological examination of the cecum showed: (1) ulceration and necrotic debris over the mucosal wall of cecum; (2) some enlarged cells with eosinophilic nuclear inclusions (Fig 1.) which were positive for cytomegalovirus (CMV) stain by CMV monoclonal antibody (clone CMV 01, Neomarkers; Fig. 2). The diagnosis of typhlitis with CMV infection was made. CMV-pp65 antigenemia assay, as determined by immunofluorescence, was negative. Three weeks of Ganciclovir was added. No more fever or abdominal pain was noted after operation, and the patient recovered gradually with normal oral intake.

Neutropenic enterocolitis or typhlitis is a clinical syndrome in neutropenic patients characterized by fever and abdominal pain. It was originally described in children following induction chemotherapy for acute leukemia [1] and subsequently reported in both adults and children with a variety of hematologic and solid malignancy, in patients with acquired immunodeficiency syndrome, and as a complication of bone marrow transplantation [2]. The development of typhlitis has historically been attributed to a variety of chemotherapeutic regimens. Mucosal injury caused by cytotoxic drugs combined with neutropenia and impaired host defense to intestinal organism leads to the occurrence of typhlitis [3]. However, in this patient, neutropenic enterocolitis is the initial presentation of acute leukemia before treatment of any chemotherapeutic agents

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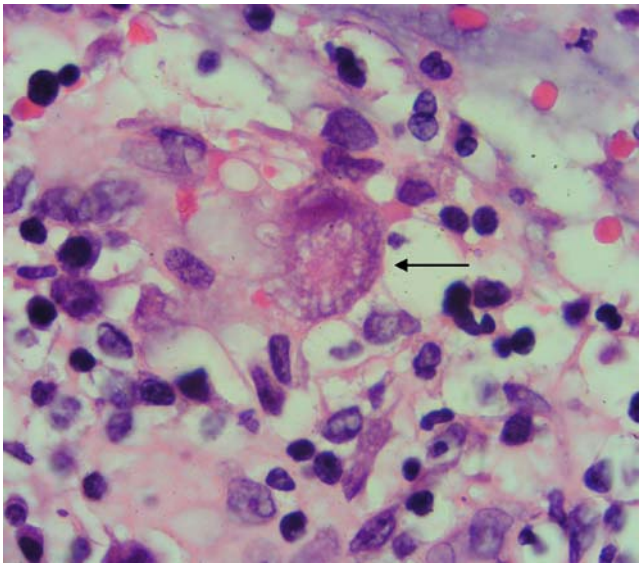

Fig. 1 Histology of cecum showing several enlarged cells with eosinophilic nuclear inclusion bodies typical of cytomegalovirus (*arrow*). Hematoxylin and eosin, magnification ×400

for leukemia. Similar cases with acute leukemia developing neutropenic enterocolitis before induction or maintenance of chemotherapeutic agents are not common but had been reported, suggesting that chemotherapy could be one of the predisposing factors; it is not an essential in the genesis of neutropenic enterocolitis [4].

CMV infection in gastrointestinal tract is most often seen in patients with the acquired immunodeficiency syndrome, inflammatory bowel disease, or those receiving immunosuppressive therapy for transplantation. It is also reported after chemotherapy for lymphoma and small cell lung cancer [5, 6] and only rarely in patients without any underlying diseases. There was only one case report of a patient with myelodysplasic syndrome developing segmentary cecal CMV colitis after induction chemotherapy with fludarabine, cytarabine, and mitoxantrone [7]. The authors attributed the etiology of CMV colitis to the fludarabine-induced CD4 lymphocyte depletion. In this case, no remarkable past history is noted, except the diabetes mellitus which may contribute to the occurrence of CMV colitis. Although the role of CMV as a primary pathogen of typhlitis in this patient is disputed, we describe the rare case of neutropenic enterocolitis associated with tissue-proven CMV infection as the initial presentation of disease. CMV colitis often presented with symptoms of watery or bloody diarrhea, abdominal pain with cramps, and fever. No other common presentations of CMV colitis, such as watery or bloody diarrhea, were noted in this patient except abdominal pain. The diagnosis of CMV colitis can be established by endoscopic findings, demonstrating CMV inclusion bodies or positive immunohistochemistry with monoclonal antibodies directed against CMV on specimens, CMV culture, or by demonstration of CMV DNA [8].

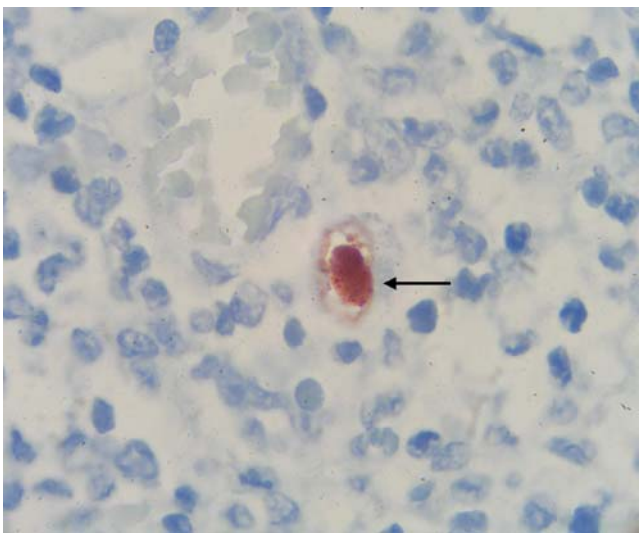

Fig. 2 Histopathology showing cells positive for nuclear immunostaining of the CMV Ag (*arrow*)

In conclusion, according to our case, neutropenic enterocolitis could develop before any chemotherapy for acute leukemia. The CMV-related enterocolitis should also be considered as the differential diagnosis in patients with typhlitis, especially in those resistant to supportive treatments and use of broad-spectrum antibiotics.

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