CASE REPORT:
DIAGNOSTIC CONSIDERATIONS IN THE TREATMENT OF ACUTE COLITIS

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A previously well 28-year-old Turkish male was diagnosed with pan-ulcerative colitis (UC) in 2006 after presenting with a 3 month history of diarrhoea (10x/day, Bristol chart score 7) and abdominal pain. Colonoscopy and biopsies demonstrated characteristic active colitis and there was no evidence of small bowel disease on barium follow through. Aside from a steroid-responsive acute exacerbation in 2007 his symptoms were otherwise well controlled on pentasa (1.5g BD) and azathioprine (200mg OD).

Recently, he was admitted via the accident and emergency department with acute abdominal pain and bloody diarrhoea within 48-hours of ingesting a chicken kebab. On examination he was apyrexial (36.5), tachycardic (HR 107), BP 123/65, with lower abdominal tenderness (but no guarding or rebound). Blood tests and plain radiographs were normal except for CRP 37 and an abdominal x-ray (AXR) showing thickened large bowel wall in left upper quadrant with normal gas pattern (no dilatation). On day 1, urgent flexible sigmoidoscopy (Figure 1) and biopsy revealed features consistent with a flare of UC (moderate recto-sigmoid erythema and multiple small rectal ulcers).

Intravenous (IV) hydrocortisone (100mg QDS) was commenced. On day 6, stool samples though negative for c.difficile grew campylobacter. Therefore, his presentation was due to campylobacter enteritis exacerbating UC. He was successfully treated with 7 days of per-oral (PO) Clarithromycin with an improved bowel habit (2x/day, Bristol chart score 7) and had an early discharge on day 7 on a reducing-dose PO steroids.

However, following discharge, despite reducing the dose of prednisolone (currently 30mg OD) and azathioprine (200mg OD), his bowel habits failed to improve further. 18 days post discharge (day 25), a follow-up outpatient flexible sigmoidoscopy demonstrated rectosigmoid colitis with some improvement from the rectosigmoid to splenic flexure indicative of mild/moderate distal colitis necessitating addition of topical agents - asacol (BD) and colifoam enemas (BD). In outpatient clinic follow-up (day 50) he complained of bloody diarrhoea (BO 9x/day, Bristol chart score 7) with cramping abdominal pain and faecal urgency.
Figure 1: Image from flexible sigmoidoscopy at presentation (day 1) showed distal descending colon with erythematous change confluent ulceration and incompletely formed stool.

Question 1: What is your immediate next step to manage this patient?

a) Abdominal x-ray
b) Stool sample for c.difficile (given recent antibiotic treatment) and MC+S (given recent c)Campylobacter enteritis)
d) Admit the patient to Gastroenterology ward
e) Restart oral prednisolone
f) Repeat flexible sigmoidoscopy

Question 2: What is most likely cause of this current presentation?

a) Exacerbation of UC
b) Infective enteritis / superadded infections
c) Ischaemic colitis
d) A or B
e) Irritable bowel syndrome triggered by recent infective enteritis.
He was subsequently admitted directly from outpatient clinic to a Gastroenterology ward (day 50). AXR showed right sided faecal loading but no bowel dilatation. Blood tests revealed CRP 10, mildly elevated ESR 32 and WCC 7.1. Stool samples were negative for c.difficile and campylobacter infection.

He was rehydrated and presumptively started on IV hydrocortisone (100mg QDS) for exacerbation of UC. A limited response to treatment after seven days of treatment, prompted repeat sigmoidoscopy (day 57), which demonstrated features consistent with chronic active colitis. Biopsies however revealed chronic active colitis with CMV rectal inclusions consistent with concurrent CMV colitis (Figure 2).

**Figure 2:** Image from repeat flexible sigmoidoscopy (day 57 post initial presentation) showing a well demarcated ‘punched out’ ulcer not typical of UC but pathognomonic of CMV colitis.
He was started on IV gancyclovir for 3-days followed by oral valgancyclovir for 3-weeks with regular laxatives for proximal constipation.

He was discharged on a reducing regimen of prednisolone (40mg OD) for 1-week reducing by 5mg/week until dose of 20mg/day. At 20mg the dose was slowly reduced by 5mg/month) as well as valganciclovir (900mg BD) for 3 weeks as per the ‘European Crohns and Colitis Organisation’ (ECCO) guidance (1). Repeat flexible sigmoidoscopy (day 80), showed a much improved mucosa.

Question 3: What is the seroprevalence of CMV within the normal adult population?

a) 5%
b) 50%
c) 20%
d) Up to 100%
e) 70%

Question 4: In patients with severe colitis approximately how prevalent is CMV within colonic tissue?

a) 100%
b) 80%
c) 30%
d) 10%
e) 50%

Question 5: How would you diagnose underlying CMV infection?

Serology (IgG & IgM)

a) PCR
b) Viral culture
c) Histology (Immunohistochemistry)
d) B & D

DISCUSSION

Whenever we encounter an acute exacerbation of UC it is important to take a full history including recent travel and any dietary indiscretions (2). The minimum laboratory investigations should be performed including ESR, CRP and microbiological testing for infectious causes. It is important to note that the ESR and CRP need not be grossly elevated or elevated at all in acute exacerbations as evident in this case; high CRPs (e.g. >100) often reflecting
co-existent infection. Additional stool and blood tests may be needed for those who have travelled abroad.

AXR is important to exclude colonic dilatation. At this point it is essential to request an urgent flexible sigmoidoscopy and biopsy (2).

Over the past decade increasing use of immunomodulators and biologic agents has revolutionised the treatment of IBD. But their increasing use and potential for opportunistic infection (from impaired immunity) has become a significant safety concern, as opportunistic infections are often difficult to recognise and cause appreciable morbidity and mortality (1).

CMV infections can present like an infectious mononucleosis affecting multiple organs, with patients at risk of developing hepatitis, colitis, oesophagitis, pneumonia, retinitis and encephalitis (3, 4). CMV is most prevalent in the developing world and poor socioeconomic groups (5). One must distinguish between CMV infection (e.g. positive serology) and CMV disease (e.g. colitis, oesophagitis, end organ damage), with very few CMV infections leading to actual disease. Nevertheless, CMV colitis can mimic an acute exacerbation of UC and is associated with poorer outcomes with a higher colectomy rate (6, 7). In patients with severe colitis, evidence of CMV has been reported in 21-36% of colonic tissue (8). Immunomodulator therapy is associated with activation of subclinical reactivation of latent CMV infection, which usually runs a self limiting course or is asymptomatic (8). Therefore, only with severe CMV infection should discontinuing immunomodulator therapy during be considered (1).

In adults, such high CMV seroprevalence rates means serology is of little diagnostic value for active infection. Detection of CMV DNA (via PCR) has superseded CMV serology for confirming CMV infection and provides rapid results and allows for qualitative and quantitative testing in a wide range of tissue samples (1). Of course histology also has a pivotal role in the diagnosis of CMV infection.

Ganciclovir (for 2-3 weeks) is the treatment of choice for CMV infection. Commenced as IV ganciclovir for 3-5 days, it is later switched to oral valganciclovir for the remainder of the treatment period (1, 8). Foscarnet is an alternative to Ganciclovir should resistance or intolerance occur (8).

In this case we have seen a patient with UC admitted on two separate occasions with what both appeared to be acute exacerbations of UC. However, investigations revealed that he was actually suffering from two separate conditions, both of which mimic UC. This highlights how in acute exacerbations of IBD it is important to promptly take stool samples to exclude underlying infection and to perform urgent flexible sigmoidoscopy to exclude infective colitis.

REFERENCES

1. Rahier JF et al, European evidence-based Consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel

Answers:
Question 1:
d) Admit the patient to a Gastroenterology ward.

Question 2:
d) Exacerbation of ulcerative colitis or infective enteritis / superadded infection.

Question 3:
d) up to 100%

Question 4:
b) 30%

Question 5:
e) PCR and histology