USGIPS Case of the Month

A 66 year old woman presented to her primary care physician with hair loss, diarrhea, nail atrophy and a significant unintentional weight loss over a period of approximately a year. She had no significant prior medical history beyond hypertension prior to her current complaints. An upper endoscopy as well as a colonoscopy with biopsies was performed with the following results.

What is your diagnosis?

a. Menetrier's disease
b. Cowden syndrome
c. Juvenile polyposis syndrome
d. Cronkite-Canada syndrome
e. Peutz-Jeghers syndrome

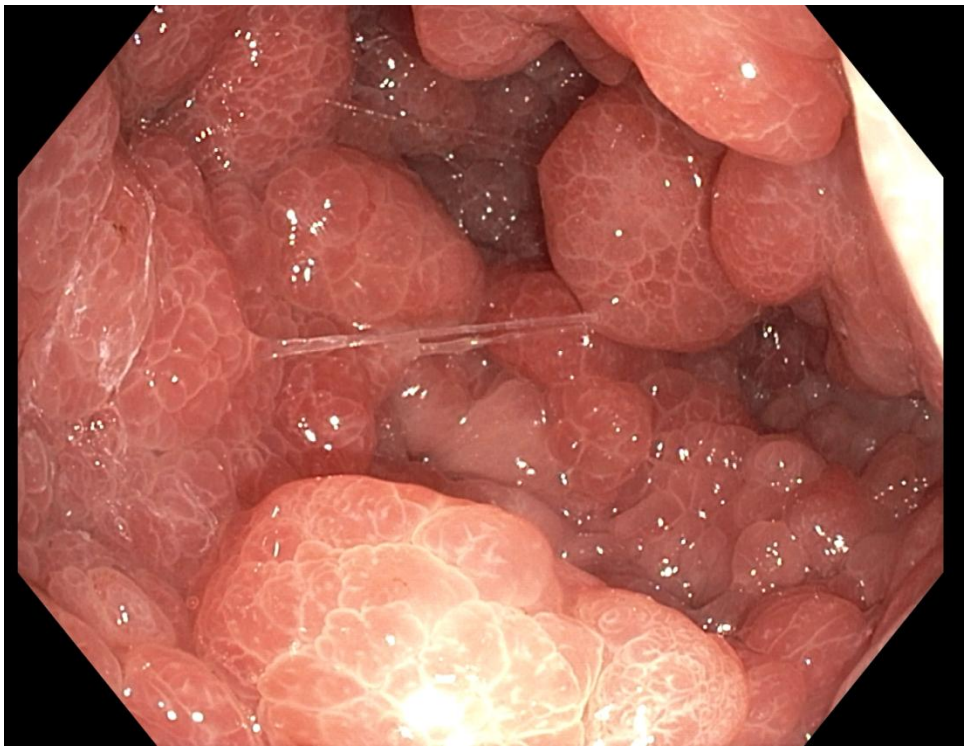

Figure 1. Endoscopic image of patient's stomach.

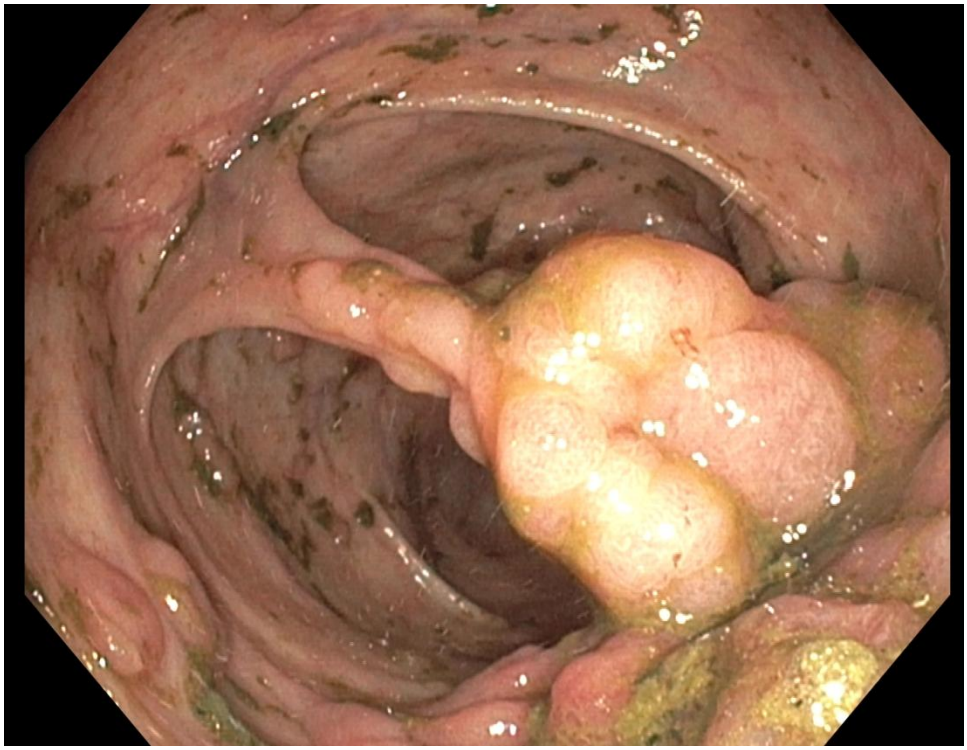

Figure 2. Endoscopic image of patient's colon.

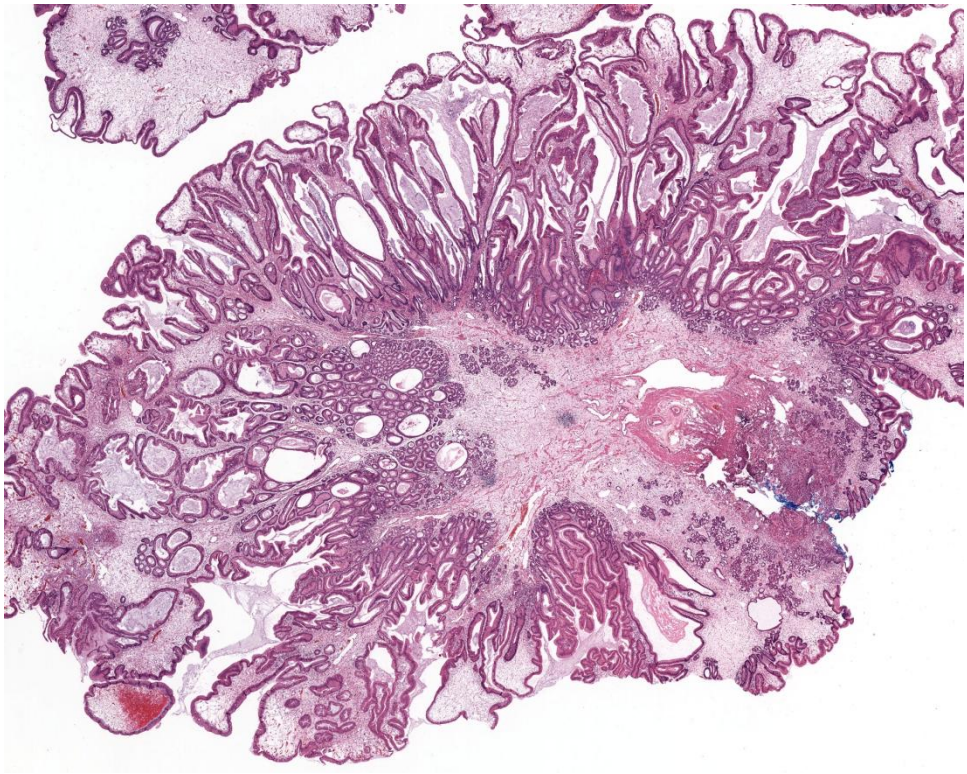

Figure 3. Gastric polyp (20x)

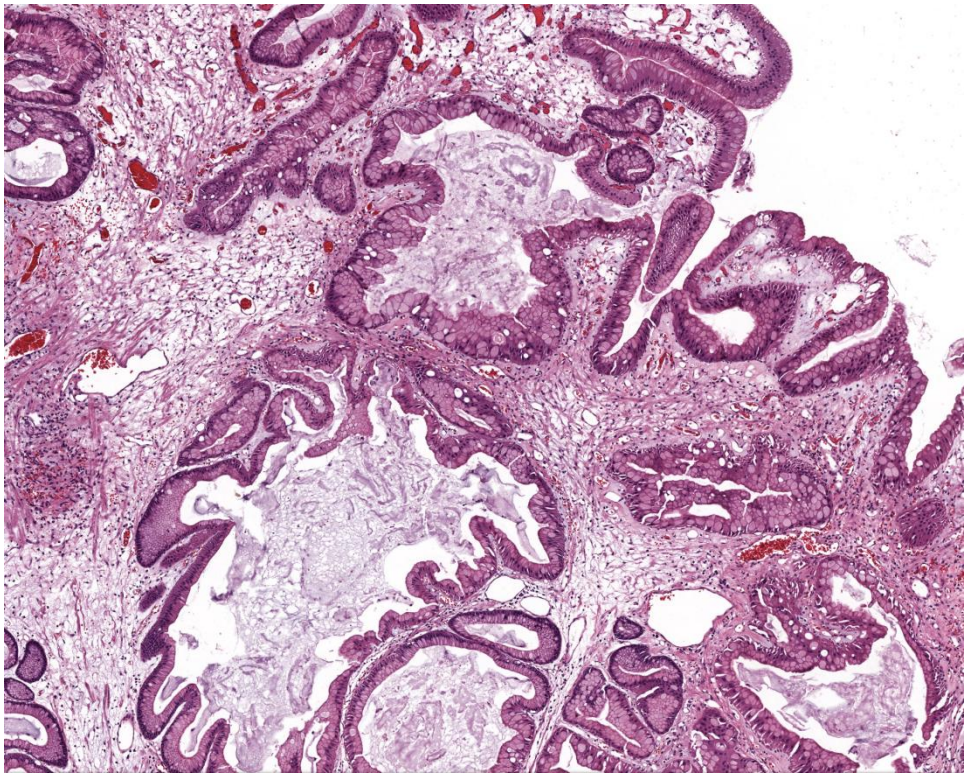

Figure 4. Gastric polyp (50x)

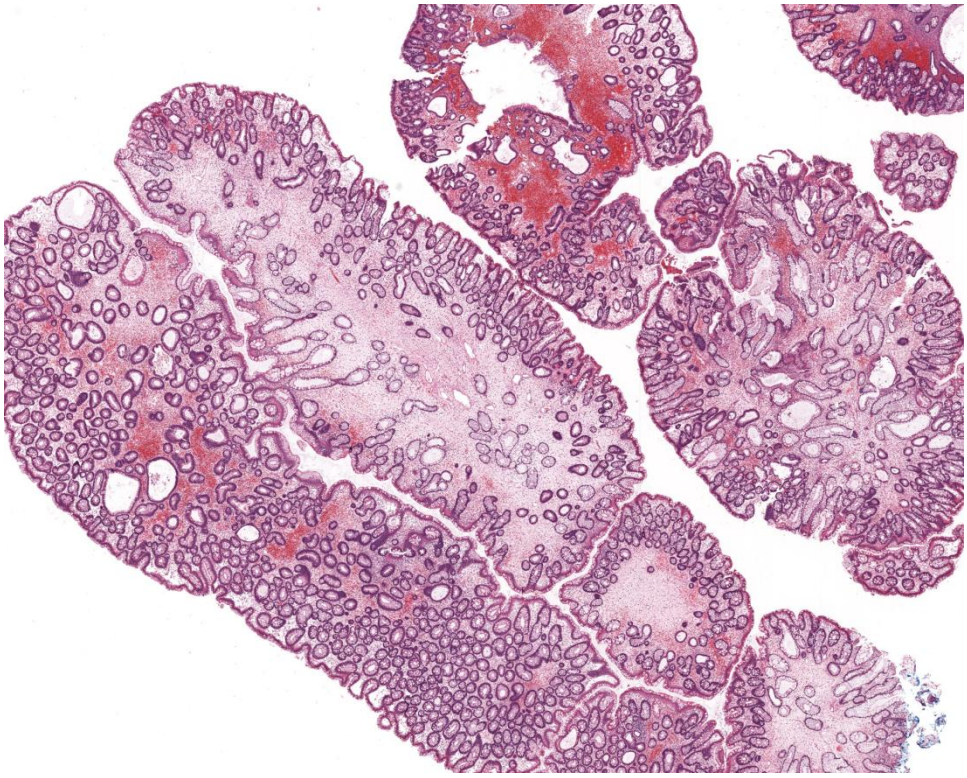

Figure 5. Colonic polyp (20x)

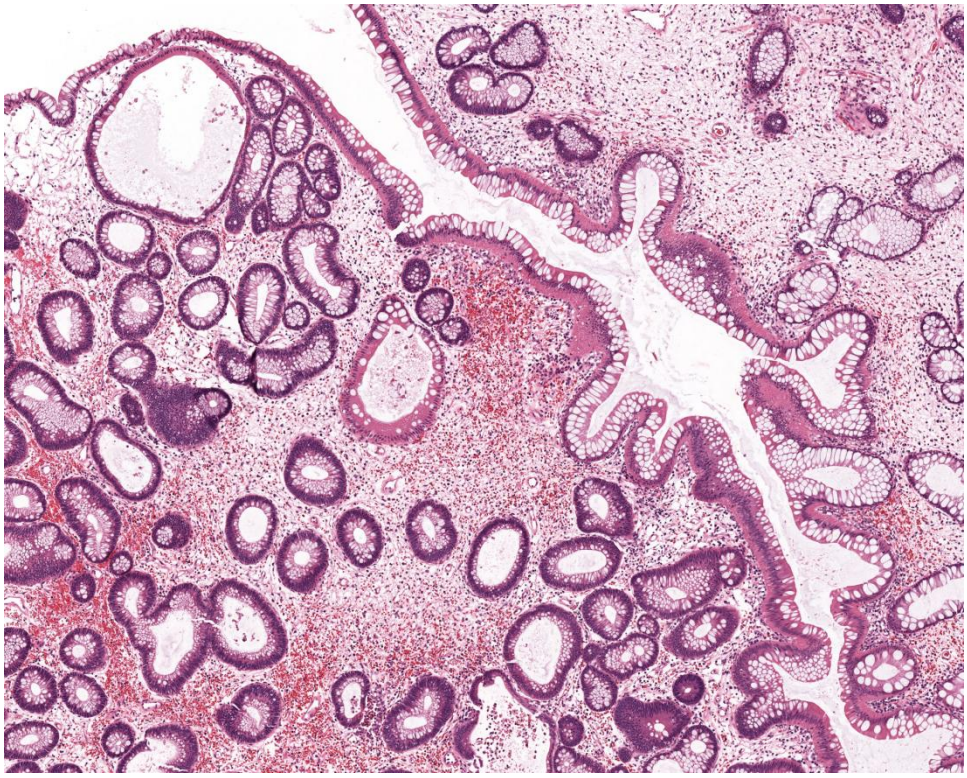

Figure 6. Colonic polyp (50x)

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Answer and Discussion

Cronkite-Canada syndrome

Cronkite-Canada syndrome is a rare polyposis condition that typically afflicts adults in their fifth or sixth decade of life.[1] In the classical clinical presentation, patients characteristically exhibit a combination of gastrointestinal symptoms such as anorexia, weight loss, diarrhea or abdominal pain as well as ectodermal changes including skin hyperpigmentation, nail dystrophy and alopecia. Additional manifestations that have been reported include peripheral edema and glossitis, both likely secondary to the associated protein-losing enteropathy.[2] Laboratory findings further support this pathogenesis and often reveal hypoproteinemia and electrolyte disturbances as well as anemia and positive fecal occult blood testing.[3]

The polyposis associated with Cronkite-Canada syndrome is typically widespread and often involves the gastrointestinal tract in its entirety, with sparing only of the esophagus. Endoscopically, these polyps are most often broad based and tend to coalesce, leaving minimal unaffected intervening mucosa. These macroscopic findings are directly reflected in the associated histologic features which include ill-defined polyps with cystically dilated glands and crypts with an associated edematous lamina propria.[4] Scattered mononuclear cells and eosinophils are typically present. These features are also characteristically appreciated in biopsies of the apparently uninvolved intervening mucosa.

Although it was originally described over sixty-years ago, the pathogenesis of Cronkite-Canada syndrome is still poorly understood.[5,6] This is in part due to the rarity of this disease, with only a few large cases series having been reported, principally out of Japan.[2] No genetic basis for this syndrome has been identified and there has been a suggestion of an immunologic dysregulation etiology.[7,8] Although consistent treatment guidelines are not established, some form of immunosuppression such as corticosteroids or azathioprine in combination with nutritional support is most often utilized. Clinical outcomes are generally poor, although they are highly variable with a small number of patients experiencing complete remission.[9]

In isolation, the gastric polyps of Cronkite-Canada are essentially histologically indistinguishable from those of several other polyposis syndromes, highlighting the importance of correlating microscopic findings with the clinical and endoscopic features of each case. The polyps of Peutz-Jeghers syndrome are most likely to be encountered in the small intestine and have a characteristic arborizing pattern associated with a smooth muscle core. Additionally, although the polyps of juvenile polyposis syndrome can appear remarkably similar to those in Cronkite-Canada, biopsies of the intervening non-polypoid mucosa in the former will appear normal, in stark contrast to the findings in the latter. The less well defined hamartomatous polyps of Cowden syndrome may also enter the differential, but these tend to be more common in the lower gastrointestinal tract and are associated with less lamina propria edema and cystic dilation. Perhaps the most obvious difference between these polyposis syndromes and Cronkite-Canada is the lack

of the associated weight loss, diarrhea and nutritional deficiencies that often accompanies Cronkite-Canada.

Finally, Menetrier's disease may at times enter the differential secondary to overlapping features in the clinical presentation and gross appearance on endoscopic examination of the stomach. However, the histologic findings of this disease including dramatic foveolar hyperplasia with little if any associated edema is distinctly different than that of Cronkite-Canada syndrome.

References

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Authors

Danielle Harrell, D.O.
Jesse Kresak, M.D.
Michael Feely, D.O.

Department of Pathology, Immunology, and Laboratory Medicine
University of Florida, College of Medicine
1600 SW Archer Road, Gainesville, FL 32610-0275