

***Strongyloides stercoralis* in a Patient With Rheumatoid Arthritis Undergoing Treatment With Etanercept**

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Biologic therapy for the treatment of autoimmune diseases such as rheumatoid arthritis leads to a series of secondary effects and complications which are ever more frequent and increasingly complicate both the management as well as the associated comorbidity. We present the case of a patient who had one of these associated complications.

Key words: Rheumatoid arthritis. *Strongyloides stercoralis*. Etanercept. Infection.

***Strongyloides stercoralis* en un paciente con artritis reumatoide en tratamiento con etanercept**

La terapia biológica para el tratamiento de enfermedades autoinmunitarias, como la artritis reumatoide, conlleva una serie de efectos secundarios y complicaciones cada vez más frecuentes y de gran complejidad tanto en el manejo como en la comorbilidad asociada. Presentamos el caso de un paciente con una de estas complicaciones asociada.

Palabras clave: Artritis reumatoide. *Strongyloides stercoralis*. Etanercept. Infección.

Clinical Case

A 29-year-old equatorian male was diagnosed with rheumatoid arthritis in 2001 and initially treated with methotrexate, non-steroidal anti-inflammatory drugs and then with hidroxycloquine, prednisone, and parenteral methotrexate. Due to a lack of symptom

improvement, mainly arthritis of the wrists, elbows, shoulders and hips, he started treatment with etanercept in 2004. After an initial clinical improvement, treatment was stopped in November 2005 because the patient presented skin vesicular and hemorrhagic lesions due to varicella zoster, as well as hepatitis A, meriting hospitalization. In February 2006 the patient is hospitalized in Manzanares due to upper gastrointestinal tract bleeding of the duodenum due to an infestation by *Strongyloides stercoralis*, during which esophageal candidiasis is also found. He is treated for those infections with nistatine and albendazole 400 mg/12 h, after which he is found to be asymptomatic and is not reintroduced to biologic therapy. After discharge, the patient is diagnosed with *Helicobacter pylori* infection, receiving eradication treatment; he presented microcytic, hypochromic anemia without an elevation of acute phase reactants in the blood analysis. After this episode he travels to his country of origin where he suspends all medication, with clinical worsening and receives local steroid infiltrations, as well as systemic steroid boluses. He is seen at the rheumatology outpatient consult in June 2006 with an exacerbation of rheumatoid arthritis, presenting swelling of the wrists, generalized joint pain, and morning stiffness that lasts 2 hours for the past month-and-a-half before the visit. In addition, the patient reported yellow-colored diarrhea of 1 week since onset, with abdominal pain and tenesmus, without blood or mucus. Because of this he was hospitalized due to a suspected reinfestation with the parasite. On the blood analysis there was microcytic, hypochromic anemia (hemoglobin 10.9 and hematocrit 33.1), which he already had presented and for which he had been receiving treatment with oral iron supplements; he also presented thrombocytosis as well as an increase in acute phase reactants with an ESR of 56 and a CRP of 2.34, as well as a rheumatoid factor of 216.09. In the urine analysis there was positive nitrites and bacteria's in the urinary sediment. In the stool samples there were *Giardia lamblia* cysts and *S stercoralis* larvae; the rest of the tests (endoscopy, serology, etc) were normal. After this finding, treatment with metronidazole and albendazole was begun, although the patient did not tolerate the latter and a consultation with the department of infectious disease was carried out at the Hospital Ramón

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y Cajal, which recommends treatment with ivermectin at a dose of 12 mg, which the patient tolerates without incidence. After discharge the patient was treated with prednisone 10 mg a day and metamizole for pain. After 2 weeks a new stool sample is taken and cultured, with negative results, and treatment with methotrexate and hydroxychloroquine was started because the patient presented clinically swelling of the wrists as well as pain on the shoulders, hands and hips and morning stiffness which lasted more than 1 hour. After the start of these DMARDs, the patient showed clinical improvement without bouts of joint swelling. A new stool culture done a month after was negative and treatment was maintained.

Discussion

S stercoralis is a human intestinal nematode with a high worldwide prevalence, although it affects subtropical regions more frequently, with approximately 10 million cases.⁶ One study shows that the prevalence in our country has recently increased,⁷ and it appears both in immunocompetent and immunodeficient patients, as well as in patients treated with corticosteroids¹ or biologic therapy, although the literature shows only 1 report which happened after treatment with etanercept,³ transplants, infection with the human immunodeficiency virus, blood diseases, malnutrition, alcoholism,⁵ and others. The latter cases are more severe. The female parasite has a preference for the digestive tract; it plants its eggs in the mucosa and liberates larvae that abandon the organism through the stools; they penetrate other organisms through the skin of by ingestion and migrate via the circulation to other organs such as the lungs.^{4,6} Autoinfection can occasionally happen for years if no adequate treatment is given. Sexual reproduction of *Strongyloides* occurs out in the open.⁶ Patients are usually asymptomatic,^{5,6} although acute manifestations such as allergic rash, cough, tracheal irritation, nausea, vomit, watery diarrhea, and abdominal pain can be present. Chronic manifestations are nausea, vomiting, constipation, epigastric pain, diarrhea, weight loss, bronchial hyperreactivity episodes, allergic rash, etc. These patients generally have eosinophilia.¹

A hyperinfection syndrome occurs in 1.5%-2.5% of immunodeficient patients with strongyloidiasis, where the patient presents the abovementioned intestinal manifestations as well as subacute intestinal obstruction, pneumonia, or lung hemorrhage. These cases can be complicated with a disseminated infection which has a high associated mortality.¹

Our patient presented an infestation by 2 parasites, one of which was present in February 2006, 3 months after the suspension of biologic therapy. However, when reinterrogating the patient, we found out that he had presented intestinal symptoms since before stopping the therapy, mainly diarrhea, abdominal pain, and dyspepsia,

making us assume that the parasite appeared while the patient was still receiving treatment with etanercept. Moreover, what called our attention was the fact that the patient presented a new infestation after receiving eradication treatment, almost one year after suspending the biologic drug, leading us to think: *a)* the patient did not take the treatment adequately and suspended it before time, leading to a new manifestation of the same parasite because we were unable to find a stool culture done after receiving treatment; *b)* the patient had reinfected himself on the trip back to his country of origin, justifying the appearance of *G lamblia*; or *c)* the patient was reinfected through contact with his close relatives. Therefore, a first infection with *S stercoralis* appeared associated to biologic therapy with etanercept, as has been previously described in the literature³ and a second one which could be the result of an inadequate eradication treatment of this infection or a new infection, taking into account that the patient received steroids, with this association also described in the literature¹ and who also presented infection by *G lamblia*.

What calls our attention the most is that in parasitic infections, arthritis can appear as a rare complication, manifested as polyarthritis and associated to intestinal symptoms. The synovial fluid of these patients does not show larvae, and it is described as a reactive arthritis, although their presence has been observed in some synovial biopsies.⁴ In addition, the case of a 44-year-old African male has been described, who had manifested *S stercoralis* associated polyarthritis since he was 18 years of age and was HLA B27 positive, with the symptoms disappearing after treatment for the parasite.² In order to carry out the differential diagnosis between rheumatoid arthritis and an infection by this parasite or secondary reactive arthritis, in addition to carrying out a complete history and a thorough examination, the best thing is to demonstrate if the clinical signs and symptoms disappears with antiparasitic treatment or, if it continues, face the fact that it may be a case of rheumatoid arthritis with a infection by the parasite, as occurred in our case in which, after eradication treatment and a negative culture, the patient persisted with joint pain, arthritis, and morning stiffness. The adequate treatment of *S stercoralis* is diverse, using drugs such as albendazole, tiabendazole, and ivermectin. However, in a study published in 2001, ivermectin is described as the most effective treatment for the eradication of *S stercoralis* larvae, especially in cases of hyperinfection, describing in vitro eradication of 100% of larvae.⁸ Therefore, it would be appropriate for those patients undergoing biologic therapy as well as for all of the patients with immune compromise and those who are originally from a country where there is a higher prevalence, to undergo a stool culture for parasites, especially in cases which present gastrointestinal symptoms. Ivermectin, which has shown a better efficacy, would also be convenient to employ for its eradication.

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