Reminder of important clinical lesson

Lymphogranuloma venereum and HIV infection: misdiagnosed as Crohn's disease

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Summary

The report describes a young Caucasian homosexual man who presented with a 4-month history of bloody diarrhoea and weight loss. Over the next 4 months he was investigated for inflammatory bowel disease and subsequently started on mesalazine and prednisolone as an outpatient. Within a month of starting treatment his symptoms worsened, leading to his self-referral to the genitourinary medicine clinic. The patient was subsequently diagnosed with advanced HIV infection and lymphogranuloma venereum infection. The patient was treated with doxycycline for 3 weeks and started on antiretrovirals. One month later the patient is symptom free with a recovering immune system.

BACKGROUND

Lymphogranuloma venereum (LGV) is a sexually transmitted infection caused by three serovars of *Chlamydia trachomatis* (serovars L1, L2 and L3). The infection is highly prevalent in parts of Africa, Asia and South America but has been rare in Western Europe for many decades. Since 2003 however, the re-emergence of rectal LGV has been described in men who have sex with men (MSM). This rectal LGV epidemic produces signs and symptoms similar to inflammatory bowel disease (IBD) including diarrhoea, purulent or mucous anal discharge and bloody proctitis.

This case highlights an important diagnosis which gastroenterologists and general practitioners (GP) in particular continue to miss. It is of relevance to all doctors in acute medicine and some surgical specialties as the clinical presentation is common and endoscopically and clinically, may be confused with IBD.

CASE PRESENTATION

A 24-year-old Caucasian homosexual man presented to his GP with a 4-month history of intermittent bloody diarrhoea, painful defaecation and 3 stones weight loss. There was no relevant medical history or family history. The patient was investigated under a general anaesthetic with rigid sigmoidoscopy which revealed a posterior anal fissure, and florid inflammation of the entire rectum and lower sigmoid. Histology of the rectal biopsies showed extensive ulceration, marked active chronic inflammatory infiltrates, numerous granulomata but no crypt abscesses. With the differential of IBD, the histology findings were thought to favour Crohn's disease. Treatment was started with mesalazine 800 mg once a day and prednisolone 30 mg once a day. His symptoms persisted with increasing anal pain over the next 2 months.

Colonoscopy was performed to evaluate the extent of his disease. This confirmed the presence of a posterior anal fissure with severe inflammation of the rectum to the recto-sigmoid. There was patchy inflammation of the

descending, transverse, ascending colon and caecum. No further biopsies were taken at this time, and the diagnosis of Crohn's disease remained unchanged.

Four months later with continued symptoms he presented to the Courtyard Clinic at St George's Hospital requesting a HIV test. The patient was diagnosed with advanced HIV infection with a CD4 count of 25 cells/mm³ (4%) and viral load of 159 000 copies/ml. A full sexual health screen was performed, and the patient was admitted for further investigation of his symptoms.

The rectum was markedly tender during proctoscopy, the rectal mucosa was erythematous with contact bleeding. A positive Chlamydia nucleic acid amplification test (NAAT) was reported by the laboratory within 24 h. This was subsequently genotyped in a reference laboratory (HPA Colindale, London, UK) and confirmed as LGV infection (figure 1A,B).

The rectal biopsies were reviewed in light of the HIV diagnosis and special stains were performed to identify alternative pathogens. The histology was reviewed and it was advised that the presence of multiple non-caseating granulomas in the submucosa was not typical of Crohn's disease. The mesalazine and prednisolone were stopped, the latter in decreasing doses over 2 weeks. His symptoms markedly improved within 2 weeks of starting doxycycline.

OUTCOME AND FOLLOW-UP

Our patient is currently symptom free and doing well. The patient was successfully treated for his LGV infection with a 3-week course of doxycycline 100 mg twice daily. Within 10 days of treatment his bloody diarrhoea had resolved and upon completion of his antibiotics he had regained his normal bowel habit. Further tests and examination during this acute admission identified untreated early syphilis, hepatitis B infection (HBsAg positive, HBcAb negative, HBsAb 0 mIU/ml, HBV DNA 1.7×10⁸ IU/ml), genital warts, molluscum contagiosum and genital herpes. In this case,

Figure 1 (A,B) Proctoscopy images of rectal mucosa.

treatment with prednisolone caused symptom deterioration and may have exacerbated the additional infections. The patient started antiretroviral therapy (Truvada and Efavirenz) 3 weeks after diagnosis. At the end of 1 month, the CD4 count improved to 153 cells/mm³ (10%) with a viral load of 374 copies/ml. Knowledge of his diagnosis has allowed the testing and treatment of his contacts, emphasising the importance of partner notification when dealing with sexually transmitted infections.

DISCUSSION

Recent outbreaks of LGV in Western Europe and the USA have been reported since 2003. This epidemic has a preponderance for MSM and behaves differently to the classical LGV infection which is highly prevalent in parts of Africa, Asia and South America. Since 2004, over 1000 cases have been diagnosed in MSM with a new surge of cases in 2010. The L2 serovar of *C trachomatis* has been identified as causing the current outbreak.^{1 2}

The symptoms and signs of infection in MSM such as proctitis presenting as severe rectal pain, mucoid and/or haemorrhagic rectal discharge, tenesmus, constipation and other features of lower gastrointestinal inflammation¹; have led to incorrect diagnosis of IBD. This misdiagnosis has been described in case reports previously,³⁻⁵ the new surge in cases this year suggests that we need to raise awareness of LGV infection to ensure patients are managed appropriately.

Further analyses of reported cases has identified a pattern of LGV infection among white MSM, the vast majority of whom were HIV positive and co-infected with hepatitis C infection.^{1 2} While sexual behaviour may account for this finding, the ulcerative nature of LGV infection is likely to increase the transmission risk of HIV and other bloodborne viruses, in the same way as with other ulcerative sexually transmitted infections such as genital herpes.

Classical LGV infection follows three clinical stages – primary, secondary and tertiary. It occurs at the site of the infection (mouth, anus, or any part of male or female genitalia). The primary lesion presents as a painless sore which may go unnoticed, and the incubation period ranges over 3–30 days. The secondary stage follows the primary lesion by 10–30 days and typically causes systemic symptoms and lymphadenopathy. *C trachomatis* serovars L1–L3 are

Table 1 Other infective causes of bowel symptoms in HIV positive patients⁷

CMV colitis
MAI infection
Salmonella enterocolitis
Campylobacter enterocolitis
Cryptosporidiosis
Microsporidiosis
Isosporiasis
Clostridium difficile
Consider sexually transmitted infections

This table summarises other causes of infective bowel symptoms that HIV positive patients may experience, highlighting that a wide differential diagnoses needs to be considered.

CMV, cytomegalovirus; MVI, *Mycobacterium-avium-intracellulare*.

lymphotropic, and cause disease by thrombolympangitis and perilymphangitis. The LGV infection therefore manifests itself with inflammation and swelling of lymph nodes and surrounding tissue. Thus clinically, patients present with tender inguinal and/or femoral lymphadenopathy which may ulcerate and discharge pus from multiple points, creating chronic fistulae. The tertiary stage of the infection has also been referred to as the genito-anorectal syndrome. This describes a few patients who do not recover following the secondary stage of infection. In these patients *C trachomatis* infection persists and causes a chronic inflammatory response, leading to destruction of involved tissues. Patients can present with proctitis, acute proctocolitis, rectal bleeding, fistulae, strictures and chronic destruction of the vulva. Lymphoedema of the genitals with persistent suppuration and pyoderma may result secondary to the destruction of lymph nodes.^{1 2}

Diagnosis of LGV infection requires a rectal swab for Chlamydia (NAAT). Positive rectal Chlamydia results are subsequently genotyped in a reference laboratory for LGV infection. Rectal swabs are currently performed in genitourinary clinics for all cases of rectal sexual exposure with symptoms. National guidelines are set to change to ensure all UK genitourinary clinics offer rectal Chlamydia testing for all MSM reporting rectal exposure. Clinicians should have a low index of suspicion for an infective cause of rectal or bowel symptoms, and LGV infection should be excluded in all patients.

Learning points

- ▶ Consider a diagnosis of HIV infection in all cases of bloody diarrhoea and weight loss.
- ▶ Sexual history taking to establish anal intercourse in MSM will indicate the need to take rectal swabs for Chlamydia. Chlamydia swabs should be available in gastroenterology clinics and swabs should be taken in all with bowel symptoms.
- ▶ Cases of suspected LGV infection should be referred to GUM teams for confirmatory tests and testing and treatment of sexual partners to reduce the risk of onward transmission and re-infection.
- ▶ LGV infection is treated with 3 weeks of oral doxycycline 100 mg twice daily.

In addition, routine HIV testing will continue to identify a large number of patients with otherwise undiagnosed HIV infection, and we are actively trying to normalise this recommendation.⁶ HIV infection itself can cause bowel symptoms in over 50% of patients at some time during their illness, the most common infective causes are summarised in table 1. In this case, misdiagnosis led

to inappropriate treatment being initiated in a severely immunocompromised individual highlighting the importance of always considering a wide number of differential diagnoses.

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Competing interests None.

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