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CASE REPORT

Severe invalidating pain syndrome associated with benznidazole therapy for Chagas' disease

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Abstract Chagas' disease is an endemic parasitic disease and constitutes an important health problem in Latin American countries. The increasing number of immigrants from these countries has resulted in a rise in diagnosis and consequently in the treatment of this disease in developed countries not familiar with this condition. Currently, benznidazole is used for treatment of this condition. However, undesirable effects have been reported with this treatment, and there are few data about continuous long-term use of this drug. We describe a case of invalidating pain syndrome in a 31-year-old Bolivian woman with Chagas' disease while receiving benznidazole therapy. Because of the number of cases with this condition will probably increase because of immigration, a better understanding of the side effects of the treatment of this disease is essential.

Keywords Benznidazole · Chagas' disease · Pain · Polyarthralgias

Chagas' disease (CD) is an endemic zoonosis caused by *Trypanosoma cruzi* and is a major cause of morbidity and mortality in most Latin American countries, with more that 10 million Latin Americans carrying the parasite [1]. However, most infected people will never have symptoms, and only 10 to 30% of them will have clinical manifestations of chronic CD, mostly affecting the heart and gastrointestinal tract [1–3]. The increasing number of immigrants from these countries has resulted in a rise in diagnosis and consequently in the treatment of this disease in developed countries not familiar with this condition [2, 3]. In addition, the transmission of the parasite by blood transfusion or organs transplantation from infected individuals has also been observed [2, 3]. Currently, benznidazole is used for treatment of CD [2, 4]. Nevertheless, undesirable effects have been reported with this treatment, and there is no experience with continuous long-term use of this drug.

We describe a case of invalidating pain syndrome in a 31-year-old Bolivian woman with CD while receiving benznidazole therapy.

Case report

The patient was admitted to the Rheumatology service because of a 1-week history of stiffness and severe pain in the shoulders, pelvic girdles, and wrists associated with a marked functional impairment. She has been living in Spain for the last 2 years. The patient referred to a previous diagnosis of CD (in her country) but without apparent associated clinical symptoms. She was previously evaluated at the Tropical Medicine Service of our hospital, and after confirming a *T. cruzi* infection (by enzyme-linked immunosorbent assay and polymerase chain reaction [PCR] detection of *T. cruzi* in blood), she began treatment with benznidazole (300 mg/day). She took the treatment only during 5 weeks because she began complaining of pain. The patient was referred to our Service to evaluate severe invalidating pain syndrome. At physical examination, she showed a marked limitation of active and passive movements of the shoulders

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and hips and also swelling and tenderness in the third metacarpal of both hands and in the right wrist. No other remarkable physical findings were observed. Radiographs of the hands, shoulders, and pelvis were all normal as well as bone scintigraphy and electromyography. Routine white and red blood cells counts, proteinogram, renal and liver function test, creatine kinase, calcium, phosphate, and serum electrolytes were all normal; erythrocyte sedimentation rate was 35 mm/h, and C-reactive protein was 1 mg/dl. The Immunological profile that included antinuclear antibodies and rheumatoid factor was negative as was the serological study (including the determination of antibodies to Rubella, Parvovirus B-19, Epstein–Barr, Cytomegalovirus, hepatitis C and B, human immunodeficiency virus, *Mycoplasma pneumoniae*, *Chlamydia*, *Brucella*, *Borrelia*, and *Treponema*); the human leukocyte antigen B-27 antigen was negative.

The patient was treated with anti-inflammatory therapy (diclofenac 50 mg/8 h), and because secondary effect of CD treatment was suspected, benznidazole therapy was discontinued. Clinical symptoms began to improve after 5 days of discontinuation of therapy and treatment with anti-inflammatory drugs, and she became free of symptoms 6 weeks later. After 1 year, *T. cruzi* detection by PCR was negative, whereas Chagas' serology remained positive. The patient remains asymptomatic after 1 year of follow-up.

Discussion

Controversies remain regarding the efficacy of benznidazole in chronic CD [3, 5]. Nevertheless, recent studies support the beneficial effect of this drug on the progression of cardiac CD [6, 7]. However, treatment with this antiparasitic drug has also been related to secondary effects, especially neuropathy, depression, headache, dermopathy, sleepiness, disorientation, or even convulsions, among others [8–10]. Undesirable effects such as minor myalgias and arthralgias have also been reported in relation to this therapy, but to our knowledge, no prior similar case has been previously published. Indeed, our patient developed a severe and invalidating pain syndrome that required hospital admission. The resolution of the symptoms after the discontinuation of therapy and the absence of any other associated disorder clearly suggest a relationship with this treatment. In this case and despite receiving a shorter duration of treatment (5 weeks) than that recommended for the treatment of CD (8 weeks), the Chagas-specific PCR was negative 1 year after treatment. As expected, Chagas' serology remained positive as seropositivity lasts for a long period despite the clearance of the parasite after treatment of chronically infected patients [11].

Because the number of cases of CD will probably increase in our country because of immigration, a better knowledge of the undesirable secondary effects of the treatment of this disease is mandatory.

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