Note

Infectious arthritis as the single manifestation of sporotrichosis: Serology from serum and synovial fluid samples as an aid to diagnosis

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Summary Sporotrichosis is a generally cutaneous, granulomatous, chronic and benign infection. Less frequently the disease may affect the joints. Articular involvement is usually characterized by monoarthritis in the absence of systemic symptoms, generally preceded by skin lesions, and frequently affects immunosuppressed individuals. We describe here the case of a healthy patient presenting knee arthritis without skin lesions, diagnosed as sporotrichosis, and treated with oral itraconazole. Serology used in this case was an invaluable tool for the diagnosis of sporotrichosis arthritis lacking skin lesions.

Key words Sporotrichosis, Arthritis, *Ss*CBF antigen, Synovial fluid, Knee

Artritis infecciosa como única manifestación de la esporotricosis: serología de muestras de suero y líquido de la sinovia como recurso del diagnóstico

Resumen En la mayoría de las veces, la esporotricosis es una infección cutánea, granulomatosa, crónica y benigna. De modo más raro, la enfermedad puede afectar las articulaciones. El comprometimiento articular en general se caracteriza por monoartrite sin síntomas sistémicos con presentación clínica habitual de lesiones cutáneas y con frecuencia despunta en las personas inmunodeprimidas. El caso descrito es de una paciente sana que presentó artritis en la rodilla sin lesiones cutáneas, con el diagnostico de esporotricosis y que fue tratada con itraconazol oral. En este caso se concluye que la sorología es una herramienta valiosa para el diagnóstico de la artritis sin lesiones cutáneas producida por el hongo *Sporothrix schenckii.*

Palabras clave Esporotricosis, Artritis, Antígeno SsCBF, Líquido sinovial, Rodilla

Systemic sporotrichosis involving other organs is rare [4]. The infection is usually acquired by traumatic inoculation of material contaminated with the dimorphic fungus *Sporothrix schenckii* present in nature. Animal transmission has been also reported [10,15]. Specific involvement of the joint is generally associated with skin lesion elsewhere, preferentially affects the knee joints and is mainly observed in immunosuppressed patients [5]. Herein we report the case of a healthy patient with articular involvement without previous skin lesions. Serology from serum and synovial fluid was helpful in the differential diagnosis of other arthritic conditions.

Case Report

An 88-year-old white woman was admitted to the Hospital Universitário Pedro Ernesto, State University of Rio de Janeiro, Brazil, for the etiological investigation of monoarthritis in the left knee. The symptoms had started 4 months earlier with arthritis in the left knee characterized by edema, erythema and local heat, which progressed to important functional limitation. The patient reported no fever, weight loss, digestive or respiratory alterations. There was no history of diabetes nor any other comorbidity except high blood pressure treated with daily oral

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dose of 12.5 mg hydroclorothiazide. She also reported no skin lesions at the site before the onset of arthritis. Oral nonsteroidal anti-inflammatory drugs, as well as intramuscular depot corticosteroids, had been administered on three occasions and intra-articular corticosteroid infiltration was performed on two occasions suspecting of a traumatic or inflammatory process. The patient had also received oral prednisone at low doses. None of the described treatments showed improvement in the patinet. Physical examination revealed no other alterations, except for arthritis in the left knee accompanied by synovial thickening and a Baker's cyst. She had no history of smoking or alcohol consumption. Ultrasound imaging of the affected joint showed a Baker's cyst which had been punctured several times. Simple radiography performed at the beginning of the disease revealed only gonarthrosis. Laboratory exams showed normochromic normocitic anemia and normal white cells count except for high eosinophils (20%), an elevated erythrocyte sedimentation rate (41 mm in the first hour); rheumatoid factor 61 UI/ml (normal value up to 15 UI/ml); Anti-nuclear factor 1/100 (dotted nuclear pattern); C-reactive protein 3.03 mg/dl (normal value up to 0.9 mg/dl); Waaler-Rose reaction 32 UI/ml (non reactive is normal); antisclero-70 antibody, anti-histone, anti-SM, anti-ENA and anti-SSA/RO all negative. Other exams were within normal values. Cytology of synovial fluid revealed cloudy, yellow color and a count of 20,000 cells/mm^3 with 80% polymorphonuclear and 20% mononuclear leukocytes and other cells (normal synovial fluid is limpid, up to 200 cells/mm^3 being 75% mononuclear and 25% polymorphonuclear). There were no malignant cells. LDH was 2,194 U/l (normal value for this patient is 72 U/l - 60% of serum value); total protein 5.1 g/dl (normal range 1-3 g/dl); glucose 63 mg/dl (normal range 70-110 mg/dl). Direct microscopy for alcohol-acid-resistant bacteria was negative and crystals were not detected. When knee arthroscopy was performed 10 ml of a viscous synovial fluid and a thickened sanguinolent synovia were removed. Direct microscopy of alcohol-acid-resistant bacilli and culture for mycobacteria in synovial fluid were both negative. Mycological examination of synovial fluid and synovial biopsy fragment resulted in negative direct microscopy but *S. schenckii* was isolated in culture. Histopathology of the synovial fragment revealed an unspecific inflammatory infiltrate of mononuclear cells with great number of plasmocytes (Figure 1). PAS and Grocott stain were both negative for fungal elements. Serology for sporotrichosis using

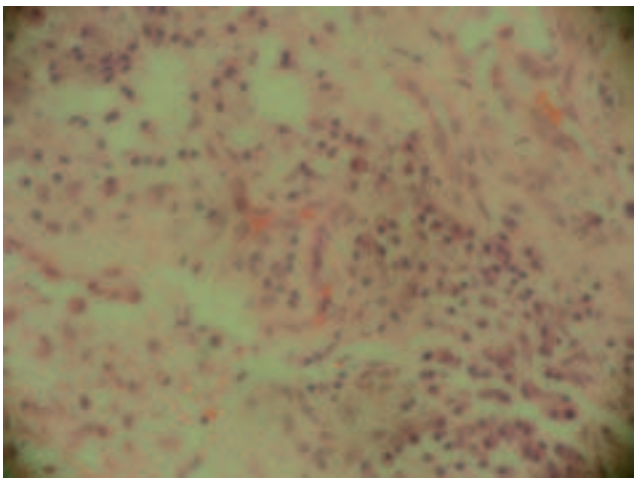

Figure 1. Synovial histopathology stained with H&E showing an inflammatory infiltrate composed mainly of mononuclear cells. Note great number of plasmocytes (arrows).

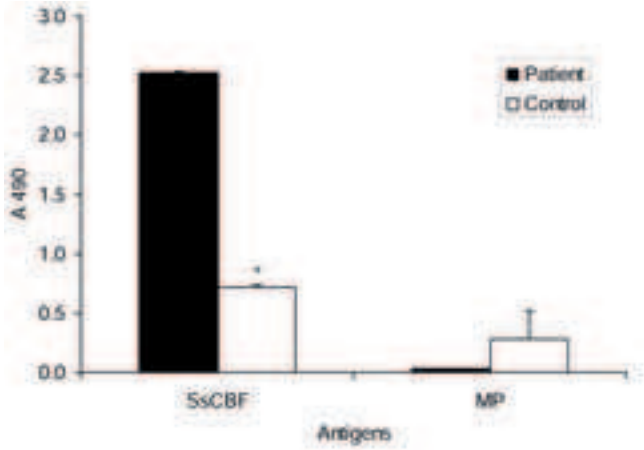

Figure 2. Detection of IgG antibodies in synovial fluid from a patient with infectious arthritis caused by *S. schenckii* and a patient with arthritis but without history of fungal infection were tested with both antigenic fractions SsCBF and MP by ELISA. *$p < 0.05$ compared with the control (Students t-test).

ELISA and the *Ss*CBF antigen fraction were performed. This fraction is recognized by IgG antibodies present in serum samples, with this test showing 90% sensitivity and 80% specificity [3]. Analysis of a serum sample revealed an IgG titer of 204,600 for a cut-off value of <6,400. Concomitant investigation of a synovial fluid sample showed a significant IgG antibody level recognizing the *Ss*CBF antigen as compared to control clinical material. The result with the *Ss*CBF antigen was quite significant and specific as shown by the non reactivity observed with an irrelevant antigenic preparation of *Saccharomyces cerevisiae* (Figure 2). Treatment with 400 mg itraconazole/day was initiated and the patient was symptom free after 3 months of treatment. Itraconazole was discontinued after a total course of six months of treatment. Eighteen months after the end of the treatment patient was still asymptomatic but death occurred due to cardiovascular disorder.

Discussion

In the State of Rio de Janeiro, Brazil, epidemic of cases of sporotrichosis had been observed since 1977 due to the transmission of the etiologic agent through contaminated animals [11]. Most of these cases have a benign and localized character usually presenting as lymphocutaneous form. We haven't seen patients with no skin lesions. In the present case, we couldn't find associated immunossupression. Arthritis was monoarticular, the patient presented no general symptoms and sporotrichosis was not suspected initially. Fungi are not a common cause of chronic monoarthritis; joint involvement without skin lesions has been observed though not a frequent finding [13,14]. Differential diagnosis must includes other infectious etiologies such as mycobacteria, common bacteria, syphilis as all as other non infectious etiologies including hypotyreoidism, amyloidosis, multiple myeloma, paraneoplastic syndrome, colagenosis. Extensive laboratory investigation is very important to establish the diagnosis. Detectable titers of serum antinuclear factor (dotted nuclear pattern); elevated levels of rheumatoid factor, total C protein, and erythrocytes sedimentation rate are unespecific and can be present in elderly people or in different infectious and inflammatory disorders. Usually, chronic fungal arthritis shows a viscous and sanguinolent aspect, a cell count ranging from 10,000 to 40,000 cells/mm^3 (polymorphonuclear leukocytes

predominate), high protein and low glucose; all laboratory findings were present in this patient [12]. High levels of LDH can be found in rheumatoid arthritis, gout and infectious arthritis [12]. Microscopic synovial pathology usually reveal a granuloma which was not present in this case, though we observed a great number of plasmocytes that may be seen in cases of sporotrichosis [6,12]. To our knowledge there is no systematic study for the serodiagnosis of sporotrichosis with a biochemically well defined antigen. A diagnostic method based on immunoelectrophoresis using a culture filtrate preparation was proposed several years ago but was only tested with a patient with cutaneous sporotrichosis [1]. The use of complex antigen mixtures such as culture filtrate preparations was proved to present a significant variation in its biochemical composition and antigenic properties [16]. Thus, this serological test was proved to be a rapid method for the differential diagnosis of arthritis caused by *S. schenckii* as already observed for other extracutaneous forms of this disease [3].

The most frequently antifungal drugs used to treat sporotrichosis are azole compounds, especially itraconazole, and amphotericin B [2]. The patient progressed well after short treatment with oral itraconazole. Follow up showed no relapses and she was in good general health. End of treatment was based on the age of patient besides favorable clinical outcome. Joint preservation in this patient was possibly due to correct diagnosis, which permitted the initiation of adequate therapy. Some patients presenting chronic joint involvement until diagnosis of sporotrichosis is made may need an arthrodesis [8,9]. According to the literature, progression of sporotrichosis with joint manifestations usually occurs in immunosuppressed patients and requires long periods of treatment to cure the disease [7]. In a review of the fungal arthritic literature from 1966 to 2001 *S. schenckii* was the agent that caused more articular sequela post-treatment [6]. In conclusion, in this patient with arthritic sporotrichosis was treated and cured within 6 months course of itraconazole for joint involvement and no skin lesion; we suggest that serologic procedures using serum samples and synovial fluid may be used as an aid for the diagnosis of extracutaneous forms of sporotrichosis although we need more studies to confirm the benefit of this ELISA test in others non-serum organic fluids; the gold standard in the diagnosis of an infectious disease is still the isolation of the etiological agent.

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