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Case Report

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Spirochetosis Mimicking Acute Appendicitis: Clinical Report and Review of the Literature

Magdalena Lüthy[a] Samuel A. Käser[a] Carolin Wagener[b] René Fahrner[a, c]

[a]Department of Surgery, Bürgerspital Solothurn, Solothurn, Switzerland; [b]Institute of Pathology, Pathology Länggasse, Bern, Switzerland; [c]Department of Surgery, Spital Thun, Thun, Switzerland

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Abstract
Introduction: Intestinal spirochetosis is sometimes found by chance in histological specimen of routine endoscopies. There are only a few cases described in the literature that spirochetosis of the appendix was mimicking acute appendicitis. We present a case of pseudoappendicitis with the histological finding of spirochetes and review the current literature. ***Case Presentation:*** A 72-year-old woman presented with pain of the lower right abdomen and previous systemic corticoid therapy. In clinical examination, there was a tenderness and pain in the right lower quadrant, and inflammation values were elevated. An abdominal computed tomography scan revealed no obvious inflammation of the appendix. A diagnostic laparoscopy was performed and revealed a macroscopically uninflamed appendix which was removed. Histology revealed spirochetosis of the appendix but no typical signs of appendicitis. The patient was treated with antibiotics for 5 days and was discharged without abdominal pain. In a clinical control 6 weeks later, the abdominal pain had disappeared and the patient was in good clinical condition. ***Discussion:*** Intestinal spirochetosis is randomly found in histological specimen during routine endoscopies, even in asymptomatic patients. There are only a few cases described with spirochetosis of the appendix causing pain and mimicking appendicitis; hence, this entity is an important differential diagnosis of pain in the right lower quadrant of the abdomen.

Introduction

Spirochetes are Gram-negative bacteria that have the ability to move actively. There are several diseases caused by this bacteria family such as syphilis caused by *Treponema pallidum* or Lyme's disease caused by *Borrelia burgdorferi* which are both members of the spirochete family.

Intestinal spirochetosis is a rather uncommon finding in humans, mostly detected by chance in histological specimen during endoscopy. For many decades, it is known that spirochetes are located in the gut. In 1967, Harland and Lee [1] presented 10 cases with intestinal symptoms such as pain, diarrhea or obstipation and detection of spirochetes, so that a potential pathogenicity of these bacteria was discussed. As in many cases no tissue inflammation was observed, it remains unclear whether the detection of spirochetes is pathognomonic for a disease and symptoms or just an incidental finding [2].

karger@karger.com
www.karger.com/iid

Correspondence to:
Samuel A. Käser, samuel.kaeser@spital.so.ch

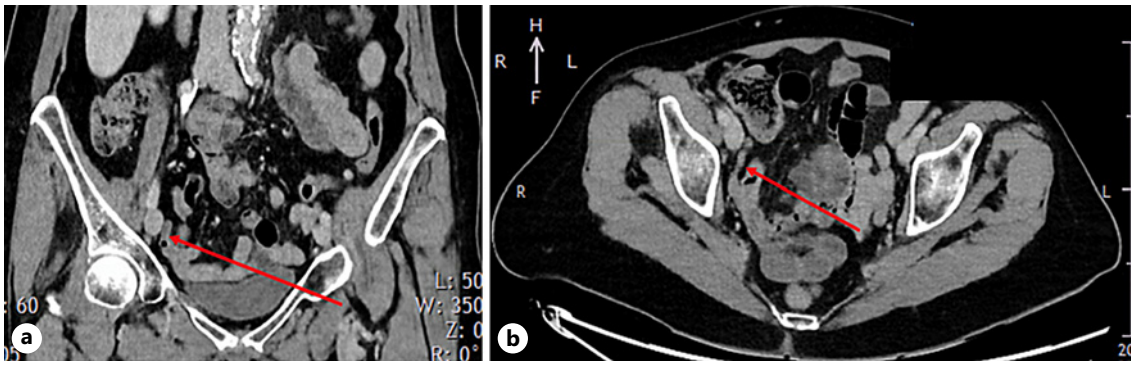

Fig. 1. Computed tomography [coronal section (**a**), axial section (**b**)] of the abdomen showing an uninflamed appendix vermiformis (red arrow).

Histologically, a basophilic band of organisms is located at the luminal surface of the epithelium, which is approximately 3 μm thick. It resembles a fuzzy fringe-like line, and the organisms stain strongly with a Warthin-Starry stain as well as with an Alcian blue and PAS stain. An immunohistochemical stain is also available. Usually, there is no invasion of the underlying tissue and no associated inflammatory response.

There are several studies showing a coincidence between immunodeficiency and intestinal spirochetosis. These patients mostly suffered from symptoms such as colitis or hepatitis, and after an antibiotic therapy with metronidazole, the patients often reported an improvement in symptoms [3, 4].

Pseudoappendicitis is described as any condition mimicking acute appendicitis with acute right lower abdominal pain and tenderness. It is often caused by chronic intestinal diseases affecting the terminal ileum, such as Crohn's disease. Another typical cause is an infection with *Campylobacter species* or *Yersinia species*, which in most cases is asymptomatic but can also mimic clinical signs of appendicitis [5]. In the current literature, there are only few case reports for pseudoappendicitis and identifying intestinal spirochetosis as potential source of symptoms.

Gan et al. [6] presented a case of a 24-year-old man with suspected appendicitis, with clinically and histologically no sign of inflammation; however, the appendix was colonized by spirochetes, which was postulated to be responsible for the abdominal pain and signs of appendicitis. Henrik-Nielsen et al. [7] found 13 cases in a series of 681 surgically removed appendices with spirochetes in otherwise histologically normal appendices (pseudoappendicitis). Westerman et al. [8] analyzed 142 appendices removed from children. They found five positive specimens for spirochetes in patients with and without acute appendicitis.

Case Presentation

A 72-year-old woman presented to the emergency department with right-sided pain in the lower abdomen and local signs of peritonitis. The pain was described as constant, stabbing, and had worsened during the previous days. She reported a cutaneous exanthema and a systemic corticoid therapy for 2 weeks which she had ceased 3 days before the admission. Blood analysis revealed elevated CRP of 184 mg/L and mild leukocytosis of 10 G/L. Prior to admission, the patient had never undergone a coloscopy.

Due to the reported symptoms and right-sided abdominal pain, with elevated inflammatory markers in the blood, there was suspicion of potential acute appendicitis, so that a computed tomography of the abdomen was performed (shown in Fig. 1). Unfortunately, the radiological findings were not conclusive and showed no distinct signs of inflammation of the gastrointestinal tract or appendix. The patient was therefore submitted to the surgical ward for clinical controls, and an antibiotic therapy with ceftriaxone and metronidazole was started. The following day, there was no improvement regarding her pain and symptoms, so that as further invasive diagnostics, an exploratory laparoscopy was performed.

During surgery, there was no intra-abdominal fluid, and the appendix was macroscopically without signs of inflammation. The only abnormal finding was a limited area of thickened retroperitoneal peritoneum, so that a biopsy was taken. Based on our departmental policy that even macroscopically normal appearing appendices should be removed to rule out histological pathology (e.g., neurogenic appendicopathy, small tumors), an appendectomy was performed.

During the postoperative course, the elevated CRP levels significantly reduced under antibiotic therapy, and the abdominal pain disappeared completely. The patient was discharged on day five after the laparoscopy.

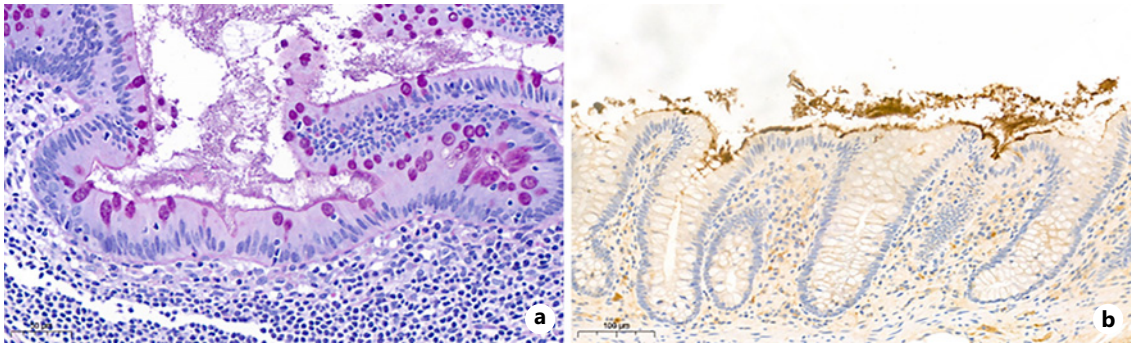

Fig. 2. Histologically, intestinal spirochetosis is characterized by a basophilic superficial band at the luminal epithelial surface of the appendiceal or colonic mucosa and can be highlighted with a PAS stain (**a**) and even immunohistochemically (**b**).

Histology was performed and ruled out an acute inflammation of the appendix, but there was coincidentally evidence of intestinal spirochetosis (shown in Fig. 2), which were irregularly distributed in the mucosa. The biopsy of the peritoneum showed no inflammation or malignancy.

After 6 weeks, the patient was seen in an outpatient setting and was in good clinical condition without abdominal pain. The skin efflorescences were still bothering her, and corticoid therapy was still administered. The advice to undergo a coloscopy was still refused, so that an affection of the entire colon with spirochetes could not be ruled out so far.

Discussion and Conclusion

We report a case of a female patient with acute abdominal pain, systemic inflammation, and systemic corticoid therapy because of an unresolved erythema of the skin. A diagnostic laparoscopy with appendectomy was performed, showing no acute inflammation of the appendix, except for proof of intestinal spirochetosis. A literature search in PubMed (search terms: "spirochetosis" and "appendicitis") for articles published in the last 50 years revealed seven reports dealing with intestinal spirochetosis affecting the appendix (shown in Table 1).

Potential risk factors of intestinal spirochetosis are poorly developed regions with low living standards, critical illness, homosexuality, and HIV infections. In HIV-positive patients as well as in immunocompromised patients and children, the likelihood to develop symptoms seems to be much higher than in every other group [13]. Although poorly developed regions are a potential risk factor for intestinal spirochetosis, there are several reports from developed countries (see Table 1). Another important issue is the fact that the pathogenicity of intestinal spirochetosis is still not completely understood. In addition to patients with unspecific clinical symptoms, there are asymptomatic carriers diagnosed during routine endoscopy. Until now, the diagnostic methods are suboptimal, and the prevalence of intestinal spirochetosis is underestimated. A recently published review and meta-analysis investigated the association of spirochetosis in patients with irritable bowel syndrome and colonic polyps [14]. The authors concluded that spirochetosis was associated with the diagnosis of irritable bowel syndrome and diarrhea but not with colonic polyps [14]. These results underline the fact that the clinical significance of intestinal spirochetosis still needs further investigation.

In our case, the systemic corticoid therapy may have influenced the development of intestinal spirochetosis. It has been reported that there is an association between immunodeficiency (side effect of immunocompromised therapy or acquired) and intestinal spirochetosis [3, 4].

A conservative treatment with antibiotics, e.g., metronidazole, has been shown to be effective, and most patients were relieved from their symptoms [13]. Furthermore, there are several reports of asymptomatic patients and coincidental detection of intestinal spirochetosis by colonoscopic biopsies [15].

After recapitulation of our patient's medical history, we found that she had a history of Lyme's disease 8 years before, which is caused by *B. burgdorferi*, a member of the spirochete family. Initially, she received antibiotic treatment after presenting characteristics of an erythema migrans, and 2 years later, neuroborreliosis was diagnosed. After intravenous antibiotic treatment for 3 weeks, the clinical signs of *Borrelia* infection disappeared. The detection of intestinal spirochetosis and the patient's history led to further assessments for *T. pallidum*, the pathogenic germ for

Table 1. Literature search (PubMed): studies presenting intestinal spirochetosis in the vermiform appendix

Authors	Year	Cases, *n*	Key findings
Gan et al. [6]	2017	1	Case report. Clinical diagnosis, macroscopically pseudoappendicitis, patient on prednisolone for asthma
Westerman et al. [8]	2013	5	Systematic retrospective histological analysis of children with acute appendicitis and pseudoappendicitis (n = 142)
Haleem et al. [9]	2003	2	Systematic retrospective histological analysis of patients with appendectomy (n = 598), spirochetosis found in histologically normal appendices
Yang and Lapham [10]	1997	4	Adults and children, suspected appendicitis, and occasional appendectomy (n = 109)
White et al. [11]	1994	1	Case report of a child with symptoms of acute appendicitis
Henrik-Nielsen et al. [7]	1985	18	Systematic retrospective histological analysis of patients with appendectomy (n = 681). Spirochetes mostly found in pseudoappendicitis
Lee et al. [12]	1971	62	Systematic retrospective histological analysis (n = 790). Spirochetes mostly found in patients with acute appendicitis

Lues, which could have explained the cutaneous efflorescences and the penetrating aortic ulcer, but all tests were negative for *T. pallidum*.

Comparable to our case, most described cases of intestinal spirochetosis and appendectomy were associated without histological detection of acute inflammation. Interestingly, reports of patients with immunodeficiency showed acute inflammation in the resected intestinal specimen [3]. Therefore, a potential conclusion may be that in healthy individuals, intestinal spirochetosis is associated without pathological alterations and perhaps no pathogenic effect. In patients with innate or acquired immunodeficiency, intestinal spirochetosis may cause infections and inflammation associated with clinical symptoms such as pseudoappendicitis, as reported in our patient.

In summary, it remains indistinct whether the clinical improvements were due to the removal of the appendix, antibiotic treatment, or a coincidence of the supportive treatment. As spirochetosis is even diagnosed in asymptomatic patients based on biopsy specimen during routine endoscopy and successful eradication of spirochetosis is not inevitable associated with symptom relief, the pathogenicity and source of symptoms of spirochetes are still debatable, and further investigations are needed.

Statement of Ethics

Approval of the Local Ethics Committee was waived due to local guidelines for case reports. Written informed consent to publish this case presentation including medial history and any accompanying images was obtained from the patient. Furthermore, this research was carried out in accordance with the National Institutes of Health guidelines and was conducted in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

All authors declare that they have no conflicts of interest.

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Author Contributions

Study conception and design: M.L., S.A.K., and R.F.; acquisition of data: M.L., C.W., and R.F.; analysis and interpretation of data: M.L., S.A.K., C.W., and R.F.; drafting of the manuscript: M.L. and R.F.; and critical revision of the manuscript: S.A.K. and C.W. All authors have read and approved the final version of this manuscript.

Data Availability Statement

Data are not publicly available due to ethical reasons. Further inquiries can be directed to the corresponding author.

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