

Recurrence of tuberculosis as a cerebral abscess in a patient with systemic lupus erythematosus

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Abstract. Infections are a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). Treatment with immunosuppressive drugs can decrease the clonal proliferation of T cells and is the main predisposing factor for tuberculosis (TB). Clinically, the extrapulmonary TB is frequent in patients with SLE due to reactivation of latent foci of primary infection or simply a reinfection. A case of young woman who presented with cerebral TB. The diagnosis was established by biopsy, which showed chronic granulomatous inflammation with areas of central necrosis, with isolated *Mycobacterium tuberculosis*. There is increasing evidence suggesting an increased severity of TB in SLE patients. This report demonstrates the necessity of monitoring the increased susceptibility to infections in SLE patients.

Key words: Tuberculosis, systemic lupus erythematosus, cerebral abscess

1. Introduction

Infections are the major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). Patients with SLE are more susceptible to infection with *Mycobacterium tuberculosis* (MB) (1). MB infection requires cellular immune response mediated by CD4 + T lymphocyte-specific antigens bacilli. Recent studies show that deficient T cell was associated with increased susceptibility to tuberculosis (TB) (2).

Clinically, the extra-pulmonary TB is frequent in patients with SLE, being common to reactivate on a latent focus of primary infection due to hematogenous spread of lymph-pulmonary TB, or simply a reinfection. Soon, those who have a history of pulmonary TB are more susceptible to have extrapulmonary (3).

Among the forms of extra-pulmonary presentation, affecting the central nervous system (CNS) is one of the least frequent. The clinical manifestation depends on the location of the lesion in the CNS, which generally grows slowly. When there's involvement of the subarachnoid space, with a normal CFS and the computed tomography (CT) presents only minor alterations, can be difficult to differentiate from other diseases. (4) Treatment of SLE with steroids and immunosuppressive drugs is the main predisposing factor for infection MB (5). The epidemiology of TB features a greater exposure to the infectious agent and is a determinant factor to increase the susceptibility (6).

The aim of this article is to present a case of cerebral abscess caused by TB in a patient with SLE in immunosuppressive therapy, highlighting the importance of approaching this disease with a differential diagnosis.

2. Case report

A female patient, 28-years-old, white, born and resident in Campos – RJ, was admitted to the emergency room complaining of left hemiparesis and right facial palsy. In the last 15 days she developed left hemiparesis progressively with concomitant right facial palsy and dysarthria. In her past medical history we could observe,

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chickenpox and mumps in childhood. Fifteen years ago, she had a SLE with lupus nephritis. She makes a regular use of azathioprine, prednisone and cyclosporine. Seven months ago, she had completed an outpatient treatment for pulmonary TB biphasic with two months of rifampicin 600mg/day, isoniazid 400mg/day, pyrazinamide 400mg/day and ethambutol 1200mg/day and four months of rifampicin 600mg/day and isoniazid 400mg/day with regular adherence to treatment.

Three months progressed, with complaints of weight loss of about five pounds in one month, cough, night sweats and mild fever. Restarted immediately an outpatient treatment for pulmonary TB, after two positive direct smears with rifampin 600mg/day, isoniazid 400mg/day, pyrazinamide 400mg/day and ethambutol 1200mg/day. During this time, with low adherence to treatment, she interrupted it for two months, when the symptoms had ceased. Eighteen days later, an episode of generalized tonic-clonic seizure preceded by a single episode of fever and mild left hemiparesis. She received a treatment at this time with carbamazepine 200mg/day.

Physical examination revealed a fever (39.5°C) and cough with yellow sputum. Lung auscultation, breathe cavity in the left apex and diffuse rales crackles. The neurological evaluation demonstrated ipsilateral Babinski sign, left hemiparesis, impaired gait and dysarthria. In the subsequent investigation conducted by a laboratory used tests such as blood count, biochemistry, western blot and cultures that were negative, and finally, CT scan revealed "a hypodense lesion in the frontal lobe in the right superior frontal gyrus with center hydrated, probably necrotic, captured with a contrast and a presence of perilesional edema" (Figure 1). The CD4 count at the time the patient with 119 cells/mm³. The images were considered suggestive for toxoplasmosis and empirical treatment was initiated with sulfadiazine 4g/day, pyrimethamine 50mg/day and folic acid 5mg on alternate days, which had no success. After results of serology for toxoplasmosis, which was negative, began cloranfenicol 500mg/day.

The patient remained without clinical improvement, so it was decided, therefore, a further research including a cerebral biopsy and a resection of the lesion, which revealed an extensive glaucomatous inflammatory chronic process with areas of central necrosis, lymphocytic halo and giant cell reaction. The Ziehl showed few bacilli.

Microscopically, the predominant cells were macrophages and lymphocytes in the middle of a

dense network of fibrin, was isolated MB. The patient developed a hypotension, tachycardia and poor general condition, which was diagnosed with *Pseudomonas aeruginosa* sepsis and later came to death.



Fig. 1. Computed tomography reveals a hypodense lesion in the frontal lobe with center hydrated, probably necrotic, capture of contrast and presence of perilesional edema.

3. Discussion

This discussion is based on the increased frequency and as well on the severity of TB in immunocompromised patients with evidence of the CD4 T cells act to control this infection and its role in the development of immunity after exposure to antigen. The CD4 T lymphocytes activate macrophages by releasing the IL-2.(7) The meeting of activated macrophages, and epithelioid cells surrounded by an infiltrate of lymphocytes, comprises the granuloma. CD8 T-lymphocytes are also important for an effective T cell immune response. Other risk factors associated with immunosuppressive therapy are the daily doses of steroids during its lasting (8,9).

A recent study suggests that for every gram of prednisone increases to 23% the risk of developing TB. To prove convincingly the effect of steroids on the immune response a MB was performed in vitro studies. It was found that cortisol in physiological concentrations can inhibit the proliferation of antibodies against mycobacterium, as well as the synthesis of IFN- γ (10). The immunosuppressive action decreases

the proliferation of the T cells, primarily by inhibiting the release of IL-2 receptor of IL-2, inducing the proliferation of cytotoxic T cells. The function of T cells mediate the cellular responses by reducing the responses of B cells which is dependent on T cells and by inhibiting the transcription of the gene for IL-2, although it also has an effect on the gene transcription of IFN- γ and IL-3. However, it also decreases the transcription of other genes, both in the induction and effectuation phases of immune response (11).

The previous episode of TB in SLE patients is a predisposing condition to the recurrence of the disease. The clinical and laboratory features may coexist in both diseases and the presentation can be varying. Often, the diagnosis of extra pulmonary TB is made by the exclusion of other diseases and helps the tuberculin test. The tuberculin test is the test which is made in cases of BCG vaccine by immunization or a previous TB. Although they are no side effects, some causes may interfere in the results of tuberculin, one of them is the recent treatment with corticosteroids (12). There may be greater difficulty in the diagnosis of extra pulmonary forms of TB, which usually allow the bacteriological confirmation of diagnosis in only about 25% of cases. The reasons for this difficulty are many and include poor access to most of the injuries and the fact they are usually paucibacillary, a situation in which the sputum is usually negative. The histopathologies of granulomatous reaction do not rule out the possibility of other diseases (12,13).

The introduction of chemotherapy, especially the BCG vaccination, which has brought remarkable change in the prevalence of CNS-TB, which today is only observed in a small percentage of cases of extra pulmonary TB. The involvement in this case, can occur in two basic ways: by the occurrence like meningoencephalitis or cerebral tuberculoma. Tuberculoma or cerebral abscess by MB is the least common form of presentation among the two forms that affect the CNS. The clinical manifestations depend on the area of the lesion, which generally grows slowly (3,4).

Radiology, contributes giving important information for the diagnosis of extra pulmonary TB, although in none of the areas have specific radiological patterns. Only in a few ways there are concomitant with active pulmonary TB and rarely there is evidence of the passage of the bacilli by the lungs. Still, the chest radiograph is mandatory, since the evidence of infection lesions is a good pointer for the diagnosis (14).

Currently, new diagnostic modalities have been used in TB. Among these all, is the determination of adenosine deaminase (ADA) and polymerase chain reaction (PCR), which may be useful in certain forms of extra pulmonary disease (15). Treatment of TB in SLE patients has the same recommendations as to any other healthy patients. After categorizing the patient, combined therapy should be initiated. The choice of regimen may depend on resistance patterns, sputum test results and patient characteristics. This scheme usually includes the combination therapy of rifampicin, isoniazid, pyrazinamide and ethambutol for two months followed by at least four months of rifampin and isoniazid. The duration of the treatment is subject to change depending on the patient's clinical condition and the response to the treatment. The decision to continue therapy for up to nine months may be indicated the presence of persistent signs and symptoms of TB, and extensive cavitory pulmonary disease on chest radiograph or a positive sputum culture in two months (16).

There is a growing clinical and experimental evidence that suggests an increased severity of infection in patients with tuberculosis LES. The significant number of cases of reactivation or reinfection MB in extra pulmonary involvement demands an extra care in the treatment of these patients. Unlike patients co-infected with TB and others diseases, there are no specific guidelines and standards for management the patients with SLE and TB. This report presents the needing to observe the increased susceptibility to infections in SLE patients.

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