

CMV Colitis Masquerading As Colon Cancer - An Unusual Presentation Of Acquired Immunodeficiency Syndrome

P K H Chow, J M S Ho, A E Ling, H S Goh

ABSTRACT

We present a case-report of a patient with a typical history and a barium enema study diagnostic of right-sided colonic cancer. Laparotomy and right hemicolectomy was carried out. Histological examination revealed Cytomegalovirus (CMV) colitis and the patient was subsequently tested positive for Human Immunodeficiency Virus (HIV).

Gastrointestinal symptoms are common in patients with Acquired Immune Deficiency Syndrome (AIDS) and up to 10% of all AIDS patients have CMV colitis. The diagnostic criteria for CMV colitis is reviewed. AIDS is likely to become more common and we stress the awareness of this condition as well as the need for preoperative colonoscopy and histological diagnosis in patients with radiological diagnosis of colorectal carcinoma.

Keywords: CMV colitis, AIDS, colorectal cancer, colonoscopy

INTRODUCTION

Cytomegalovirus (CMV) is an ubiquitous beta herpesvirus which usually causes subclinical infections in children and young adults. The virus is then carried for life but remains latent. When there is compromise of T-lymphocyte mediated immunity as seen in organ transplantation, lymphoid neoplasia and Acquired Immunodeficiency Syndrome (AIDS), CMV reactivation syndromes can develop. These manifest as retinitis, gastroenteritis or fulminant disseminated disease. In HIV infection, CMV reactivation syndromes usually appear late at the advanced stage of the disease.

While CMV infection is common in the general population, gastrointestinal CMV involvement is, with few exceptions, found almost exclusively in compromised hosts and may involve any part of the gut from oesophagus to rectum⁽¹⁾. The colon is the most common site of involvement and as many as 10% of AIDS patients have CMV colitis^(2,3). Such patients present with severe, intractable diarrhoea, weight loss, fever, and rectal bleeding or melaena or with complications of the colitis such as bleeding or perforation⁽⁴⁾.

We present a case-report of CMV colitis masquerading as caecal cancer which led to the diagnosis of AIDS.

CASE REPORT

A 46-year-old hawker presented with a one-month history of abdominal discomfort and change of bowel habits in the form of intermittent constipation and watery diarrhoea. There was occasional fresh bleeding per rectum. He also complained of loss of weight of about 10 kg over the same period of time. Clinical examination was normal and a barium enema showed a constant narrowing in the caecum suggestive of cancer (Fig 1).

The patient had a laparotomy and right hemicolectomy was performed. On cutting open the specimen, the caecum

and ascending colon showed multiple tiny ulcers each about 0.2 to 0.3 cm in diameter. There was no evidence of perforation of the ulcers and the intervening mucosa was markedly oedematous, resulting in an overall narrowing of the lumen. The ileocaecal valve was also congested with tiny ulcers measuring 0.2 cm in diameter. There was no evidence of diverticular disease. The patient made an uneventful post-operative recovery and was discharged five days after his surgery.

Histological examination of the resected specimen showed that the ulcers were superficial, involving mucosa and submucosa only (Fig 2). Scattered amidst the inflammatory cellular infiltrate at the ulcer bases and the lining blood vessels were cells with enlarged nuclei containing prominent basophilic inclusions (Fig 3 and 4).

Immunoperoxidase stains for cytomegalovirus showed marked positivity in these cells, confirming the presence of cytomegalovirus infection. The mucosa adjacent to the areas of ulceration showed granular atrophy suggesting ischaemic changes. There was no evidence of malignancy in the specimen.

The patient readmitted himself a few weeks later for bleeding and painful piles for which haemorrhoidectomy was carried out. He was found to have proctitis with oedematous rectal mucosa and contact bleeding.

HIV infection was suspected when CMV colitis was diagnosed. On closer questioning, the patient gave a history

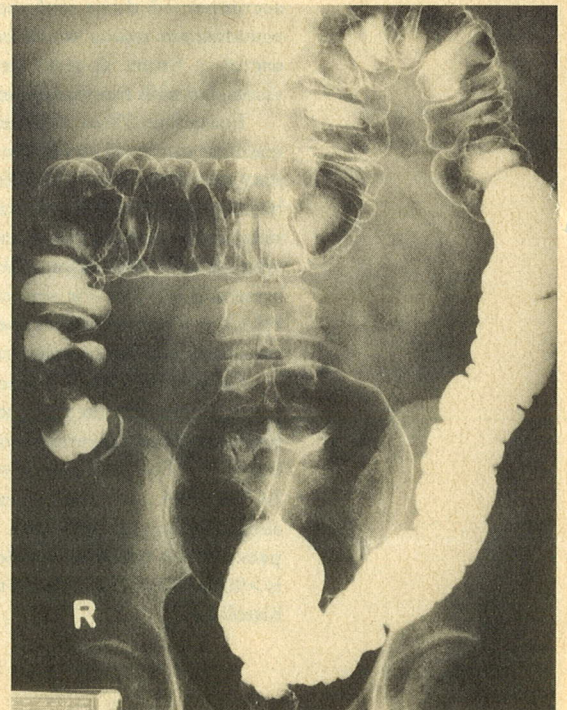


Fig 1

Department of
Colorectal Surgery
Singapore General Hospital
Outram Road
Singapore 169608

P K H Chow, MBBS,
M Med (Surg), FRCS (Edin)
Registrar

Department of Pathology
Singapore General Hospital

J M S Ho, MBBS, MRCPATH
Senior Consultant

A E Ling, MBBS, FRCPA
Consultant Virologist

Gleneagles Medical Centre
6 Napier Road #04-08
Singapore 258499

H S Goh, BSc, MBBS, FRCS
Consultant

Correspondence to:
Dr P K H Chow

Department of General Surgery
Singapore General Hospital

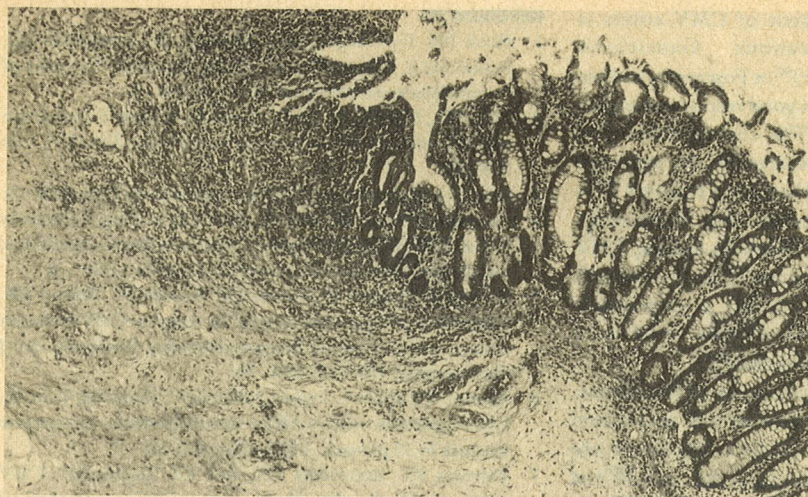


Fig 2

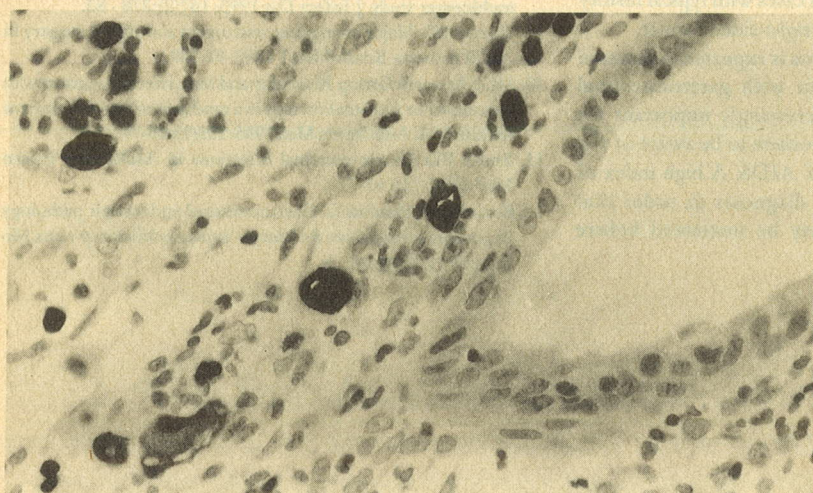


Fig 3

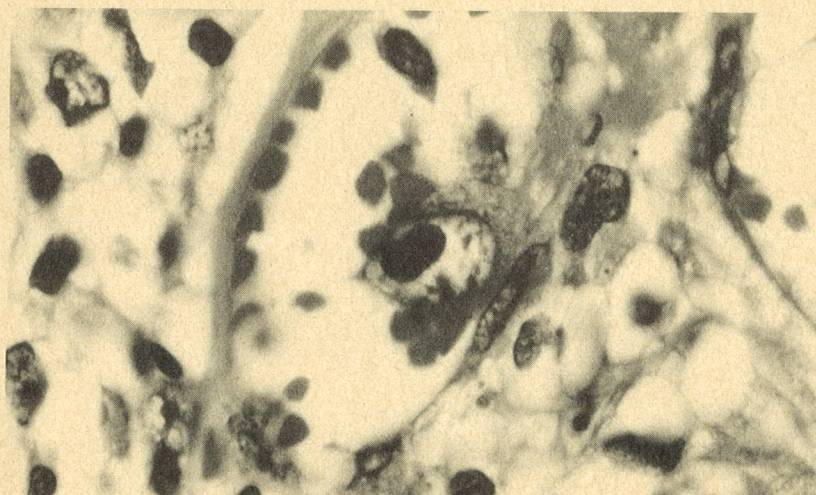


Fig 4

of multiple unprotected sexual exposure with prostitutes. At both admissions, clinical examination was normal with no evidence of adenopathy nor hepatosplenomegaly. Chest X-ray was normal.

The patient was subjected to full haematological and serological examination. These showed a leucocyte count of $3.38 \times 10^9/L$ with a differential count of 47% polymorphonuclear cells, 34% lymphocytes and 12% monocytes. Haemoglobin was 9.8g/dL and platelet count was $190 \times 10^9/L$. Peripheral blood film was normal. Liver function tests were normal with no increase in the levels of serum aminotransferases. CMV antibody level using complement fixation methods was 64.

Circulating lymphocyte subpopulation counts showed TCD_4 at 13.4% (26.6 - 37.0) and TCD_8 at 55.0% (16.3 - 27.1), with absolute counts of TCD_4 at 129 cells/UL (342 - 929) and TCD_8 at 529 cells/UL (103 - 717). CD_4/CD_8 ratio was 0.2 (1.0 - 2.2). The patient's HIV status was determined by a positive enzyme immunoassay (EIA) for HIV antibodies (Abbot, 3rd generation EIA), and confirmed by Western Blot (Genelabs Diagnostic, Singapore).

The patient has been informed of his HIV status and has been referred to the Communicable Disease Centre for counselling and further management.

DISCUSSION

Cytomegalovirus colitis is one of the most common and potentially serious opportunistic pathogens of the gastrointestinal tract in AIDS patients. It reportedly affects up to 10% of all AIDS patients^(2,3). Virtually all organs of the alimentary tract are susceptible to CMV disease. The most common manifestation of enteric cytomegalovirus disease is colitis and this usually presents with severe, intractable diarrhoea, weight loss, fever, and rectal bleeding or melaena⁽⁴⁾. The presentation is therefore non-specific and common to many other gastrointestinal conditions.

The underlying pathology is believed to be a CMV-induced endothelial vasculitis that results in ischaemia and possibly transmural infarction. Patients with CMV colitis may also present with complications of the colitis, namely bleeding, perforation and necrotising colitis requiring emergency laprotomy and resection. The prognosis in this case becomes grave.

Diagnosis is by endoscopy which shows submucosal haemorrhage and diffuse mucosal ulceration⁽⁵⁾. Endoscopic findings are however non-pathognomonic and gross lesions ranging from erythematous patches to deep and wide coalescing ulcers may be found. The absence of endoscopic ulcerative lesions however has a 98% negative predictive value⁽⁶⁾. Multiple endoscopic biopsies should be carried out as the disease is multifocal and the biopsy specimen should be sent for viral culture of CMV, antigen assay and histopathology for intranuclear CMV inclusions. Biopsies from the caecum are more likely to be diagnostic⁽⁷⁾. Most authorities diagnose CMV associated gastrointestinal disease when the biopsy specimen shows cytomegalic inclusion cells with surrounding inflammation.

Barium enema is non-definitive as CMV colitis mimicks other forms of colitis⁽⁴⁾. The barium enema may be normal. CMV colitis simulating carcinoma has not been previously reported in the literature.

When diagnosed, management of CMV colitis is primarily medical. Intravenous Ganciclovir (dihydroxypropoxymethyl guanine)⁽⁹⁾ or Foscarnet (sodium phosphonoformate) are used with good response rates but are not without side-effects⁽⁹⁾. The clinical efficacy of intravenous Ganciclovir and Foscarnet for the treatment of CMV colitis is fairly similar. Most trials reported 57% to 75% improvement rate with either drug. These drugs could lead to the elimination of ulcerative lesions, CMV intranuclear lesions and CMV culture from the colon⁽⁶⁾. Although these drugs have shown a reasonable improvement rate for treatment, its role as life-long suppressive agents for colitis is uncertain⁽¹⁰⁾.

Surgery is indicated for complications of the disease. Mortality is high when complications such as perforation or necrotising colitis occur as these patients are immunocompromised. Post-operative mortality of 28% at day one and 71% by one month has been reported⁽¹¹⁾.

In this patient, preoperative colonoscopy could have diagnosed the CMV colitis. With increasing incidence of HIV infection and CMV colitis, there is a greater need for colonoscopic examination even in cases with typical history and barium enema diagnostic of right-sided cancer.

The incidence of AIDS patients is expected to increase and many of them will present with gastrointestinal symptoms⁽¹²⁾. It will become increasingly important for surgeons and other health-care workers to be aware of the gastrointestinal manifestations of AIDS. A high index of suspicion is required for early diagnosis in order that appropriate early treatment may be instituted before complications develop.

REFERENCES

1. Hirsh MS. Cytomegalovirus infection. In: Isselbacher KJ, Braunwald E, Wilson JD et al, editors. *Harrison's Principles of Internal Medicine*. McGraw Hill, 1994:794 - 6.
2. Drew WL, Mint XL, Miner RC, Sands M, Ketterer B. Prevalence of CMV infection in homosexual men. *J Infect Dis* 1981; 143: 188 - 92.
3. Sohn N. In the rectum in AIDS. *Pract Gastroenterol* 1988; 12:50 - 60.
4. Frager DM, Frager JD, Wolf EL, Rand LG, St. Onge G, Mitsudo S, et al. CMV colitis in Acquired Immunodeficiency Syndrome: radiological spectrum. *Gastroent Radio* 1986; 11:241 - 6.
5. Culpepper-Morgan JA, Kotler DP, Scholes JV, Tierney AR. Evaluation of diagnostic criteria for mucosal CMV inclusion disease in the Acquired Immunodeficiency Syndrome. *Am J Gastroenterol* 1987; 82:1264 - 70.
6. Mentec H, Lepout C, Lepout J, Marche C, Harzic M, Vilde JL. Cytomegalovirus colitis in HIV-1 infected patients: a prospective research in 55 patients. *AIDS* 1994; 8(4):461 - 7.
7. Hinnant KL, Rotterdam HZ, Bell ET, Tapper ML. CMV infection of the alimentary tract: a clinico pathological correlation. *Am J Gastroenterol* 1986; 81:73 - 88.
8. Dieterich DT, Kotler DP, Busch DF, Crumpacker, Du Mond C, Dearmand B. Ganciclovir treatment of cytomegalovirus colitis in AIDS: a randomised, double-blind, placebo controlled multicenter study. *J Infect Dis* 1993; 167(2):278 - 82.
9. Wexner SD. Major emergency and urgent abdominal surgery in AIDS patients. *South Med J* 1988; 81:589.
10. AIDS Research Group. Morbidity and toxic effects associated with ganciclovir or foscarnet therapy in a randomised cytomegalovirus retinitis trial. *Arch Intern Med* 1995; 155(1): 65-74.
11. Smith PD. Gastrointestinal infections in AIDS. *Ann Intern Med* 1992; 116 63-77.
12. Bonacini M, Skodras G. Gastrointestinal endoscopic pathology in patients seropositive for human immunodeficiency virus. *Mo Med* 1993; 90(2):85 - 9.