Brushing Up on Brush Borders: Intestinal Spirochetosis Diagnosis and Management

Joy E. Fesen, M.D.¹, Ethar K. Al-Husseinawi, MBChB², Jessica R. Newman, D.O.³

¹Tulane University School of Medicine, New Orleans, LA
Department of Internal Medicine
University of Kansas Medical Center, Kansas City, KS
²Department of Pathology
³Department of Internal Medicine, Division of Infectious Diseases

Received May 27, 2021; Accepted for publication July 28, 2021; Published online Nov. 5, 2021
https://doi.org/10.17161/kjm.vol14.15535

INTRODUCTION

Intestinal spirochetosis was first described in 1967.⁴ 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.² Symptoms most commonly associated with adult cases of intestinal spirochetosis include abdominal pain with watery diarrhea.³ Adolescent cases of intestinal spirochetosis may present with nausea and failure to thrive, along with diarrhea.⁴ 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/μL 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).

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.

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-nc-nd) License. (CC-BY-NC-ND 4.0: https://creativecommons.org/licenses/by-nc-nd/4.0/)

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.
DISCUSSION

Spirochetes are classified into *Spirochaetaceae*, *Leptospiraceae*, and *Brachyspiraceae* based on morphologic and phylogenetic differences. Brachyspiraceae species *Brachyspira pilosicoli* and *Brachyspira aalborgi* are the most commonly identified organisms in human intestinal spirochetosis. 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. 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. 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. Most published case series recommend metronidazole, ceftriaxone, meropenem, tetracycline, moxifloxacin, and chloramphenicol. Most published case series recommend metronidazole as an initial treatment.

Some debate exists regarding whether intestinal spirochetosis is a disease process or merely intestinal colonization. One reason for this uncertainty is the high incidence of coinfection with other enteric bacteria. 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. In one series looking at 20 cases, 70% had CD4 lymphocyte cells > 200/µL. In a large series investigating colorectal biopsies in Japan, there was a slightly higher incidence of intestinal spirochetosis in patient with HIV. 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 vermiiform appendix. 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. The proposed pathogenic mechanism for diarrhea associated with this disease is micrivialis destruction caused by spirochetal attachment. Furthermore, when a significant population of enterocytes become attached it may lead to a physical restriction of electrolyte and water resorption adding to diarrhea.

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.

ACKNOWLEDGEMENTS

Full informed consent was obtained from the patient for the publication of his information and imaging.

We thank Dr. John Bonino in the Division of Gastroenterology, Department of Internal Medicine at the University of Kansas Medical Center for his aid in the clinical care of this patient. We also would like to extend thanks to Dr. Stephanie Wood in the Department of Pathology at the University of Kansas Medical Center for her assistance in the preparation and interpretation of the biopsy specimen.

REFERENCES

1. Harland WA, Lee FD, Krasewski A, Gordon J, McSevney D. Intestinal spirochaetosis. Gut 1971; 12(2):126-133. PMID: 5548558.
2. Tsinganou E, Gebbers JO. Human intestinal spirochetoisis - A review. Ger Med Sci 2010; 8(Doc1). PMID: 20200654.
3. Körner M, Gebbers JO. Clinical significance of human intestinal spirochetosis - A morphologic approach. Infection 2003; 31(5):341-349. PMID: 14556061.
4. Koteish A, Kannangai R, Abraham SC, Torbenson M. Colonic spirochetosis in children and adults. Am J Clin Pathol 2003; 120(6):828-832. PMID: 1467970.
5. Lee JJ, Hampson DJ. Genetic characterisation of intestinal spirochaetes and their association with disease. J Med Microbiol 1994; 40(5):365-371. PMID: 8176724.
6. Mikosza AS, La T, de Boer WB, Hampson DJ. Comparative prevalences of *Brachyspira aalborgi* and *Brachyspira* (Serpulina) pilosicoli as etiologic agents of histologically identified intestinal spirochetosis in Australia. J Clin Microbiol 2001; 39(1):347-350. PMID: 1136797.
7. Brooke CJ, Riley TV, Hampson DJ. Evaluation of selective media for the isolation of *Brachyspira aalborgi* from human faeces. J Med Microbiol 2003; 52(7):599-513. PMID: 12748271.
8. Hampson DJ, The spirochete *Brachyspira pilosicoli*, enteric pathogen of animals and humans. Clin Microbiol Rev 2017; 31(1):e00087-17. PMID: 29187397.
9. Gebbers JO, Mader HP. Human intestinal spirochetoisis: Unusual findings. Microecol Therap 1989; 18:214-252.
10. Brooke CJ, Hampson DJ, Riley TV. In vitro antimicrobial susceptibility of *Brachyspira pilosicoli* isolates from humans. Antimicrob Agents Chemother 2003; 47(7):2354-2357. PMID: 12821498.
11. Pehgni PL, Gunceron JG, Sharma A. Improvement of chronic diarrhea after treatment for intestinal spirochetoisis. Dig Dis Sci 2000; 45(10):1006-1010. PMID: 10795768.
12. Surawicz CM, Roberts PL, Rompalo A, Quin TN, Holmes KK, Stamm WE. Intestinal spirochetosis in homosexual men. Am J Med 1987; 82(3 Spec No):587-592. PMID: 3826122.
13. Erikson LA, Torgersen MS. Intestinal spirochetoisis. Mayo Clin Proc 2020; 95(2):427-428. PMID: 32029097.
14. García-Hernandez D, Valls-Mayans M, Coll-Estrada S, et al. Human intestinal spirochetosis, a sexually transmissible infection? Review of six cases from two sexually transmitted infection centres in Barcelona. Int J STD AIDS 2021; 32(1):52-58. PMID: 33223216.
15. Ena J, Simón-Aylón A, Pasquau F. Intestinal spirochetosis as a cause of chronic diarrhea in patients with HIV infection: Case report and review of the literature. Int J STD AIDS 2009; 20(11):803-805. PMID: 19843615.
16. Tateishi Y, Takahashi M, Horiguchi S, et al. Clinicopathologic study of intestinal spirochetosis in Japan with special reference to human immunodeficiency virus infection status and species types. Analysis of 526 consecutive colorectal biopsies. BMC Infect Dis 2015; 15:13. PMID: 25382884.
17. Rodgers FG, Rodgers C, Shetton AP, Hawkey CJ. Proposed pathogenic mechanism for the diarrhea associated with human intestinal spirochetes. Am J Clin Pathol 1986; 86(5):679-682. PMID: 3776923.

Keywords: infectious disease, gastroenterology, microbiology, brush border, spirochete infection