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CASE REPORT | COLON

Colorectal Cancer Associated with *Strongyloides stercoralis* Colitis

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ABSTRACT

Strongyloides stercoralis colitis is a severe but easily curable disease with a high mortality rate if left untreated. Strongyloidiasis can persist up to several decades and may lead to a chronic colitis similar to that seen in inflammatory bowel disease (IBD), and the two are often confused. Chronic colitis from IBD is associated with an increased risk of colorectal cancer, so it is plausible that chronic colitis from strongyloidiasis may carry a similar risk. Our case report associates chronic *Strongyloides* colitis and colorectal cancer.

INTRODUCTION

Strongyloides stercoralis is a helminth endemic in tropical and subtropical regions of Latin America, sub-Saharan Africa, and Southeast Asia.[1] In the United States, infection is prevalent but not endemic, with individuals living in rural Appalachia, World War II veterans, and immigrants from endemic regions representing the majority of documented cases.[2,3] Several small studies in select populations within the United States have shown that as many as 6.1% of individuals sampled were infected, and as many as 46.1% were infected when immigrants from endemic areas were sampled.[3] An estimated 30-100 million people are infected worldwide.[4] Infection may be life-long, and individuals may be susceptible to chronic inflammation of the gut and colon.[5]

CASE REPORT

A 47-year-old Colombian man with a history of vitiligo and chronic anemia was admitted with chronic, intermittent abdominal pain, fatigue, and an unintentional 25-pound weight loss over 6 months. He denied rectal bleeding, melena, or diarrhea, as well as risk factors for ulcer. The patient emigrated to the United States 6 years prior and denied recent travel. There was no personal or family history of colon polyps, colorectal cancer, celiac disease, or inflammatory bowel disease (IBD).

Physical exam was notable for vitiligo and pallor. A complete blood count with differential revealed microcytic anemia with hemoglobin 3.1 g/dL and eosinophilia 26.4%. Laboratory studies revealed iron and vitamin B12 deficiencies, positive intrinsic factor blocking antibody, albumin 3.0 g/dL, and a positive fecal occult blood test. Erythrocyte sedimentation rate and C-reactive protein were normal. After transfusion of 5 units of packed red blood cells, the patient underwent and esophagogastroduodenoscopy (EGD) and colonoscopy.

The EGD revealed chronic inflammation of the gastric antral gland mucosa, suggestive of atrophic gastritis of autoimmune type, and a grossly normal duodenum. These were biopsied to exclude occult celiac disease. Colonoscopy was consistent with chronic colitis from the cecum to the sigmoid; the mucosa was friable with loss of vascular markings, haustral folds, and a matted, tacked down quality to the right colon mucosa when biopsies were taken. The ileum, distal colon, and rectum were spared. The ascending colon harbored a 3-cm ulcerated mass (Figure 1).

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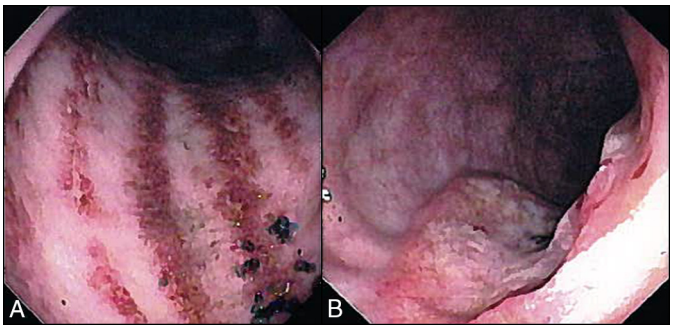

Figure 1. (A) Colon with friable granular mucosa, linear erosions, and confluent loss of vascular markings and haustral folds. (B) A 3-cm ulcerated mass identified in the ascending colon.

Surrounding biopsies were taken to exclude dysplasia in the setting of potential IBD. Biopsies of the colitis showed mild crypt distortion with lymphoplasmacytosis and eosinophilic infiltrate within the lamina propria. Biopsies of the colon mass revealed invasive low-grade adenocarcinoma with no evidence of surrounding mucosal dysplasia (Figure 2). Duodenal biopsy revealed organisms morphologically compatible with *S. stercoralis* (Figure 3). Fecal ova and parasite analysis also identified *S. stercoralis*. No worms were identified on colon pathology.

Multidisciplinary tumor board reached consensus for treatment of infectious colitis rather than dysplastic IBD, given the patient's country of origin, chronic anemia, and endoscopic and pathological findings. He was treated with ivermectin 200 μg/kg on day 1 and repeated 24 hours later. Eradication of *S. stercoralis* was confirmed with repeat stool studies. The work-up for metastatic disease was negative, and extended right hemicolectomy with ileocolic anastomosis was successful. Surgical pathology revealed transmural chronic eosinophilic inflammation associated with a stage IIB colorectal cancer. Risks and benefits of oxaliplatin- or capecitabine-based chemotherapy options were outlined, including the potential for hyperinfection syndrome, and the patient deferred adjuvant therapy. Iron deficiency anemia and eosinophilia normalized postoperatively. Surveillance colonoscopy

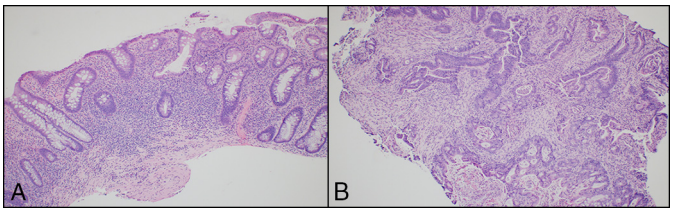

Figure 2. (A) Colon with mildly active, chronic, non-specific colitis characterized by lymphoplasmacytosis and eosinophilia within the lamina propria, as well as crypt distortion (200x magnification). (B) Colon biopsy showing invasive adenocarcinoma characterized by irregular glands lined with dysplastic epithelium in a desmoplastic stroma (200x magnification).

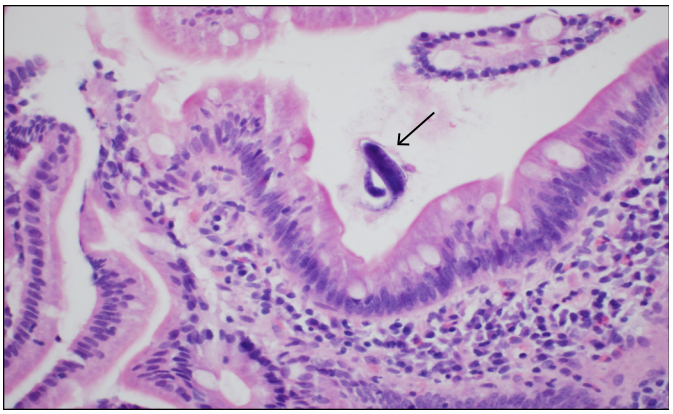

Figure 3. Duodenal biopsy showing *Strongyloides stercoralis* rhabditiform larvae (arrow) (200x magnification).

at 6 months and 2 years revealed a grossly normal colonic remnant without microscopic evidence for colitis or dysplasia.

DISCUSSION

Studies support the idea that chronic colitis can predispose an individual to colorectal cancer as demonstrated in patients with IBD. IBD-associated colorectal cancer has been decreasing in western countries, while an increased occurrence has been seen in Asian countries secondary to the increased incidence of IBD.[6,7] A direct relationship exists between colorectal cancer risk and extent and duration of disease.[8] Population-based studies from Winther et al. estimated the cumulative risk of colorectal cancer to be 0.4% at 10 years, 1.1% at 20 years, and 2.1% at 30 years.[9] Rutter et al found the cumulative risk to be 0% at 10 years, 2.5% at 20 years, and 7.6% at 30 years.[10] Söderlund et al found the cumulative risk to be 1.5% at 10 years, 3.8% at 20 years, and 7.6% at 30 years.[11]

Chronic infections with viruses, bacteria, and parasites contribute to an estimated 18% of all cancers.[12] Three helminth infections are classified as carcinogenic to humans: *Schistosoma haematobium* is associated with urinary bladder cancer, and *Clonorchis sinensis* and *Opisthorchis viverrini* are associated with cholangiocarcinoma.[13] In vitro studies have shown that substances secreted and excreted by different nematode species can induce proliferation of tumor cell lines.[14]

Due to the autoinfective life cycle of *S. stercoralis*, strongyloidiasis is a chronic infection that may go untreated for decades because the majority of patients are asymptomatic.[15] *S. stercoralis* has been associated with cancers in the past and can be seen on gastric biopsies with concomitant atrophic gastritis and gastric adenocarcinoma, and its larvae have been isolated from the bile of patients with biliary tract cancer.[16-18]

A major concern with strongyloidiasis is hyperinfection syndrome with rapid dissemination. Hyperinfection syndrome can be seen in iatrogenically immunosuppressed patients and

carries a mortality rate that approaches 100%.[19] Azathioprine and 6-mercaptopurine have been associated with this syndrome, but by far the strongest and most specific association is with glucocorticoids.[20-22] One explanation may be its acute suppression of eosinophilia and lymphocyte activation. Another may be a direct effect on the parasite as glucocorticoids may accelerate the transformation of rhabditiform to invasive filariform larvae or rejuvenate reproductively latent females.[22]

Diagnosis must be prompt to avoid these complications. Eosinophilia is not universally present but may be the only clue of a parasitic infection. Definitive diagnosis is usually made by detecting larvae in the stool, but parasite burden may be low and excretion intermittent in more than 70% of cases, so the diagnois can be missed.[23] Endoscopy can aid in detection, with rates approaching 70% seen with duodenal biopsies.[15,24] This parasite is also an infamous and dangerous mimicker for Crohn's disease, particularly ulcerative colitis (UC) as they share many endoscopic features. *Strongyloides* colitis can be distinguished from UC by transmural colonic inflammation, eosinophilic-rich infiltrate within lamina propria, relatively intact crypt architecture, skip-pattern inflammation, distal attenuation, rectal sparing, and presence of larvae.[24]

Another important issue is colorectal cancer, as IBD-associated neoplasia requires a restorative proctocolectomy with ileal pouch-anal anastomosis.[25] Therefore excluding IBD may allow for a segmental colectomy to be performed. Our case report associates chronic *Strongyloides* colitis and colorectal cancer. In at-risk populations, it is imperative to screen for this parasite and eradicate it if present, because longstanding disease may be a risk factor for colorectal cancer and the initiation of immunosuppression can have detrimental effects.

DISCLOSURES

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