“Crystal Crater”
Sevelamer-Induced Rectal Ulcer: A Rare Cause of Lower Gastrointestinal Bleeding from a Common Medication

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ABSTRACT

Sevelamer carbonate is widely available and used medication to control hyperphosphatemia in chronic kidney disease patients. Gastrointestinal side effects are common, however, there are only 2 published case reports of sevelamer causing lower gastrointestinal bleeding.

A 35 year old male with end stage renal disease (ESRD) secondary to IgA nephropathy presented with bright red stools. On the day of admission, while undergoing hemodialysis, patient had sudden onset hematochezia, 11 episodes approximately 100-150mL per episode with slight rectal pain. Initial laboratory examinations showed low haemoglobin at 8.4 g/dl from a baseline of 9.1 g/dl, which went further down to 6 g/dl, normal clotting parameters. Colonoscopy showed edematous rectal mucosa with intervening normal pinkish mucosa approximately 3-4cm from the anal verge with ulcerations and whitish exudates, with the largest measuring 5cm. Endoscopic biopsies of the rectal ulcers showed fragments of colonic mucosa with severe active inflammation, dense fibrinopurulent exudate, granulation tissue, and few yellow brown, crystalline materials, which are morphologically consistent with sevelamer crystals. Sevelamer was discontinued, patient sent home with Sucralfate enema 1 gram per rectum twice daily for two weeks. As of the time of writing this case report, approximately 7 months after, hematochezia has not recurred.

Though sevelamer induced rectal ulcers causing gastrointestinal bleeding are rare, attending nephrologists, gastroenterologists and pathologist should be aware of the possibility of the drug's effects as well as the typical morphological features on biopsy to establish the diagnosis - which would lead to prompt recognition and discontinuation of the offending drug.

INTRODUCTION

Sevelamer carbonate is a widely available and used medication for the treatment of hyperphosphatemia in patients with chronic kidney disease. It has been USFDA-approved since October 2007. Sevelamer is an orally administered ion-exchange resin which binds phosphate within the intestinal lumen, limiting absorption and thus, lowering serum phosphate levels[1]. Gastrointestinal side effects are common, including, but not limited to: vomiting (22%), nausea (20%), diarrhea (19%), dyspepsia (16%), abdominal pain (9%), flatulence (8%), and constipation (8%)[2]. After searching thoroughly through the Pubmed database, there are only 2 published case reports of sevelamer causing lower gastrointestinal bleeding[3,4]. We report a young patient with end stage renal disease on maintenance medications, including sevelamer and maintenance hemodialysis who presented with lower gastrointestinal bleeding.

CASE

A 35 year old male with end stage renal disease (ESRD) secondary to IgA nephropathy presented with bright red stools. On the day of admission, while undergoing maintenance hemodialysis, patient had sudden onset passage of bright red stools, 11 episodes approximately 100-150mL per episode with slight rectal pain. On review of systems, he had occasional constipation, described as occasional passage of hard stools. There was no abdominal pain, nausea, vomiting, weight loss, abdominal distention, weight loss, dizziness, syncope and change in stool caliber. He is maintained on hemodialysis thrice weekly and takes sevelamer, erythropoietin and iron sulphate + folic acid for 3 years due to ESRD, and clonidine as needed, telmisartan + amlodipine for his hypertension. He had no previous abdominal surgery or family history of colonic malignancy. Initial physical examination showed stable vital signs, pale conjunctiva with a nodular, soft tissue lesion 3-4cm from the anal verge and dull red dried blood per rectum on digital rectal examination. Initial laboratory examinations showed a low haemoglobin at 8.4 g/dl from a baseline of 9.1 g/dl, which went further down to 6 g/dl, normal prothrombin and partial thromboplastin time. Haemoglobin was stabilized via blood transfusions were done during dialysis and careful hydration. Patient was then prepared for colonoscopy.

Colonoscopy showed edematous rectal mucosa with intervening normal pinkish mucosa approximately 3-4cm from the anal verge with ulcerations and whitish exudates, with the largest measuring 5cm. (Figure 1) Multiple biopsies were taken and sent for histopathology.

Endoscopic biopsies of the rectal ulcers showed fragment of colonic mucosa with abundant neutrophils in the glandular epithelium and crypt lumens. The stroma shows granulation tissue

formation characterized by edema, vascular proliferation and inflammation with fibrinopurulent exudates admixed with the tissue fragments. Few yellow brown crystalline materials is present in the exudates, exhibiting a fish scale appearance on higher magnification. (Figure 2) Findings would be consistent with a medication-induced ulceration. Patient has been taking his Sevelamer tablets (Renvela) at 800 mg/tab thrice a day for the past 3 years. Sevelamer was discontinued, patient was sent home with Sucralfate enema 1 gram per rectum twice daily for two week. As of the time of writing this case report, approximately 7 months after, hematochezia has not yet recurred.

DISCUSSION

Sevelamer causing gastrointestinal mucosal injury is a rare occurrence. There are only two published case reports documenting sevelamer as the cause of rectal ulcerations with lower gastrointestinal bleeding. The first case involved a 62 year old patient with end stage renal disease presenting the lower gastrointestinal bleeding secondary to stercoral ulcers[3]. Histopathology showed denuded mucosa with acute and chronic inflammation. However, sevelamer crystals were not found, association was only assumed; since the patient was taking sevelamer with associated constipation for one month. The 2nd case reported a 72 year old patient also with end stage renal disease who took sevelamer 1600 mg orally thrice a day for 2 months presenting with rectal pain and blood tinged stools. Sigmoidoscopy revealed circumferential ulcerations and exudates with sevelamer crystals present on histopathological examination of the rectal ulcers[4]. Sevelamer was discontinued and substituted with calcium acetate.

Swanson et. al, also published case series[5] of sevelamer crystals in the gastrointestinal tract. They reported the first description of sevelamer crystals in gastrointestinal mucosal specimens and how to differentiate it from Kayexalate and Cholestyramine crystals. They described sevelamer crystals displaying a broad, curved, irregularly spaced fish scales with a characteristic 2 toned color imparted by bright pink linear accentuations with a rusty yellow background on hemotoxylin and eosin stain; which is seen in the histopathology specimen of our patient. In their case series, sites of involvement included the esophagus, small bowel and colon with associated mucosal damage, acute inflammation, extensive ulceration, ischemia, inflammatory polyp or necrosis.

The histopathologic findings of severe active inflammation, with granulation tissue and dense fibrinopurulent exudate would point to a foreign body reaction rather than a viral, bacterial or

neoplastic cause. Together with the presence of few brownish crystalline materials in the exudates, we highly believe that sevelamer has directly caused rectal mucosal injury in our case.

Conclusion

We presented a case of a young patient with end stage renal disease who presented with severe lower gastrointestinal bleeding necessitating blood transfusion and volume replacement. This is the second reported case of sevelamer directly causing rectal ulcer or bleeding. Though sevelamer induced rectal ulcers causing gastrointestinal bleeding are rare, attending nephrologists, gastroenterologists and pathologist should be aware of the possibility of the drug's effects as well as the typical morphological features on biopsy to establish the diagnosis - which would lead to prompt recognition and discontinuation of the offending drug.

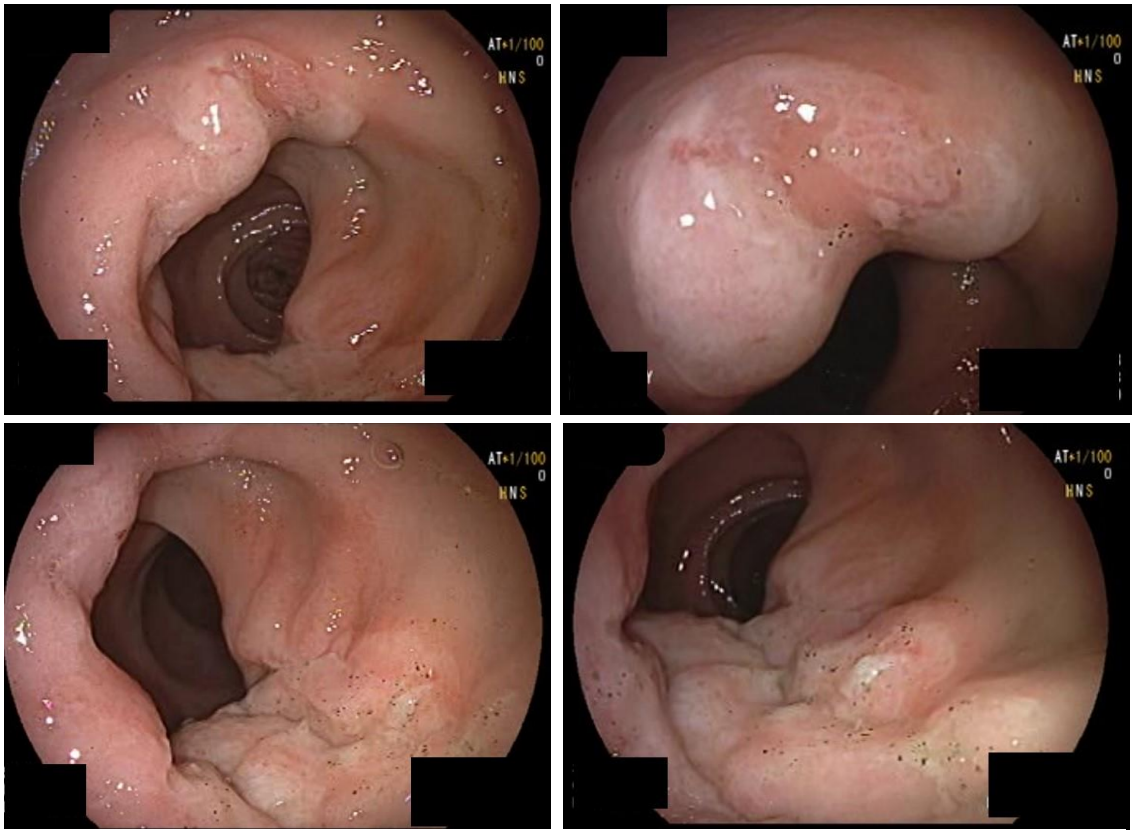

Figure 1. Rectal mucosa 3-4 cms from the anal verge with ulcerations and whitish exudates

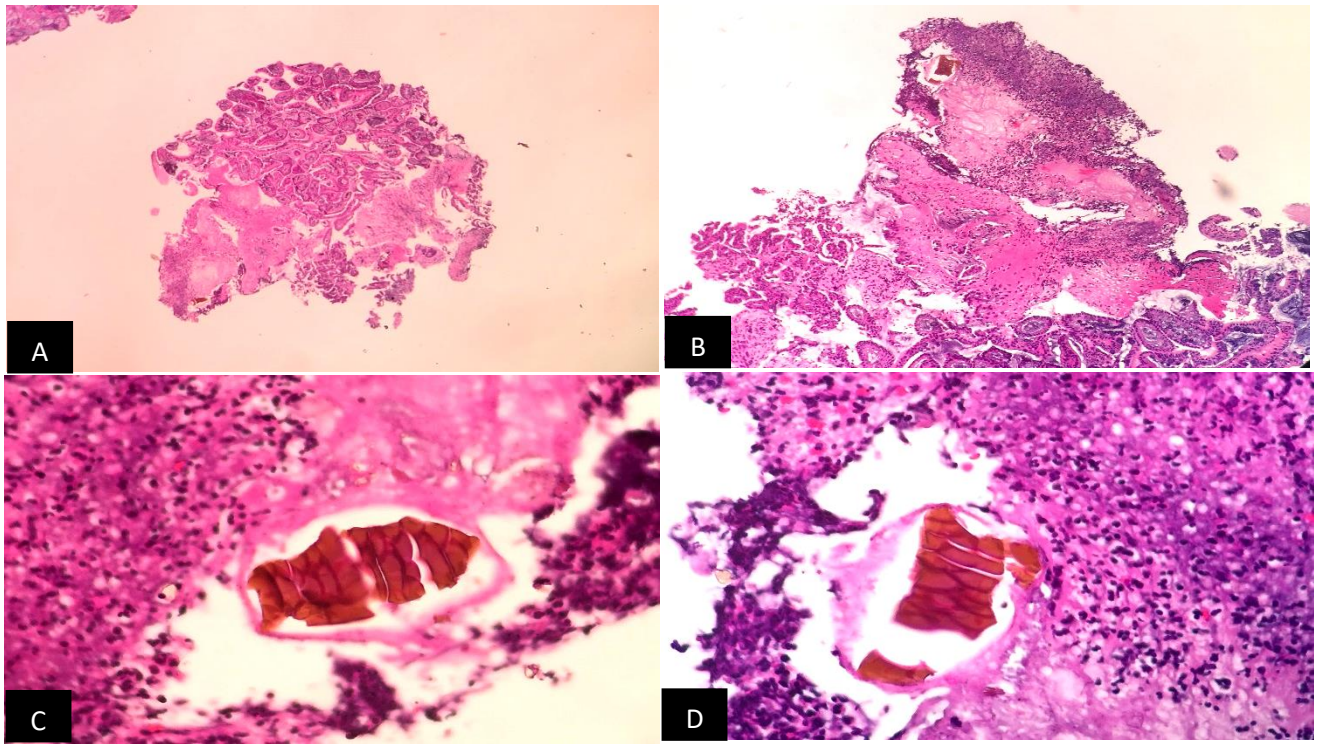

Figure 2. Histopathology of the Rectal Mucosa. A. Scanner view (40x) B. Low power view (100x) C and D. High power view (400x) showing characteristic fish scale pattern of sevelamer crystals.

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