Clinical History: A 79 year-old cachectic and chronically ill appearing man presented to the emergency department complaining of general weakness, vomiting, and diarrhea for 4-5 days. Further questioning revealed that he had undergone a 60 lb weight loss over 2 years with intermittent bouts of abdominal bloating, nausea, and non-bloody diarrhea during that time. Labs revealed hypoalbuminemia, but were otherwise unremarkable. Upper and lower endoscopy, and CT enterography were unremarkable. He underwent diagnostic laparotomy; the surgeon noted "thick exudate and discoloration involving the proximal small bowel, and dark brown discoloration of the distal ileum." Two segments of small bowel were resected. On gross exam the serosa showed gray-brown discoloration, but otherwise no other abnormal findings. Representative microscopic photos are presented for your review:

Figure 1. Low power view of small bowel

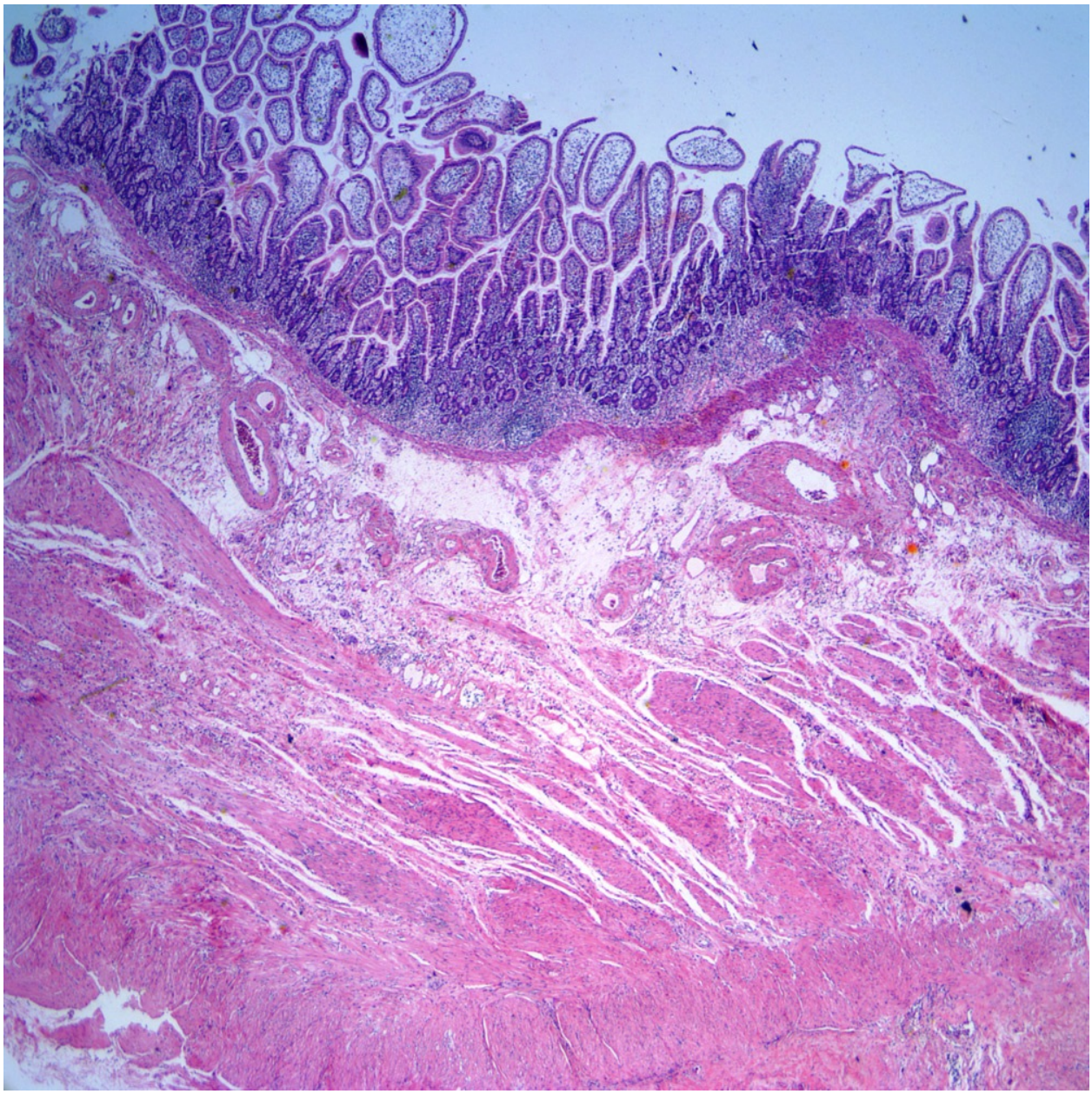


Figure 2: Muscularis propria

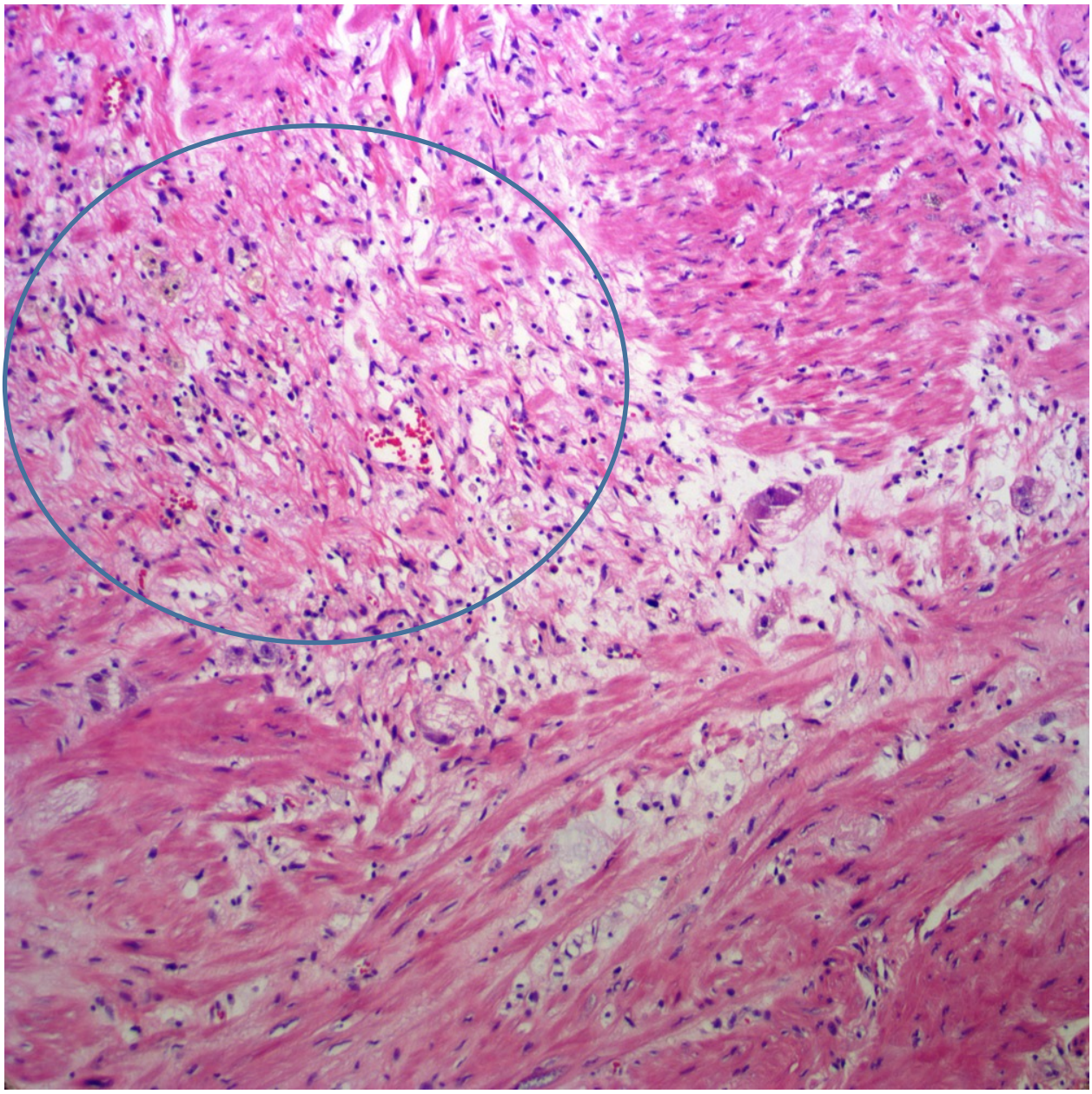


Figure 3. High power view of muscularis propria

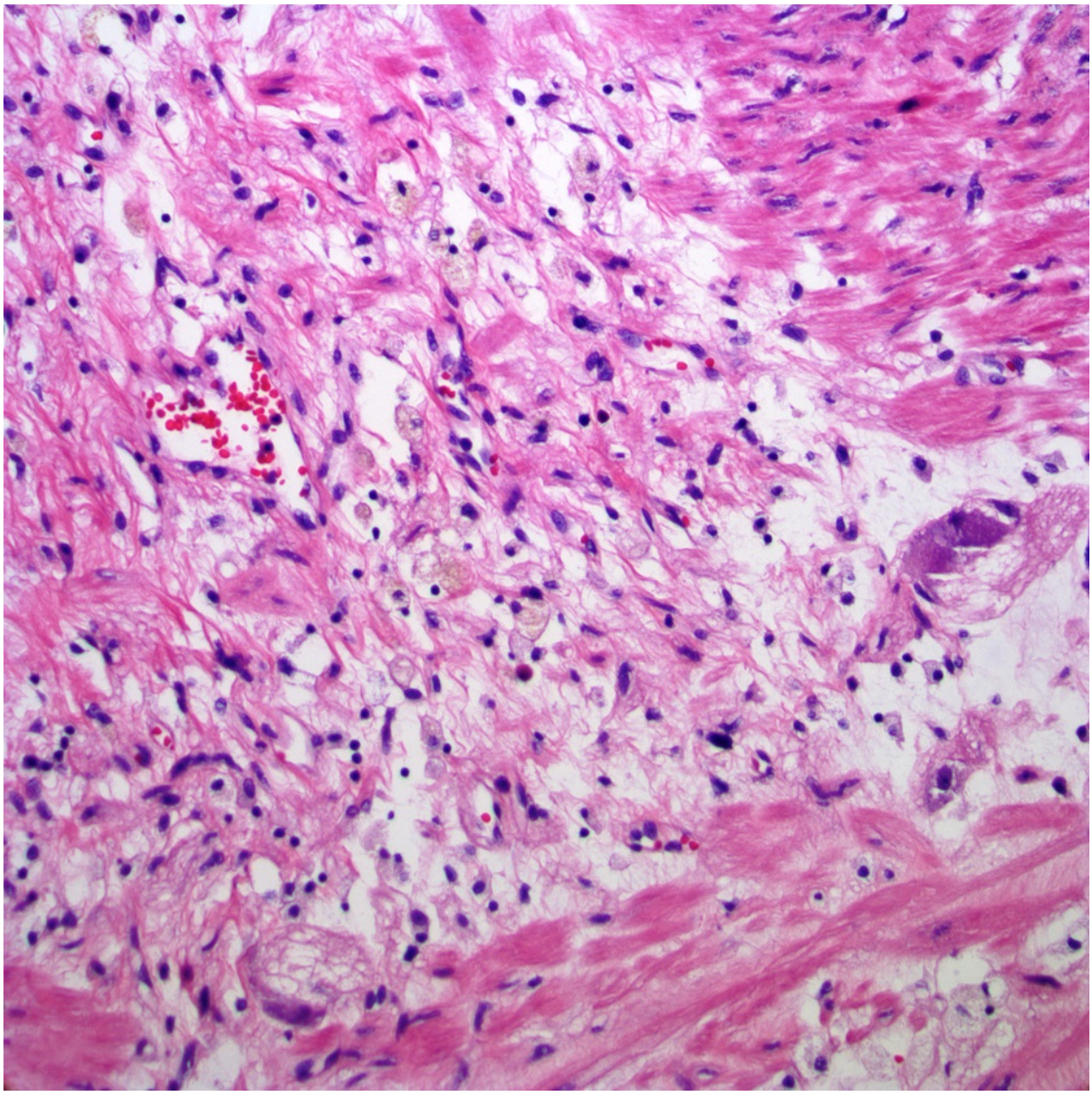
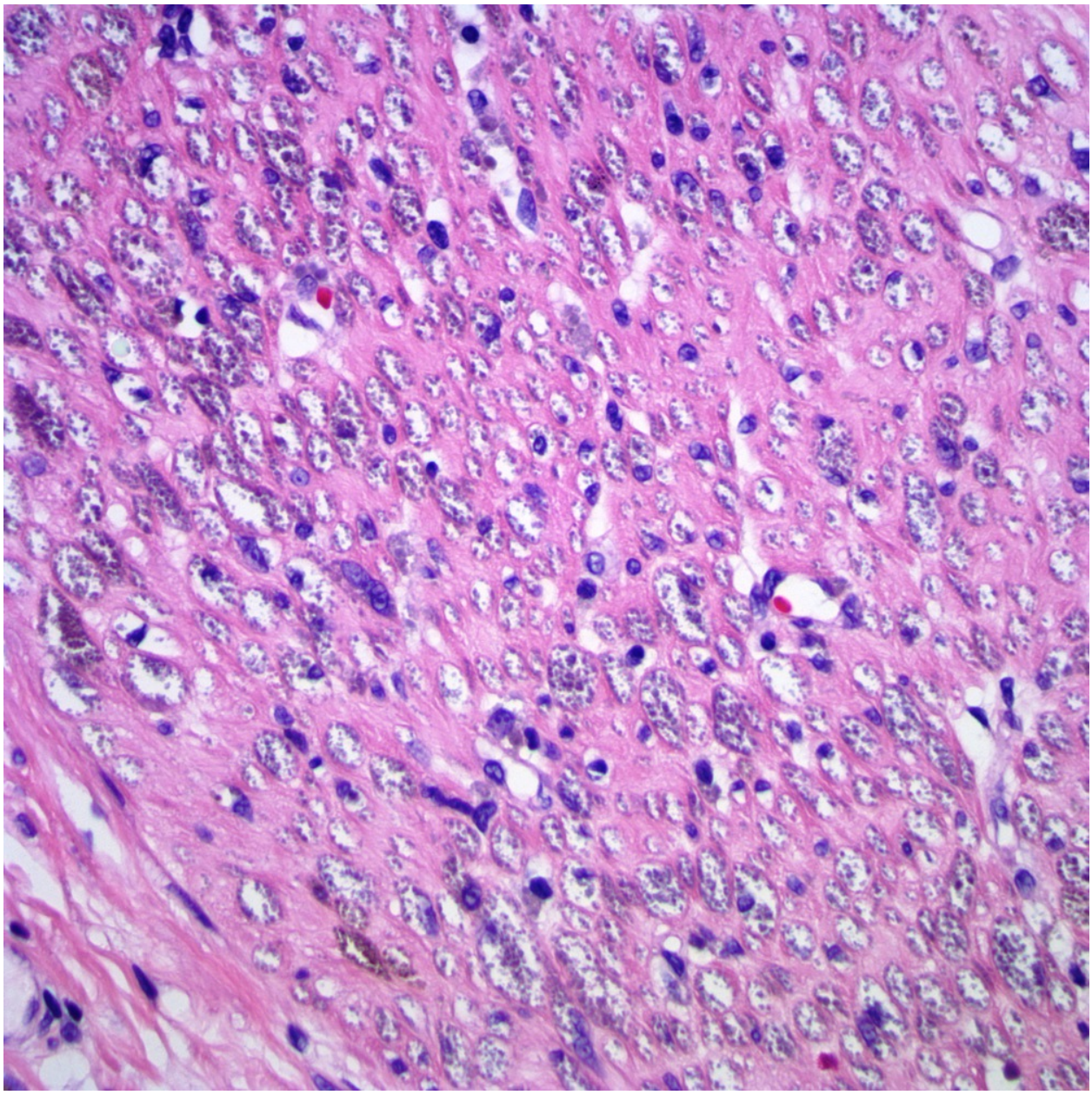


Figure 4. Another area of muscularis propria



Special stains included Fontana-Masson, iron, and PAS-D, pictured respectively below:

Figure 5. Fontana-Masson

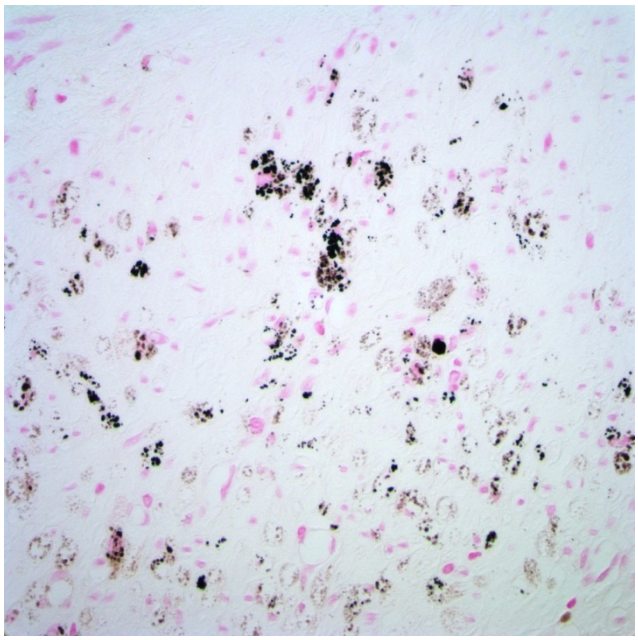


Figure 6. Iron stain

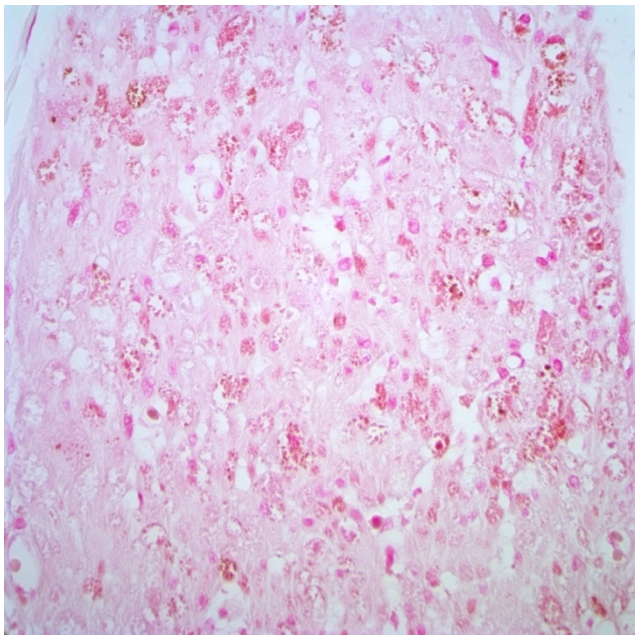
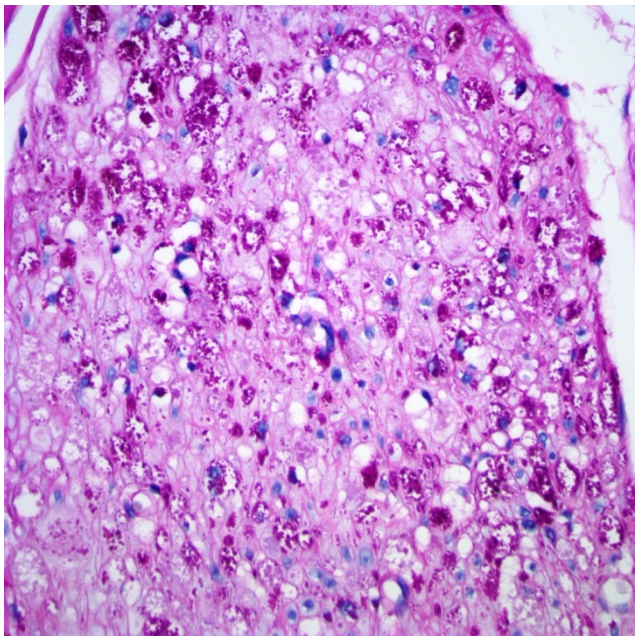


Figure 7. PAS-D stain



What is the correct diagnosis?

A) Malakoplakia

B) Brown bowel syndrome

C) Hemochromatosis

D) Melanosis coli

Answer: B) Brown bowel syndrome.

B) Brown bowel syndrome (BBS) is characterized by deposition of light brown, granular, lipofuscin-like pigment within the muscularis propria and muscularis mucosa, (Figures 2-4). This imparts a brown discoloration to the bowel. The pigment is PAS-D and Fontana-Masson positive and iron stain negative, as seen in Figures 7, 5, and 6, respectively. Mucosal lymphangiectasia is occasionally seen. It most often occurs in the small bowel, but can also be seen in the stomach and colon. Electron microscopy reveals mitochondrial damage and pigment concentrated in the perinuclear Golgi region.

A), C), and D) Malakoplakia typically consists of a dense histiocytic infiltrate with characteristic Michaelis-Gutmann bodies. Michaelis-Gutmann bodies are small intracytoplasmic concretions that are positive for calcium and iron. Hemochromatosis can cause deposits of iron in the GI tract, including the epithelial cells and the macrophages. The pigment is positive on iron stain, showing the typical Prussian blue reaction. In contrast, BBS pigment is negative on iron stain. Melanosis coli is associated with laxative use (such as anthraquinone laxatives), which induces apoptosis. It is characterized by pigmented macrophages located within the lamina propria, rather than the smooth muscle cells of muscularis propria as seen in BBS. Like BBS, the pigment seen in melanosis coli is PAS and Fontana-Masson positive.

Discussion:

Pigmentation of the bowel was first described by the German pathologist Dr. Ernst Wagner in 1861, but the association with malabsorption and vitamin E deficiency was recognized by Dr. Alwin Pappenheimer in a 1946 paper describing 4 autopsy cases, in which he noted that laboratory studies in vitamin E deficient rats produced similar changes. Since that time (nearly 70 years later), only about 27 cases have been reported in the literature.

BBS is usually associated with malabsorptive gastrointestinal disease and vitamin E deficiency. Vitamin E is an antioxidant that prevents peroxidation of unsaturated fatty acids. It has been postulated that this deficiency may result in oxidized lipids which cause mitochondrial damage and the resulting brown pigment. Some authors have reported clinical improvement and regression of the pigment with long-term vitamin E supplementation. Others have reported clinical improvement without resolution of the pigment. It is still unclear whether BBS is a primary disease or is a non-specific sequela of severe malabsorptive gastrointestinal disease.

In the current case, after the diagnosis was made a vitamin E level was drawn: 3.0 (ref. range 5.7-19.9 mg/dL). The patient was started on oral vitamin E therapy and 2 months later his vitamin E level was 9.2, he had regained 15 lbs, his appetite had improved, and his vomiting and diarrhea had resolved.

References

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