

## Brushing Up on Brush Borders: Intestinal Spirochetosis Diagnosis and Management

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### INTRODUCTION

Intestinal spirochetosis was first described in 1967.<sup>1</sup> Diagnosis is based on colon biopsy histology where spirochetal microorganisms are found attached to the apical cell membrane of colorectal epithelium as a pseudo-brush border. Higher risk groups include those living in poorly developed nations, persons living with human immunodeficiency virus (HIV), and men who have sex with men.<sup>2</sup> Symptoms most commonly associated with adult cases of intestinal spirochetosis include abdominal pain with watery diarrhea.<sup>3</sup> Adolescent cases of intestinal spirochetosis may present with nausea and failure to thrive, along with diarrhea.<sup>4</sup> Many case patients are asymptomatic.

This case highlighted a patient diagnosed with intestinal spirochetosis after years of nonspecific abdominal symptoms. The diagnosis of this rare condition requires ruling out common etiologies and a detailed inspection of colon biopsy histology.

### CASE REPORT

A 46-year-old man with HIV infection and exocrine pancreatic insufficiency was referred for colonoscopy with symptoms of intermittent diffuse abdominal cramping, nausea, and diarrhea of unexplained origin for several years. He had no improvement with lipase-protease-amylase capsules for pancreatic enzyme replacement (taken as two capsules three times daily with meals and one capsule with snacks). His work-up included negative *Clostridium difficile* PCR, *Giardia* and *Cryptosporidium* fecal antigens, stool culture, stool acid fast stain (no cyclospora, cryptosporidium or isospora seen), and syphilis antibody. The patient had a normal complete blood count with differential, thyroid stimulating hormone level and fecal fat percentage on two random collections, tissue transglutaminase antibody level, vitamin B12 level, and vitamin D (25-OH) total. At the time of his planned procedure, the patient denied fever, chills, night sweats, unintentional weight loss, vomiting, hematochezia, and melena. Otherwise, his recent review of systems was unremarkable.

The patient did not use tobacco, alcohol, or recreational drugs. He lived in a house with his son and denied sexual partners for several years, though in the remote past had male and female partners. He had no recent travel history though had been to Iraq and the desert southwest United States in the past. He was not working. He had no animal exposures aside from dogs. He did not consume raw meat or uncooked shellfish. He had not been swimming in the recent past.

On physical examination, the patient was afebrile and in no distress. Cardiac, pulmonary, and abdominal examinations demonstrated no abnormal findings. His most recent absolute CD4+ T-cell count was

140 cells/ $\mu$ L with an HIV viral load of 37,700 copies/mL. Serum white blood cell count was normal. Computed tomography scan of the abdomen and pelvis with contrast demonstrated homogeneous enhancement of the pancreas without mass, ductal dilation, parenchymal calcification, or peripancreatic inflammatory changes. He had normal caliber small bowel and colon, and a normal appendix with no free fluid or mesenteric lymphadenopathy. There was a tiny nonobstructive right renal calculus.

Colonoscopy revealed a normal appearance of the colon. Biopsy of colonic mucosa was performed, demonstrating no active inflammation or architectural distortion. On histologic examination, typical organisms were found adherent to the surface epithelium as a pseudo-brush border (Figure 1). A Warthin-Starry stain highlighted the organisms (Figure 2).

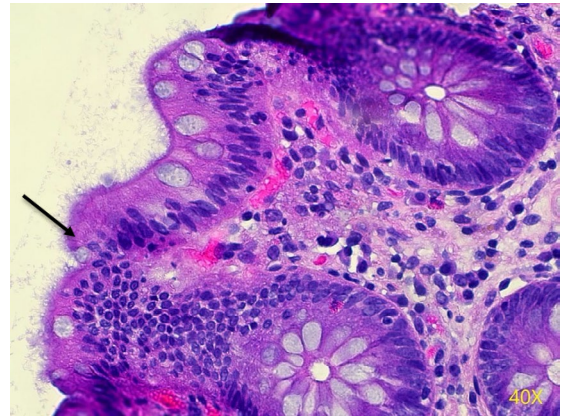


Figure 1. Typical organisms were found adherent to the surface epithelium as a pseudo-brush border.

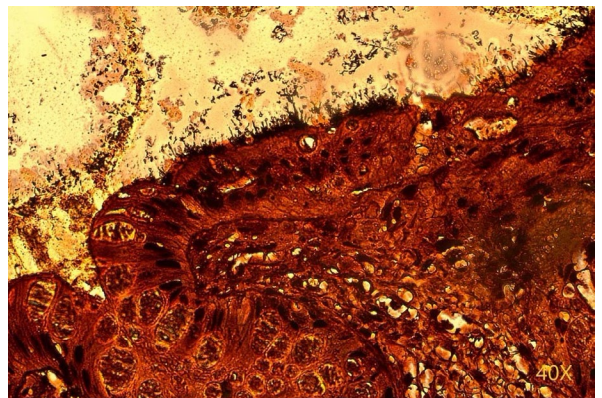


Figure 2. A Warthin-Starry stain highlighted the typical organisms.

This patient with HIV infection, a low CD4+ cell count, a lengthy history of abdominal cramping, nausea, and diarrhea without definitive alternative diagnosis, and normal findings on colonoscopy was found via colonic biopsy to have spirochetal organisms adherent to the surface of the colonic mucosa. These findings were consistent with a diagnosis of intestinal spirochetosis. The patient was prescribed a seven day course of metronidazole. One month following the therapy, he had subjective improvement in cramping abdominal pain as well as improvement in both quantity and consistency of his loose stools.

## DISCUSSION

Spirochetes are classified into *Spirochaetaceae*, *Leptospiraceae*, and *Brachyspiraceae* based on morphologic and phylogenetic differences.<sup>2</sup> *Brachyspiraceae* species *Brachyspira pilosicoli* and *Brachyspira aalborgi* are the most commonly identified organisms in human intestinal spirochetosis.<sup>5</sup> These fastidious anaerobes grow between 6 and 14 days at around 38.5°C on artificial culture media and brain heart infusion agar with 10% bovine blood and spectinomycin plus polymyxin B, respectively.<sup>6,7</sup> Their main host species include pigs and chickens, where they can cause diarrhea, failure to thrive, and delayed egg production. The bacteria are shed in feces leading to the proposed mechanism of infection being transmission by the fecal-oral route or exposure to contaminated water with higher colonization rates in developing countries.<sup>8,9</sup> When observed with in vitro antimicrobial susceptibility of *Brachyspira pilosicoli*, the pathogen has been found to be susceptible to metronidazole, ceftriaxone, meropenem, tetracycline, moxifloxacin, and chloramphenicol.<sup>10</sup> Most published case series recommend metronidazole as an initial treatment.<sup>2,11,12</sup>

Some debate exists regarding whether intestinal spirochetosis is a disease process or merely intestinal colonization.<sup>13</sup> One reason for this uncertainty is the high incidence of coinfection with other enteric bacteria.<sup>14</sup> In some case series, risks such as men who have sex with men, HIV virus infection, and co-infection with *Neisseria gonorrhoeae* or *Chlamydia trachomatis* were suggested.<sup>15</sup> In one series looking at 20 cases, 70% had CD4 lymphocyte cells >200/microL.<sup>15</sup> In a large series investigating colorectal biopsies in Japan, there was a slightly higher incidence of intestinal spirochetosis in patient with HIV.<sup>16</sup> Visualization of mucosa with colonoscopy contributed little to diagnosis, as the findings rarely correlated with disease severity, but can be used to rule out other pathologies.

Intestinal spirochetosis has been identified from proximal colon to rectum and within the vermiform appendix.<sup>2</sup> Diagnosis is made with biopsy. Histology findings along the intercryptal epithelial layer show diffuse blue fringe on hematoxylin-eosin stain. Spirochetes subsequently can be visualized on Warthin-Starry or Dieterle silver impregnation stains.<sup>12</sup> The proposed pathogenic mechanism for diarrhea associated with this disease is microvillus destruction caused by spirochetal attachment.<sup>17</sup> Furthermore, when a significant population of enterocytes become attached it may lead to a physical restriction of electrolyte and water resorption adding to diarrhea.<sup>8</sup>

In our patient, it was difficult to confirm if the spirochetes were pathogenic. In the months subsequent to the diagnosis, he had recurrent diarrhea that improved without intervention and an additional episode that improved with a repeat short course of metronidazole.

## CONCLUSIONS

Diagnosis of intestinal spirochetosis should be considered for a patient with unexplained chronic, watery diarrhea and abdominal pain, particularly in a patient with HIV infection. Work-up should include a thorough review of history, *Clostridium difficile* PCR, *Cryptosporidium*

and *Giardia* fecal antigen testing, and colonoscopy to rule out alternative diagnoses. Diagnosis of intestinal spirochetosis can be confirmed with biopsies of colonic mucosa viewed on Warthin-Starry stain which will reveal spirochetal organisms adherent to mucosa surface. Patients with intestinal spirochetosis can be treated with a course of metronidazole, although symptoms may resolve spontaneously.

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