CASE REPORT

Solitary ascending colon ulcer diagnosed as gastrointestinal CMV disease

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SUMMARY

A 42-year-old woman with a history of cholangiocarcinoma on adjuvant chemotherapy with capecitabine presented with painless haematochezia. She was found to have an isolated twenty-five mm ulcer in the ascending colon. Biopsies of the ulceration demonstrated typical cytomegalovirus (CMV) inclusions and her peripheral blood CMV PCR was significantly elevated. This is an unusual case of a solitary proximal colon ulcer. Non-steroidal anti-inflammatory drugs, inflammatory bowel disease and malignancy, are the most frequent causes of isolated ulcers in the proximal colon. Gastrointestinal (GI) CMV disease most commonly causes CMV colitis and is considered rare outside of the transplant population and other severely immunosuppressed patient groups. Patients who have received chemotherapy may also be at risk for GI CMV disease. The diagnosis should be suspected in patients who present with haematochezia or watery diarrhoea within a broad window of time after receiving chemotherapy.

BACKGROUND

Haematochezia is the term used to describe blood loss from the rectum.¹ The volume of blood loss and clinical stability of the patient often suggest the aetiology. High volume blood loss in unstable patients can be due to a large source of bleeding proximal to the colon. However, most cases of haematochezia are caused by bleeding distal to the ligament of Treitz.^{1,2}

Gastrointestinal (GI) cytomegalovirus (CMV) disease is an erosive process that can occur at any location in the GI tract and most often occurs in severely immunosuppressed patient groups such as those with acquired AIDS and transplant recipients.^{3,4} CMV disease affecting the lower GI tract has a wide clinical spectrum, but typically presents with acute or chronic diarrhoea and lower GI bleeding.⁵ Colonoscopy findings are also variable and include normal mucosa, haemorrhagic erythema and colitis that is often severe and widespread.³ The most common pattern is multiple ulcerations with at least one large ulceration exceeding 2 cm in diameter.⁶

Emerging literature highlights the importance of CMV disease in patients with lower degrees of immunosuppression than traditionally appreciated. For example, CMV colitis can occur in immunocompetent patients in an intensive care unit setting, in patients with multiple comorbid chronic diseases and in the elderly.⁷

CASE PRESENTATION

A 42-year-old woman with a history of cholangiocarcinoma had undergone a Whipple surgery (pancreaticoduodenectomy) within the preceding year. Her condition was complicated by the development of a biliary stricture and portal venous compression resulting in portal hypertension, oesophageal varices and internal haemorrhoids. She was receiving adjuvant chemotherapy with capecitabine and finished her third cycle 5 weeks prior to presentation. She had been on a dose of 1500 mg twice daily for 14-day cycles repeating every 28 days. Her next cycle had been scheduled to start the day after she presented for admission. Her other medications were notable for a proton pump inhibitor, beta blocker and pancreatic enzymes. She was not on steroid therapy and denied use of non-steroidal anti-inflammatory drugs.

She presented to the emergency room with two episodes of painless haematochezia. She was admitted and had multiple additional episodes of haematochezia, but remained clinically stable and did not require a blood transfusion.

INVESTIGATIONS

A colonoscopy was performed during her hospitalisation. The procedure revealed an isolated 2.5 cm ulceration in the ascending colon without evidence of ongoing bleeding (figure 1). A biopsy of the ulcer was taken and multiple cytoplasmic inclusions consistent with CMV infection were reported on the pathology report. On learning the result of the colonoscopy, a peripheral CMV PCR assay was ordered. The test returned positive a few days later with >3 900 000 copies/mL.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for painless haematochezia includes diverticulosis, bleeding internal haemorrhoids, malignancy, angiodysplasia, ischaemic colitis and post-procedural bleeding.^{1,2} Haematochezia may also be present in cases of brisk upper GI source of bleeding, which may include bleeding oesophageal varices, peptic ulcer disease and angiodysplasia within the small bowel.^{1,2}

The differential diagnosis for solitary ulceration within the proximal colon on colonoscopy includes malignancy, inflammatory bowel disease (IBD), medication side effect, chemical injury and infection.⁵ Among medications, non-steroidal anti-inflammatory drugs are directly implicated in colonic ulceration.^{5,8,9} Infectious aetiologies include CMV infection, amoebiasis and tuberculosis.¹⁰

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Figure 1 The isolated 2.5 cm ulcer in the ascending colon.

TREATMENT

The patient was prescribed oral valacyclovir 1000 mg three times daily based on the results of her pathology report. She was advised to take the medication for 21 days.

OUTCOME AND FOLLOW-UP

Since no active bleeding was seen during her colonoscopy, she was discharged the following day. The results of her peripheral blood CMV PCR and characteristic biopsy findings returned about 4 days later. The clinical picture was revealed to be GI CMV disease at that time and she was notified via telephone of the results. She deferred inpatient anti-viral treatment and was instead prescribed oral valacyclovir as an outpatient. She received follow-up with her local oncologist for continued chemotherapy. She reportedly had resolution of her diarrhoea within a month of her initial discharge from the hospital.

DISCUSSION

The clinical presentation of painless, low volume haematochezia suggests a source of bleeding distal to the ligament of Treitz.^{1 2} Given that this patient was known to have portal hypertension and internal haemorrhoids on a prior colonoscopy, a bleeding internal haemorrhoid was thought to be the most likely source before her procedure. The finding of an isolated ulceration in the proximal colon was unexpected and led to the consideration of other diagnoses.

The colonoscopy finding of a solitary ulceration in the proximal colon is uncommon. In a review, Ona *et al* estimated that this finding occurred in one to two out of every one thousand colonoscopies.¹¹ However, their review did not separate patients who underwent colonoscopy due to anaemia or blood loss, which suggests this finding is even less frequent than reported. The differential diagnosis for a solitary proximal colon ulcer includes malignancy, IBD, medication side effect, chemical injury and infection.^{5 11} In addition to CMV, other infectious causes of colonic ulceration include amoebiasis and tuberculosis.¹⁰ Regarding medication, multiple groups have shown an association between non-steroidal anti-inflammatory drug (NSAID) use and colonic ulceration.^{5 8 9} Her history did not support NSAID use as a cause. Her biopsy findings did not show malignant cells or findings consistent with IBD but instead revealed intracellular inclusions suggestive of CMV infection.

The most frequent symptoms of an isolated ulcer in the proximal colon are right lower quadrant abdominal pain, haematochezia and constipation.¹¹ Isolated, large ulcerations have been reported

among the endoscopic features of GI CMV disease.^{3 6} Outside of the colon, CMV disease is associated with ulcer formation in the oesophagus, stomach and small intestine. Within the oesophagus, ulcerations are classically described as serpiginous, but frequent large ulcerations or isolated large ulcerations are also reported.¹² Less commonly, CMV can produce enteritis and ulcerative disease in the small intestine and stomach. The diagnosis of CMV within the GI tract is based on a combination of biopsy results, serological testing and detection of viraemia in the blood. The gold standard for diagnosis is biopsy and immunohistochemical staining for CMV showing characteristic intracellular inclusions with an 'owl's-eye' appearance.^{3 12} Tissue findings have been shown to be 93% sensitive and 100% specific for confirming the diagnosis.¹³ Serology with IgM antibody testing against CMV is highly sensitive for recent infection when positive but does not confirm active disease.¹⁴ Tests based on detecting viraemia include PCR for CMV. This test has a lower sensitivity ranging from 81%–87% and thresholds for positive results differ between hospitals.¹⁵

In a patient with abdominal pain associated with watery or bloody diarrhoea, CMV is often considered among the differential diagnoses, when there is a known immune compromising condition. However, this diagnosis may not be entertained among those without obvious immunosuppression or in those who are immunocompetent. GI CMV infection is classically described as occurring in patients with AIDS and recipients of bone marrow or organ transplants.³ There is a growing body of literature highlighting the importance of CMV reactivation beyond the classically described setting. Other factors including age and comorbidities such as chronic kidney disease may produce sufficient immunosuppression to allow development of GI CMV disease.⁷ We found several case reports and a meta-analysis describing immunocompetent patients diagnosed with GI CMV disease.^{7 16} In the meta-analysis, patients were categorised as immunocompetent based on normal leucocyte count, absence of AIDS and not having received chemotherapy. Another study showed that receiving chemotherapy increased risk of development of CMV infection within a 3-month window of time.⁴ Our patient was likely predisposed by receiving a third cycle of capecitabine approximately 5 weeks prior to presentation. However, the patient did not exhibit laboratory evidence of immunosuppression such as neutropaenia or lymphopaenia. Given the diversity of chemotherapy drugs currently used, with varying degrees of immunosuppression ranging from minimal to complete bone marrow suppression, additional work is needed to clarify which chemotherapy regimens, patient comorbidities and degree of immunosuppression are necessary to allow clinically apparent reactivation of CMV infection. Until further evidence clarifies which patients are at highest risk, clinicians should consider CMV infection among the differential causes of diarrhoea and lower GI bleeding in patients who have received chemotherapy within a broad window of time.

Learning points

- ▶ Gastrointestinal (GI) cytomegalovirus (CMV) disease can cause isolated proximal colon ulceration in patients presenting with haematochezia.
- ▶ Patients who have received chemotherapy within a broad window of time should be considered at risk for GI CMV disease.
- ▶ Additional work is needed to clarify what degree of immunosuppression is necessary to allow development of GI CMV disease.

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