Calcium Polystyrene Sulfonate Induced Necrotizing Ulcerative Enterocolitis - Not Just an Innocent Bystander

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Authors’ contributions

This work was carried out in collaboration among all authors. Author KHC conceptualized the case, performed literature review and wrote the initial draft. Author AM provided histology input and pictures. Author WZYD managed the patient, assisted with the initial draft and performed literature search. Author RM provided expert opinion and helped in reviewing the draft. All authors read and approved the final manuscript.

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ABSTRACT

Introduction and Aims: Resins are non-absorbable medications that facilitates ion exchange and are commonly used in the treatment of hyperkalemia. Crystal deposition by these resins could result in and aggravate colonic mucosal damage. This rare but serious adverse event is under-recognized and is reportedly associated with life-threatening enterocolitis. We would like to present a case of necrotizing ulcerative enterocolitis in a patient with acute dysentery with concomitant calcium polystyrene sulfonate (CPS) prescription.

Case Presentation: An 85-year-old lady presented to us with generalized abdominal pain and bloody diarrhea for one week. She was febrile, dehydrated and lethargic. Her abdomen was soft with non-specific generalized mild tenderness. Other clinical examination was unremarkable. Laboratory indices revealed raised inflammatory markers with acute on chronic kidney disease (CKD). Relevant findings include hyperkalemia, metabolic acidosis and tall-tented T waves on her electrocardiographic (ECG) recordings. A working diagnosis of acute dysentery complicated by
CASE PRESENTATION

1. INTRODUCTION

Calcium polystyrene sulfonate (CPS), alongside sodium polystyrene sulfonate (SPS) are cation exchange resins which are widely used in hyperkalemic patients. Their usage is often safe and effective and as a result, physician oversight to the rare instances of adverse events may happen along the way. Though supplanted mostly by better access to hemodialysis facilities in many hospitals, CPS is still used when there is a delay in organizing for more definitive management. It is also pertinent to note that access to hemodialysis may not always be available in rural, outlying hospitals. The literature is replete with reports on SPS being well associated with necrotizing colitis but that of CPS is less well-described.

2. CASE PRESENTATION

Our patient was an 85-year-old pleasant lady with a background of chronic hypertension, advance osteoarthritis of both her knees and CKD stage IV. She has been fairly well prior to her recent illness. Aside from the above, she was also seeking over-the-counter aids for chronic constipation and joint pain. Her chief complaints were that of low-grade fever, generalized abdominal pain and bloody diarrhoea for one week. Clinical examination was unremarkable aside from signs of dehydration and non-specific abdominal tenderness on superficial palpation.

Relevant blood investigations revealed hemoglobin of 10.8 g/dL (range 12.0-15.0 g/dL), total white count of 9.5 x 10^9/L (range 4.0-10.0 x 10^9/L), lactate of 1.88 mmol/L (range 0.5-2.2 mmol/L) and C-reactive protein of 131 mg/L (normal <5.0 mg/L). Her renal parameters were significantly deranged with features of acute on CKD with potassium of 7.2 mmol/L (range 3.5-5.1 mmol/L), urea of 60.6 mmol/L (range 3.5-7.0 mmol/L) and creatinine of 354 umol/L (range 50-98 umol/L). There was also compensated metabolic acidosis where her pH levels were 7.350 (range 7.320-7.420) and bicarbonate of 13.8 mmol/L (24.0-28.0 mmol/L), Liver function was normal. Blood and stool cultures yielded no growth until the end of her stay.

She was admitted to the general medical ward where resuscitative measures continued from the emergency department. As part of the ongoing management, she was started on broad-spectrum antibiotics (intravenous ceftriaxone 2 g daily and intravenous metronidazole 500 mg three times a day), intravenous fluids per protocol for fluid resuscitation, oral CPS powder 15 g three times daily and a cocktail regime of 10% calcium gluconate, insulin and 50% dextrose. The latter two was prescribed as a temporizing measure to reverse hyperkalemia and for cardioprotective measures.

Despite this, her condition deteriorated by day three and she started developing new bouts of massive hematochezia which necessitated blood transfusion. An urgent colonoscopy arranged revealed extensive and continuous colonic and distal ileal ulceration of varying sizes with diffuse mucosal denuding and sloughing (Figs. 1 and 2). Blood clots could be seen at regular intervals though upon flushing, no exact bleeding point was encountered.

The mucosal surface was friable and bleeds easily on direct contact. As our preliminary culture results were still pending, multiple targeted biopsies were sampled from the ulcer...

Keywords: Calcium polystyrene sulfonate; resin-based colitis; necrotizing enterocolitis; colonic crystal deposition.

Discussion and Conclusion: This case highlights the negative prospect of prescribing CPS to patients with any forms of colitis as it could further worsen the underlying pathology. One needs to be mindful of the adverse event and consider a higher threshold for prescribing it in certain cases.

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edge and base. The histopathology results reported findings of extensive mucosal ulceration and necroinflammatory exudates with presence of basophilic crystalloid material on the ulcer surface. These ‘fish scales’ material stained positive with acid fast stain giving it a dark magenta colored (Figs. 3 and 4). The report further described absence of infectious elements and no features of chronic inflammation or ischemic colitis. Collectively with the above clinical scenario and through multidisciplinary discussions, we were convinced that these features were compatible with CPS-induced colitis. We were also mindful that their presence could have aggravated the pathology of initial infective colitis.

The medication was stopped prior to the colonoscopy as haemodialysis was commenced earlier on. About five doses of the CPS (a cumulative total of 75 g) was served and despite corrective measures and supportive care, our patient succumbed a week after the colonoscopy.

Fig. 1. Diffuse and continuous mucosal erythema with pseudomembrane, inflammation and ulceration with no intervening normal mucosa within the right-sided colon

Fig. 2. Diffuse and continuous mucosal inflammation with punched out ulcers seen in the left-sided colon
Fig. 3. A segment of the necroinflammatory colonic mucosa with ulceration seen. Notice the purplish basophilic-stained crystal which adopts a rectangular ‘fish-scales’ shape (blue arrow) (hematoxylin and eosin stain x100)

Fig. 4. Dark magenta coloured crystals can be better appreciated here (acid fast stain x100)
3. RESULTS AND DISCUSSION

Colonic pathology associated with CPS are less reported than SPS and literature are confined to mostly case studies and one systematic review for the latter [1,2]. The pathophysiology as to how CPS induced mucosal injury is not well-known and postulations on direct trauma has been offered [3]. Co-prescription with sorbitol was at one point considered to induce mucosal injury but later observations reported that the resins alone might equally be as toxic to the intestinal tract [4-6].

As to whether an underlying colonic pathology would need to be present to serve as a nidus for necrotizing enterocolitis to occur remains unknown. It is however interesting to note that in patients who were afflicted with colonic pathologies, they were found to be either critically ill or possessed significant comorbidities to begin with [7-9]. This complicates the scenario further as patients who possessed multiple medical comorbidities were also of advanced age and are known to commonly harbour other potential colonic pathologies such as complicated diverticular disease and ischemic colitis. Critically ill patients on the other hand were exposed to the risk of hospital acquired infections such as Clostridium difficile, drug-induced, ischemic and infectious colitis. The endoscopic pathology encountered may not be any different compared to resin-based necrotizing enterocolitis. The presence of crystal deposits in histology may not necessarily translate immediately to resin-induced colitis. Additionally, description on the pathological slides regarding colitis may also overlap with other common colonic pathologies making it hard to identify the exact cause [10].

Nevertheless, we are aware that SPS (with or without sorbitol) and recently, CPS are infrequently associated with mucosal damage, transmural inflammation and even perforation leading to drastic complications such as peritonitis and death [1,11,12]. This highlights the importance of a combined clinical, laboratory, endoscopic and histopathological assessments in ruling out more common causes before considering CPS-induced mucosal necrosis. Due to the paucity of strong evidence and specific recommendations, remedial actions with regards to any underlying problems and cessation of resin-based agent should occur concurrently and close observation of the patient made in liaison with the respective disciplines involved.

In our patient despite the absence of positive blood and stool cultures, the presence of fever, bloody diarrhea and raised inflammatory markers were sufficient in pointing us towards infective colitis. Inflammatory bowel disease does not occur acutely and not at this age. There were no features of diverticular disease and even though CT scan could not be performed for fear of contrast-related nephropathy, the diffuse colonic involvement is not classical for ischemic colitis. There were no potentially competing drugs that could cause colitis and stool for Clostridium difficile toxin and glutamate dehydrogenase were negative.

The late presentation which was later compounded by hospital acquired infection in addition to her underlying comorbidities and advance age was not favourable to her recovery. Though we have never investigated this further, the underlying chronic constipation, presumably from slow-transit constipation may have prolonged contact time with CPS and further worsen the injury [12]. We do believe that her precedent problem began with infection and compounded by CPS-induced colitis.

4. CONCLUSION

Our case serves to highlight a potentially rare adverse event pertaining to a commonly prescribed resin in our hospitals nationwide. Though it may not necessarily translate into avoiding the usage of CPS as evidence goes, the treating physician needs to be mindful of a selective group of patients that are susceptible to developing CPS-induced necrotizing enterocolitis.

We recommend their avoidance in cases of suspected colitis manifesting as hematochezia which includes but are not limited to infectious colitis and ischemic colitis. Alternatives such as calcium gluconate should be considered for its proven cardioprotective effect while awaiting hemodialysis. Another point to note is that of delayed colonic transit time which is more profound in patients with suspected bowel obstruction, ileus or a background history of chronic constipation. In our opinion, resins should be avoided altogether in these cases.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.
ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES