Intestinal Necrosis Associated with Orally Administered Calcium Polystyrene Sulfonate Without Sorbitol

Philippe Goutorbe, Ambroise Montcriol, Guillaume Lacroix, Julien Bordes, Eric Meaudre, and Jean-Baptiste Souraud

OBJECTIVE: To describe a case of extensive intestinal necrosis with oral intake of calcium polystyrene sulfonate without sorbitol.

CASE SUMMARY: A 73-year-old woman was admitted to the emergency department with abdominal pain. Abdominal computed tomography (CT) scan showed widespread dilatation of the bowel. The diagnosis of acute colonic pseudoobstruction was made. On day 3, her serum potassium level rose to 5.6 mEq/L. It was treated with hydrocortisone 100 mg/day and calcium polystyrene sulfonate 15 g/day via nasogastric tube from day 3 to day 6. On day 6, the severe abdominal pain recurred, with abdominal tenderness. CT scan showed pneumoperitoneum and peritoneal effusion. At surgery, 2 lenticular jejunal perforations and an ischemic cecum were found. Microscopic findings indicated that the transmural abscess contained massive inflammatory infiltrate and the cecal mucosa showed ulceration and inflammation with a fibrinous and purulent coating. Small gray-purple or blue angulated crystals were embedded in the cecal and most of the jejunal mucosal ulcers. On day 19, the patient died of multiple organ failure after her third laparotomy.

DISCUSSION: Ion-exchanging resins are given orally or by retention enema for the treatment of hyperkalemia. The most commonly used and best-established resin is sodium polystyrene sulfonate. However, it is known to promote colonic necrosis when sorbitol is also given or especially in patients with renal failure or postoperative ileus. Calcium polystyrene sulfonate is another ion-exchange resin. There are few reports of adverse effects in the literature. Our case is interesting for 2 reasons: the resin given was calcium polystyrene sulfonate and sorbitol was not used.

CONCLUSIONS: Like sodium polystyrene sulfonate, calcium polystyrene sulfonate is an ion-exchanging resin that can promote bowel necrosis. We believe that it should not be used with sorbitol or when bowel transit time is slowed.

KEY WORDS: adverse effects, calcium polystyrene sulfonate, chemically induced pathology, intestinal diseases, oral cation exchange resins, sodium polystyrene sulfonate.

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Sodium polystyrene sulfonate is a well-known ion-exchange resin given orally or as a retention enema for the treatment of hyperkalemia. Digestive tract necrotization is a well-known complication, especially when sorbitol is used with sodium polystyrene sulfonate, or in patients with renal failure or postoperative ileus.[1,2] Calcium polystyrene sulfonate is another new ion-exchange resin of interest in chronic renal failure because it provides calcium without sodium intake. To our knowledge there are only 3 reports of colonic ulcer with this resin.[3-5] Nevertheless, in these cases ulcers were limited to the mucosa without any bowel perforation. We describe a case of extensive intestinal necrosis following the use of calcium polystyrene sulfonate without sorbitol. For this event the Naranjo adverse drug reaction score indicates that it is probable that there was an adverse drug effect.[6]

Case Report

A 73-year-old white woman was admitted to the emergency department with abdominal pain. She had a history of

Author information provided at end of text.

chronic pulmonary obstructive disease, which was treated with general corticosteroid therapy (methylprednisolone 2 mg/day). On admission, her temperature and hemodynamic status were normal. Abdominal computed tomography (CT) scan showed widespread dilatation of the bowel. There was no peritoneal effusion or intestinal obstruction. The diagnosis of acute colonic pseudoobstruction (Ogilvie's syndrome) was made. Endoscopic exsufflation showed healthy colonic mucosa. On day 3, the serum potassium level rose to 5.6 mEq/L, which was attributed to adrenal insufficiency. It was treated with hydrocortisone 100 mg/day and calcium polystyrene sulfonate 15 g/day via nasogastric tube from day 3 to day 6. Daily additional treatments included 3 g of acetaminophen, 3 g of magnesium sulfate, and an intravenous perfusion of 2000 mL of isotonic saline.

On day 6, severe abdominal pain recurred, with abdominal tenderness and early signs of shock. Abdominal CT scan showed pneumoperitoneum and peritoneal effusion. During surgery, 2 lenticular jejunal perforations and an ischemic cecum were found. The necrotic bowel was resected with 2 anastomoses. The pathology report showed right hemicolectomy including 12 cm of colon and 22 cm of ileum. In the cecum, the mucosa near the appendix showed an area of brown ulceration in contact with a 5-cm submucosal abscess, containing a purulent exudate, but no pseudomembranes. The ileum showed some white fibrinous coating of the serosal surface. A longitudinal 28-cm long opening of the resected jejunum showed small mucosal areas with nonconfluent aphthous erosions and reddish or sometimes greenish areas on the serosal surface. Microscopic findings included transmural abscess massive inflammatory infiltrate, and ulceration and inflammation of the cecal mucosa with a fibrinous and purulent coating. Small gray-purple or blue angulated crystals were embedded in the cecal and most of the jejunal mucosal ulcers (Figure 1). Fewer were in the luminal area (Figure 2). These crystals stained dark red with periodic acid-Schiff (PAS) stain (Figure 3); with acid-fast stain, they were refractile but did not exhibit refringence under polarized light. The residual colonic and jejunal mucosa, submucosa, and muscularis propria were unremarkable, and there was no evidence of vascular thrombosis, cholesterol emboli, or fibrin emboli.

On day 11, a second episode of shock occurred. Exploratory laparotomy showed peritonitis due to rupture of the colonic anastomosis. The pathologist reported that on resection of 19-cm small bowel, mucosa looked normal but an important white "deposition" was present on the serosal surface. Microscopic findings included small mucosal ulcerations with crystals as described above. Numerous crystals, neutrophils, and fibrin covered the serosa.

On day 17, a third laparotomy became necessary. There was extensive necrosis of the small intestine, due to a mesenteric infarction. The pathologist reported a small bowel fragment of 3 cm with oxblood red color. Microscopic findings showed that the entire mucosal structure

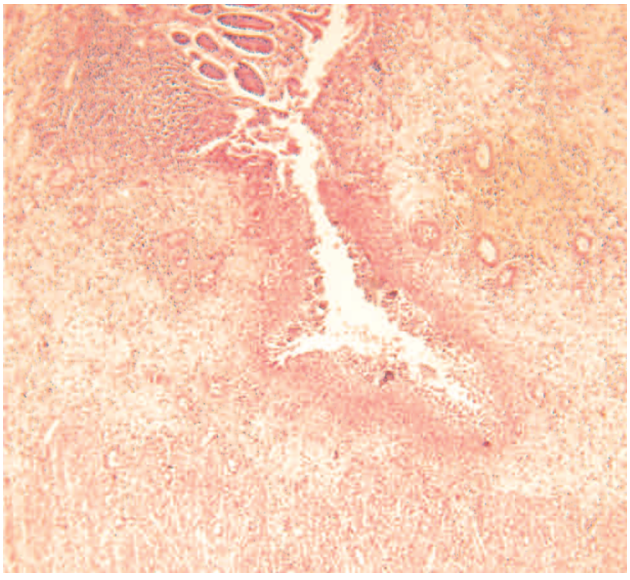

Figure 1. Small gray-purple or blue angulated crystals are embedded in the cecal and most of the jejunal mucosal ulcers.

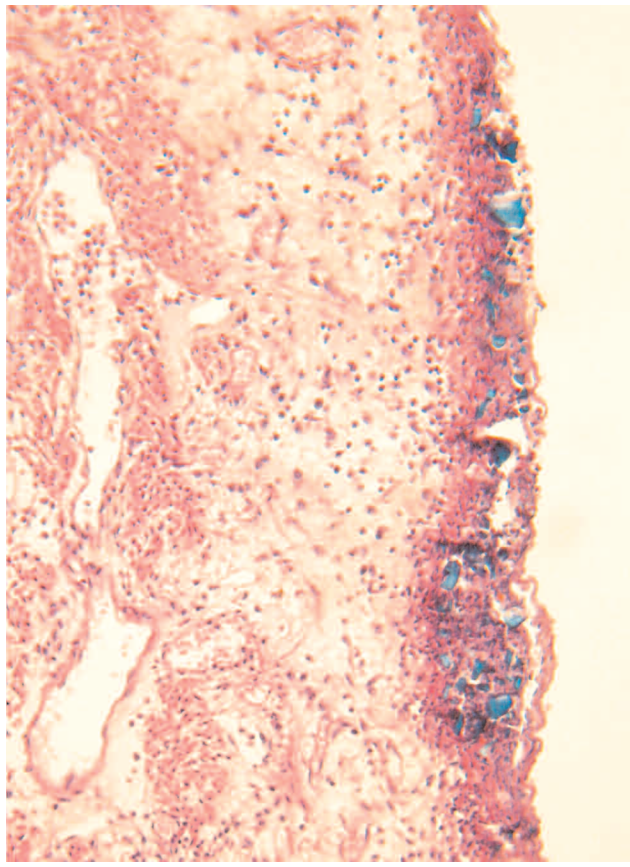

Figure 2. The crystals are present on the serosal surface, which has a coating of fibrin and neutrophils.

was infarcted with crystals in some areas, submucosa was edematous and hemorrhagic, and crystals were present on ischemic serosa.

The patient died 2 days later of multiple organ failure.

Discussion

Ion-exchanging resins are given orally or by retention enema for the treatment of hyperkalemia. The most commonly used and best established is sodium polystyrene sulfonate. It is known to promote colonic necrosis, especially in uremic patients; when sorbitol is also given; and in postoperative ileus.[1,7,8] The lesions are usually predominantly in the distal ileum and right colon, and pseudomembranes and mucosal ulceration are often observed. Partial or total wall necrosis is frequent and may be complicated by perforation with peritonitis. Microscopic examination of the surface of these ulcerations showed quadrangular, gray-blue crystal clusters, colored red by PAS, showing the Ziehl acid-fast stain.[1,9] However, such crystals are not always pathologic and may not be significant in cases of colonic necrosis.

Calcium polystyrene sulfonate is another ion-exchange resin of interest in chronic renal failure because it provides intake of calcium, rather than sodium. There are few reports of adverse effects in the literature. Gastric radio-opaque masses in very-low-birth-weight infants, a case of delayed colonic ulcer in a 77-year-old woman who had also been given sorbitol, and intestinal obstruction in a 74-year-old man have been reported.[5,10-12]

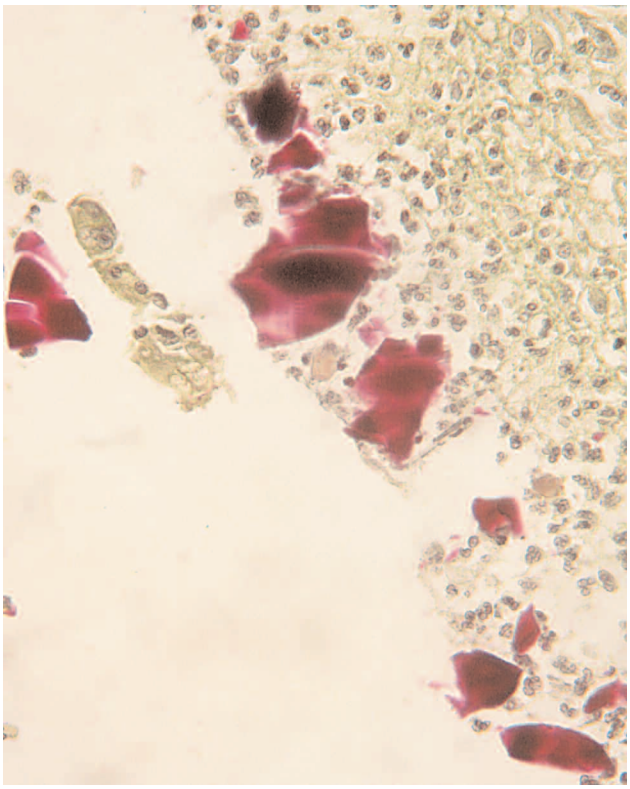

Figure 3. These crystals stain dark red with periodic acid-Schiff (PAS) stain and with acid-fast stain. They are refractile but do not exhibit refringence under polarized light.

Our case is interesting for 2 reasons: the resin is calcium polystyrene sulfonate and sorbitol was not used. In clinical and experimental reports, sorbitol is thought to be the main contributor to intestinal necrosis associated with use of an ion-exchange resin. The experimental study of Lillemoe et al. is the most impressive.[1] In rats, sorbitol alone and sodium polystyrene sulfonate in sorbitol enemas promoted colonic necrosis; on the other hand, sodium polystyrene sulfonate alone and saline enemas were safe.

The main differential diagnosis includes ischemic disease, infections such as *Clostridium difficile* colitis or enterohemorrhagic *Escherichia coli*, drug-induced lesions such as those caused by nonsteroidal antiinflammatory drugs, and even chronic conditions such as collagenous colitis, radiation colitis, and Crohn's disease. Our patient showed no evidence of ischemic colitis, such as geographic ulcers, hyalinized lamina propria, and withered or atrophic crypts, hemorrhage, or hemosiderin deposition. There were no lymphoid aggregates or granulomas, which are typical of Crohn's disease. The differential diagnosis of sodium polystyrene sulfonate crystals is cholestyramine crystals, which are more intensely basophilic and opaque, and are red with PAS, as with sodium polystyrene sulfonate, but pink with acid-fast stain.[1] Furthermore, this patient was not administered cholestyramine.

In summary, a conclusive report on this reaction has already been published. Because the colonic perforation appeared after the calcium polystyrene sulfonate was given, alternative causes of this perforation were eliminated, and crystals of calcium polystyrene sulfonate were identified in the cecal and the jejunal mucosa, we believe that this perforation is secondary to the oral administration of calcium polystyrene sulfonate. The Naranjo probability scale indicated a probable adverse drug reaction.

To our knowledge, this is the first reported case of fatal extensive intestinal necrosis following use of calcium polystyrene sulfonate without sorbitol. In this case, ileus is probably the most important risk factor. Like sodium polystyrene sulfonate, calcium polystyrene sulfonate is an ion-exchanging resin that can promote bowel necrosis. We believe that it should not be used with sorbitol or when bowel transit time is slowed (eg, in the case of postoperative ileus).

Philippe Goutorbe MD, Clinical Specialist, Head of Department of Intensive Care, Sainte Anne Military Teaching Hospital, Toulon, France

Ambroise Montcriol MD, Clinical Specialist, ICU, Sainte Anne Military Teaching Hospital

Guillaume Lacroix MD, Clinical Specialist, ICU, Sainte Anne Military Teaching Hospital

Julien Bordes MD, Clinical Specialist, ICU, Sainte Anne Military Teaching Hospital

Eric Meaudre MD, Clinical Specialist, ICU, Sainte Anne Military Teaching Hospital

Jean-Baptiste Souraud MD, Clinical Specialist, Anathomopathology, Sainte Anne Military Teaching Hospital

Correspondence: Dr. Goutorbe, goutorbephil@live.fr

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