Felty’s Syndrome and Kala-azar: A challenge for the rheumatologist
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ABSTRACT
Case report of a patient with rheumatoid arthritis who developed severe neutropenia, splenomegaly and was diagnosed with Felty’s syndrome. The patient later developed Kala-azar. Both diseases have similar clinical and laboratory presentation, making the differential diagnosis difficult. The present case report aims at drawing attention to the identification of visceral Leishmaniasis infection in patients with rheumatic diseases, as well as possibility of a patient with Kala-azar mimicking a set of symptoms of systemic rheumatic disease.

Keywords: rheumatoid arthritis, Felty’s syndrome, Leishmaniasis visceral, Kala-azar, leukopenia, febrile neutropenia.

INTRODUCTION
We present a case report of a patient with Felty’s syndrome who was admitted at the hospital due to febrile neutropenia and met the clinical, epidemiological, and laboratory criteria for visceral leishmaniasis.

CASE REPORT
A 49-year-old patient had had a diagnosis of rheumatoid arthritis 13 years before, in addition to secondary Sjögren’s syndrome, hemoglobinopathy C, and essential systemic arterial hypertension. She was admitted at the Service of Rheumatology of Hospital Santa Casa de Belo Horizonte in December 2006 for evaluation of pancytopenia. At the time she was diagnosed with Felty’s syndrome, as in addition to the erosive arthritis, she also had fever, splenomegaly, leukopenia (2,000 leucocytes/mm³) at the expense of neutropenia (220 neutrophils/mm³) and thrombocytopenia (93,000 platelets/mm³).

Myelogram was performed with nonspecific findings and absence of parasites. Other infectious and hematological diseases were ruled out, among which, myelodystrophy. Subsequently, the patient was admitted at the hospital several times due to febrile neutropenia (Table 1), and the myelogram results were always negative for parasites. In February 2009, during another hospital stay due to neutropenia, 2 indirect immunofluorescence tests for visceral leishmaniasis were carried out, due to the presence of a patient and dogs with the disease in the peridomical areas, of which results were both positive (1/80 and 1/160, respectively). Once again, the myelogram showed no parasites and an abdominal US showed mild hepatosplenomegaly. Blood cultures were negative. The treatment for visceral leishmaniasis, as established by the Ministry of Health of Brazil for more severe cases with comorbidities, was initiated with liposomal Amphotericin B at a dose of 3 mg/kg/day for 10 days, whereas the patient was maintained on broad-spectrum antibiotic therapy for febrile neutropenia. The patient presented distributive shock soon after the end of the
Amphotericin B therapy and was referred to the Intensive Care Unit, where she developed multiple-organ failure and died.

DISCUSSION

The differential diagnosis among the several causes of neutropenia constitutes a challenge in clinical practice. In patients with rheumatoid arthritis, the diagnosis of autoimmune neutropenia, of Felty’s syndrome subtype, can only be attained after ruling out other causes of neutropenia (Table 2). In the case reported here, the extensive propedeutics carried out during the hospital stay in 2006 allowed the diagnosis of Felty’s syndrome to be established.

Autoimmune neutropenia is a rare immunohematological condition that can be idiopathic or associated with several diseases, such as rheumatoid arthritis (RA). It is caused by the appearance of autoantibodies against mature neutrophils or myeloid precursors and can be classified as primary or secondary. The secondary form is mainly associated with autoimmune diseases such as RA, in the forms of Felty’s syndrome and large granular T lymphocytes leukemia, as well as systemic lupus erythematosus, primary biliary cirrhosis, Sjögren’s syndrome, and systemic sclerosis.

Felty’s syndrome comprises a triad of rheumatoid arthritis, neutropenia and splenomegaly. It occurs in less than 1% of the patients with RA. The cause of neutropenia is multifactorial and includes granulocytopenia deficiency and peripheral neutrophil sequestration, with an increase in bacterial infections and consequent increase in mortality. More than 95% of the patients have a positive rheumatoid factor, the antinuclear factor is positive in 47%-100% of the cases and 78% of the patients are HLA-DR4*0401-positive.

In 2009, 2 years after the diagnosis of Felty’s syndrome, there was serological evidence of leishmaniasis in two indirect immunofluorescence tests, in addition to important epidemiological data. According to the Ministry of Health, individuals from endemic areas who present with fever, splenomegaly, and immunofluorescence titers of 1:80 or higher are considered confirmed cases of visceral leishmaniasis, as long as other diagnoses are ruled out. Formerly, no serological tests had been carried out, but in the authors’ opinion, the diagnosis of Kala-azar was highly unlikely, due to the long time period between the neutropenia start and the evolution with hemodynamic instability and therefore, the patient had been kept without specific treatment for infection during the previous 3 years.

In the last two decades, visceral leishmaniasis has made an alarming comeback, being a potentially fatal infection in immunocompromised patients. A case similar to the one reported here was described by Moreau K et al., in a patient with RA who had been diagnosed with Felty’s syndrome. The patient presented fever, hepatosplenomegaly, leukopenia, and hypergammaglobulinemia. After several months, the identification of *Leishmania donovani* amastigotes in the control myelogram changed the diagnosis of this case into visceral leishmaniasis.

Fernández-Guerrero ML et al. described a series of ten immunocompromised patients with visceral leishmaniasis, of which two had SLE, three had had kidney
transplants, three were HIV-positive, and the other two had hematological neoplasias.

Spleen aspirate examination is the diagnostic method with the highest sensitivity (96.4%), followed by bone marrow aspirate (70.2%) for the diagnosis of visceral leishmaniasis. The serological tests, however, are indirect methods for parasite detection and due to its practical characteristic, must precede, whenever possible, the parasitological tests and can even replace them, in some instances. The indirect immunofluorescence has good sensitivity, but can have cross-reactions with other microorganism antigens, such as Trypanosoma, Mycobacterium, Plasmodium and Schistosoma.

In a retrospective study of six patients with visceral leishmaniasis, Sakkas LI et al. observed several laboratory abnormalities (cytopenias, hypergammaglobulinemia, rheumatoid factor, direct coombs, antinative DNA, and anticardiolipin IgM), similar to those found in SLE. Recent publication in our country emphasizes these findings. Pizzorni C et al. recommend that serological monitoring for leishmaniasis must be carried out in individuals that live in endemic areas during therapy with anti-TNF monoclonal antibodies, since cytokine-induced macrophage activation and tissue granuloma formation, activities related to controlling this disease, are inhibited during the use of this medication.

The present case report shows the importance and difficulty to attain a differential diagnosis between visceral leishmaniasis and Felty’s syndrome. Most often, this is a great challenge in clinical practice due to the similarity of symptoms and blood count results of the two pathologies and considering that immunosuppressive therapy in patients with leishmaniasis can be fatal.

REFERENCES