

CASE REPORTS

IBD or strongyloidiasis?

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ABSTRACT

Introduction: Strongyloides has been shown to infrequently mimic inflammatory bowel disease (IBD) or to disseminate when a patient with IBD and unrecognized strongyloides is treated with immunosuppression.

Case report: A man from Ecuador, living in Spain for years, with a history of type 2 diabetes mellitus and psoriasis treated with topical corticosteroids, was admitted to the hospital with an 8-month history of diarrhoea. Blood tests showed hyperglycemia, hyponatremia, elevated CRP and faecal calprotectin. Colonoscopy suggested IBD. The patient improved with steroids, pending biopsy results, and he was discharged. Biopsies were compatible with IBD, but careful examination revealed strongyloides. He was given a prescription of albendazole. He had to be readmitted due to SIADH, which resolved with fluid restriction. Upon discharge albendazole was prescribed again. The patient skipped most of the out-patient-clinic visits. He returned a year later on 10 mg/week methotrexate, asymptomatic, with 20% eosinophilia, and admitting he had never taken the strongyloides treatment for economical reasons. He then received a week of oral albendazole at the hospital. Biopsies and blood cell count were afterwards normal (eosinophils 3.1%) and serology for strongyloides antibodies was negative.

Discussion: This case is of interest for four rarely concurring reasons. It's a worm infection that mimics IBD; the infection was diagnosed by colon biopsy; the infection caused a SIADH; and, most interestingly, even though the patient is on immunosuppression, he remains asymptomatic.

Key words: IBD. Strongyloides stercoralis. SIADH. Immunosuppression.

CASE REPORT

A 41-year-old man from Ecuador, living in Spain for twelve years, with a history of lactose intolerance, type 2 diabetes mellitus treated with oral antidiabetic medication, and psoriasis treated with topical corticosteroids for years, was admitted to the hospital with an 8-month history of diarrhea. He referred six to eight liquid stools per day, day

and night, without pathological products, except for an occasional episode of bleeding. Recently, he noticed associated epigastric pain, fever and chills, headache, weakness and anorexia. On physical examination, the patient was thin and moon-faced. He had psoriatic plaques on abdomen and limbs, an overall decrease in strength, and epigastric and right upper quadrant mild tenderness. He was hemodynamically stable; his temperature was 37 °C. Chest and abdominal X-rays showed no abnormalities and stool culture was negative.

Blood tests showed hyperglycemia 216 mg/dL, hyponatremia 121 mmol/L, increased acute phase reactants (CRP 80.9 mg/L), malnutrition parameters (urea 10 mg/dL, creatinine 0.38 mg/dL, uric acid 1.2 mg/dL, total cholesterol 106 mg/dL, albumin 2.8 g/dL), IgG 4623 mg/dL and fecal calprotectin of 116 mg/kg. The blood count showed no abnormalities. *Klebsiella pneumoniae* was isolated from the urine culture. The rest of the analysis (including renal function, autoantibodies, celiac disease antibodies, thyroid hormones and serology for hepatotropic virus, HIV and syphilis) and abdominal ultrasound were normal. The tuberculin skin test (Mantoux test) was also negative.

Empirical treatment was started with ciprofloxacin, metronidazole and nutritional support, awaiting colonoscopy. The colonoscopy revealed an edematous mucosa from the anal margin to the cecum, with areas of loss of vascular pattern and submucosal hemorrhage, alternating with non-affected areas. The transverse and descending colon were the most affected, presenting pseudopolyps and aphthae. The terminal ileum was normal. The endoscopic image was compatible with Crohn's disease colitis, as first option, or infectious colitis, as second.

Given the endoscopic suspicion of inflammatory bowel disease (IBD) in a patient with other autoimmune disorders and that he was already on wide-spectrum antibiotics, with minimal clinical recovery, 5-ASA and oral corticosteroids

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were added to the treatment. Insulin treatment was required for adequate glycemic control once steroids were begun. The patient showed significant clinical improvement, regaining appetite and normalizing bowel movements. He was discharged, pending pathology result.

Biopsy samples obtained during the colonoscopy showed intense transmural, linfoplasmocytic inflammation and pseudogranulomatous formations with criptitis, which were compatible with IBD, but careful examination revealed strongyloides (Figs. 1 and 2).

With a diagnosis of colitis secondary to strongyloides, which had mimicked IBD, we prescribed albendazole 400 mg every 12 hours (Ivermectine was not available) and switched prednisone to hydrocortisone 60 mg daily, the latter due to hyponatremia and suspected secondary adrenal insufficiency.

Days later, a sigmoidoscopy was performed to control the response to treatment. It showed more subtle lesions. During the examination, the patient presented an episode of dizziness and headache.

On examination, the patient was weak and had the rounded face and muscular atrophy previously mentioned as well as multiple psoriatic skin lesions. His blood pressure was 98/52 mmHg. Laboratory tests revealed hyponatremia with a lowest value of 118 mmol/L, hypokalemia (3 mmol/L) and hypochloremia (85 mmol/L). Protein-energy malnutrition and anemia due to iron-deficiency were also present.

He was readmitted to the hospital, this time in the Endocrinology Department. To establish the cause of isovolemic hypotonic hyponatremia (plasmatic osmolarity 237 mOsm/kg) thyroid hormones and cortisol levels were measured. TSH and T4L levels were normal and serum cortisol levels were decreased (8 mcg/dL) considering the patient was being treated with 60 mg id of oral hydroaltesone.

The available results of blood tests taken 5 months before admission revealed mild or moderate hyponatremia with normo- or hypokalemia.

Normal saline was infused and the patient was supplemented with oral sodium chloride, with no natremia improvement. The urine sodium level was 64 mmol/L and urine osmolarity was increased (527 mOsm/kg), suggesting the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Moderate fluid restriction was started (700 mL id) with an improvement of natremia (126 mOsm/L). CT scan showed an unspecific colitis and tumor markers were negative.

On-line research, using the terms “syndrome of inappropriate antidiuretic hormone secretion” and “strongyloidiasis”, revealed an association between the two, although few publications were found. The patient was discharged with the diagnosis of SIADH secondary to strongyloidiasis, recommending another week of anti-parasitic medication, following fluid restriction as done during hospitalization.

The patient did not go to the endocrinology outpatient clinic, but available results of blood tests prescribed by his general practitioner showed normal natremias (134-138 mOsm/L). After missing the next out-patient-clinic visits, he very recently returned to visit the gastroenterologist. He had gained weight, remained asymptomatic and, although still moon-faced, he had much less muscular atrophy and had general well being. He had a recent blood test which was normal, except for eosinophilia of 20%. He had occasionally been followed by the endocrinologist near his home (he did not attend regularly), the general practitioner and a dermatologist. He was on oral antidiabetic drugs, topical steroids, and 10 mg/week oral methotrexate (for his psoriasis), but he said he never took the albendazole, because he had not been able to afford it. He then received a week of oral albendazol at the hospital. Blood cell count

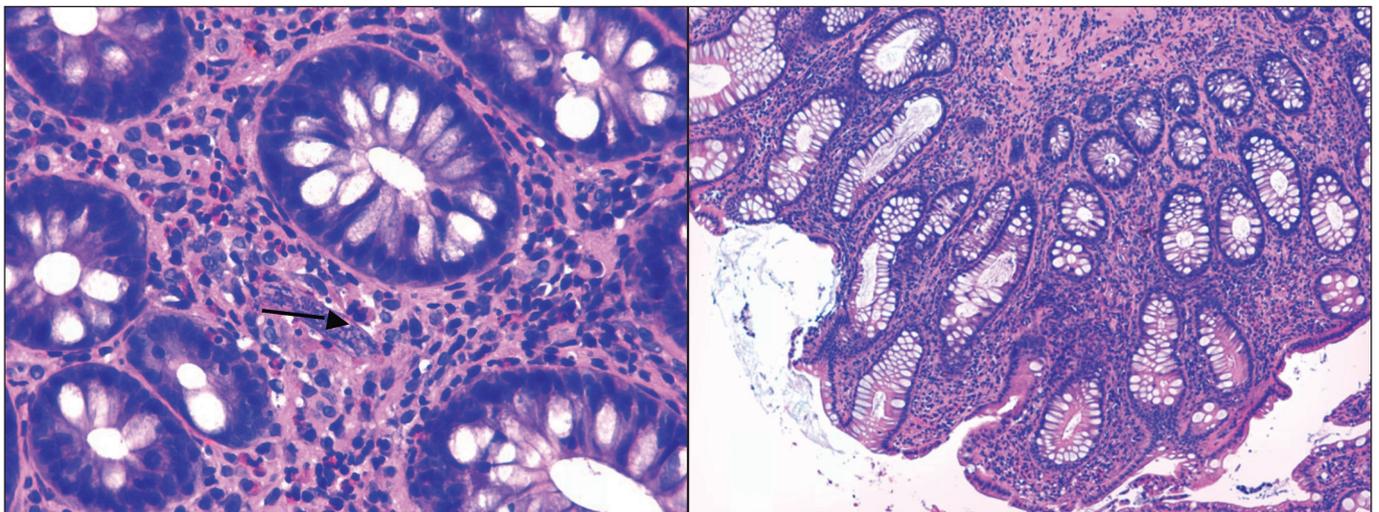


Fig. 1. Biopsy fragment of colonic mucosa. Parasites compatible with strongyloides are present within the lamina propria eliciting a marked inflammatory response with lymphoplasmacytic and eosinophilic infiltrate intracryptic and intraepithelial. Reactive changes are present in adjacent glands (H&E).

was afterwards normal (eosinophils 3.1%) and serology for strongyloides antibodies was negative. A rectosigmoidoscopy was performed and the mucosa was macro and microscopically normal, without parasites.

DISCUSSION

This case is of interest for four rarely concurring reasons. It is a worm infection that mimics IBD; the infection was diagnosed by colon biopsy in formaldehyde; the infection caused a SIADH; and the patient remains asymptomatic with topical steroids and methotrexate. Few cases that show how strongyloid infection can mimic an IBD flare (1,2) or cases of SIADH secondary to strongyloidiasis infection have been published. Most have been diagnosed microbiologically, using stool recollection, duodenal aspirate or serology, not by colonic biopsy processed in formaldehyde. Even fewer cases (none to our knowledge) have shown stabilization and improvement with steroids and methotrexate, which have historically shown worsening of strongyloides infection.

Strongyloides stercoralis is an endemic nematode in tropical and temperate areas around the world. *S. stercoralis* infection includes five clinical syndromes: Carrier state, acute infection with Löffler's syndrome, intestinal infection with chronic diarrhea, hyperinfection syndrome and disseminated disease. The infection is asymptomatic in most cases. When there are symptoms, they are usually sporadic and long lasting, more often affecting the digestive tract (epigastric pain, dyspepsia, diarrhea and chronic malabsorption), respiratory (cough and bronchospasm) and skin (pruritus). However, immunosuppression states, such as hypogammaglobulinemia immunosuppression, AIDS, Cushing syndrome, treatment with antineoplastic chemotherapy, corticosteroids, and other immunosuppressants, can entail hyperinfection or disseminated presentations that can be serious and sometimes fatal (3).

The administration of corticosteroids is a major risk factor for the conversion of a chronic low-grade infection into a fulminant one with high mortality. In order to avoid this complication, screening for strongyloidiasis in patients requiring initiation of intensive treatment with corticosteroids, such as inflammatory bowel disease, may be recommended. Eosinophilia, particularly in those who have travelled to endemic areas, is suggestive of infection. However in immunocompromised patients it is frequently absent. The sensitivity of a single coproparasitologic stool test (30%) can be increased with serial parasitological studies (4). Duodenal biopsy is another useful tool, but it can be falsely negative in cases where the nematode has not invaded the mucosa, or may be misdiagnosed as eosinophilic duodenitis, if there are few parasites, especially in unsuspected cases, in low prevalence countries. The Baermann technique or silver agar method increases the sensitivity of the biopsy study. Serological tests are

sensitive and specific (5) but there may be false positives. Before immunosuppression, a duodenal aspirate should be performed in patients with positive serology and negative parasitological results.

Chronic enterocolitis and malabsorption can result from a high parasite load. The colitis is usually on the right side and the endoscopic findings include loss of vascular pattern, edema, aphthous ulcers, erosions, serpiginous ulcers and xanthoma-like lesions. Strongyloidiasis' hallmarks include patchy inflammation, distal attenuation of disease, eosinophilic infiltration, and, characteristically, a relatively intact architecture of the crypts and the submucosa, although some cases have presented criptitis and granulomatous-like lesions.

Our patient had strongyloides-colitis symptoms, which are quite similar to those in IBD. He, curiously, had worsened on reducing the topical steroids, and improved when oral steroids and 5-ASA were given. Initially, when he was clinically worse and had stopped steroids for three months, he did not have eosinophilia, which appeared when he was on topical steroids again, asymptomatic, and had started on methotrexate. Endoscopically, his colitis was more apparent on the transverse and left colon (instead of the characteristic right side) and, macroscopically, it did not match either Crohn's or ulcerative colitis, but they could not be excluded because this type of parasite infections are not frequently seen in Spain. The pathology gave the diagnosis.

As Ben-Horin et al. point out (2), the diagnosis can be over-looked by the inexperienced or unsuspecting pathologist (6) or may be mistaken for eosinophilic gastroenteritis (7). The first pathologists to look at the sample were residents. They saw very inflamed tissue, compatible with IBD, and some tubular structures that called their attention, which their supervisor staff member confirmed as strongyloidiasis.

Regarding his readmission at the hospital, physical examination and laboratory tests met the established criteria for SIADH diagnosis as defined by Bartter and Schwartz (1697), with euvolemic hyponatremia and inappropriate urine concentration. The absence of respiratory or neurological symptoms (dizziness and headache resolved with SIADH treatment) that would raise suspicion of disseminated strongyloidiasis infection differentiated our case from those described previously, where SIADH was due to pulmonary strongyloidiasis infection. As in other published cases (8,9), given the absence of other etiologies of SIADH (including drugs), it seems reasonable to attribute this disorder to the infection by *Strongyloides stercoralis*.

The pathogenesis of hyponatremia in patients with SIADH due to strongyloides infection remains unknown. Hayashi hypothesizes that anorexia associated with the infection triggers the SIADH, along with a direct or indirect effect of the nematode on the increased ADH secretion (9).

Despite the absence of a hyperinfestation strongyloidiasis syndrome, our patient suffered from protein-energy

malnutrition and was being treated with corticosteroids that may have contributed to the progression of the infection (3). However, we are not aware of corticosteroid treatment's influence on SIADH development nor has bibliographical research revealed any association. SIADH requires symptomatic treatment; etiological treatment for strongyloidiasis should be promptly started. According to the feasible severity of the infection, some authors support universal treatment including asymptomatic patients in order to prevent parasitic dissemination.

This case made us research infrequent causes of colitis and SIADH. SIADH is a rare complication due to strongyloides infection. It is mainly associated with disseminated strongyloidiasis infection, but its pathogenesis remains unknown. Although parasitic eradication should be started promptly, our patient confessed a year later that he had not taken the worm treatment. However, he *was* on pharmacological immunosuppression, which seemed surprisingly to partially block the effects of his parasite infection, and his blood tests only revealed eosinophilia. Contrary to what has been published to date, immunosuppression has not worsened his strongyloidiasis infection.

As Buonfrate et al. comment in their meta-analysis (10), western doctors do not usually think about strongyloidiasis, but rather look for underlying IBDs. Does an underlying IBD explain his response to steroids and methotrexate, or, as Greenstein's group has previously pointed out with regard to other microorganisms, is the immunosuppressive treatment responsible for inhibiting, but not killing the germs (11,12)? Is his asymptomatic state with eosinophilia a result of immunosuppression "blocking" the development of IBD, a shift of intestinal flora after a long-term immigration, and worms conferring a TH2 response that is supposed also to decrease the possibilities of IBD presentation? In mice, reappearance of allergic and atopic conditions has been observed when *S. stercoralis* is treated (13-15). Since the patient has been erratic in follow-up and treatment, he has been hospitalized for worm treatment. We will try to improve his adherence to visits and treatment to check on worsening of his already known aberrant

immune conditions, and on the look-out for possible new ones (mainly IBD).

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