CASE REPORT

Large bowel perforation secondary to CMV colitis: an unusual primary presentation of HIV infection

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SUMMARY

We report a case of HIV-associated *Cytomegalovirus* colitis complicated by large bowel perforation. A 62-year-old man of same-sex relationship was not known to have HIV, but a diagnosis of inflammatory bowel disease was made early in his admission, with steroid treatment initiated. He was later confirmed to be HIV positive, and found to have multiple microperforations of the bowel necessitating ileocecectomy and Hartmann's procedures.

BACKGROUND

This case illustrates how *Cytomegalovirus* (CMV) colitis can manifest with symptoms and signs mimicking inflammatory bowel disease (IBD). Histological findings may reveal CMV inclusions if supplementary testing is requested, which can aid diagnosis. However, this is not routinely performed. Misdiagnosis can prove detrimental to patient care due to variances in treatment.

An estimated 26% of people with HIV remain undiagnosed. Studies suggest that nearly 50% of HIV cases are confirmed late resulting in delays to antiretroviral treatment.¹ This case illustrates how HIV infection should be considered in this cohort of patients within primary care. Early confirmation reduces the risk of complications.

Repeat HIV testing is indicated in individuals who have previously tested negative but have continued risks of exposure, men who have sex with men (MSM), patients with a history of intravenous drug use and in antenatal care.²

CASE PRESENTATION

A 62-year-old man of same-sex relationship first presented to his general practitioner with arthralgia primarily affecting the hip and ankle joints. He was originally diagnosed with osteoarthritis. He then developed a constellation of symptoms that included: persistent bloody diarrhoea with faecal incontinence, bloating, dyschezia, significant weight loss and stomatitis.

One week prior to his acute admission, he had attended a gastroenterology clinic where coeliac screens had proved negative, and arrangements were made for further investigation with gastroscopy and colonoscopy.

Over the course of the 2 months prior to his acute admission, he had been started on multiple medications for his symptoms including loperamide, lactulose, mebeverine and anal steroid creams. Despite these medications, there had been no improvement to his symptoms.

This man had a history of hypertension, hypercholesterolaemia and asthma. He was an ex-smoker with no relevant family history of illness.

He was admitted to hospital having collapsed while using the toilet. On general inspection the patient looked cachectic and unwell, with clinical signs of anaemia. Cardiovascular examination was unremarkable. Respiratory assessment revealed sparse crackles in the left lung base. On examination of the abdomen, there was generalised tenderness in the absence of guarding and bowel sounds were normal. Rectal examination was not performed.

His admission observations (pulse 95, blood pressure 120/60 mm Hg, respiratory rate 14 breaths/min, temperature 36.8°C) were within normal limits.

The patient's blood tests on admission revealed severe microcytic anaemia (haemoglobin (Hb) 88 g/L, mean corpuscular volume 63.5 fL), moderate hyponatraemia (126 mmol/L), thrombocytosis ($1141 \times 10^9/L$) and mildly raised white cell count ($12.2 \times 10^9/L$).

A sexual history was taken in the acute medical unit (AMU), revealing that this man was in an open relationship, with multiple recent partners. Consent was obtained for an HIV test.

Urgent sigmoidoscopy was performed the day following his arrival. This revealed severe colitis from the anus to sigmoid and beyond, leading to a diagnosis of 'probable IBD' (figure 1). He was started on intravenous hydrocortisone and asacol. Four biopsies from the sigmoid and two from the anus were taken. Histology was reported a day later: 'clinically, if infection can be ruled out, the features are suggestive of IBD'.

The day following this histology report, preliminary HIV tests returned positive. A decision was made not to inform the patient of these initial results until further tests confirmed the diagnosis, unless his condition deteriorated and became life-threatening.

The patient was promptly reviewed by the consultant for infectious disease. They determined that a diagnosis of infective colitis had to be considered but that the patient should remain on hydrocortisone. Investigations for Lymphogranuloma venereum (LGV) serology and CMV studies—these included serology testing and PCR of the blood—were requested. Following examination, the patient was treated for oesophageal candidiasis and possible hairy leukoplakia, although the lateral margins of the tongue could not be fully visualised to confirm this. Funduscopy was unavailable.

Concerns were later expressed that the recently initiated steroids could be blinding more ominous abdominal symptoms. An abdominal X-ray revealed

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Figure 1 Thickening to descending colon and associated extraluminal gas, in keeping with contained perforation.

multiple dilated large bowel loops with no abnormality shown on the chest X-ray. CT scan was requested, revealing a 'contained perforation at the splenic flexure, with collection of mostly gas and a small amount of fluid' (figure 2). Findings were in keeping with sigmoid colitis. No immediate surgical intervention was required, with medical management considered appropriate.

Following deterioration in the patient's clinical state, an erect chest X-ray was requested. This found 'significant free gas under the right hemidiaphragm'. This prompted immediate surgical review and intervention.

DIFFERENTIAL DIAGNOSIS

1. IBD
2. Bowel malignancy
3. Infective colitis
4. Diverticulitis

TREATMENT

A laparotomy was performed. The splenic flexure was mobilised to free the perforation. Numerous microperforations of the transverse and descending colon were discovered. The surgical team proceeded to undertake both ileocecectomy and Hartmann's procedures.

Histology of the resected bowel described features as those of 'IBD favouring a Crohn's colitis'. Supplementary reporting from immunostaining for CMV revealed 'areas of ulceration showing

Figure 2 Sigmoidoscopy performed on this patient revealed a cobblestone appearance, initially suggestive of a Crohn's colitis.

positive nuclear staining in some cells, suggestive of CMV infection'. PCR testing was also performed on a 10 cm section of the resected bowel. Two of the three samples taken tested positive for CMV.

Both CMV serology (IgG positive) and PCR blood testing (17 288 IU/mL) confirmed a diagnosis of CMV. Further HIV testing revealed an absolute CD4 count of 142 cells/ μ L. Treatment for CMV was continued with ganciclovir. Fluconazole was used to treat oesophageal candidiasis. Antiretroviral agent Triumeq (50 mg dolutegravir sodium/600 mg abacavir sulfate/300 mg lamivudine) was started following assessment by an infectious diseases consultant.

Following surgery, several postoperative complications ensued.

Regular drops in Hb were treated with repeated blood transfusions. No identifiable cause was established despite extensive investigations. Omeprazole and tranexamic acid were added to the patient's drug regimen.

Prior to planned discharge, the patient experienced midline wound discharge with accompanying signs indicative of intra-abdominal sepsis. CT scan discovered 'multiple walled off intraperitoneal collections' but 'no detectable fistula'. Tazocin and vancomycin were used to treat Gram-positive cocci and Gram-negative bacilli infection.

The patient was eventually discharged home, more than 2 months after his arrival. He has since made full recovery, with regular outpatient follow-up in the colorectal clinic.

DISCUSSION

Most instances of CMV disease in HIV-positive patients occur in the setting of advanced immunosuppression associated with CD4 count <50 cells/ μ L.³ The most commonly affected site is the colon (47%). Duodenum (21.7%), stomach (17.4%), oesophagus (8.7%) and rarely small bowel (4.3%) are all susceptible. Patients with CD4 count <50 cells/ μ L are considered at the highest risk of life-threatening complications, of which gastrointestinal tract bleeding and colon perforation are the most common.⁴

Very few studies reference the similarities in presentation between CMV colitis and IBD. In one such paper, the difficulty in establishing CMV colitis with certainty is acknowledged—with histological findings of CMV inclusions in tissue samples supporting the diagnosis.⁵ Similar difficulties were encountered with this individual. His initial management focused on a suspected diagnosis of ulcerative colitis.

Figure 3 Cytomegalovirus inclusion body (marked with an arrow). Note that the cell is large with a clear halo around the nucleus and appears like an 'owl's eye'.

Review of the literature suggests CMV colitis remains a diagnostic challenge.^{6–9} PCR of colonic tissue and immunostaining are considered the two most effective means of diagnosis. The latter typically reveals basophilic intranuclear inclusions (figure 3).¹⁰ However, multiple biopsies are often required to confirm diagnosis, as viral inclusions are most frequently found within endothelial cells located in the deeper layers of the bowel. Recent literature suggests that neither serological studies nor cultures of biopsy are essential in making a diagnosis. Viral culture was previously the gold standard, though results take several weeks to return. Neither blood PCR nor serological tests are able to differentiate between past and current infection.^{5 11}

BHIVA guidelines identify several clinical indicators that necessitate HIV testing. Gastroenterological indicators include 'chronic diarrhoea of unknown cause', 'oral candidiasis' and 'weight loss of unknown cause'—all of which this man had been suffering from. However, BHIVA makes no reference to the role of HIV testing in patients who are about to start immunosuppression treatment. We have seen in this case how significant the consequences of immunosuppression can be in a HIV-positive patient. The European Crohn's and Colitis Organisation (ECCO) state in their guidelines that in all adolescent and adult patients with IBD testing for HIV 'should always precede commencement of immunomodulator therapy'.¹²

Patient's perspective

- ▶ I was told following initial tests that I had a severely inflamed lower bowel, and that it would have to be surgically removed and...a colostomy bag fitted. This was quite unexpected, and rather frightening, as it was about to have quite an impact on my future lifestyle, and also possible physical attributes. But not to be outdone by fate's little quirks, just before I was due to go into surgery, I was visited by two (specialist) nurses who informed me...I was HIV positive. I had always been mindful of unprotected sexual activity, and the 'it won't happen to me' mentality. The combination of both sets of news was for me absolutely devastating, and really depressing.
- ▶ The one thing I have since thought about was why did the nurses...deem it necessary to break the news about my HIV status at that point in time, and not leave it until after my operation...which would have caused me far less stress and worry, when I was obviously very ill and at such a low point?
- ▶ After the initial operation I had some internal bleeding which required further investigation, at which time I (and my partner) was told that...that there was the possibility of death. However, the bleeding did stop, and I have since been discharged. I have gained weight and physical strength, and more importantly, I have mentally returned to being the belligerent b*****d as what I was before.
- ▶ I have always been a strong character, both physically and mentally, and I believe both these factors have helped me through the situation.
- ▶ I am very grateful for the efforts of all the medical staff who had to put up with me during my stay.

Learning points

- ▶ CMV colitis shares many similarities in clinical presentation and histological analysis with inflammatory bowel disease. Always consider this as a differential, particularly where risk factors for immunocompromise exist (figure 2).
- ▶ If infective colitis secondary to CMV is being considered as a diagnosis, immunostaining for CMV inclusion bodies should be requested alongside any routine histology (figure 3). This, in addition to PCR of colonic tissue, is considered the most effective investigation to diagnose CMV colitis.^{5 11}
- ▶ In undiagnosed cases of acute diarrhoea with negative stool cultures, referral should be made to secondary care. Endoscopy may be required.¹³
- ▶ This patient's reflection raises an interesting ethical dilemma. Is life-threatening illness enough to warrant breaking bad news at such a critical time in someone's care?
- ▶ The majority of services across the UK expected to apply BHIVA recommendations for HIV testing will have a low prevalence of HIV within their local populations. For regions such as the Fylde Coast, the number of men who have sex with men, intravenous drug users and other at-risk groups is comparatively higher. Such areas may benefit from a more focused set of guidelines.²

Contributors DRB was involved in the acute care of this patient working as an FY1 on medical nights, and subsequently followed up this patient's outcome to compile the case study. DRB and ST provided an acute medicine input and slant, with advice on the most relevant and applicable information from the case. HV selected appropriate images taken during the patient's admission, detailing the findings shown. PI reviewed the final stages of the case report to ensure that necessary information had not been missed and that all key learning points were covered. This was particularly useful given that this patient had resided on PI's ward during their stay.

Competing interests None declared.

Patient consent Obtained.

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