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CASE REPORT | COLON

A Successful Steroid-Sparing Approach in Cronkhite-Canada Syndrome

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ABSTRACT

Cronkhite-Canada Syndrome (CCS) is a rare, sporadic polyposis condition. The literature on CCS consists mostly of case reports. Although disease presentation has been well-described, there is no consensus on the management of CCS. We present a severe case of CCS that demonstrated clinical and endoscopic response to corticosteroids. This response was maintained with azathioprine. This case provides additional experience on a therapeutic strategy to induce and maintain a durable corticosteroid-free remission.

INTRODUCTION

Cronkhite-Canada Syndrome (CCS) is a rare nonhereditary polyposis condition first described in 1955.[1] Given the rare incidence of CCS, there is no consensus on therapy. Currently, corticosteroids are the mainstay of CCS therapy. The experience with steroid-sparing regimens remains limited. We present a case of CCS where remission was induced by corticosteroids and maintained by azathioprine.

CASE REPORT

A 71-year-old white man with irritable bowel syndrome, diabetes, and atrial fibrillation on warfarin developed abdominal pain with alternating constipation and diarrhea after many years of stable gastrointestinal symptoms. Esophagogastroduodenoscopy (EGD) and colonoscopy revealed antral erythema and 2 colonic polyps. Pathology revealed inactive chronic gastritis and 2 diminutive tubular adenomatous polyps; there was no evidence of microscopic colitis or *Helicobacter pylori*. Over the course of 9 months, symptoms worsened and he lost 15 pounds unintentionally. Examination revealed alopecia and onychodystrophy (Figure 1). Laboratory tests revealed low ferritin, hemoglobin, protein, and albumin. Stool guaiac was positive. Repeat EGD and colonoscopy performed 1 year after the previous endoscopic evaluation showed innumerable antral, ileal, and colonic polyps (Figure 2). Both polyps and the intervening mucosa were biopsied; no polypectomies were attempted. Pathology showed foveolar hyperplasia with chronic gastritis in the stomach and lamina propria inflammation with cystically dilated crypts and glands in the colon (Figure 3).

This was consistent with typical CCS histological findings of edematous lamina propria, architectural distortion of mucosal glands and crypts, and scant mononuclear inflammatory cell infiltrate.[2] The differential diagnosis of CCS consisted of other polyposis syndromes including familial adenomatous polyposis, Peutz-Jeghers syndrome, juvenile polyposis syndrome, and phosphatase and tensin homolog hamartoma tumor syndrome. In general, these polyposis syndromes can be differentiated by their own characteristic clinicopathologic features. Juvenile polyps and CCS polyps can appear endoscopically and histologically identical.[3] Typical histological findings of CCS are found in polypoid mucosa and nonpolypoid mucosa; this is a key distinguishing feature of CCS. Combining the clinical manifestations, polyposis on endoscopy, and the characteristic histologic findings, the patient was diagnosed with CCS. The patient's symptoms of abdominal pain and diarrhea persisted despite initial therapy of oral nutritional support and antidiarrheal medication. Prednisone was initiated at 40 mg daily and his symptoms improved, however, he developed cognitive side effects of confusion. There is limited literature describing cases of CCS achieving steroid-free clinical remission with

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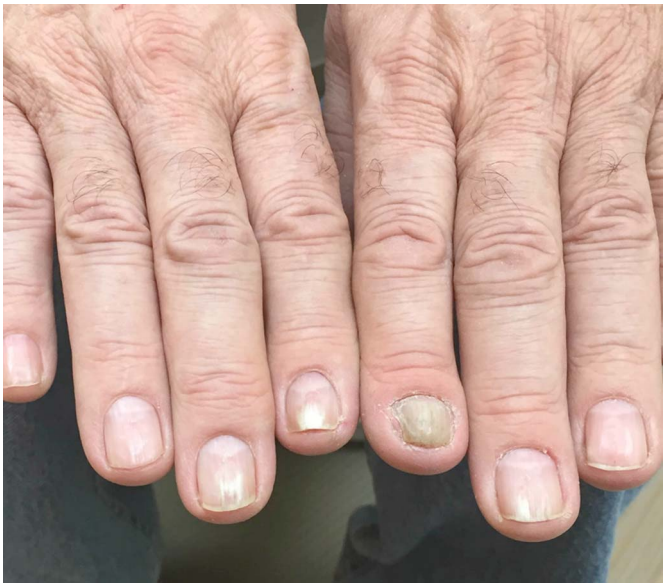

Figure 1. Onychodystrophy present bilaterally on fingernails.

azathioprine monotherapy. Varying doses of azathioprine had been used as monotherapy or in combination with other immunosuppressants. After a comprehensive discussion of alternative therapy options with the patient, who was wary of long-term immunosuppression, he agreed to a dose of 1.25 mg/kg/d of azathioprine (the literature described a dose of 2 mg/kg/d). The prednisone was tapered off after 6 weeks of therapy and azathioprine was initiated. Corticosteroid side effects resolved on prednisone taper and CCS symptoms remained controlled on azathioprine without adverse effects. The patient was able to regain weight and onychodystrophy improved as well. After 8 months of immunosuppressive therapy, repeat EGD and colonoscopy were performed. In comparison to findings 1 year ago at diagnosis, the repeat endoscopy at 1 year after diagnosis demonstrated near resolution of polyposis (Figure 4).

DISCUSSION

There are about 500 cases of CCS described in the literature with an estimated incidence of 1 per million persons per year.[4,5] The average age at CCS diagnosis is the early 60s and there is a male predominance.[6] Most of the cases originate from Japan. CCS commonly presents with diarrhea, weight loss, alopecia, and dermatologic manifestations of onychodystrophy and hyperpigmentation. Complications include protein-losing enteropathy, gastrointestinal bleeding, intussusception, and gastrointestinal cancers, mainly gastric and colon.[7] This condition carries significant morbidity with a 5-year mortality up to 55% due to gastrointestinal bleeding, congestive heart failure, and sepsis.[5] The polyposis is typically hamartomatous and diffuse involving the entire gastrointestinal tract except the esophagus.[8] Management of CCS commonly consists of corticosteroid therapy and nutritional support.[6,9,10] An autoimmune etiology of CCS has been suggested and case reports have described the beneficial response of immunosuppressive therapies: azathioprine, anti-tumor necrosis factor antibody, cyclosporine, and sirolimus.[11–16] This case contributes additional experience to the limited literature on azathioprine as a viable steroid-sparing strategy in CCS.

This patient presented with hallmark features of CCS including diarrhea, onychodystrophy, and diffuse polyposis. This case demonstrated that disease can develop rapidly, which can lead to complications such as malabsorption, malnutrition, gastrointestinal bleeding, and obstruction. Our case highlighted the importance of an endoscopic evaluation, given the severity of symptoms despite an unremarkable endoscopic evaluation 1 year before. Unfortunately, the patient did not tolerate prednisone therapy but he demonstrated clinical and endoscopic response to low-dose azathioprine. This case underscored the dramatic response of this disease to immunosuppressive therapy and the ability to maintain remission with low-dose azathioprine. The patient demonstrated near resolution of

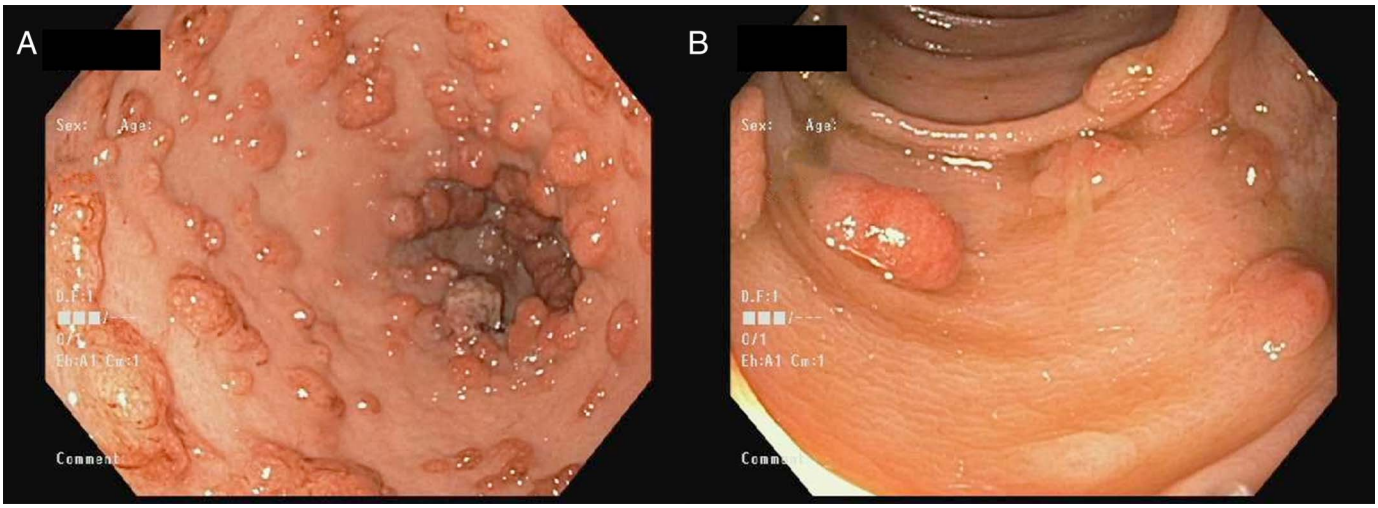

Figure 2. (A) Esophagogastroduodenoscopy revealing numerous gastric polyps in the antrum, and (B) colonoscopy revealing numerous descending colonic polyps.

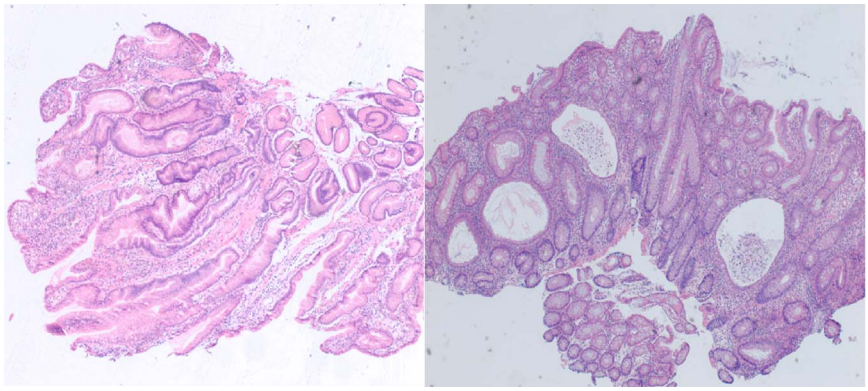

Figure 3. Pathology showing foveolar hyperplasia and chronic gastritis (left); chronic inflammation in the lamina propria, cystically dilated crypts and glands (right).

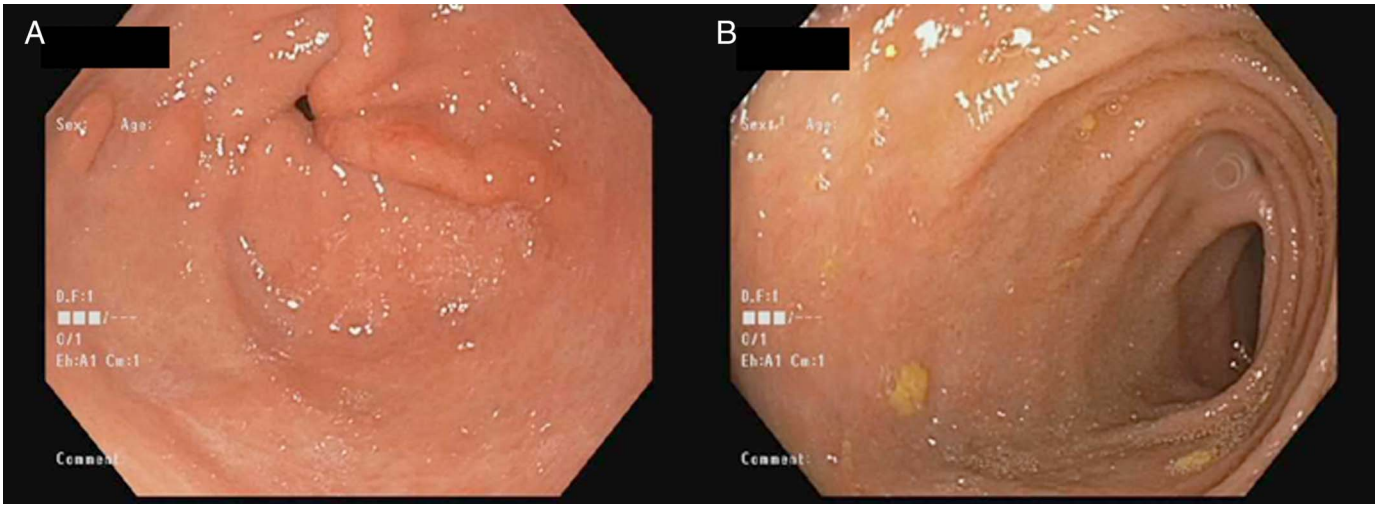

Figure 4. (A) Follow-up esophagogastroduodenoscopy of antrum, and (B) follow-up colonoscopy revealing near resolution of polyps on antrum.

polyposis with 6 weeks of prednisone and 26 weeks of azathioprine. It is important to be aware of this constellation of symptoms and to refer for endoscopic evaluation. Early diagnosis is crucial to identifying and treating a disease with significant mortality that can respond rapidly to immunosuppression.

DISCLOSURES

Author contributions: All authors drafted the manuscript and approved the final draft submitted. EJ Mao and S. Fine are the article guarantors.

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Informed patient consent was obtained for this case report.

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