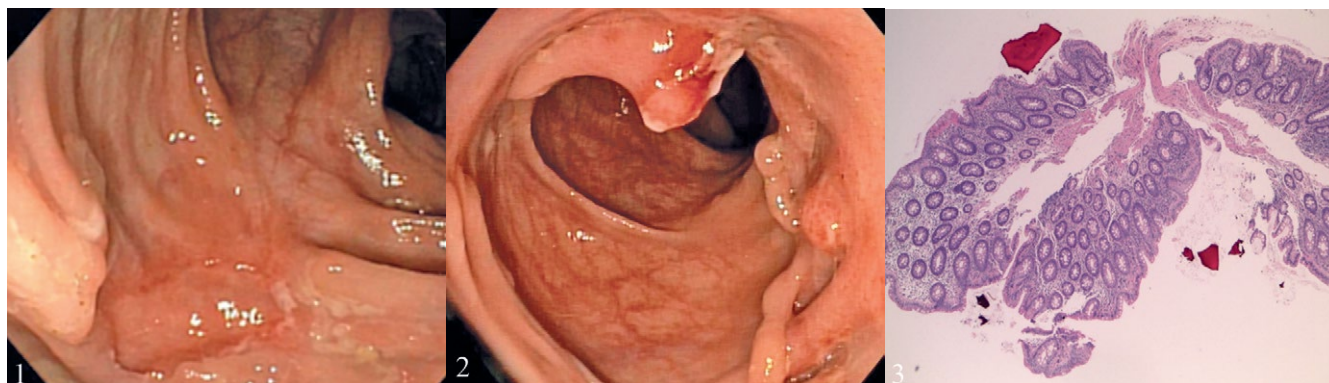


An Exceptional Cause of Drug-Induced Colitis: Cholestyramine

Joana C. Branco¹, Gonçalo Alexandrino¹, António Alves^{2,3}, Jorge Reis¹

1) Gastroenterology Department, Professor Doutor Fernando Fonseca Hospital, Lisbon; 2) Pathology Department, Professor Doutor Fernando Fonseca Hospital, Lisbon; 3) Pathology Institute, Faculty of Medicine, University of Lisbon, Lisbon, Portugal



An 82-year-old woman was evaluated for watery chronic diarrhea. Her past medical history was irrelevant. During the last 4 months she had around 5 bowel movements daily, without blood, present also during nighttime. Laboratory analysis showed mild anemia (hemoglobin 10.4g/dL), mild leucocytosis (10,300/ μ L), and increased C-reactive protein level (4.59mg/dL). The stool cultures, including ova and parasites, and *Clostridium difficile* were negative. She was initially empirically treated with probiotics, loperamide and cholestyramine with partial resolution of symptoms. An ileocolonoscopy performed two months later revealed deep ulcerations (Fig. 1) and various cicatricial areas (Fig. 2) involving all colorectal mucosa. The histological examination demonstrated slight architectural distortion with regenerative aspects; lymphoplasmacytic infiltrate, eosinophils and neutrophils were depicted in the lamina propria. In the necrotic areas, rhomboid orange/eosinophilic crystals (Fig. 3, H&E 40x), without „fish-scale” pattern, were found. These features were compatible with crystal-associated colitis induced by cholestyramine.

This crystal-associated colitis is very rare, and to our knowledge, only one case reported cholestyramine as causative agent [1]. The responsible crystals are: resins (namely kayexalate) and sevelamer, with different characteristics revealed by histology. Kayexalate crystals show a quite specific morphology: rhomboid or triangular, basophilic, with “fish-scale” pattern [2]. Cholestyramine crystals appear orange or basophilic, angulated, and are distinguished from kayexalate by their greater opacity and lack of “fish-scale” pattern. Both crystals stain red with periodic acid-Schiff staining: kayexalate is red with an acid-fast staining, whereas cholestyramine is pink [2].

Sevelamer and kayexalate crystals are associated with chronic renal failure and show “fish-scale” pattern; however, sevelamer has a two-toned color (yellow/pink), and are magenta with the acid-fast stain [3].

The time between the drug intake and the appearance of symptoms or the diagnosis of colitis is not yet fully known, especially for cholestyramine. For kayexalate, Harel et al. [4] analyzed a total of 58 cases, of which 51 were given kayexalate for acute treatment of hyperkalemia (with 5 patients taking only a single dose) and 7 were on treatment for more than 1 month. The median time to symptoms, in the case of patients taking kayexalate for acute treatment, was 2 days (1-5 days).

Attention should be paid to the clinical history with an adequate medication review, because of the overlapping of color and morphology of these crystals [3].

Corresponding author: Joana Carvalho e Branco,
cbranco.joana@gmail.com

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