Toxic megacolon: remember cytomegalovirus

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CASE REPORT

A 63-year-old female retired clerical officer was admitted with a 1-week history of profuse diarrhoea. The patient had been diagnosed with non-Hodgkin's lymphoma 4 years previously, and a human immunodeficiency virus (HIV) test at that time was negative. She had received two regimens of chemotherapy, and had been in remission for 3 months with a normal leukocyte count. The diarrhoea was watery with no blood or mucus, and associated with mild nausea and diffuse left-sided abdominal pain relieved by defaecation. The patient had a mild pyrexia and scanty bowel sounds, but the abdomen was not distended. Full blood count and full biochemistry were normal apart from the white cell count (13.8×10^9/litre — predominantly neutrophils and monocytes). Initial blood cultures and routine viral serology were negative, but the latter was never repeated. Stool samples were negative for bacteria, parasites and toxins.

One week into the admission, the patient developed toxic megacolon. Computed tomography scan showed non-specific colitis with no evidence of lymphoma relapse. Soluble contrast enema revealed no mechanical obstruction. Fibreoptic sigmoidoscopy showed non-specific inflammation of colonic mucosa, with no organisms on routine microbiology. A single stool sample revealed *Clostridium difficile* toxin, and intravenous vancomycin was administered for 14 days, with partial clinical improvement. However, the diarrhoea and megacolon recurred dramatically, and the patient developed atrial fibrillation. At laparotomy, multiple perforations of dilated toxic colon had been walled off by small bowel, stomach and pancreas, with no evidence of lymphoma. A subtotal colectomy, small bowel resection, sleeve gastrectomy and partial pancreatectomy was performed. The patient died from sepsis and multiorgan failure 1 week later. Histopathology from the resected specimen showed severe colitis of indeterminate type, and immunohistochemistry obtained postmortem revealed cytomegaloviral colitis (*Figure 1*).

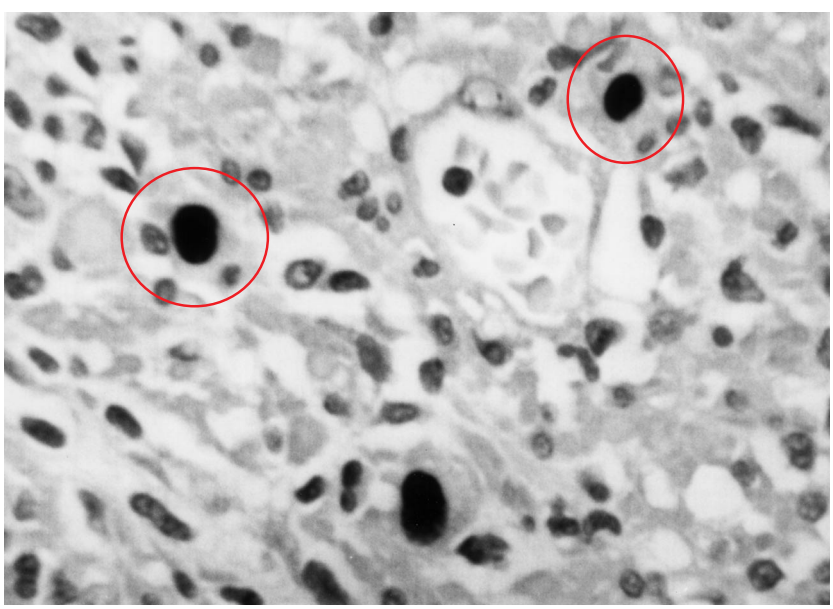

Figure 1. Immunocytochemistry (x350 overall magnification) from colon specimen resected from this patient showing three cytomegalovirus-positive cells (circled).

INTRODUCTION

This article reports a fatal case of toxic megacolon caused by cytomegaloviral colitis in a patient with non-Hodgkin's lymphoma in remission. This treatable condition must be considered early in any patient with bloody diarrhoea, including those without obvious evidence of immunocompromise.

DISCUSSION

Human cytomegalovirus (HCMV) is a highly species-specific herpesvirus spread by person–person contact, blood transfusion or tissue transplantation. It is well known that in the context of significant immunocompromise, especially human immunodeficiency virus (HIV) infection and organ transplantation, HCMV colitis is a potentially life-threatening disease. In healthy people, HCMV colitis can occur subclinically or cause mild diarrhoea, and is considered self-limiting. However, reports suggest that this disease can cause local complications such as fistulas and strictures in patients without immunocompromise (Ng et al, 1999), and may be fulminant in immunocompetent patients with comorbidity (van Wijk et al, 1997; Grimsehl et al, 1999).

HCMV colitis presents with diarrhoea, vomiting and abdominal pain. Bloody diarrhoea is characteristic, but not an absolute prerequisite to consideration of the diagnosis. HCMV immunoglobulin (Ig) G antibodies are

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present in 40–100% of healthy adults in developed countries (de Jong et al, 1998), and a rise in this titre or the appearance of IgM antibodies in seronegative individuals represents reactivation/primary infection respectively.

Alternatively, active viraemia can be detected by the demonstration of high levels of the virus in blood buffy coat cells/urine or HCMV DNA in plasma. Lower levels may be attributed to carrier status, but are significant in the immunocompromised.

Plain radiographs and computed tomography scans show non-specific colitis, often with colonic wall thickening and mural ulceration (Murray et al, 1995). Full colonoscopy with right-sided biopsies are preferable to sigmoidoscopy in the absence of colonic dilatation (Combes et al, 1995).

Clinical and endoscopic appearances may suggest pseudomembranous colitis; indeed both types of colitis may coexist and stool sample results may thus act as a 'red herring' as in this case. Definitive diagnosis is often by histopathology of biopsy samples, showing characteristic intranuclear viral inclusion bodies which give 'owl's eye' appearances, and may also show non-caseating granulomas in patients with active cell-mediated immunity.

Antiviral treatment with intravenous gancyclovir should be commenced immediately in any patient in whom HCMV colitis is suspected. This is usually effective even in significant immunocompromise and during chemotherapy (Oshima et al, 1999). In patients with progressive colitis, HCMV hyperimmune globulin may be added, or other antivirals such as foscarnet or cidofovir substituted, but toxic megacolon at risk of perforation merits urgent colectomy.

The prognosis in the immunocompetent is favourable, except in the presence of significant comorbidity (Marts et al, 1994; Grimsehl et al, 1999). **HM**

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