

Kayexalate-induced Colon Necrosis and Colon Stricture: A Case Report

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Abstract

Hyperkalemia in patients with renal insufficiency could be life-threatening. One method for treating hyperkalemia is with sodium polystyrene sulfonate (kayexalate), a cation-exchange resin. While some minor gastrointestinal disturbances, such as constipation, anorexia, and nausea, are known side effects, there have also been reports of serious gastrointestinal complications. Here, we present a Taiwanese female patient with acute diarrhea, acute kidney injury, and hyperkalemia who developed colon necrosis with bloody stool as a result of oral kayexalate treatment. This case later complicated with colon polyp formation and stricture. Careful use of the drug could help avoid unnecessary complications.

Key Words: kayexalate, colon necrosis, hyperkalemia

Introduction

Kayexalate is a cation-exchange resin used to treat life-threatening hyperkalemia. Some minor gastrointestinal disturbances were known to be the side effects of the agent¹. However, there have been some serious gastrointestinal complications reported². The additional insult of iatrogenic colonic ischemia, ulcerations and necrosis superimposed on a critical illness may lead to perforation and even mortality of the patient². The case reported here involves a patient with colon necrosis presenting with bloody stool, which later complicated into the formation of inflammatory polyps and colon stricture, caused by oral kayexalate in a patient with diarrhea, acute kidney injury, and hyperkalemia.

Case report

One 81-year-old female was admitted to the hospital due to severe diarrhea following the use of bisacodyl (one of laxative agents) 10mg usage. She had a history of senile dementia, but no prior history of diabetes, hypertension or other systemic disease. She had normal renal function before this admission, with a serum creatinine of 0.75 mg/dL. Notably, She had a history of chronic constipation and regularly took 20 mg of sennosides daily. Acute diarrhea and weakness developed one day after the administration of an additional 10mg of bisacodyl.

On physical examination, she had an acute ill-looking appearance. Her blood pressure was 91/47 mmHg, pulse rate 50 beats per min, respira-

tory rate 16 breaths per min and body temperature 36.6°C. The head was normal and supple. Cardiac and lung examinations were unremarkable, with clear lung sounds. The abdomen was soft, with no localized pain, rebounding pain or muscle guarding; however, hyperactive bowel sounds were present. Poor skin turgor was observed. Laboratory tests were as follows: white blood cell count 8,760/mm³, hemoglobin 10.6g/dL, and platelet count 156,000/L. Serum BUN and Cr were 111 mg/dL and 4.5 mg/dL, respectively. Serum electrolytes showed sodium at 136 mMol/L and potassium at 6.1 mMol/L. An electrocardiogram (ECG) showed only sinus bradycardia. Based on the diagnosis of enterocolitis and acute kidney injury with hyperkalemia, fluid resuscitation and oral 5g kayexalate three times daily were prescribed. The appropriate antibiotic was initially administered. Acute onset of colic abdominal pain and severe bloody stools occurred 3 days later. On clinical examination she had a tender abdomen without signs of peritonitis. Serial stool cultures, especially for *Clostridium difficile*, were negative. Due to severe bloody stools following the previous

treatment, a colonoscopy was performed. Colonoscopy (Fig.1) revealed extensive friable mucosa with ulceration and erythematous mucosa with edematous change extending from the sigmoid colon to the ascending colon. Pathological examination of the colitis tissue showed kayexalate crystal deposition (bright purple crystals) surrounding by granulation tissue and inflammatory cells, compatible with kayexalate-induced colitis (Fig.2A). Fig.2B (100x magnifications) revealed acute inflammatory cells and necrotic debris, compatible with acute colon necrosis.

Given the diagnosis of kayexalate-induced colitis, conservative treatments including bowel rest were prescribed. Subsequently, her condition gradually improved, and she was discharged in a better state one month later. After discharge, the patient

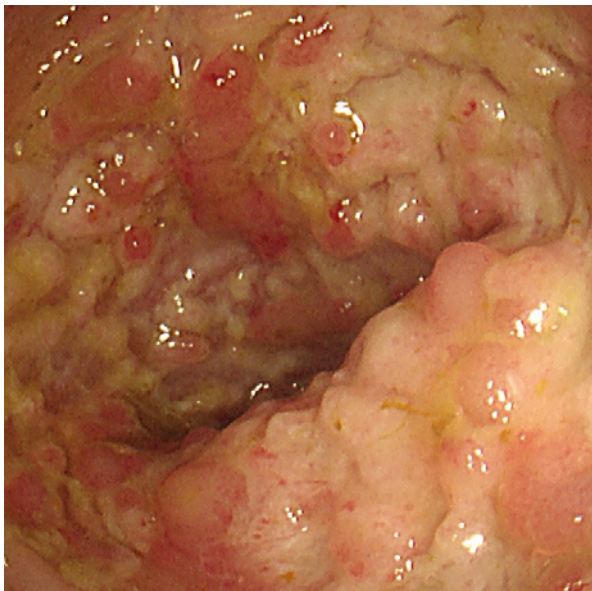
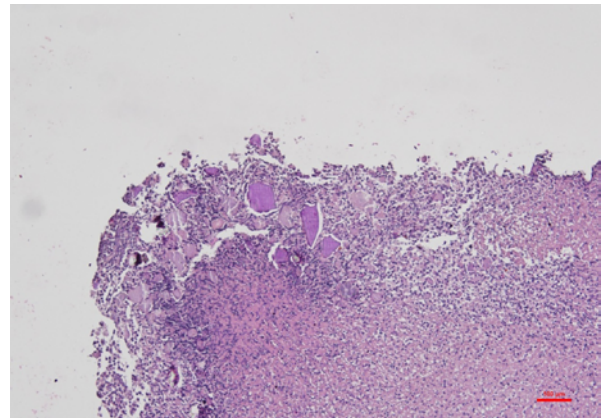
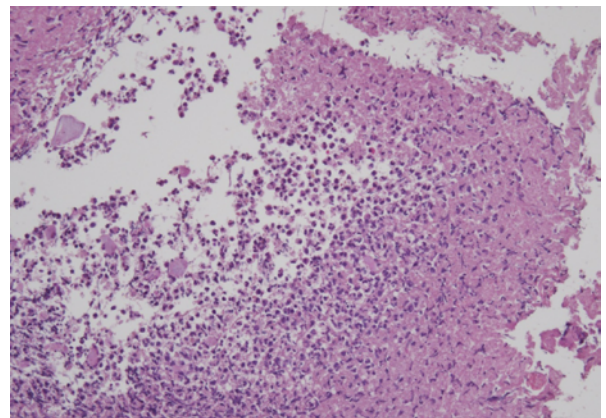


Figure 1. Colonoscopy revealed extensive friable mucosa with ulceration and erythematous mucosa with edematous change from the sigmoid colon to the ascending colon.



A. Kayexalate (bright purple crystals) surrounding by granulation tissue and inflammatory cells (40x)



B. Acute inflammatory cells and necrotic debris (100x)

Figure 2.

denied recurrent bloody stools or diarrhea, but continued to have poor bowel movements. A repeat colonoscopy performed six months later (Fig.3A and Fig.3B) showed improved extensive colitis. However, it still revealed segmental colitis with mucosal hyperemia and erosion in the sigmoid colon (Fig.3A). Colon stricture and pseudopolyp formation were also noted in this segment (Fig.3B). Histopathology of the colitis tissue (Fig.4A) still showed



A. Sigmoid colon colitis with mucosal hyperemia and erosion



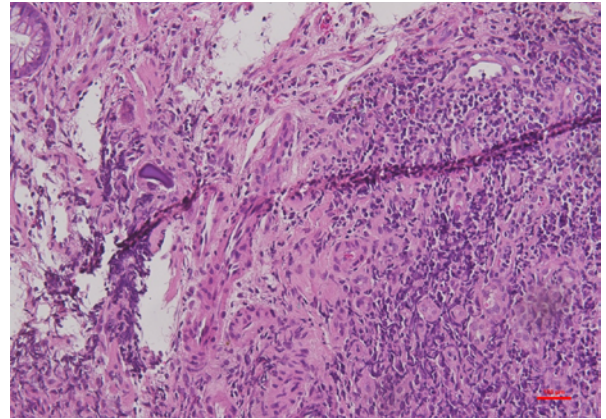
B. Sigmoid colon stricture and pseudopolyp formation

Figure 3.

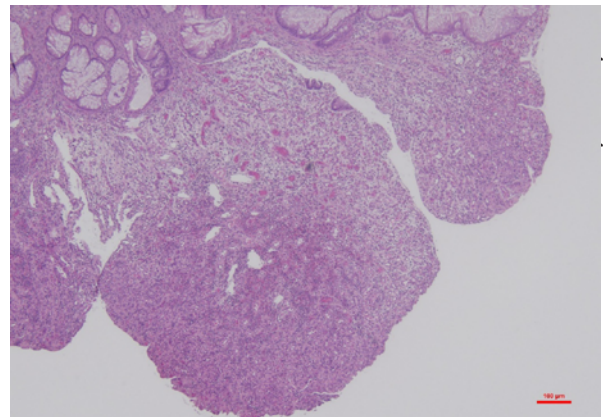
scanty kayexalate crystals (bright purple crystals) within granulation tissue, consistent with kayexalate-induced colitis. The colon pseudopolyp pathology (Fig. 4B) revealed a polypoid configuration with focal surface erosion and granulation tissue, consistent with chronic inflammation. Given the absence of symptoms, apart from constipation, only clinical observation was prescribed.

Discussion

Kayexalate is an ion-exchange resin that exchanges sodium for potassium in the gastrointestinal tract, particularly in the colon. It increases fecal potassium excretion and was approved by the Food



A. Scanty Kayexalate (bright purple crystals) present within granulation tissue (200x)



B. Colonic mucosa in a polypoid configuration with focal surface erosion, granulation tissue (abundant thin walled and dilated vessels surrounded by mixed neutrophilic and lymphoplasmacytic inflammation) (expanded lamina propria) and absent fibrosis (20x)

Figure 4.

sis of the terminal ileum and colon associated with its use began to accumulate^{4,5}.

Minor gastrointestinal disturbances, such as constipation, anorexia, and nausea were mentioned frequently¹. However, some healthcare professionals may not recognize that there are other serious side effects, such as colonic ischemia, ulcerations and necrosis, perforation and even mortality². The true incidence of colonic necrosis after kayexalate use is unknown. A retrospective cohort study reported an incidence of 0.14% (95% CI, 0.03%–0.40%) in hospitalized patients prescribed oral kayexalate with sorbitol⁶. Another study by Gerstmann et al.⁷ noted a 0.27% overall incidence, with a higher rate of 1.8% in the postoperative period. However, mortality in these severe gastrointestinal injury cases can be as high as 33%².

While there was evidence demonstrating sorbitol rather than kayexalate as the contributing factor of the colonic necrosis^{4,5,8}, this case did not involve the use of sorbitol. The exact mechanism of kayexalate-induced colonic necrosis remains unknown. Prior reports have indicated that various risk factors, including chronic kidney disease, end-stage renal disease, solid organ transplantation, postoperative status, hypovolemia, peripheral vascular disease, and immunosuppressive therapy, may contribute to gastrointestinal injury associated with kayexalate use^{9–12}. One possible mechanism is that elevated renin levels, commonly seen in renal insufficiency, predispose patients to nonocclusive mesenteric ischemia via angiotensin-mediated vasoconstriction¹³. In this case, kayexalate-induced colitis may have resulted from acute kidney injury combined with hypovolemia and diarrhea-related enteritis.

The colon is the most common site for kayexalate-induced gastrointestinal injuries². Diagnosing kayexalate-induced colitis via colonoscopy can be challenging, as its findings often mimic other conditions like ischemic colitis^{14,15}, non-specific ulcers¹⁶, or pseudotumors¹⁷. A definitive diagnosis of kayex-

alate-related mucosal necrosis relies on identifying the characteristic angulated kayexalate crystals with a mosaic pattern¹⁸ in specimens. Biopsies of affected areas typically show basophilic or violet crystals embedded in the mucosal surface, along with superficial inflammatory exudate on H&E staining¹⁸. For example, Chou et al.¹⁴ documented a case where a young uremic patient developed colonic necrosis after taking oral kayexalate with sorbitol. The patient's colonoscopy images showed multiple, isolated, well-demarcated ulcers in the splenic flexure and transverse colon, with some linear ulcers along the colon's longitudinal axis. Given the ulcer pattern, ischemic colitis was initially considered the most likely diagnosis. The correct diagnosis of kayexalate-induced colitis was later confirmed when bright purple kayexalate crystals were found in ulcerated debris or embedded within the colonic lamina propria. In some case reports or review of the Literature^{6,7,19}, these crystals can be found in biopsies from colonoscopies or in surgical specimens. Surgical specimens are usually required for more severe cases involving complications like colon perforation^{7,20,21}, obstruction^{22,23}, or stricture^{24,25}.

A colonoscopy in our case revealed extensive friable mucosa with ulceration and erythematous mucosa exhibiting edematous change, extending from the sigmoid colon to the ascending colon. The major clinical differential diagnosis included ischemic, infectious, inflammatory, or drug-induced colitis. The diagnosis was later confirmed by the identification of kayexalate crystals. Additionally, these crystals can persist for up to six months and may lead to colon stricture and pseudopolyp formation.

Despite a Food and Drug Administration black-box warning regarding its use with sorbitol and ongoing debate about its efficacy in reducing serum potassium levels, kayexalate continues to be widely prescribed for the management of acute and chronic hyperkalemia^{7,26,27}.

To determine whether kayexalate is appropriate for the patient, we should consider the patient's potassium level, ECG rhythm, hypovolemia status, comorbid conditions, contraindications, drug interactions and status of bowel movement. The administration of these resin agents in the elderly with decreased bowel function due to conditions, such as enteritis and acute kidney injury, poor intestinal perfusion, should be approached with caution.

Based on this case report and a review of the literature, kayexalate should be used with extreme caution in patients with diarrhea and hyperkalemia, especially ECG did not reveal hyperkalemia change. Alternative methods such as adequate hydration, glucose/insulin/bicarbonate injections or hemodialysis should be considered for managing hyperkalemia in these patients.

If severe kayexalate colitis unfortunately occurs, immediate cessation of the drug is paramount. The initial management plan should involve supportive care with a focus on fluid replacement and electrolyte management. For suspected secondary infections or complications, antibiotics should be promptly initiated. Nutritional support, such as dietary adjustments or enteral nutrition, should be considered if the patient cannot tolerate oral intake. Close monitoring is crucial to observe for signs of improvement or deterioration and to adjust treatment as needed. Surgical intervention may be necessary in severe cases with complications like perforation or significant necrosis^{7,20,21}.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images

and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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聚苯乙烯磺酸鈉引發的大腸壞死及大腸狹窄： 一個病例報告

黃國智

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摘要

高鉀血症在腎功能不全的患者中可能是危及生命的。治療高鉀血症的一種方法是使用聚苯乙烯磺酸鈉 (Kayexalate)，這是一種陽離子交換樹脂。已知此藥物的一些輕微副作用包括便秘、食慾不振和噁心。然而，一些嚴重的胃腸道併發症也有可能發生。在此，我們報告了一例台灣女性患者，因急性腹瀉伴有急性腎損傷及和高鉀血症，口服 Kayexalate 後造成結腸壞死，伴有血便，該病例後來發展為結腸息肉形成和狹窄，小心使用這類藥物應能避免不必要的併發症。