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CASE REPORT

Dark Bowels: A Case of Severe Progressive Pseudomelanosis Duodeni

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ABSTRACT

Pseudomelanosis in the gastrointestinal tract consists of black pigmentation of the mucosa. The colonic manifestation is a relatively common and benign condition that has been well-described in the literature. However, duodenal pseudomelanosis is a rare form of this condition with unclear pathophysiology and etiology. Very few cases have been reported and several hypotheses have been published as to its cause, however none have been scientifically confirmed.

An 80-year-old female with past medical history of atrial fibrillation on apixaban, congestive heart failure, chronic kidney disease, and anemia on iron supplementation was admitted to the hospital for chest pain and hemoglobin of 6.1g/dl. The patient underwent esophagogastroduodenoscopy (EGD) that revealed a non-bleeding 2 cm gastric ulcer, erosive gastritis, pseudomelanosis grastri, and marked pseudomelanosis duodeni. At that time, she was taking amiodarone, amlodipine, clonidine, carvedilol, hydralazine, apixaban, asprin, ferrous sulfate, and pantoprazole. Her folate level was, 16 ng/ml (within normal limits). Pathology results of biopsies taken during the endoscopy confirmed aggregates of macrophages in the lamina propria with CD68 positive immunostaining. The macrophages contained black granular material consistent with pseudomelanosis duodeni. Iron stain (Prussian blue) and Melan-A were both negative. One year later, the patient presented again with melena and anemia, and repeat EGD showed significant progression of the pseudomelanosis.

It is recognized that the pigment consists primarily of ferrous sulfide, but other component elements such as calcium, potassium, aluminum, magnesium, and silver have been noted as well. Some data suggest that an association exists with chronic conditions such as congestive heart failure; hypertension; chronic kidney disease; folate deficiency; some medications including diuretics, beta blockers, and iron supplements; as well as gastrointestinal bleeding. The differential diagnosis can include hemochromatosis, brown bowel syndrome, metastatic melanoma, and ischemic bowel, making differentiation difficult and complex. Here we present a case of an 80-year-old female who was found to have pseudomelanosis duodeni for whom we were able to document significant progression of the condition over a period of one year. This phenomenon of rapid documented progression of psuedomelanosis duodeni is highly unusual and has never before been described in the medical literature to our knowledge. It illustrates the paucity of information regarding the mechanism underlying psuedomelanosis duodeni and its clinical consequences.

INTRODUCTION

Pseudomelanosis in the gastrointestinal tract is from black pigmentation of the mucosa. It is more commonly seen in the colon and extracolonic pseudomelanosis is rare. Duodenal pseudomelanosis is a rare and benign condition with uncertain etiology and pathophysiology. The pigment consists of ferrous sulfide, however other elements such as calcium, potassium, aluminum, magnesium, and silver have also been identified (1). An association may exist with gastrointestinal bleeding and chronic conditions such as congestive heart failure, hypertension, chronic kidney disease, folate deficiency. Pseudomelanosis may also be associated with the use of medications including diuretics, beta blockers, and iron supplements (2, 3).

Due to its rarity, the reporting of longitudinal follow up of pseudomelanosis duodeni to identify progression or resolution is not generally available. Herein we describe the clinical findings in an 80-year-old woman who was found to have pseudomelanosis duodeni which significantly progressed over a period of one year.

CASE PRESENTATION

An 80-year-old woman presented with an episode of generalized weakness, shortness of breath, palpitations, and melena. She had a medical history of atrial fibrillation, hypertension, congestive heart failure, chronic kidney disease, diabetes mellitus, peripheral vascular disease, chronic anemia, and coronary artery disease for which she had coronary artery bypass grafting a number of years prior to presentation. She was receiving iron supplementation for her anemia. Her other medications included apixaban, amiodarone, amlodipine, clonidine, carvedilol, hydralazine, aspirin, and pantoprazole.

The patient had prior gastrointestinal bleeding and esophagogastroduodenoscopy (EGD) performed one year prior to presentation due to melena, which demonstrated a non-bleeding 2 cm gastric ulcer, erosive gastritis, pseudomelanosis gastri, and pseudomelanosis duodeni (Figure 1).

On presentation, the patient's vital signs were within normal limits. Physical exam was remarkable for conjunctival pallor and tachypnea. Digital rectal exam demonstrated melena in the rectal vault. The patient's hemoglobin was 6.1 g/dL and she received 1 unit of packed RBCs. EGD demonstrated erosive gastritis, a 2 cm gastric ulcer, as well as pseudomelanosis gastri with marked pseudomelanosis duodeni (Figure 2). When compared to EGD images from 1 year prior, there was significant progression of the melanosis from speckled deposits to complete discoloration of the epithelium. Histopathology of prior biopsies confirmed the presence of aggregates of macrophages in the lamina propria with CD68 positive immunostaining, contain black granular material consistent with pseudomelanosis duodeni (Figure 3). Iron stain (Prussian blue) and Melan-A were both negative. No endoscopic biopsies were taken during the hospitalization. The patient's melena resolved and upon stabilization the patient was discharged on a proton pump inhibitor and sucralfate. Apixiban was resumed 3 days after discharge, and aspirin was subsequently resumed.

DISCUSSION

Pseudomelanosis duodeni (PD) was first described in 1976 (4). Although there are subsequent reports of PD, its pathogenesis and clinical significance are still uncertain. Studies suggest that the pigment does not originate from melanin and vary based on its location throughout the gastrointestinal tract, hence its name "pseudomelanosis."

Pseudomelanosis coli is strongly associated with excessive laxative use. Anthracene derivatives in laxatives are thought to interfere with normal physiological functions of the epithelium leading to apoptosis. Macrophages within the lamina propria phagocytize these cells leading to lipofuscin pigment accumulation and black/brown discoloration (5). However, there is no association between laxative abuse and PD. In PD, pigmentation consists of iron sulfide deposition (6). This is believed to be due to hemorrhage within the gastrointestinal tract with subsequent phagocytosis of erythrocytes, and the degradation products thereof remain within the lysosomes of macrophages within the lamina propria (7). The main constituent of the pigmentation is iron and there is evidence of an association of PD with chronic diseases such as heart failure; renal failure; hypertension; diabetes; gastrointestinal bleeding; and medications and therapies such as hydrochlorothiazide, furosemide, hydralazine, beta blockers, digoxin, and iron supplements, and hemodialysis (8, 9, 10).

PD is most common among women aged 60-70. PD can appear clinically suspicious and provoke clinical uncertainty. The differential diagnosis includes hemochromatosis, brown bowel syndrome, and metastatic melanoma. During intestinal surgery, PD may mimic the appearance of ischemic bowel, making differentiation difficult. Biopsies may stain positive for melanin (Melan-A, Masson-Fontana) or iron (Prussian blue), however there is not a standardized staining pattern used for diagnosis (9, 10, 11). The histopathology of the biopsies obtained from this patient was negative for both iron and melanin. This may be attributable to the variable sulfur content of the pigment in PD, which has been demonstrated by ultrastructural studies. Additionally, this is consistent with other histological studies carried out on PD biopsies where Prussian blue staining is unpredictable (9, 11).

PD is generally an incidental finding and there are no current recommendations for follow up. Thus, there is limited evidence supporting the progression or the resolution of PD (9). There is one report indicating that the discontinuation of oral iron therapy, and the substitution of intravenous iron therapy resulted in complete resolution of PD after 3 months (13, 14).

This patient was observed to have significant progression of PD. Images from the initial endoscopy demonstrated scattered speckling of pseudomelanosis throughout the duodenum. Images from the follow up EGD one year later demonstrate brown/black discoloration of the entire duodenum. Although no official grading system is in place for PD, some have proposed a grading system for pseudomelanosis coli in which grade III was the most severe and described as dark black colonic mucosa with linear or spotted boundary with normal mucosa (15).

Several potential risk factors for PD exist in this patient: (a) chronic iron therapy, and (b) active GI bleeding. The duodenum is the main site of iron absorption and coupled with excessive oral iron supplementation and/or gastrointestinal bleeding PD may develop (12). Hydralazine, has also been suggested as a contributor to PD. Some patients have had complete resolution of PD several months after discontinuation of hydralazine. Similarly, PD has been reported in association with beta-blocker therapy, which was also part of this patient's therapeutic regimen (8, 9). Congestive heart failure may contribute to the development of PD formation via vascular congestion, extravasation of red blood cells, and subsequent hemolysis and phagocytosis.

CONCLUSIONS

We describe a patient who had demonstrable progression of PD over a period of one year. Many factors that may be associated with or contribute to the development of PD. This patient was taking a beta-blocker, hydralazine, and oral iron, and had congestive heart failure, diabetes mellitus, and chronic

kidney disease. This atypical progression of PD is attributed to the contributions of each therapeutic agent and underlying clinical process.

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Conflict of Interests: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and report no conflicts of interest.

Keywords: Pseudomelanosis duodeni, melena

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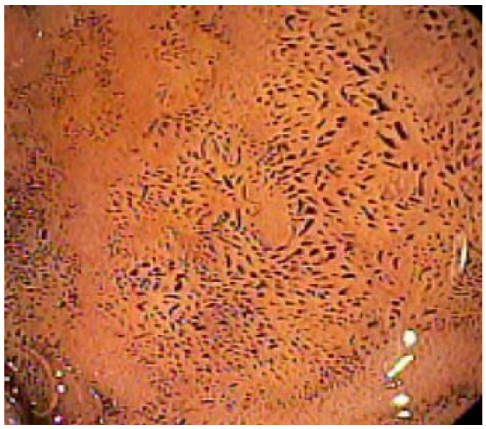

Figure 1. Initial esophagogastroduodenoscopy (EGD) findings

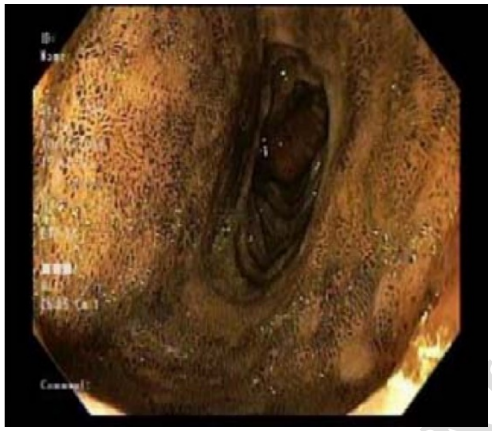

Figure 2. Esophagogastroduodenoscopy (EGD) findings at 1 year after presentation

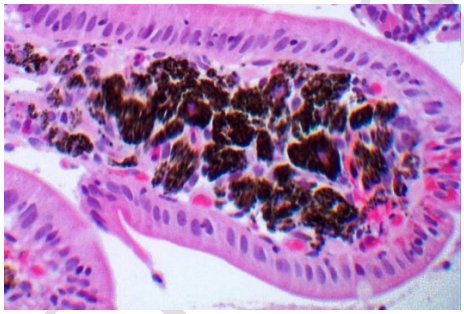

Figure 3. Pathology slide demonstrating aggregates of macrophages in the lamina propria with CD68 positive immunostaining, contain black granular material