The Use of Deep Snare Biopsies to Diagnose Cronkhite-Canada Syndrome

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ABSTRACT

Cronkhite-Canada syndrome is a rare sporadic polyposis syndrome that presents with dermatologic and neurologic symptoms in addition to nutritional deficiencies. It can mimic alternate pathologies, such as Menetrier disease, making adequate histologic sampling with deep snare biopsies necessary for tissue comparison. We present a case report of Cronkhite-Canada syndrome that demonstrates the importance of deep tissue sampling for adequate diagnosis and treatment initiation.

INTRODUCTION

Cronkhite-Canada syndrome (CCS) is a rare nonhereditary polyposis syndrome initially reported by Leonard Cronkhite and Wilma Canada in 1955.1 Given its rarity, diagnosis can be challenging because it can mimic other hyperplastic and nonhyperplastic gastropathies, such as Menetrier disease (MD). We present a case of CCS where repeat deep tissue sampling was the link for an adequate medical diagnosis.

CASE REPORT

A 68-year-old Japanese woman with a history of endometriosis presented to clinic with a 2-year history of 30 pound unintentional weight loss, chronic diarrhea accompanied by abdominal pain and occasional blood, and diminished sense of taste. She also noted skin hyperpigmentation, loss of her nails, and a gradual onset of peripheral neuropathy in her toes, which progressed to muscular weakness in the lower extremities. Family history was notable for liver cancer in her mother, but otherwise was negative for autoimmune processes. Laboratory tests completed at symptom onset showed a normal complete blood count, comprehensive metabolic panel, folate, vitamin B12, and thyroid function studies. HIV was negative. Anti-nuclear antibodies were positive, but complements were normal, and serum protein electrophoresis showed elevated alpha-2 globulins. Colonoscopy and upper endoscopy completed 10 months after symptom onset identified 2 colonic polyps (tubular and inflammatory polyps) and 1 gastric polyp (fundic gland polyp), but were otherwise unremarkable. Computed tomography completed 20 months after symptom onset showed prominent gastric folds with a filling defect in the small bowel. A subsequent magnetic resonance imaging enterography, however, showed no evidence of a small bowel lesion. She was evaluated by hematology, endocrinology, rheumatology, and neurology with no diagnoses found.

Given her ongoing symptoms, she was then referred to an academic gastrointestinal center for further evaluation. On physical examination, she had onychodystrophy of fingers and toenails and hyperpigmentation of the palms and soles of her feet (Figure 1). Repeat laboratory evaluation was significant for normocytic anemia, with a hemoglobin drop from 13.7 g/dL to 9.3 g/dL within 6 months, hypoalbuminemia of 2.6 g/dL, a low total protein of 5.5 g/dL, hypocalcemia, and low vitamin B12. Celiac serologies and repeat urine and serum protein electrophoresis were normal. Owing to the thickening of her stomach seen on the prior computed tomography scan, an upper endoscopy was performed, which revealed polypoid mucosal changes of the gastric antrum and body and...
duodenum (Figures 2 and 3). Biopsies of the distal stomach obtained with a cold forceps demonstrated tortuous foveolae and lamina propria edema. Congo red staining was negative. Based on the initial histology, the leading differential diagnosis included MD.

The decision was made to repeat upper endoscopy and colonoscopy in 1 month with snare resection for deeper tissue sampling and to determine background mucosal involvement. Repeat upper endoscopy and colonoscopy revealed extensive pedunculated and sessile polyps localized to the distal stomach, terminal ileum, and right colon, with the largest measuring 21 mm (Figure 4). Tissue obtained with snare resection of a gastric and colonic polyp demonstrated cystically dilated crypts and prominent stromal edema, morphology that was nearly identical when compared with the background nonpolypoid colonic mucosa (Figures 5 and 6). This morphology in combination with the clinical context was most compatible with a diagnosis of CCS.

DISCUSSION
CCS is a rare nonhereditary polyposis syndrome characterized by diarrhea, alopecia, skin hyperpigmentation, and tongue atrophy accounting for the loss of taste. Anemia, nutritional deficiencies, and hypoalbuminemia are most commonly seen on laboratory examination on account of the protein-losing enteropathy.
Endoscopic evaluation is highlighted by hamartomatous polyps in the stomach and small and large intestine while sparing the esophagus.

Gastric mucosa can be thickened, mimicking MD and other rare hyperplastic and nonhyperplastic gastropathies. Adequate histologic sampling of the gastric and colonic polyps and surrounding background mucosa with deep snare biopsies is necessary for tissue comparison. Although foveolar hyperplasia and lamina propria edema can be seen with superficial samples in both CCS and MD, as seen in our patient’s first upper endoscopy, deeper tissue samples allow for better assessment of the mucosal architecture and pit-to-gland compartment. While MD has orderly architecture with glands retained in parallelism, CCS key distinguishing histology demonstrates architectural distortion of glands and crypts within the polyps and background non-polypoid mucosa. In our case, the nearly identical histologic features of the polyps and background/nonpolypoid mucosa in the clinical context of dermatologic changes were most compatible with CCS. CCS was further differentiated from MD given the characteristic location of mucosal involvement. Unlike MD, which concentrates in the gastric body and spares the gastric antrum and duodenum, CCS polyps can distribute throughout the entirety of the digestive tract, simultaneously affecting the antrum and intestines with esophageal sparing.

Distinguishing between CCS and MD is important given their variation in treatment. While definitive treatment of CCS is still being explored, patients have responded with symptomatic and endoscopic remission after corticosteroid or azathioprine administration. If left untreated, CCS can lead to fatal outcomes, including malnutrition, gastrointestinal bleeding, and infection. After the diagnosis of CCS, our patient was started on 40 mg prednisone for 2 months and tapered by 10 mg monthly thereafter for a goal of 8 months of treatment. Follow-up esophagogastroduodenoscopy and colonoscopy were performed 4 months after prednisone initiation. While esophagogastroduodenoscopy and colonoscopy showed similar polypoid mucosa, the patient reported symptomatic improvement with improvement of nail growth, 11 pound weight gain, return of taste, and diarrhea resolution. The decision was made to continue with the 20 mg prednisone therapy and reassess in several months for endoscopic remission.

**DISCLOSURES**

Author contributions: N. Filipek: drafting and finalization of the manuscript, data and image collection, and is the article guarantor. P. Dromparis: acquisition and interpretation of histology. IA Hujoel: critical revision of the manuscript.

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