CASE REPORT

Recurrent cytomegalovirus colitis: a rare case of immune reconstitution inflammatory syndrome

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SUMMARY

Cytomegalovirus (CMV) colitis usually occurs in patients with advanced immunosuppression when the CD4 count is <50 cells/ μ L. We reported a case of recurrent CMV colitis in a patient with HIV who presented with profuse lower gastrointestinal bleed. This was a case of immune reconstitution inflammatory syndrome (IRIS) manifesting as CMV colitis and has been reported only once in the literature previously. This patient had a CD4 count of 157 cells/ μ L and undetectable viral load after being on antiretroviral therapy (ART) for 5 months, which was consistent with IRIS. The diagnosis of CMV was confirmed by a colonoscopy and a biopsy. This case highlights the fact that CMV colitis can manifest despite a moderately preserved CD4 count and the clinicians must have a high index suspicion for IRIS syndrome especially when someone was recently started on ART. Since effective treatment is available, it is important not to miss the diagnosis of CMV colitis.

a well-described entity in IRIS; however, it is extremely rare to have CMV-IRIS manifesting as colitis. In the literature to date, there is only one case that has been reported. The management of IRIS includes treating the opportunistic infection as soon as possible. The timing regarding continuation of ART and role of anti-inflammatory agents remains controversial.

CASE PRESENTATION

A 52-year-old woman originally from Liberia was admitted for lower abdominal pain, rectal pain and bleeding per rectum. The bleeding was described as profuse and bright red of 1 week duration. She denied any recent sexual activity including rectal intercourse. She had a medical history of HIV/AIDS, cerebral toxoplasmosis, CMV colitis, ambulatory dysfunction, protein calorie malnutrition and deep venous thrombosis. Her current medications included emtricitabine/tenofovir, raltegravir, trimethoprim/sulfamethoxazole and rivaroxaban.

Approximately 5 months ago, she was diagnosed with HIV at a different hospital where she was found to have biopsy-proven CMV colitis. Her initial CD4 count was less than 20 cells/ μ L and viral load was 196 584 copies/mL. The patient was treated with intravenous ganciclovir (5 mg/kg/dose) for 7 days. ART was started 2 weeks after initiation of ganciclovir. The patient recovered after a complicated course and was discharged to a nursing home on ART and valganciclovir (900 mg two times per day). This was subsequently stopped at the nursing home after 21 days since she was symptom free. Prior to this hospital admission, she did not receive any form of treatment with ART.

She presented to our hospital 5 months after the diagnosis of AIDS was made. Her physical examination was significant for diffuse abdominal tenderness and positive for gross blood in the rectal vault. However, her vital signs were normal and she was admitted to the general medical floors.

INVESTIGATIONS

On admission, her haemoglobin level was 12.5 g/dL (baseline 13–14 g/dL), platelets 3.38×10^5 per litre and international normalised ratio 1.5. CD4 count was 157 cells/ μ L and the viral load was undetectable. A CAT scan of the abdomen and pelvis (CTap) with contrast revealed faecal impaction and proctitis.

An emergent colonoscopy was not done since she was haemodynamically stable. The rivaroxaban

BACKGROUND

Immune reconstitution inflammatory syndrome (IRIS) is the paradoxical worsening of an existing disease process or the appearance of a new disease process or an infection after initiation of antiretroviral therapy (ART). This is secondary to a dysregulated immune response that occurs after ART is initiated. IRIS is usually seen in patients who have a low CD4 count and a high viral load at the time of ART is started. Cytomegalovirus (CMV) manifesting in the form of retinitis or uveitis is

Figure 1 Multiple large rectal ulcers with oozing vessels and seven clips were used to achieve haemostasis.

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Figure 2 A white-based ulcer at the ileocecal valve.

was stopped on admission. However, the following day, the patient had a frank haematochezia and a haemoglobin drop of 4 units. Emergent colonoscopy was performed and it demonstrated multiple large rectal ulcers 1–2 cm in size with visible vessels and oozing. The area was injected with epinephrine solution 1:10 000 and seven clips were used to stop the bleeding (figure 1). A white-based ulcer was seen in the caecum, which was biopsied (figure 2). The remainder of the colon appeared normal except for diverticulosis.

On day 3 of the hospitalisation, the patient had worsening abdominal pain, and a repeat CTap was obtained which demonstrated moderate to severe diffuse thickening of the caecum, ascending colon, transverse colon and descending colon (figure 3). The bowel wall measured up to 1.7 cm in thickness (figure 4). There was no evidence of obstruction, ischaemia or any abscess.

During the hospital course, the patient subsequently developed severe diarrhoea resulting in non-gap metabolic acidosis. Stool studies were negative for *Cryptosporidium*, *Giardia*, *Cyclospora*, *Mycobacterium avium* complex (MAC), *Shigella*, *Salmonella* and *Clostridium difficile*. Blood and sputum cultures showed no evidence of mycobacterium. Immunohistochemical stain of the ulcer was positive for CMV (figure 5).

Figure 3 CAT scan of the abdomen and pelvis axial cut points to the thickened bowel wall of the colon.

DIFFERENTIAL DIAGNOSIS

1. *Clostridium difficile* colitis.
2. CMV-IRIS colitis.
3. *Cyclospora*-induced diarrhoea.
4. MAC-causing diarrhoea.
5. *Shigella* toxin diarrhoea.

TREATMENT

The patient required 5 units of packed red blood cells during the episode of massive gastrointestinal bleed and was transferred to the intensive care unit for close monitoring. Once the diagnosis of CMV was made, she was started on intravenous ganciclovir at 5 mg/kg two times per day. Since there was a strong suspicion for severe IRIS, ART was continued and prednisone at 1 mg/kg was initiated.

OUTCOME AND FOLLOW-UP

Unfortunately her hospital course was complicated by respiratory failure and disseminated intravascular coagulation. She eventually expired.

DISCUSSION

Gastrointestinal disease by CMV in patients with AIDS is a rare but serious complication in the modern era. CMV gastrointestinal disease in AIDS was first reported in 1983; however, it became rare after ART became available in 1995–1996.¹ The risk factors include prior CMV infection and a CD4 count of

Figure 4 CAT scan of the abdomen and pelvis coronal cut points to thickened bowel wall of the ascending colon.

Figure 5 Immunohistochemical stain of the ulcer was positive for cytomegalovirus.

<50 cells/ μ L. It is extremely rare to have CMV infection with a CD4 count >100 cells/ μ L.²

IRIS is a widely recognised complication of ART. It occurs in 10%–25% of the patients started on ART.³ This can present either as the paradoxical worsening of symptoms when the patient is started on ART or can be the unmasking of an opportunistic infection. This was initially present in this patient but was not clinically evident; however, initiation of ART acted as a trigger. We believe that this patient made an initial recovery with ganciclovir but once ART was started, the patient had a florid immune response resulting in severe colitis. This is evident from the fact that the patient had a rise in CD4 count along with a massive reduction in viral load over the period of 5 months and subsequent worsening of symptoms. The mechanism of IRIS is similar to a type IV hypersensitivity reactions that occur as levels of HIV RNA drop and the immunosuppressive effects of HIV infection are controlled.⁴ IRIS can occur anywhere between 2 weeks and 2 years after ART initiation.⁴

This case is unique because CMV colitis as a manifestation of IRIS is rare and not well documented. Common pathogens associated with IRIS include *Mycobacterium tuberculosis*, *Mycobacterium avium* complex, CMV, *Cryptococcus* and *Pneumocystis*. CMV retinitis and uveitis are well-known associations of IRIS; however, colitis secondary to CMV in association with IRIS has been reported only once before.⁵

Although rare, CMV colitis is the second most common presentation of CMV disease in patients with AIDS.⁶ Colitis usually presents with abdominal pain, malaise and anorexia. Profuse watery diarrhoea occurs sporadically. Perforation and haemorrhage are other severe life-threatening complications.^{7,8}

Endoscopy with biopsy is key to diagnose CMV colitis. Oesophagitis can present with large shallow ulcers, but colitis can manifest as punctate or deep ulcers. The gold standard to diagnose CMV is by histopathology. Histopathology is characterised by inflammation or necrosis of the mucosa along with intranuclear and intracytoplasmic inclusions.

Treatment includes induction therapy with ganciclovir at a dose of 5 mg/kg every 12 hours for 3–5 days followed by oral valganciclovir for a total of 2–3 weeks.⁹ Guidelines on duration of therapy is based on clinical improvement and not based on CD4 count. This is something that needs to be studied further.

This case highlights the fact that CMV colitis can manifest despite a moderately preserved CD4 count of 150 and the clinician must have a high index suspicion for IRIS syndrome, especially when someone was recently started on ART. Since effective treatment is available, it is important not to miss the diagnosis of CMV colitis.

Learning points

- Patients with HIV can have cytomegalovirus (CMV) infection despite a moderately preserved CD4 count >150 cells/ μ L, especially with recent initiation of antiretroviral therapy.
- CMV–immune reconstitution inflammatory syndrome colitis is rare but lethal disease process; it is important not to miss the diagnosis since effective treatments are available.
- Endoscopy with biopsy is the key to diagnose CMV colitis.
- The current guidelines regarding duration of treatment for CMV colitis is based on clinical resolution and not CD4 count. This needs further investigation.

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