

Gastric pseudomelanosis (report of a case and review of literature)

Abstract

Gastric pseudomelanosis is exceedingly rare. To the best of our knowledge, there have been only six reported cases in the literature of gastric pseudomelanosis. We report a case of an 86 year-old woman with marked iron deficiency anemia who was found to have characteristic speckled pattern of grey-black pigmentation on endoscopic examination. Histologically, the gastric biopsy revealed characteristic aggregates of sub epithelial macrophages with coarse brown-black pigment present within the lamina propria. This pigment had focal and patchy positive staining for iron. These changes were consistent with pseudomelanosis. The previously reported six cases had similar clinicopathological features. Although the exact pathogenesis of gastric pseudomelanosis is unknown, it is benign and has not been associated with malignant transformation or worsening of any underlying medical conditions.

Keywords: gastric pseudomelanosis, subepithelial pigmented macrophages, severe mitral regurgitation, hypertension, mild coronary artery disease

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Jin-Ping Lai,¹ Ada R Quintana,¹ Giao Vuong²

¹Department of Pathology, Saint Louis University School of Medicine, USA

²Division of Gastroenterology and Hepatology, Saint Louis University School of Medicine, USA

Correspondence: Jinping Lai, Department of Pathology, Saint Louis University, 1402 South Grand Boulevard, St. Louis, MO 63104, USA, Tel +1 314-577-8475, Fax +1 314-577-613, Email jinpinglai@slu.edu

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Introduction

Pseudomelanosis is a rare benign condition characterized by pigment deposition within subepithelial macrophages in the lamina propria, typically in duodenal mucosa. Rare cases have been reported in gastric mucosa. It can occur at any age and has been reported in association with upper GI bleeding, chronic renal failure, hypertension and diabetes mellitus. To the best of our knowledge, only six cases have been reported. We describe the clinicopathological features of an interesting case with similar features as the six cases previously described and a review of the literature to better understand this rare entity.

Case presentation

An 86 year old with a history of stage III chronic kidney disease, hypertension, atrial fibrillation, mild coronary artery disease, severe mitral regurgitation, iron deficiency anemia without overt bleeding, and rheumatoid arthritis was admitted to our institution for syncope. The patient complained of occasional right lower quadrant pain that resolved with lying flat, however denied changes in appetite or weight loss. She was on chronic iron therapy and stated that her stools were usually black in color. The patient's outpatient medications included coumadin, hydralazine, cyanocobalamin (Vitamin B12), metoprolol, ferrous sulfate, famotidine, calcium acetate, folic acid, levothyroxine, prednisone, simvastatin and tramadol.

GI was consulted for marked anemia (Hemoglobin of 6.8g/dL). Upper GI endoscopy was done to evaluate her marked iron deficiency anemia and showed a few localized small erosions in the gastric body. There was no stigma of recent bleeding. However, in the greater curvature of the gastric body there was a localized mucosal abnormality characterized by darkly pigmented discoloration that "did not wash off" (Figure 1A). Biopsies were taken with a cold forceps for histology. The duodenum appeared normal.

Histologically, the gastric biopsy revealed characteristic subepithelial pigment deposition. Aggregates of subepithelial

macrophages with coarse brown-black pigment were seen within the lamina propria (Figure 1B-1C). This pigment had focal and patchy positive staining for iron (Figure 1D). These changes were consistent with pseudomelanosis.

Due to the benignity of gastric pseudomelanosis, this lesion was not further evaluated for. The syncopal episode was determined to be orthostatic which responded to IV fluids. The patient was also transfused 2units of PRBCs and discharged with uneventful follow up.

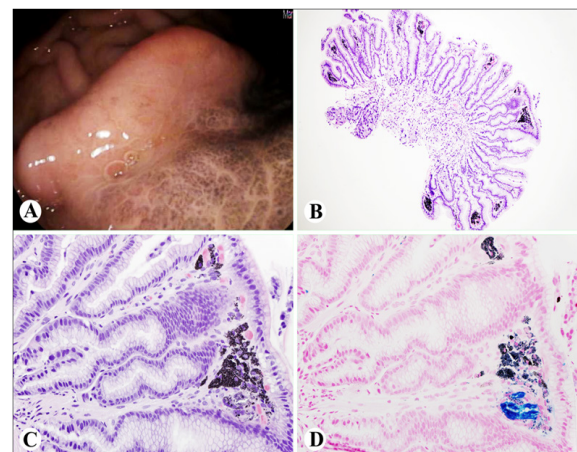


Figure 1 Gastric pseudomelanosis.

A: Upper GI endoscopy shows darkly pigmented discoloration at the great curvature; B-C: Histologically, aggregates of subepithelial macrophages with coarse brown-black pigment are seen within the lamina propria (H&E stain, B: 100x; C: 400x); D: The pigment shows focal and patchy iron staining (Perls' Prussian blue stain, 400x).

Discussion

Only 7 cases of gastric pseudomelanosis have been reported to our knowledge, including this current case. In the seven reported

cases, all but one patient was female (The gender of one patient was not given in the literature). The ages ranged from 60 to 86 with an average age of 73.4 years. In the seven reported cases, all patients suffered from multiple medical problems (One case report did not discuss comorbidities). Of the cases with known comorbidities, common medical problems included chronic renal insufficiency, anemia and hypertension. All patients were taking ferrous sulfate and at least six of the seven patients were on an antihypertensive

medication. In all cases the endoscopic findings showed dark pigmentation in the gastric mucosa corresponding to subepithelial pigmented macrophages histologically.¹⁻⁶ No evidence of malignant transformation or worsening of any underlying medical conditions was reported (Table 1). Although gastric pseudomelanosis is a rare entity, physicians should be aware of it to facilitate a prompt diagnosis and avoid unnecessary testing.³

Table 1 Clinical pathologic findings in the six reported cases and current case of gastric pseudomelanosis

Case	Age	Sex	Comorbidities	Medications	Clinical presentation	Endoscopic findings	Histologic findings	Follow up
Weinstock LB et al. ¹	74	Female	Chronic renal insufficiency (Creatinine 4.6 mg/dL), anemia	Ferrous sulfate	Asymptomatic	Dark pigmentation of the antral mucosa	Presence of iron sulfide granules in the lamina propria, confirmed by Prussian blue stain	Unknown
Rustagi T et al. ²	60	Female	Chronic kidney disease, hypertension, iron deficiency anemia, coronary artery disease, type 2 diabetes mellitus, hypertension	Ferrous sulfate, hydralazine, furosemide, carvedilol, clopidogrel, insulin	Hypertensive urgency and intermittent nausea and vomiting for 2 days	Patchy erythema in the antrum with thick mucosal folds and a diffuse peppered gray-black pattern in the stomach Dark pigmentation of the pylori antral mucosa; the remainder of the gastric mucosa appeared normal	Aggregates of macrophages with coarse black-brown cytoplasmic pigment within the lamina propria	No further episodes of vomiting and was discharged with uneventful follow-up
Kibria R et al. ³	79	Female	Hypertension, congestive heart failure, iron deficiency anemia	Ferrous sulfate, furosemide, carvedilol, bupropion, escitalopram	Postprandial epigastric pain and early satiety for 2 months, along with 10 lb weight loss	Speckled pattern of black pigmentation seen throughout the stomach and duodenum	Prussian blue stain indicated hemosiderin deposition	Unknown
Alraies MC et al. ⁴	83	Female	Diabetes mellitus, hypertension, coronary artery disease, hypothyroidism, chronic renal failure	Ferrous sulfate, furosemide, hydralazine, Hydrochlorothiazide, isosorbide mononitrate, levothyroxine, esomeprazole, atorvastatin, insulin, metoprolol, diltiazem and aspirin	Epigastric pain for 1 day with black stool	Multiple millimeter coffee-colored lesions in the gastric body, duodenal bulb and second portion of duodenum	Pigment in stromal macrophages ; iron staining (Perl's) was negative for the presence of iron sulfide granules in the lamina propria	No recurrent bleeding and discharged with uneventful follow-up
Ochoa Palominos A et al. ⁵	60	Male	Hypertension, ischemic heart disease, idiopathic retroperitoneal fibrosis, chronic kidney failure, iron deficiency anemia	Ferrous sulfate, furosemide, doxazosin, atenolol, acenocoumarol	Rule out esophageal-gastric varices		Blackish-brown deposits within the lamina propria macrophages. Confirmed presence of iron deposits using Perl's technique	Uneventful follow-up

Table Continued

Case	Age	Sex	Comorbidities	Medications	Clinical presentation	Endoscopic findings	Histologic findings	Follow up
Antaki F et al. ⁶	73	Unknown	Unknown	Ferrous sulfate, hydralazine	Dysphagia	Dark pigmentation of the gastric mucosa inside a small hiatal hernia	Pigment deposition at the level of the lamina propria	Unknown
Quintana A (2015, current case)	86	Female	Hypertension, chronic kidney disease, iron deficiency anemia, Afib, coronary artery disease	Ferrous sulfate, hydralazine, famotidine, cyanocobalamin, metoprolol, folic acid, levothyroxine, prednisone, simvastatin and tramadol	Severe anemia and syncope	Gastric greater curvature with darkly pigmented discoloration that "did not wash off"	Subepithelial coarse brown-black pigmentation deposition in macrophages; patchy positive for iron	Discharged with uneventful follow-up

The exact pathogenesis and etiology for pseudomelanosis is not clear, however it has been associated with hypertension, chronic kidney disease, anemia, diabetes mellitus and gastrointestinal bleeding.^{1,2,5} Many common medications including antihypertensive drugs such as hydralazine and furosemide, propranolol, methyldopa, thiazides and iron sulfate have been implicated in pseudomelanosis. Although no definite etiology or mechanism has been identified, it is thought that the large size of the particles that cause pigmentation are difficult to absorb and subsequently cause pigmentation deposition.⁵ Hydralazine, furosemide and hydrochlorothiazide contain sulfur, which has been postulated to promote deposition of pigment in the duodenum.²

The classic endoscopic findings of pseudomelanosis of the gastrointestinal tract are discrete, flat, black or brown speckled pigmentation of the gastric, duodenal, and jejunal mucosa. In the present case, only the stomach was involved. Histologic examination is necessary for diagnostic confirmation and to exclude other conditions associated with deposition of pigment seen endoscopically such as post-hemorrhagic deposition of hemosiderin, hemosiderosis/hemochromatosis, metastatic melanoma and substance ingestion such as charcoal or barium sulfate.² Microscopically, the pigment is located subepithelially in mucosal macrophage lysosomes, but can also be found in extracellular space or in epithelial cells. Various ancillary histochemical stains can be utilized to help characterize the pigment, including Masson-Fontana stain and Perls' Prussian blue stain. Iron stains are typically negative or only focally positive. In the current case, Prussian stain is focally positive for iron deposition.

The pigment in hemosiderosis/hemochromatosis is finely granular, brown to black particles in epithelial cells which stain diffusely positive for iron. In advanced iron overload disorders, iron is deposited in parenchymal cells throughout the body, including the parietal cells in the stomach. Studies have shown that the pigment of pseudomelanosis is composed of a mixture of ferrous sulfide, ferrum sulfate, lipomelanin, hemosiderin, ceroid, pseudomelanin, lipofuscin and lipofuscin-like pigment. The deposited pigment can also contain aluminum, calcium, magnesium, potassium, sulfur, silica, and silver.^{1,2}

As mentioned previously, histochemical stains can be utilized to help characterize the pigment, including Masson-Fontana stain and Perls' Prussian blue stain. Because the pigment is made up of a mixture of pigments, iron stains are typically negative or only focally positive. It is important to note that Prussian blue stain can give a false-negative reaction if ferrous oxide is present instead of ferrous sulfide.

Conclusion

Our case had numerous risk factors that are known to cause pseudomelanosis. Among the patient's risk factors was the administration of ferrous sulfate supplements as well as hydralazine, both have been implicated in the development of pseudomelanosis. The other six patients reported in the literature also had similar comorbidities including iron deficiency anemia on oral iron therapy and hypertension on antihypertensive medications. Pseudomelanosis of the upper gastrointestinal tract is benign and has not been associated with malignant transformation or worsening of any underlying medical conditions.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

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