An unusual recurrent ileocolonic injury

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Abstract

Potassium binders (Kayexalate® and Sorbisterit®) are commonly used to treat hyperkaliemia. They are made of sodium or calcium polystyrene sulfonate. Their use is associated with multiple adverse effects including ileocolonic (or more rarely upper digestive tract) injuries which can lead to necrosis or perforations. This side effect is mostly seen in patients with chronic kidney disease or constipation. It presents with abdominal pain, diarrhea or hematochezia. The diagnosis is made when the histo-logical analysis of samples from the erythematous or ulcerated digestive wall finds polystyrene sulfonate crystals embedded in the mucosa. This diagnosis can be suspected by taking a careful initial drug inventory, if the clinician is aware of this rare but serious adverse effect. The lack of specificity of clinical symptoms and endoscopic lesions makes this inventory even more essential. Treatment is mainly supportive and requires cessation of the drug, while surgery is inevitable in the most severe cases. (Acta gastroenterol. belg., **2021,** 84**, 666-668**).

Keywords: Polystyrene sulfonate, hyperkaliemia, chronic kidney disease, colitis, necrosis.

Introduction

Potassium binders are widely used to treat hyperkaliemia since the 1970s. Among their side effects, one is serious and life threatening: gastrointestinal tract necrosis (1). Indeed, colonic injury (more rarely gastric or small intestine lesions) ranging from mucosal erythema to extensive necrosis, including ulcers or perforations, have been associated with the intake of these drugs, mainly in patients with chronic kidney disease (CKD) (2,3). This adverse effect remains largely unknown to practitioners, even among gastroenterologists.

Case report

A 56-year-old man presented to the emergency department with a 2-day history of abdominal pain in the right lower quadrant, non-radiating and associated with non-bloody vomiting. He reported a chronic tendency to constipation that was unchanged. He denied having fever, melena or hematochezia. His medical history included end stage renal disease (ESRD) due to polycystic kidney disease for which he had been on dialysis 3 times a week for 3 years, arterial hypertension, hypercholesterolemia, insulin-requiring type II diabetes, as well as asymptomatic cecal ulcers found on screening colonoscopy 1 year earlier. Biopsies of these ulcers were non-specific. Outpatient medications consisted of atorvastatin, acetylsalicylic acid, sodium bicarbonate, phosphate binder, potassium binder (Sorbisterit®) and pantoprazole. He denied smoking and had no known allergy.

On admission, parameters showed tachycardia at 124/min and hypertension at 156/92 mmHg, he was afebrile. His physical examination found normal cardiopulmonary auscultation, but guarding on palpation of the right lower quadrant. He had normoactive bowel sound. Significant laboratory values included white blood cell count of 16,000/µL with 82% neutrophils, as well as an increase in CRP to 202 mg/L. Unsurprisingly in view of his ESRD, serum creatinine and potassium were increased (respectively 10.6 mg/dL and 6.9 mEq/L), while bicarbonate was low (16.4 mEq/L). Liver and pancreatic function tests were normal, while LDH was increased to

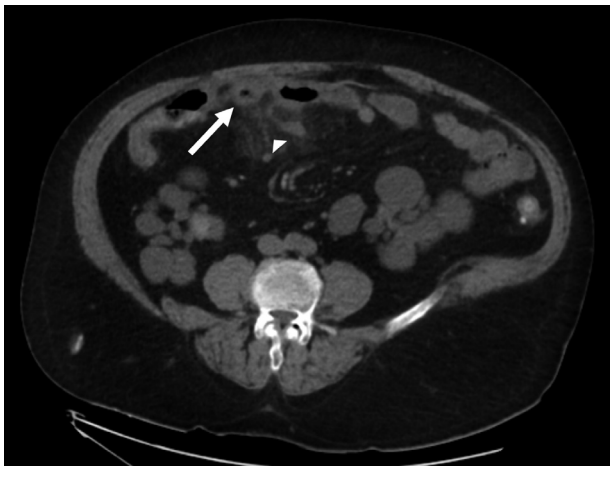

Figure 1.

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Submission date : 01/10/2020
Acceptance date : 02/12/2020

294 U/L (normal: 135-225). An abdominal computerized tomographic (CT) scan was performed, which showed ileitis with wall thickening of the terminal ileum and stranding of adjacent fat (Fig. 1).

Patient was admitted for complementary assessment. Stool cultures and examination for *C. difficile* were negative. Abdominal CT scan with injection of contrast medium showed good permeability of mesenteric and portal vessels.

Due to good clinical and biological evolution under empiric antibiotics (Amoxicillin-clavulanic acid), infectious ileitis was suspected and patient was discharged home on day 4.

He presented again to the emergency department 9 days after his discharge for recurrence of abdominal pain, this time associated with diarrhea and fever (38.7 °C). His blood sample showed an increase in CRP (168 mg/L, compared to 88 mg/L at discharge). Repeated abdominal CT scan showed in addition to the ileitis, the presence of two tiny extra-visceral air bubbles suggesting a minimum digestive perforation. Conservative treatment has been adopted given his stable clinical condition. He was re-admitted, under broad spectrum IV antibiotics (Piperacilin-Tazobactam). Colonoscopy was performed after 5 days of clinical and biological improvement, which showed localized ulcers surrounded by erythema in the transverse colon and the hepatic flexure (Fig. 2). There was no loss of vascularity of surrounding mucosa.

To our surprise, endoscopic appearance of the terminal ileum was normal. Biopsies at the edges of colonic ulcers were taken, which revealed ulcerated colonic mucosa, with infiltration of inflammatory cells around polystyrene Sulfonate (PS) crystals, embedded in the mucosa (Fig. 3).

The differential diagnoses (infection, ischemia and chronic inflammatory bowel disease) having been reasonably excluded, and in view of the histological findings, the diagnosis of ulcerative ileocolitis due to PS was retained, and this drug was suspended. The outcome was then favorable, without no recurrence after 6 months of follow-up.

Cross-sections on the biopsies of the cecal ulcerations found in the screening colonoscopy 1 year earlier were made. They showed, in less abundance, these same crystals embedded in the mucosa.

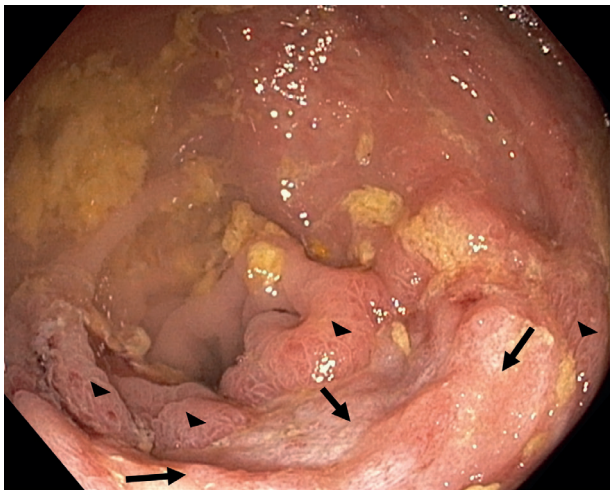

Figure 2.

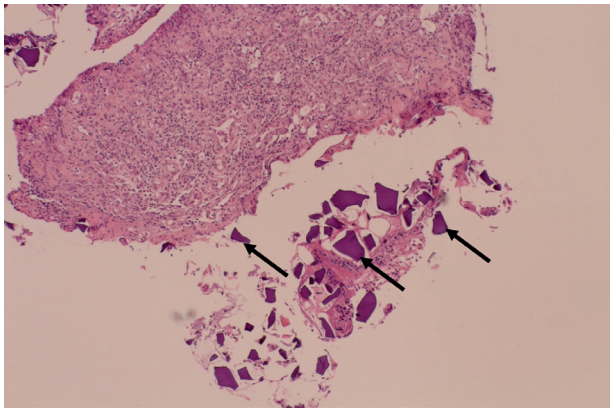

Figure 3.

Discussion

Sodium or calcium PS are cation exchange resins. Their mechanism is to exchange their bound sodium or calcium for intraluminal potassium (4). In this way, they prevent the absorption of potassium from the lumen of the digestive tract and decrease serum potassium. They were approved by the FDA in 1975 (5). Because they tended to provide constipation, sorbitol was initially added to PS solutions for its laxative effect (6). The first case of colonic lesion due to PS was described in 1987 by Lillemoe et al., in patients treated with enemas combining PS and sorbitol who developed colonic necrosis (1). Lillemoe then conducted an experimental study on uremic rats, that suggested that the necrosis was due to sorbitol rather than PS. This led the FDA to remove resins with a high rate of sorbitol (7). Later, cases of colonic necrosis after intake of PS without sorbitol were observed, questioning the attribution of digestive damage to sorbitol rather than to PS (8). The clinical case we herein describe is also illustrative of that. Indeed, despite what its name might suggest, Sorbisterit® does not contain sorbitol.

Ileocolonic injuries due to PS occur in up to 1% of patients treated with these resins, and are probably underestimated because of the lack of awareness of this side effect (9). 91% of cases of digestive tract lesions due to PS appear in patients with CKD (8). Constipation and ileus are other predisposing factors, by slowing transit and increasing the contact time of the resins with the digestive mucosa (10,11). Cases of upper digestive tract injuries (stomach, duodenum) have also been described more rarely (3). The lesions can appear a few hours or days after a one-time use of PS (9). They can sometimes also appear several years after the initiation of chronic intake of PS, for a reason still unknown to this day. The precise pathophysiology remains unclear. An alteration of the intestinal microcirculation and a release of

prostaglandins are suspected (2). CKD may therefore be a risk factor through splanchnic vasoconstriction induced by the activation of the renin angiotensin aldosterone system existing in the context of renal disease.

The diagnosis is made, after exclusion of differential diagnoses, when typical crystals (striated, polygonal and basophilic) are found in the intestinal mucosa of erythematous or ulcerated regions (12). These crystals have a characteristic "broken glass" appearance. In the most severe cases, transmural involvement of the wall is observed, raising the risk of perforation. The main differential diagnoses that should be ruled out are infection, ischemia, drug-related ileocolitis (mainly nonsteroidal anti-inflammatory), or chronic inflammatory bowel disease. The prognosis depends on the injured organ, the extent, and depth of the lesions. In the most severe cases, extensive colonic necrosis can occur, with an alarming mortality of 36% (13). In contrast, upper digestive tract injury related to PS has a better prognosis (14).

In the absence of specific treatment, the management is supportive and empirically consists on the cessation of PS. In the most severe cases, surgical resection is inevitable.

In patients with multiple risk factors, a low potassium diet and drug alternatives should be preferred. One of the therapeutic possibilities against hyperkalemia is Patiromer, a different potassium binder available since 2018. However, due to its high cost, the use of this drug in clinical practice remains uncommon.

Conflict of interest

None.

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