CLINICAL CASE

CHRONIC DIARRHEA AND INTESTINAL SPIROCHETOSIS: A CASE HIGHLIGHTING THE IMPORTANCE OF HISTOLOGICAL DIAGNOSIS. A CASE REPORT.

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Abstract

Human intestinal spirochetosis is an uncommon cause of chronic diarrhea caused by colonic colonization by *Brachyspira* species. We report the case of a 56-year-old man with chronic watery diarrhea, weight loss, and occasional fecal incontinence. Laboratory tests and colonoscopy were unremarkable. Colonic biopsies and immunohistochemical analysis confirmed intestinal spirochetosis. Treatment with metronidazole led to complete symptom resolution. This case highlights the importance of considering intestinal spirochetosis in the differential diagnosis of chronic diarrhea, even in patients without risk factors or endoscopic abnormalities.

Keywords: Intestinal spirochetosis, chronic diarrhea, *Brachyspira*, immunohistochemistry, colonoscopy.

Introduction

Chronic diarrhea, defined as the emission of loose stools for more than four weeks, is one of the most common reasons for referral to gastroenterology clinics and poses a diagnostic challenge due to the wide variety of potential etiologies, including inflammatory, infectious, functional, malabsorptive, endocrine, and neoplastic causes. Clinical guidelines recommend a systematic approach based on the medical history, physical examination, and targeted laboratory and microbiological tests, with the goal of distinguishing between organic and functional causes and determining the need for further diagnostic tests[1,3].

Despite advances in diagnostic techniques, a proportion of patients continue to present with an inconclusive initial

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Royo Esteban A, Alarcón García L, Polo Cuadro C, Yagüe Caballero C, Casas Deza D, Pascual Oliver A. Chronic diarrhea and intestinal spirochetosis: a case highlighting the importance of histological diagnosis. A case report. RAPD 2026;49(5):170-173. DOI: 10.37352/2026495.3

evaluation, especially when endoscopic findings are macroscopically normal. In this context, it is necessary to consider less common conditions within the differential diagnosis. Among these, human intestinal spirochetosis is a rare and likely underdiagnosed cause of chronic watery diarrhea, the diagnosis of which typically depends on histopathological examination due to the absence of specific endoscopic findings[2,4].

Intestinal spirochetosis is defined by the colonization of the colonic mucosa by anaerobic spirochetes of the genus Brachyspira, primarily Brachyspira aalborgi and Brachyspira pilosicoli[5]. Although it is a well-recognized disease in veterinary medicine, especially in poultry and swine, its clinical significance in humans remains a subject of debate. It was first described in 1967 by Harland and Lee, and to date, only a few cases have been reported in the literature. In the largest series published to date in our setting, the prevalence of ID was estimated at 0.7% (8/1,174) among patients with chronic watery diarrhea[10]. Transmission appears to occur primarily via the fecal-oral route, although the exact mechanism of transmission is unknown[2].

The reported prevalence varies depending on the population studied and the geographic area, being higher in developing countries and among certain at-risk groups, particularly people with human immunodeficiency virus (HIV) infection and men who have sex with men (MSM). However, cases have also been reported in immunocompetent individuals with no apparent epidemiological risk factors, which makes clinical suspicion even more difficult[6-8].

From a clinical standpoint, intestinal spirochetosis may be asymptomatic or present with nonspecific symptoms such as chronic watery diarrhea, abdominal pain, bloating, or weight loss[9]. Endoscopically, the mucosa is usually normal; therefore, the diagnosis depends largely on histological examination, in which a filamentous basophilic band adherent to the colonic epithelium ("*false brush border*") is classically observed and confirmed by special stains or immunohistochemistry[8].

We present the case of an immunocompetent patient with long-standing chronic watery diarrhea and a macroscopically normal colonoscopy, whose definitive diagnosis of intestinal spirochetosis was established through histopathological examination.

Clinical case

We present the case of a 56-year-old man with no significant medical or surgical history who was referred to the Gastroenterology department for chronic diarrhea that had persisted for more than one year. He presented with predominantly watery, liquid stools—occasionally explosive—accompanied by episodes of fecal incontinence and intermittent abdominal pain unrelated to bowel movements. He also reported a weight loss of approximately 6 kg since the onset of symptoms, with no fever or emissions of pathological material.

Regarding epidemiological history, the patient reported that his wife had had a *Clostridioides difficile* infection more than one year before the onset of his symptoms. He denied recent travel, consumption of non-potable water, risky sexual practices, relevant epidemiological exposure, or use of toxic substances, supplements, or medications. The physical examination was entirely normal, with no abnormal abdominal findings.

A complete laboratory workup was performed, including a complete blood count, biochemical panel, C-reactive protein, thyroid panel, and serology tests, all of which were normal. Celiac disease was ruled out based on normal IgA levels and negative antitransglutaminase antibodies.

The microbiological stool analysis revealed a positive PCR result for *Blastocystis hominis*, this finding was considered of uncertain significance given the debated pathogenicity of the organism and the patient's clinical persistence.

Given the persistence of symptoms and the absence of conclusive findings, a colonoscopy was performed with serial biopsies to rule out microscopic colitis. During the examination, the colonic mucosa appeared macroscopically normal, with no inflammatory lesions, ulcerations, or vascular abnormalities. Histological examination of the colonic biopsies revealed the presence of a basophilic filamentous band adherent to the surface epithelium, consistent with intestinal spirochetosis, which was subsequently confirmed by a positive immunohistochemical test for spirochetes (Figure 1).

Following the diagnosis, treatment was initiated with metronidazole 500 mg every 8 hours for 10 days, resulting in complete resolution of the diarrhea and disappearance of the gastrointestinal symptoms upon completion of treatment.

Discussion

Human intestinal spirochetosis is a rare condition and is likely underdiagnosed, especially in immunocompetent patients without classic risk factors. Although it has traditionally been associated with HIV infection and MSM, there are an

DOI: 10.37352/2026495.3

increasing number of case reports in the general population, suggesting that its actual prevalence may be underestimated[6-8].

The true pathogenic significance of intestinal spirochetosis remains controversial, as in some individuals it may present as an incidental finding. However, various studies have demonstrated an association between colonization by *Brachyspira spp.* and chronic gastrointestinal symptoms—particularly watery diarrhea, abdominal pain, and weight loss—with clinical improvement following antibiotic treatment, as was the case in our patient[9,10].

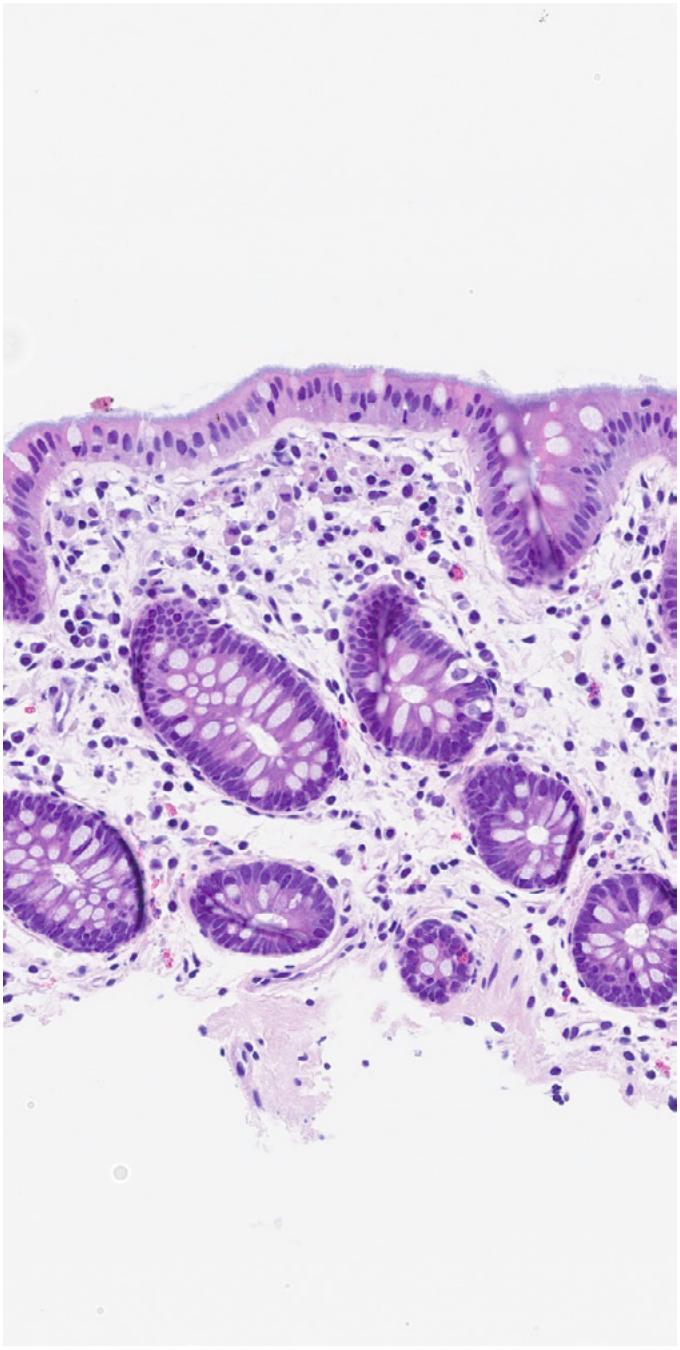


Figure 1. ***Large intestine mucosa showing a bluish, feathery band on the surface of the epithelium (H&E).***

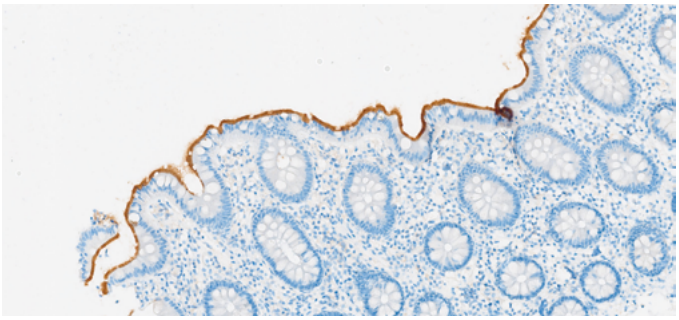


Figure 2. ***Immunohistochemical staining for spirochetes showing positive expression on the colonic surface (spirochete IHC).***

One of the most clinically significant aspects is the difficulty in diagnosis. Most patients have normal endoscopic findings; therefore, the diagnosis depends primarily on histopathological examination[8]. The characteristic lesion consists of a basophilic pseudo-brushed band on the colonic epithelium, corresponding to the adhesion of spirochetes to the mucosal surface. Confirmation can be achieved using special stains such as Warthin-Starry or through immunohistochemical and molecular techniques[4].

In our case, the diagnosis was reached after ruling out the most common causes of chronic diarrhea and thanks to the systematic collection of biopsies despite the macroscopically normal appearance of the mucosa, which highlights the importance of maintaining a broad, multidisciplinary diagnostic approach.

Another point of interest is the concomitant detection of Blastocystis hominis in stool. Although this protozoan has been linked to gastrointestinal symptoms in certain studies, its pathogenic role remains controversial, and current guidelines do not consider a causal relationship to be proven in all immunocompetent patients; therefore, its detection must be interpreted within the context of the individual clinical presentation[3,10,11].

Clinical resolution following metronidazole administration is consistent with a possible etiological role for intestinal spirochetosis; however, this association should be interpreted with caution. The available evidence remains insufficient to establish an unequivocal causal relationship between colonization by *Brachyspira spp.* and gastrointestinal symptoms, as most published studies are retrospective or consist of case series. A recent meta-analysis confirmed the association between intestinal spirochetosis and gastrointestinal symptoms, although it highlighted the low quality of the evidence and the inability to establish causality[13].Furthermore, metronidazole is active against various anaerobic microorganisms and protozoa and is also one of the therapeutic options for patients with small intestinal

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bacterial overgrowth (SIBO); therefore, it cannot be ruled out that the clinical improvement was influenced, at least in part, by mechanisms other than the treatment of *Brachyspira spp.* colonization[12].

Furthermore, the lack of specific tests to rule out SIBO constitutes a limitation of our case. Similarly, it cannot be completely ruled out that the response to metronidazole reflected the simultaneous treatment of another condition sensitive to this antibiotic. However, the pathologic demonstration of intestinal spirochetosis, the exclusion of the most common causes of chronic diarrhea, and the complete resolution of symptoms following treatment support the notion that this condition may have played a clinically relevant role in the presentation of the case. In any case, given the observational nature of this isolated clinical case and the currently available evidence, it is not possible to establish a definitive causal relationship between the pathologic finding and clinical improvement[4,10,13,14].

Metronidazole remains the most frequently used antibiotic in published symptomatic cases, although the available evidence comes primarily from retrospective series and case reports, with no randomized clinical trials or specific guidelines defining the therapeutic indication. Consequently, the decision to initiate treatment must be individualized based on symptoms, the clinical context, and the reasonable exclusion of other causes of chronic diarrhea[4,13,14].

This case illustrates the need to consider intestinal spirochetosis as part of the differential diagnosis of chronic watery diarrhea, even in the absence of classic risk factors or endoscopic findings, and highlights the fundamental role of histopathological examination in the diagnosis of rare conditions. It also highlights the importance of critically interpreting the response to antibiotic treatment, avoiding unequivocally attributing clinical improvement to the histopathological finding in the absence of studies that establish a causal relationship.

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DOI: 10.37352/2026495.3