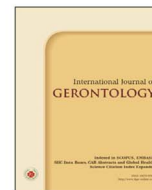




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Case Report

Intestinal Bleeding Caused by Combined Cytomegalovirus Enteritis and Adverse Effect of Kalimate in Elderly: A Case Report

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SUMMARY

Gastrointestinal (GI) bleeding is one of the major indications for hospitalization in the elderly. The most common causes of GI bleeding in elders include peptic ulcer, diverticular disease, angiodysplasia, colitis, and adverse effects of medications. Kalimate (calcium polystyrene sulfonate) is commonly used to treat hyperkalemia, which has rare but severe complications of colonic necrosis and perforation. Cytomegalovirus (CMV) infection of the GI tract is uncommon and can be fatal. Here we present the case of a 73-year-old female with GI bleeding caused by combined cytomegalovirus enteritis and adverse effect of Kalimate.

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1. Introduction

Gastrointestinal (GI) bleeding is a serious and life-threatening emergency that affects a large number of elderly people. After experiencing GI bleeding, elderly patients face a higher risk of mortality. The number of deaths resulting from a bleeding episode each year is increasingly attributed to these patients, representing 10% of the total.¹ Peptic ulcer, diverticular disease, and angiodysplasia are the most common causes of major bleeding in elderly.¹ However, there are other factors that can lead to GI bleeding, such as inflammatory bowel disease, liver disease, infectious colitis, and drug-induced injury. Furthermore, the causes of gastrointestinal bleeding can often involve multiple contributing factors simultaneously. Cytomegalovirus (CMV) infection is rare in previously immunocompetent patients. Sodium polystyrene sulfonate (Kayexalate) or its analogs, calcium polystyrene sulfonate (Kalimate) is a cation-exchange resin frequently used in managing hyperkalemia among individuals with chronic kidney disease (CKD). The rare occurrence of intestinal necrosis and perforation represents extremely severe complications linked to the use of this medication. Here, we present a case of GI bleeding in the elderly caused by combined cytomegalovirus enteritis and adverse effects of Kalimate.

2. Case presentation

A 73-year-old female patient presented to the emergency department due to syncope and tarry stool passage. The patient had a medical history of type 2 diabetes mellitus, essential hypertension, stroke, chronic obstruction pulmonary disease, and chronic kidney disease under hemodialysis. After admission, her initial laboratory examinations detected anemia and hyperkalemia (5.8 mmol/L).

Esophagogastroduodenoscopy revealed gastric ulcer, chronic duodenitis, and lymphangiectasia; the colonoscopy showed colitis. However, no active bleeding was found in either esophagogastroduodenoscopy or colonoscopy. Computed tomography showed no evident contrast extravasation into intestinal loops. Angiography was also performed in the celiac trunk, superior mesenteric, and inferior mesenteric arteries; however, no active bleeding nor vascular abnormality was observed. Due to a high suspicion of small intestinal bleeding, an intra-operative enteroscopy was performed. It showed several bleeding ulcers measuring up to 10 mm in the jejunum and ileum (Figure 1); therefore, small intestinal segmental resection was performed. The resected ileum measured 23.5 cm in length and 6 cm in circumference. The serosal surface showed dark red discoloration. The mucosa had several skipped ulcers and a long linear ulcer at the anti-mesenteric side, approximately 13 cm in length. Microscopically, the sections showed a segment of the small intestine with several areas of mucosal ulceration. Some basophilic crystals were found in the ulcer bed, which showed a red color on the periodic acid-schiff and acid-fast stains, consistent with Kalimate crystals (Figure 2A, 2B). There were plump epithelioid cells with large nuclei seen in the ulcer base that were negative for CK and CD34, while some were positive in the CMV immunohistochemical stain, indicating CMV infection (Figure 2C, 2D). Combined histological findings and immunohistochemical stain results demonstrated intestinal ulcer with CMV infection and deposition of Kalimate crystals. The CMV serology test showed high immunoglobulin G levels (> 250 AU/ML). After surgical treatment and intensive care, the patient passed away one week later due to bradycardia and hypotension.

3. Discussion

Gastrointestinal bleeding affects many elderly people and is a frequent indication for hospitalization.^{1,2} Identifying the cause and location of GI bleeding is one of the greatest challenges for clinicians.

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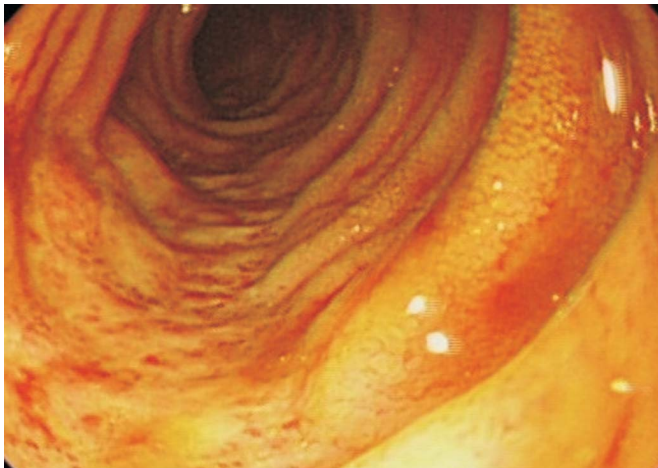


Figure 1. Image of intra-operative enteroscopy. There are several bleeding ulcers in the middle segment of small intestine.

Common risk factors for GI bleeding in the elderly patients, include the use of antiplatelet agents, anticoagulants, nonsteroidal anti-inflammatory drugs, a personal history of peptic ulcer disease, esophageal varices, angiodysplasia, colitis, and colonic diverticular disease.³

Colitis is a colonic inflammatory process and the main causes are ischemia, infections, and ulcerative colitis.⁴ Several pathogens may cause infectious colitis; bacterial and viral infections account for most cases.⁵ The most frequent bacterial colitis includes *Clostridium difficile*, *Salmonella*, *Escherichia coli*, and *Shigella*.⁵ Common causes of viral colitis include norovirus, rotavirus, adenovirus, and CMV.⁵ CMV infection usually affects immunocompromised patient and immunocompetent hosts with risk factors such as old age, diabetes mellitus, chronic kidney disease, and end-stage renal disease.⁶ CMV infection can be an asymptomatic or tissue-invasive disease, and some patients develop intestinal perforation and require surgical treatment.⁶ Diagnosing of CMV infection is challenging because of its diverse presentations, and the most common endoscopic finding is ulcers, similar to other colitis.⁶ Histopathology is the gold standard in diagnosing CMV infection. CMV infection can be fatal and cause up to 21% in-hospital and 40% overall mortality rates.⁶ CMV colitis is the most common type of CMV infection; however, CMV enteritis has the worst outcome.⁶ Antiviral therapy can improve prognosis; therefore, early CMV enterocolitis diagnosis is essential.

Drug-induced injury of the GI tract is also a common cause of GI bleeding, and crystal deposition (iron and kayexalate) is one of the major causes.⁷ Hyperkalemia is a common electrolyte disorder in patients with CKD, which can lead to fatal cardiac arrhythmias.^{8,9} Kayexalate or Kalimate are sodium or calcium polystyrene sulfonates, that act as exchange resins between sodium or calcium, and potassium ions, widely used to treat hyperkalemia. Adverse drug effects involving the GI tract with Kalimate or Kayexalate are rarely present, and not more than 200 cases have been reported in the literature.⁸ However, these drugs have been reported to be associated with colon necrosis and cause high mortality rates.⁸ Colon is the most commonly involved organ.⁸ The diagnosis is based on pathologic findings of the basophilic crystal materials in the necrotic ulcer base of mucosa and within the necroinflammatory debris.^{10,11} Due to the serious GI adverse effect of Kayexalate or Kalimate, physicians should carefully assess the patient's intestinal motility, underlying disease, and comorbidity before prescription.

Multimorbidity, the co-occurrence of at least two factors within a person, increases with age and exacerbates the risk of GI bleeding.

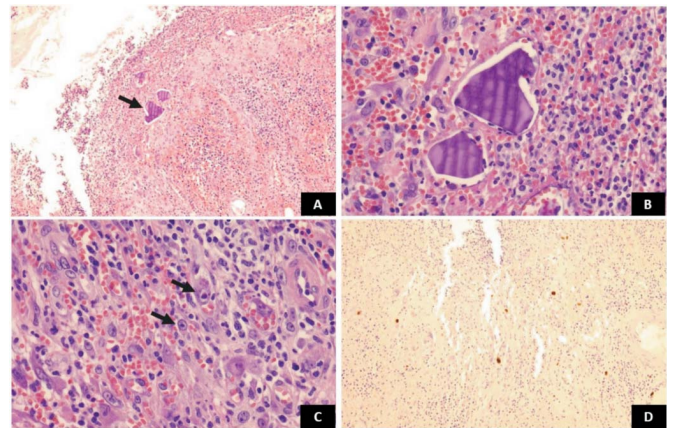


Figure 2. Microscopical feature of intestinal specimen. (A) Some crystals (arrow) embedded in the inflamed granulation tissue of ulcer base. (B) The crystals are basophilic with irregular edge. (C) There are some plump, epithelioid cells with large nuclei and peri-nuclear halo (arrow). (D) The cytomegalovirus (CMV) immunostain shows positive in those large cells, indicating CMV infection.

In our case, the ulcer areas of the intestinal mucosa presented with CMV infection and deposition of Kalimate crystals. To our knowledge, this is the first reported case of intestinal bleeding caused by combined cytomegalovirus enteritis and adverse effects of Kalimate.

4. Conclusion

GI bleeding is common in the elderly. Peptic ulcers, diverticular disease, and angiodysplasia are the most common causes of bleeding. However, other less common causes, such as infectious enterocolitis or drug-induced injury, should be considered. CMV infection of the GI tract is uncommon and can be fatal. Kalimate or Kayexalate are commonly used in treating hyperkalemia and may be associated with severe GI adverse events. Physicians must be cognizant of the risk of adverse events when prescribing such medication. Careful evaluation of the patient's underlying disease, clinical presentation, and medical history will help to provide the patients with the most appropriate treatment.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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