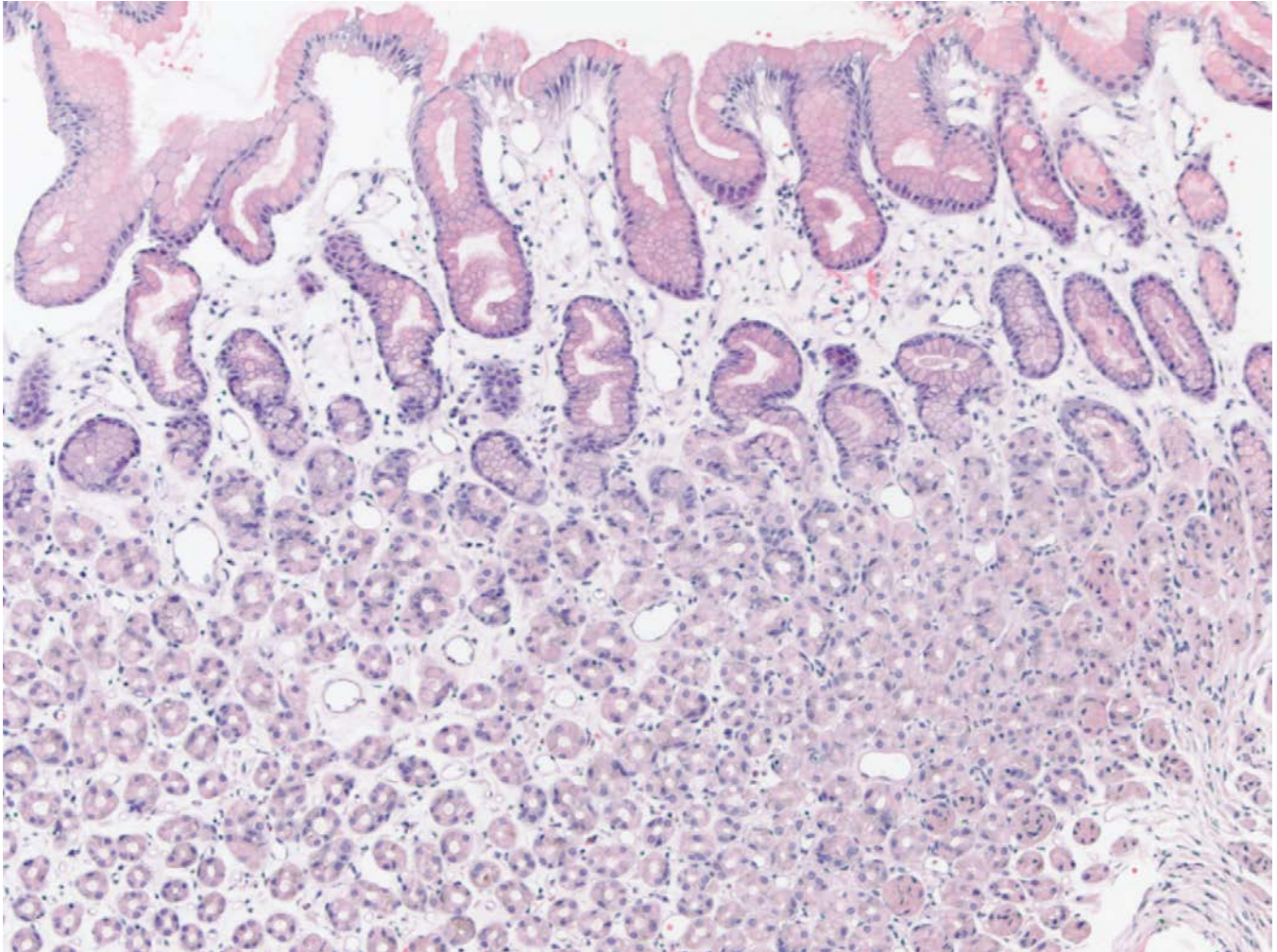
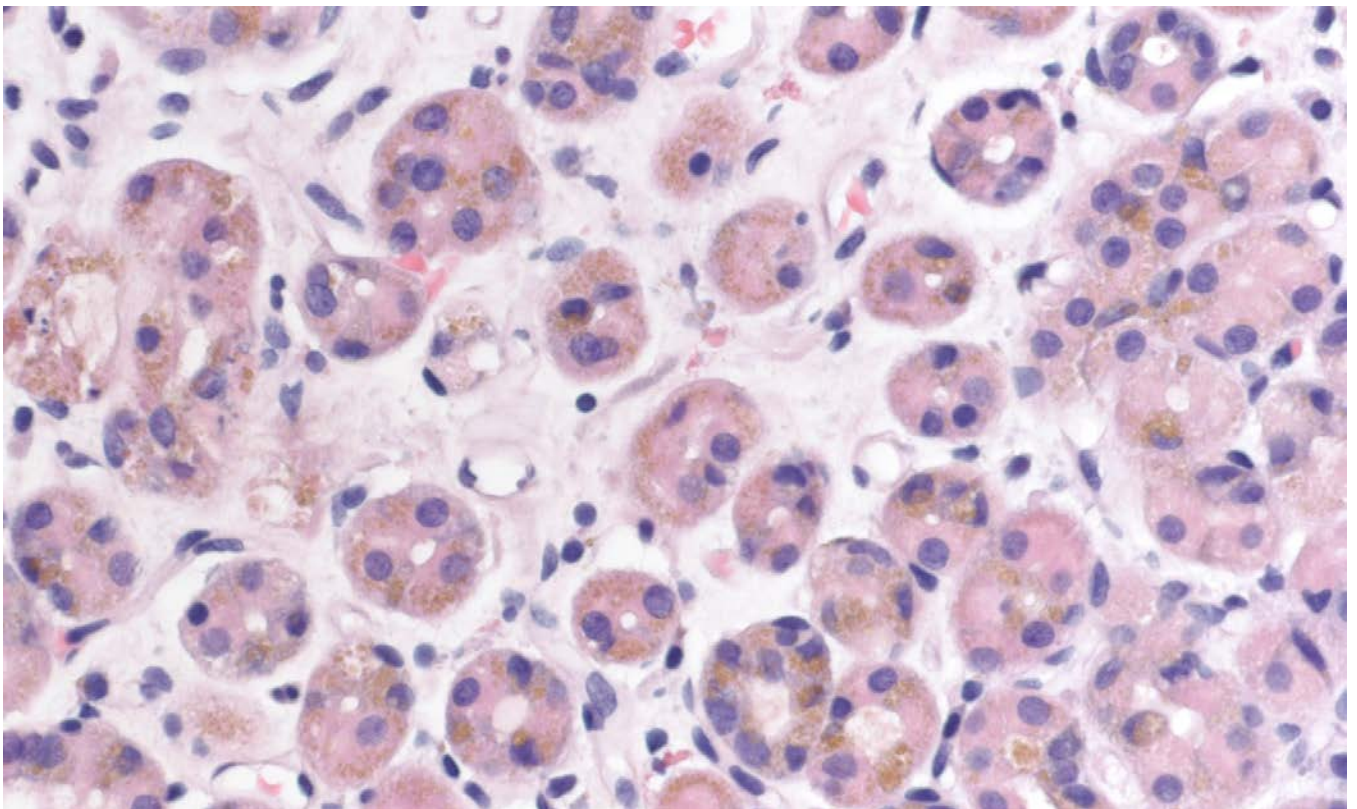
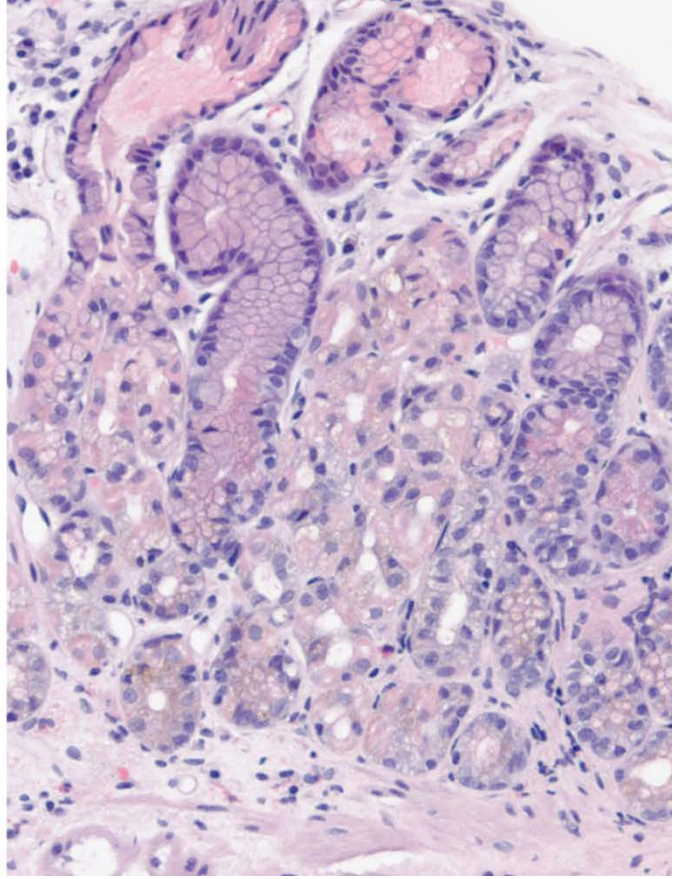
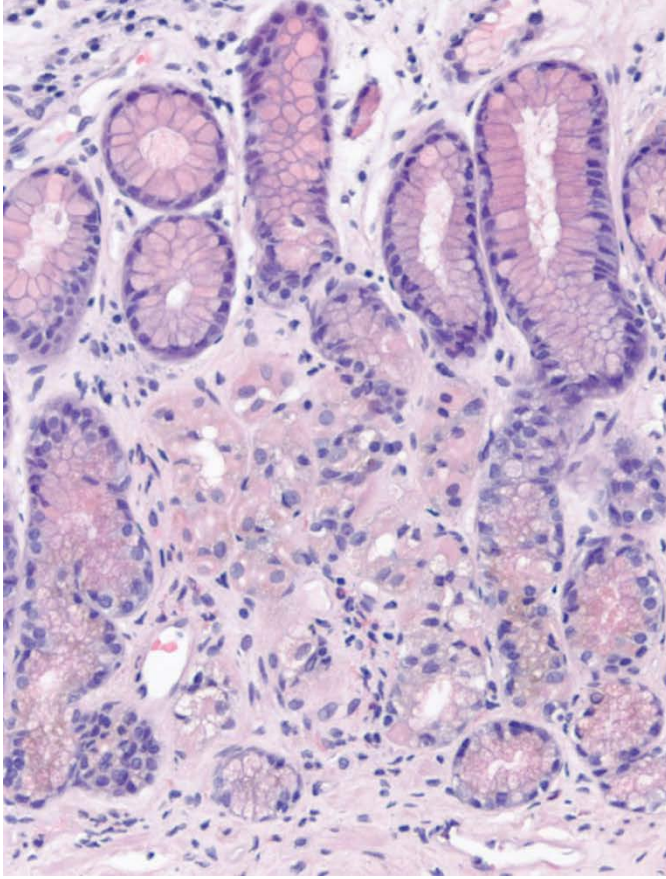


CASE HISTORY:

A 76-year-old woman with alcoholic cirrhosis underwent an esophagogastroduodenoscopy for evaluation of anemia and screening for varices. Her medications included lactulose, rifaximin, and zinc sulfate. Endoscopy showed a small, nearly completely healed pre-pyloric ulcer and a nodular mucosal pattern in the stomach that was consistent with mild portal hypertensive gastropathy; the esophagus and duodenum appeared unremarkable. Random biopsies were obtained from the stomach. Representative H&E images are provided below.

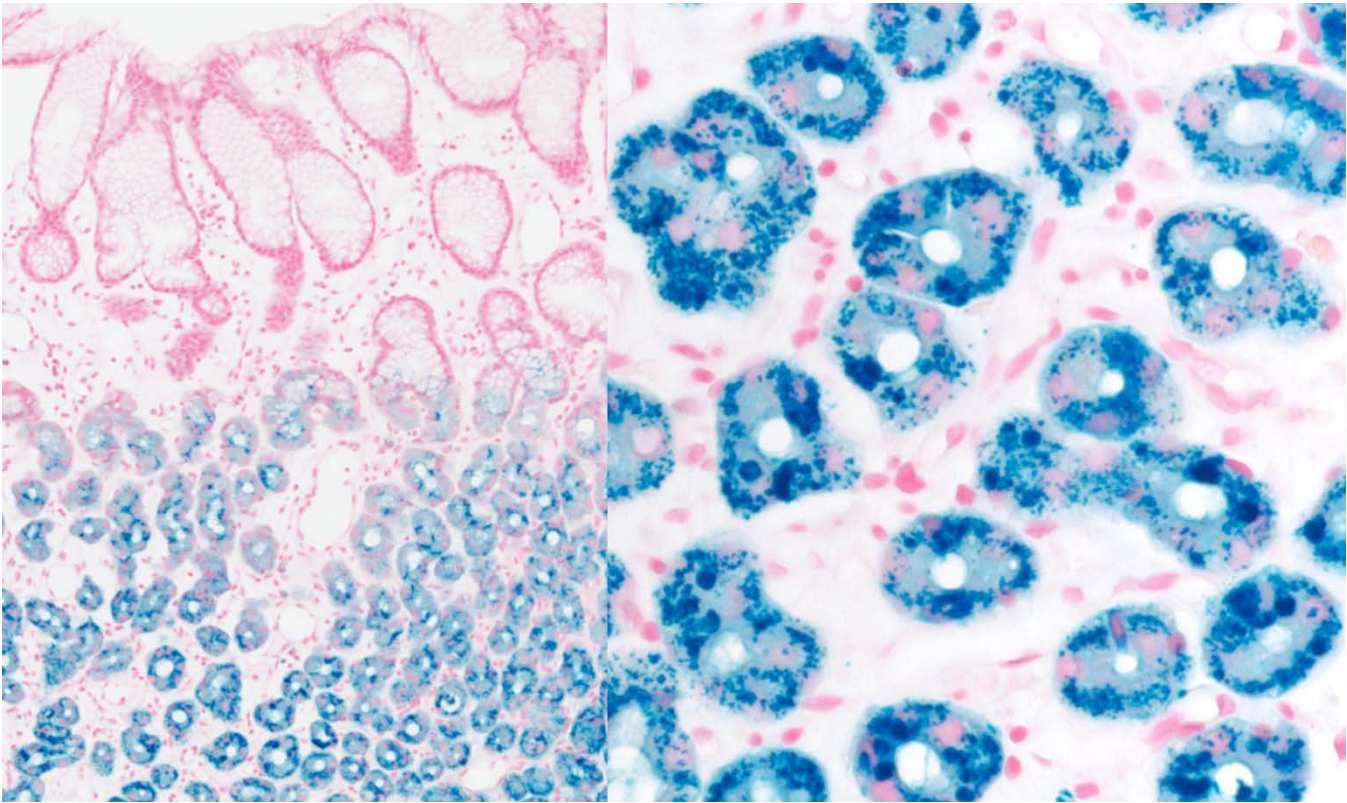
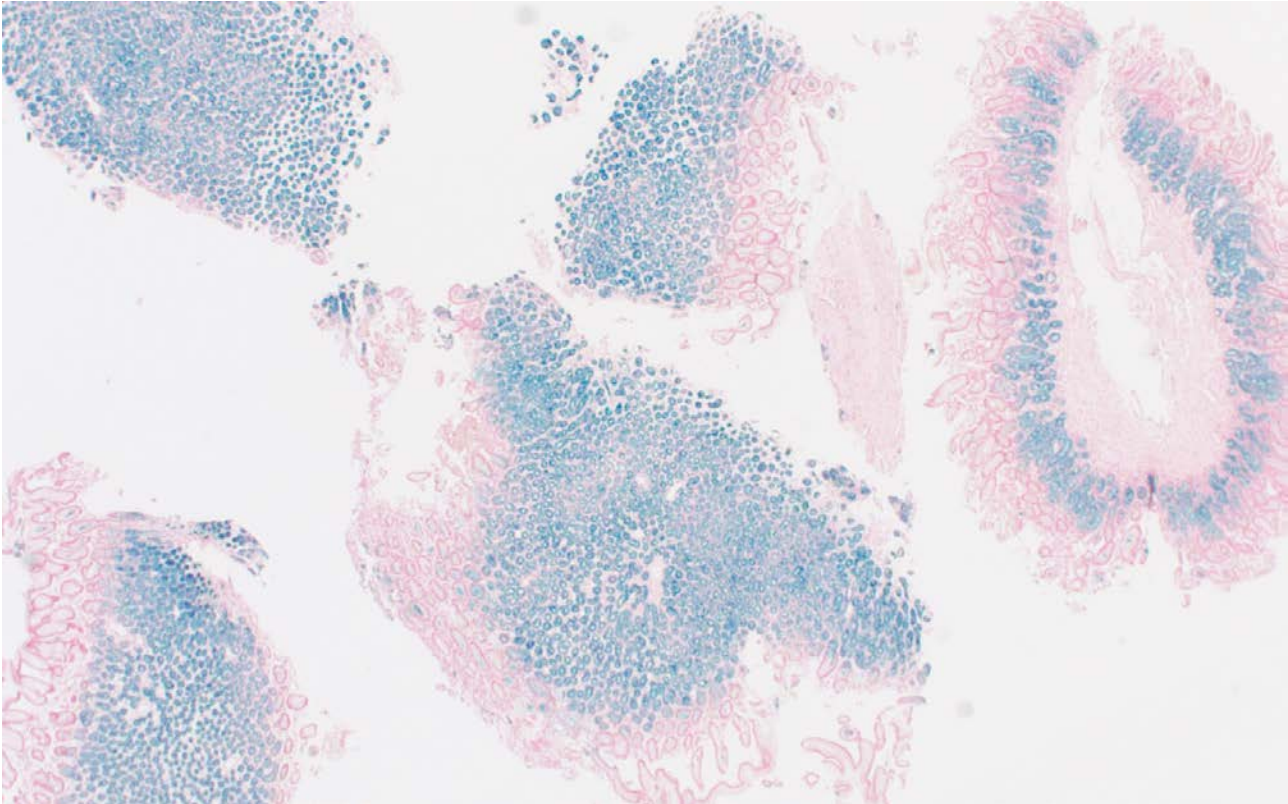




Which of the following best describes these findings?

- A. Gastric mucosal calcinosis
- B. Gastric mucosal siderosis
- C. Lanthanum deposition
- D. Gastric pseudomelanosis
- E. Minocycline-induced gastric mucosal pigmentation

A Prussian blue histochemical stain was performed and images are provided below.



This finding has been found to be associated with which of the following? Select all that apply.

1. Alcohol abuse
2. Hereditary Hemochromatosis
3. Chronic hepatitis C
4. Chronic hepatitis B
5. Wilson's disease

Gastric mucosal siderosis (Choice B) is the best answer:

The findings in this case illustrate gastric mucosal siderosis. Histologically, the findings can be subtle at low power, but at higher magnification, intracytoplasmic brown, refractile granules can be seen in glandular epithelium, predominantly within the glands and pits; the Prussian blue stain confirms that the granules are composed of iron.

Marginean et. al. in "Gastric Siderosis: Patterns and Significance," characterized histologic patterns of iron deposition in gastric mucosa and determined disease associations. They described three patterns of gastric siderosis:

Pattern A, "nonspecific gastric siderosis" consists of iron deposition predominantly in macrophages and stromal cells; this pattern is associated with gastritis and apparent previous mucosal injury/hemorrhage, but rarely with iron medications.

Pattern B, "iron-pill gastritis," is almost always associated with oral iron medications and consists of predominantly extracellular, coarse, crystalline aggregates of iron with background mild gastritis or reactive gastropathy. These extracellular deposits of iron tend to be luminal or in the superficial lamina propria, especially when seen with epithelial injury or erosions.

Pattern C, "gastric glandular siderosis," consists of iron deposition in glandular epithelium (including foveolar, antral, chief, and parietal cells), with increasing intensity on Prussian blue stain in deeper glands, which can be seen in patients with cirrhosis (from alcohol, HBV, or HCV) and in some patients with hereditary hemochromatosis.

While pattern C is the least common, it is important to recognize, as work-up for hemochromatosis or portal hypertension should be considered if there is not a known clinical history or explanation. Our case is an example of pattern C in a patient with alcoholic cirrhosis. Subsequent *HFE* gene studies were negative for H63D, C282Y, and S65C mutations in our case.

Gastric mucosal calcinosis (Choice A) is incorrect:

Gastric mucosal calcinosis most frequently occurs in the setting of hypercalcemia and/or hyperphosphatemia in patients with chronic renal disease, but can also be seen in patients taking aluminum-containing antacids or in those on isotretinoin or sucralfate therapy. Endoscopically, the gastric mucosa may show 1-5 mm, white, flat plaques or nodules. On microscopic exam, amorphous, basophilic deposits are seen within the superficial lamina propria of gastric mucosa, sometimes surrounded by macrophages. A von Kossa stain will highlight deposits of gastric mucosal calcinosis, which are composed of calcium, phosphorus, aluminum, and chlorine.

Lanthanum deposition (Choice C) is incorrect:

Lanthanum carbonate is a noncalcium-containing phosphate binder that is used to manage hyperphosphatemia in patients with chronic kidney disease on dialysis. Endoscopically, lanthanum deposition can appear as white, annular mucosa, erosions, erythema, or polypoid lesions. Histologically, biopsies often show expansion of the lamina propria by histiocytes and multinucleated giant cells. Within these histiocytes, the lanthanum varies from granular and amorphous to coarse purple or brown material. The background gastric mucosa often has the appearance of chemical/reactive gastropathy. A von Kossa stain should be negative for calcium and Prussian blue stain may show focal, faint positivity.

Gastric pseudomelanosis (Choice D) is incorrect:

Pseudomelanosis refers to spotty brown or black pigmentation of gastrointestinal mucosa seen on endoscopy and occurs more commonly in the small intestine rather than the stomach. It is associated with upper GI bleeding, chronic renal failure, hypertension, and diabetes mellitus. Pseudomelanosis appears as granular brown to black pigment within macrophages in the lamina propria. The pigmented material in pseudomelanosis is negative or focally positive on Prussian blue stain.

Minocycline-induced gastric mucosal pigmentation (Choice E) is incorrect:

Minocycline is a tetracycline antibiotic used to treat a number of infections and conditions, including acne vulgaris and rosacea. To our knowledge, it is not known to cause gastric mucosal discoloration, but its deposition is well-known in other body sites. Minocycline can deposit within the thyroid gland and skin, leading to black pigmentation and discoloration. In the skin, the pigment varies from golden brown to black and is contained within macrophages, especially around vessels and sweat glands. The pigment from minocycline stains with Fontana-Masson; Prussian blue stain can be positive or negative in the pigment.

For the second part of the question, as discussed above, alcohol abuse, hereditary hemochromatosis, chronic HCV, and chronic HBV are associated with gastric glandular siderosis, but Wilson's disease is not (**1-4 are correct**).

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