



Case report

Life-threatening gastrointestinal bleeding caused by cytomegalovirus-induced duodenal ulcer in a patient with AIDS: A case report

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ABSTRACT

Background: The reasons for gastrointestinal bleeding among patients with acquired immune deficiency syndrome (AIDS) were complex. Here we present an unusual case of life-threatening gastrointestinal bleeding caused by a cytomegalovirus-induced duodenal ulcer in an AIDS patient.

Case presentation: A 31-year-old male with AIDS was admitted on July 18, 2023, complaining of abdominal pain for 38 days and intermittent hematochezia for 12 days. During his hospitalization, gastrointestinal endoscopy attributed gastrointestinal bleeding to a giant duodenal ulcer. Furthermore, cytomegalovirus (CMV) infection was confirmed as the reason for the ulcer through metagenomic next-generation sequencing (mNGs), hematoxylin-eosin (HE) staining, and immunohistochemistry (IHC) staining for the biopsy tissue. The patient's gastrointestinal bleeding was stopped by interventional embolization. Following a 4-week course of anti-CMV treatment, the giant duodenal ulcer was cured.

Conclusions: For AIDS patients with gastrointestinal bleeding, the CMV-induced gastrointestinal ulcer should be considered. Comprehensive methods (mNGs, HE staining and IHC staining for biopsy tissue) were benefit for confirmed diagnosis. Beside anti-CMV treatment, the interventional embolization is a choice for hemostasis.

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1. Introduction

As known, the mortality of alimentary tract hemorrhage is still high, and the reasons is multifactorial. The major reasons include gastroduodenal ulcer, varices, gastritis, stress ulcer, etc [1]. For AIDS patients, the reasons of gastrointestinal bleeding are more complex, the opportunistic infection(OI) should be specially considered [2]. CMV infection is a common OI for AIDS patients, which can cause life-threatening and tissue-invasive risks, especially for alimentary tract and fundus [3,4]. The typical clinical types of CMV-caused gastrointestinal disease are colitis, esophagitis and gastritis, which rarely leads to severe bleeding [5]. Here we present a case of AIDS patient with life-threatening gastrointestinal bleeding caused by cytomegalovirus-induced duodenal ulcer.

2. Case presentation

A 31-year-old male was admitted to hospital on July 18, 2023 with a chief complaint of abdominal pain for 38 days and intermittent hematochezia for 12 days. The patient experienced the onset of abdominal pain on June 9, 2023 and was hospitalized from June 16 to July 18, 2023 in local hospital. The puncture biopsy for lymph node was performed due to multiple enlarged retroperitoneal and intermesenteric lymph nodes, the histopathological examination did not show malignant tumor or infective pathogens. After receiving antibacterial treatment (intravenous meropenem, 1.0g Q8h for 7 days), antifungal treatment (intravenous voriconazole, 200mg Q12h for 10 days), and diagnostic anti-tuberculosis treatment, the abdominal pain was not improved. On July 6, 2023, the patient presented with hematochezia. The pharmacological hemostasis therapy were provided, however, there was no improvement in the bleeding.

The patient had a history of men who have sex with men(MSM). He was confirmed with HIV infection on April 6, 2023, with a CD4⁺ T lymphocyte count of 2 cells/ μ L and an HIV viral load of 5,021,465 IU/mL. Between April 13 and May 9, 2023, the patient was hospitalized for septic shock, disseminated aspergillosis, COVID-19, and syphilis.

The physical examination revealed emaciation, pale eyelids and skin, mild epigastric tenderness and rebound pain, as well as subcostal accessibility of the liver and spleen.

Laboratory tests revealed hemoglobin level was 59g/L(normal range 130–175g/L), platelet count was 49×10^9 /L(normal range 125–350 $\times 10^9$ /L), albumin of 27.2g/L(normal range 40–55g/L), CMV-DNA and CMV IgM were negative, and CMV IgG was positive. CT scan revealed enlarged retroperitoneal and intermesenteric lymph nodes and hepatosplenomegaly.

After admission, the patient presented with intermittent hematochezia and consistently low hemoglobin levels, subsequently leading to a life-threatening hemorrhagic shock. Comprehensive treatments (fasting, proton pump inhibitor therapy, blood transfusion, etc) were performed. There was a reduction in bleeding episodes, then the gastroduodenoscopy and colonoscopy were performed, a giant ulcer measuring about 1.5cm in diameter at the duodenal bulb was observed (Fig. 1A). CMV was found by metagenomic next-generation sequencing analysis(mNGs) for the biopsy tissue. The hematoxylin-eosin(HE) staining revealed characteristic intranuclear inclusion bodies(Fig. 2A) and the immunohistochemistry (IHC) staining further confirmed a positive reaction for antigens of CMV (Fig. 2B). The large duodenal ulcer was considered to be caused by CMV infection, so intravenous ganciclovir (250mg Q12h) was provided. In the initial stage of anti-CMV treatment, patients experienced reduced gastrointestinal bleeding. However, hematochezia recurred after one week of anti-CMV treatment. For hemostasis, interventional embolization was performed on the gastroduodenal artery, the patient's bleeding was stopped. Following a 2-week course of anti-CMV treatment, a reduction in both the extent and depth of the duodenal ulcer was observed via gastroduodenoscopy(Fig. 1B). By anti-CMV treatment with 4 weeks, substantial healing of the ulcer was observed(Fig. 1C). Subsequently, antiretroviral therapy (ART) was resumed for AIDS. The patient's condition was assessed as stable based on a follow-up telephone call three months later.

3. Discussion

The hematochezia arises from a complex array of etiologies. For persistent upper gastrointestinal bleeding poses a life-threatening risk, the diagnostic is challenging, especially for AIDS patients. Our case contributed a better understanding of diagnosis and treatment

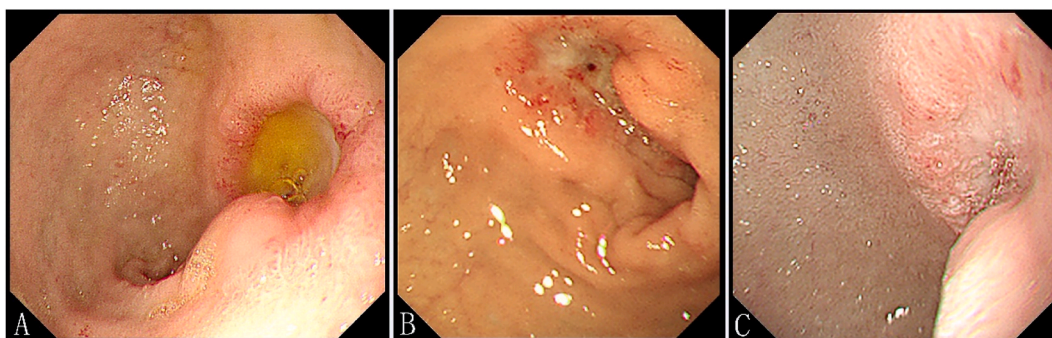


Fig. 1. Gastroduodenoscope pictures taken from the patients. A. The duodenal ulcer before anti-CMV treatment. B. The duodenal ulcer after anti-CMV treatment for 2 weeks. C. The duodenal ulcer after anti-CMV treatment for 4 weeks.

of gastrointestinal bleeding caused by CMV-induced duodenal ulcer in AIDS patients.

CMV infection can cause disseminated or localized end-organ disease in AIDS patients. The commonest clinical manifestations of severe CMV end-organ disease are retinitis, colitis, esophagitis and gastritis [5]. Some studies had indicated that the clinical manifestations of CMV-caused duodenitis and duodenal ulcers are characterized by non-specific symptoms including initial presentation with epigastric abdominal pain, bloating, nausea and vomiting, and advanced stages with melena, hematemesis and hematochezia [6–9]. Our patient suggested the ulcer caused by CMV infection should be considered for AIDS patients with life-threatening gastrointestinal bleeding.

Diagnosing duodenal ulcers caused by CMV infection is challenging. The detection of plasma CMV-DNA, CMV IgG, and CMV IgM levels is the most common method for screening CMV infection in the clinical practice [10]. Positive results for these markers indicate the presence of CMV infection, however, they do not provide evidence of end-organ disease associated with an active CMV infection. Endoscopy plays a crucial role in diagnosing gastrointestinal CMV infection. Nevertheless, studies have shown that identifying CMV based on endoscopic appearance is difficult due to nonspecific presentations such as ulcerations, erosions, and mucosal hemorrhage [7, 9,11]. Therefore, detection for biopsy tissue obtained via endoscopy provided more benefits for diagnosis. According to the guideline, the diagnosis of CMV end-organ disease typically relies on clinical presentation and detection of the virus in tissue samples [3]. Our former study demonstrated that HE staining and IHC staining are pivotal diagnostic techniques for detecting CMV infection in tissue sample [12]. Metagenomic next-generation sequencing (mNGS) is a novel culture-independent sequencing approach for detecting pathogens to identify various pathogens (bacteria, viruses, fungi, and parasites) in clinical samples, which also provide the more accurate method for detecting CMV infection in tissue samples [13]. In our case, the patient did not present with any other typical symptoms with CMV infection (fever, retinitis, enteritis, esophagitis etc.). Moreover, the negative blood CMV-IgM and CMV-DNA brought challenges for an accurate diagnosis. The endoscopy revealed a significant duodenal ulcer, and subsequent HE staining for tissue biopsy revealed the presence of inclusion bodies. Further IHC staining and mNGs of tissues confirmed the diagnosis of CMV infection. Therefore, our case suggests that combining mNGS for tissue samples with histopathological examination (HE staining and IHC staining) can provide robust diagnostic evidence for duodenal ulcers caused by CMV infection.

Delayed treatment might increase the mortality for gastrointestinal bleeding caused by CMV infection [8]. So anti-CMV treatment should be provided as soon as possible when the etiology was confirmed. The hemorrhage still recurred in our patient with one week anti-CMV treatment, which suggested anti-CMV treatment is not enough for hemostasis in short time, especially for giant ulcer. The endoscopic hemostasis might lead to a risk of perforation because the ulcer was deep, and surgical intervention might result in higher risk for the patient. Therefore interventional embolization therapy provide as an optimal option for managing the bleeding of ulcer caused by CMV infection ulcers. The other observation from our case is that AIDS patients with giant duodenal ulcer caused by CMV infection should receive a sufficient duration of anti-CMV treatment, preferably lasting at least 4 weeks. According to the current guideline, a duration of 21–42 days is recommended for anti-CMV therapy in cases of colitis or esophagitis caused by CMV infection [3]. Another study also demonstrated that a longer duration of anti-CMV treatment exceeding 14 days was associated with improved survival [14]. Therefore, ensuring a longer course of treatment could lead to an improved prognosis.

4. Conclusion

For AIDS patients with life-threatening gastrointestinal bleeding, the gastrointestinal ulcer caused by CMV infection should be considered. The analysis of mNGs, as well as HE staining and IHC staining based on biopsy tissue, are crucial for accurately identifying CMV-induced gastrointestinal ulcers. Beside anti-CMV treatment, the interventional embolization is a choice for hemostasis. Additionally, at least 4-week course of anti-CMV treatment for managing giant duodenal ulcers may result in an enhanced prognosis.

Ethics statement

Informed consent was obtained from the patient for the publication of all images, clinical data and other data included in the main manuscript.

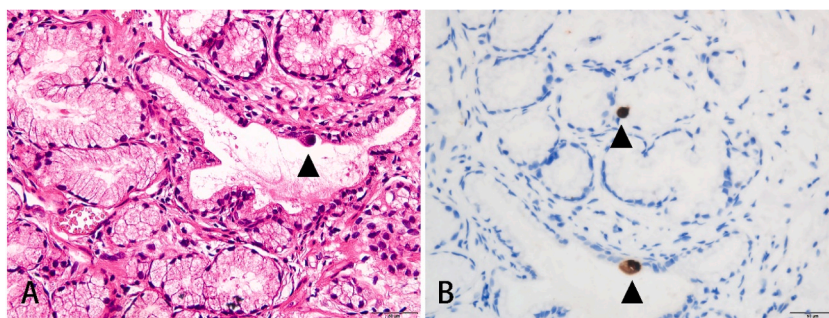


Fig. 2. Microscopic picture for the biopsy taken from the duodenum ulcer. A. The intranuclear inclusion body (triangle) in the epithelial cell of the mucosa of the duodenum. H&E \times 400. B. Immunohistochemistry staining for CMV (triangles). IHC \times 400.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Shihui Song: Writing – original draft. **Wei Guo:** Investigation. **Shi Zou:** Data curation. **Feng Zhou:** Data curation. **Mingqi Luo:** Formal analysis. **Li Chen:** Data curation. **Ke Liang:** Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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