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CASE REPORT | COLON

Colonizing the Unlikely: *Brachyspira* in an Immunocompetent Patient

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ABSTRACT

Chronic diarrhea is a common condition that medical professionals often encounter. We present an unusual case of chronic diarrhea in a relatively young, immunocompetent man that was attributed to *Brachyspira*. The patient's clinical presentation was not specific, and he underwent workup for common infectious, inflammatory, and autoimmune causes, all unrevealing. During colonoscopy, no abnormalities were detected; however, histopathology revealed the presence of *Brachyspira*. Following a course of metronidazole, the patient showed marked improvement in his diarrhea. It is worth noting that the patient's social history did not align with the established risk factors mentioned in the existing literature.

INTRODUCTION

Chronic diarrhea is a frequently encountered concern in gastroenterology clinics, with infectious causes often at the forefront of diagnostic considerations. *Brachyspira*-induced diarrhea is an underrecognized entity. In this report, we raise awareness about *Brachyspira* as a rare but notable cause of chronic diarrhea, even in immunocompetent patients, emphasizing the importance of considering uncommon pathogens in diagnosing persistent gastrointestinal symptoms.

CASE DESCRIPTION

A 42-year-old man with a medical history of giardiasis presented to gastroenterology clinic due to persistent diarrhea. He reported a decade of watery bowel movements twice daily, with no blood, mucus, or nocturnal episodes. His symptoms did not appear to be diet-related, and he was not taking any medications. Notably, his travel history included trips to Costa Rica, Puerto Rico, and the Bahamas within the past 3 years. He denied experiencing weight loss, decreased appetite, abdominal pain, fevers, chills, joint symptoms, or skin changes. There was no known family history of cancers or gastrointestinal disorders.

Despite a comprehensive infectious workup, which included examinations for ova and parasites, stool culture, *Helicobacter pylori* stool antigen testing, and stool-based Cryptosporidium and Giardia direct fluorescent antibodies, all these tests returned negative. Fecal calprotectin was elevated at 623 μg per grams (μg/g). In addition, serum testing for celiac disease using tissue transglutaminase immunoglobulin A antibodies and total immunoglobulin A level were negative. Owing to his persistent decade-long diarrhea, a colonoscopy was deemed necessary for further evaluation. The procedure revealed normal-appearing colonic lumen, with random biopsies taken throughout the colon using a cold forceps to rule out microscopic colitis. Pathology results from the descending colon and rectum indicated the presence of spirochetes, specifically *Brachyspira*, as confirmed by a positive Warthin-Starry stain (Figures 1, 2, and 3).

Upon further inquiry into the patient's social history, it was discovered that he engaged in high-risk sexual activities with both men and women. Subsequent workup for sexually transmitted infections was initiated, including testing for HIV, syphilis, gonorrhea, and

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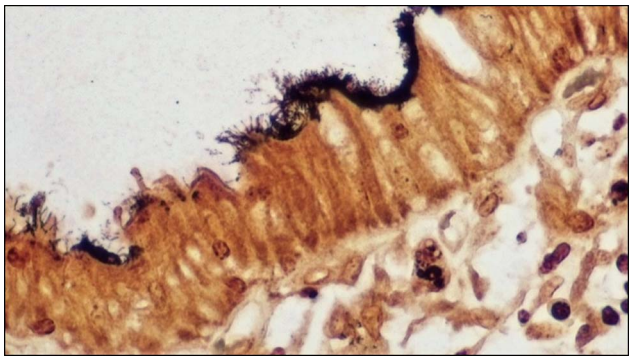

Figure 1. Warthin-Starry special stain, when viewed at 400× magnification, highlights the spirochetes in black.

chlamydia, all of which yielded negative results. As a result, the patient was referred to an infectious disease clinic, where the team recommended a course of treatment using oral metronidazole at a dosage of 500 mg every 6 hours for 10 days. Following the successful completion of this therapy, the patient reported a marked improvement in his chronic diarrhea.

DISCUSSION

Brachyspira, a genus of flagellated anaerobic spirochetes discovered in 1980, resides in the large intestines of various animals, including primates, dogs, pigs, birds, and humans.[1,2] The term *Brachyspira* originates from the Greek term "*Brachy*," meaning short, mirroring its size range of 2–13 μm.[3,4] *Brachyspira hyodysenteriae* is clinically significant for its role in swine dysentery while 2 other *Brachyspira* species, *Brachyspira pilosicoli*, and *Brachyspira aalborgi*, have been linked to human intestinal spirochetosis.[5,6] Notably, *B. pilosicoli* is associated with diverse conditions in different species, including porcine colonic spirochetosis, avian intestinal spirochetosis, and chronic diarrhea in dogs, highlighting the genus's importance in veterinary and human pathology.[5,7]

Intestinal spirochetosis occurs when numerous *Brachyspira* attach to colonocytes, forming a false brush border.[5] Colonocytes within both the small and large intestines are essential for

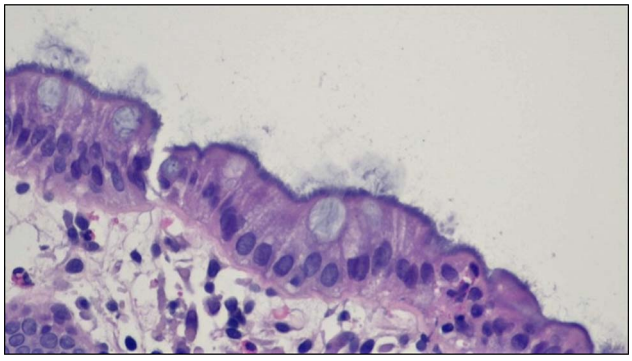

Figure 2. At a magnification of 400×, a hematoxylin and eosin-stained section reveals a basophilic fringe, which is formed by the organisms carpeting the luminal surface.

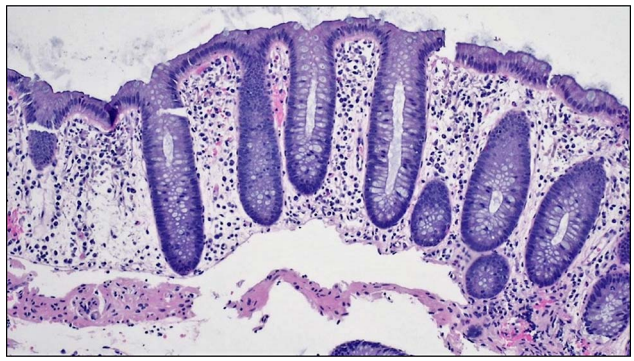

Figure 3. At 100× magnification, a hematoxylin and eosin-stained section displays a subtle, fuzzy appearance of the colonic epithelium surface, with no significant signs of active or chronic inflammation.

maintaining homeostasis, facilitating water and electrolyte absorption and safeguarding against pathogenic bacteria.[8] The severity of symptoms directly correlates with the extent of spirochete invasion, leading to cellular damage and structural alterations in the intestinal epithelium. Diarrhea results from the reduced absorption capacity of the impaired epithelium.[9] Studies have indicated that *Brachyspira* involvement leads to cell membrane destruction, glycocalyx defects, and mitochondrial swelling, involving intracellular and macrophage phagolysosomes.[5] Furthermore, reactive intraepithelial mast cells and immunoglobulin E plasma cells may play a role in the condition's pathogenesis.[10] The variations in human intestinal spirochetosis pathogenesis among different *Brachyspira* species remain unexplored, primarily due to a lack of species identification in many case reports.[2]

Brachyspira colonization is predominantly observed in developing countries and among immunocompromised individuals, like those with HIV or underlying malignancies.[11] In some cases, it is incidentally discovered during colonoscopies performed for unrelated reasons in immunocompetent patients.[2,12] Transmission of *Brachyspira* has been observed to occur through the fecal-oral route, along with zoonotic transmission by contact with infected animals, their feces, or contaminated water.[12,13] Given *Brachyspira*'s association with gonococcal and *Shigella flexneri* coinfections, sexual transmission is another potential mode of transmission.[14] In symptomatic adults, the infection can manifest as watery diarrhea, abdominal pain, weight loss, and bloody stools.[2] In children, the symptoms may mimic inflammatory bowel disease and include persistent diarrhea, rectal bleeding, abdominal pain, weight loss, decreased appetite, and failure to thrive.[15]

Regarding diagnostic modalities, culturing *Brachyspira* is uncommon due to limited selective media capable of controlling anaerobic bacterial overgrowth.[2,11] *Brachyspira* species grown on blood agar at 37°C exhibit varying degrees of hemolysis, ranging from strong to weak beta.[16] The incubation period is typically 3–5 days, but *B. aalborgi* may require up to 2 weeks. In some cases, *Brachyspira* species can be detected in blood

cultures after a 10-day incubation period, especially in spirochetemia.[5,16] These spirochetes can be visualized under phase-contrast or dark field microscopy as slender, comma-shaped, or spiraled organisms.[5] Nowadays, a definitive diagnosis of intestinal spirochetosis relies on colonic biopsies, which reveal the organism's presence through the Warthin-Starry silver nitrate stain.[2] Although not yet universally available, diagnosis can also be achieved by conducting polymerase chain reaction on deoxyribonucleic acid extracted from stool samples, using species-specific probes.[11]

Intestinal spirochetosis is treated with systemic antibiotics. *B. pilosicoli* isolates are susceptible to tetracycline, metronidazole, ceftriaxone, meropenem, and chloramphenicol, as determined by susceptibility testing.[17] Treatment typically consists of oral metronidazole, with adults taking 500 mg 3 times daily for 10 days.[13,15]

We present a unique case of symptomatic intestinal spirochetosis in an immunocompetent patient, defying the established risk factors documented in the literature. Traditional risk factors of this condition include immunosuppression, disruptions in gut flora as seen in inflammatory bowel disease (IBD), frequent antibiotic use, poor hygiene practices, or close contact with infected animals.[1,5,13] However, the patient's history of high-risk sexual behavior with same-sex partners, in the absence of a known immunocompromised state, warrants further investigation as a potential risk factor for *Brachyspira* colonization. Moreover, his decade-long history of diarrhea suggests a possible role of chronic *Brachyspira* infection in the development of intestinal disorders. Recent metaproteomic research has indicated that *Brachyspira* colonization is notably more prevalent in individuals with irritable bowel syndrome with diarrhea.[10,18] Given the appropriate clinical context, colonic spirochetosis should be considered in the differential diagnosis for chronic diarrhea.

DISCLOSURES

Author contributions: J. Tidwell designed the work, drafted the work, gave final approval, and is the article guarantor; J. Fusco and M. Nguyen drafted the work, and gave final approval; GH Nam provided and interpreted pathology slides; S. Goldenberg made critical revisions and gave final approval.

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REFERENCES

1. Tsinganou E, Gebbers JO. Human intestinal spirochetosis--a review. *Ger Med Sci.* 2010;8:Doc01.
2. Norris SJ. Hiding in plain sight: Colonic spirochetosis in humans. *J Bacteriol.* 2019;201(21):e00465–19.
3. Schmidt T. Spirochetes. In: *Encyclopedia of Microbiology 4E.* Cambridge, Massachusetts Academic Press, 2019, pp 283–98.
4. 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 5265 consecutive colorectal biopsies. *BMC Infect Dis.* 2015;15:13.
5. Hampson DJ. The spirochete Brachyspira pilosicoli, enteric pathogen of animals and humans. *Clin Microbiol Rev.* 2018;31(1):e00087–17.
6. Gelberg H. Alimentary system and the peritoneum, omentum, mesentery, and peritoneal cavity. In: *Pathologic Basis of Veterinary Disease 6E.* St. Louis, Missouri Mosby, 2017, pp 324–411.
7. Sykes JE. Miscellaneous enteric bacterial infections. In: *Infectious Diseases of the Dog and Cat 5E.* Philadelphia, Pennsylvania W.B. Saunders, 2021, pp 797–801.
8. Blachier F, de Sá Resende A, da Silva Fogaça Leite G, Vasques da Costa A, Lancha Junior AH. Colon epithelial cells luminal environment and physiopathological consequences: Impact of nutrition and exercise. *Nutrire.* 2018;43(1):2.
9. Smith J, Johnson A. Understanding Brachyspira infections: A comprehensive review. *J Infect Dis.* 2020;25(4):123–35.
10. Jabbar KS, Dolan B, Eklund L, et al. Association between Brachyspira and irritable bowel syndrome with diarrhoea. *Gut.* 2021;70(6):1117–29.
11. Westerman LJ, de Boer RF, Roelfsema JH, et al. Brachyspira species and gastroenteritis in humans. *J Clin Microbiol.* 2013;51(7):2411–3.
12. Alsaigh N, Fogt F. Intestinal spirochetosis: Clinicopathological features with review of the literature. *Colorectal Dis.* 2002;4(2):97–100.
13. Guzman Rojas P, Catania J, Parikh J, Phung TC, Speth G. Intestinal spirochetosis in an immunocompetent patient. *Cureus.* 2018;10(3):e2328.
14. Garcia-Hernandez D, Vall-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):52–8.
15. Helbling R, Osterheld MC, Vaudaux B, Jaton K, Nydegger A. Intestinal spirochetosis mimicking inflammatory bowel disease in children. *BMC Pediatr.* 2012;12:163.
16. Mirajkar NS, Phillips ND, La T, Hampson DJ, Gebhart CJ. Characterization and recognition of Brachyspira hampsonii sp. nov., a novel intestinal spirochete that is pathogenic to pigs. *J Clin Microbiol.* 2016;54(12):2942–9.
17. Brooke CJ, Hampson DJ, Riley TV. In vitro antimicrobial susceptibility of Brachyspira pilosicoli isolates from humans. *Antimicrob Agents Chemother.* 2003;47(7):2354–7.
18. Fan K, Eslick GD, Nair PM, et al. Human intestinal spirochetosis, irritable bowel syndrome, and colonic polyps: A systematic review and meta-analysis. *J Gastroenterol Hepatol.* 2022;37(7):1222–34.