

DIAGNOSIS OF DISSEMINATED TOXOPLASMOSIS BY POLYMERASE CHAIN REACTION IN BRONCHOALVEOLAR LAVAGE FLUID OF A PATIENT WITH AIDS

DIAGNÓSTICO DE TOXOPLASMOSE DISSEMINADA ATRAVÉS DE TÉCNICA DE REAÇÃO EM CADEIA DA POLIMERASE REALIZADA NO LAVADO BRONCO-ALVEOLAR DE PACIENTE COM SIDA

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ABSTRACT

Pulmonary toxoplasmosis is a challenging diagnosis in immunosuppressed patients with nonspecific clinical picture and radiologic findings. We present a case of pneumonia due to *Toxoplasma gondii* diagnosed by polymerase chain reaction (PCR) in the bronchoalveolar lavage (BAL) fluid of a patient with acquired immunodeficiency syndrome (AIDS). Coinfection with *Pneumocystis jirovecii* was found in the same specimen. Direct examination and culture for bacteria, mycobacteria and other fungus were negative. Despite the intensive management, respiratory compromise evolved rapidly, with the need for ventilatory support. Acute respiratory distress syndrome developed, and the patient died of multiple organ failure. This case illustrates that a high index of suspicion is necessary for diagnosis of pulmonary toxoplasmosis, a potentially fatal condition. Due to high diagnostic performance, PCR in BAL fluid should be included in the evaluation of immunosuppressed patients with nonspecific pulmonary diseases.

Keywords: PCR; HIV; AIDS; toxoplasmosis; disseminated toxoplasmosis

RESUMO

O diagnóstico de toxoplasmose pulmonar em pacientes imunossuprimidos é difícil, devido ao quadro clínico e aos achados radiológicos inespecíficos. Neste artigo, relatamos o caso de uma paciente com síndrome da imunodeficiência adquirida (SIDA), que apresentou pneumonia por *Toxoplasma gondii* diagnosticada através de reação em cadeia da polimerase (PCR) no lavado bronco-alveolar (LBA). A paciente apresentava co-infecção com *Pneumocystis jirovecii*. Os demais exames microbiológicos, como bacterioscópico, cultural para bactérias, micobactérias e fungos, foram negativos. Apesar do manejo intensivo, a paciente evoluiu com síndrome do desconforto respiratório agudo e óbito por falência múltipla dos órgãos. Este caso demonstra que um alto índice de suspeita clínica é necessário para o diagnóstico de pneumonia por *Toxoplasma gondii*. Devido ao seu desempenho diagnóstico, o PCR para *Toxoplasma gondii* no LBA deve ser incluído na avaliação de pacientes imunossuprimidos com quadros pulmonares inespecíficos.

Unitermos: PCR; HIV; SIDA; toxoplasmose; toxoplasmose disseminada

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Pneumonia due to *Toxoplasma gondii* is an uncommon and underdiagnosed condition. It is usually a result of reactivation of a latent chronic infection (1). Immunosuppressed patients are particularly susceptible to the disseminated disease (2). Most cases occur in patients who have undergone bone marrow (3) or heart transplantation, and less often, in those with acquired immunodeficiency syndrome (AIDS) (4-6). Pulmonary toxoplasmosis can present as isolated pneumonitis or as part of a disseminated disease. It is difficult to diagnose and is frequently discovered only at autopsy (4,7). Screening for the infection can be done by serology, but this strategy lacks specificity. The radiographic patterns of toxoplasmosis are nonspecific (1). Lung biopsy or fiber-optic bronchoscopy (FOB) with bronchoalveolar lavage (BAL) are essential, since direct identification of the organism is the gold standard for diagnosis. The amplification of the *T. gondii* DNA by polymerase chain reaction (PCR) is a promising technique for diagnosis. PCR was shown to be sensitive and highly spe-

cific for detecting toxoplasmic disease (8-10). We report a case of disseminated toxoplasmosis in an AIDS patient diagnosed by PCR in BAL.

CASE REPORT

A 63-year-old, white, female patient was referred to a tertiary hospital because of a 2-week history of dry cough and fever. Her medical records disclosed a history of an infiltrating ductal carcinoma of the breast, stage IIIA (pT2pN2M0), resected 7 months earlier and treated with three cycles of adjuvant chemotherapy with cyclophosphamide, doxorubicin and fluorouracil (CAF). After the third cycle, 2 months earlier, she developed febrile neutropenia, which resolved after treatment with cefepime. Despite resolution of fever, incomplete hematological recovery was observed (persistent leukopenia), and chemotherapy was withheld. On admission, the patient was febrile, in breathing distress and oral thrush was noted. She had pancytopenia, hypoxemia with an elevated alveolar-arterial gradient and

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lactate dehydrogenase (LDH) of 1,590 mg/dL. Thoracic radiograph showed bilateral diffuse infiltrates. Antibiotics for coverage of community acquired pneumonia and *Pneumocystis jirovecii* infection were started. The patient developed mental confusion and underwent brain computed tomography (CT) that showed a left frontal hypodensity with discrete contrast impregnation and another hypodensity on the right thalamic region that did not enhanced on contrast imaging. Lumbar puncture showed the following results: opening pressure = 180 cmH₂O, leucocytes = 1/mm³, protein = 30 mg/dL, glucose = 40 mg/dL (serum = 74 mg/dL), adenosine deaminase (ADA) = 3 U/L. Non-reactants venereal disease research laboratory (VDRL) and fluorescent treponemal antibody absorbed (IFI-FTABs) tests, direct examination and culture for bacteria, fungus and mycobacteria were negative. PCR for mycobacteria, toxoplasmosis, herpes zoster (HZV) and John Cunningham (JC) viruses were also negative. An ELISA anti-HIV test was positive. Serology for *T. gondii* was positive for immunoglobulin G (IgG) and negative for immunoglobulin M (IgM). A presumptive diagnosis of toxoplasmic encephalitis was made, and clindamycin, pyrimethamine and folinic acid were added to sulfamethoxazole-trimethoprim (SMT-TMP). A fiber-optic bronchoscopic BAL was performed. Direct examination for *Pneumocystis jirovecii* and PCR for *Pneumocystis jirovecii* and *T. gondii* were positive. Direct examination and culture for bacteria, mycobacteria and other fungus were negative. Despite the intensive management, respiratory compromise evolved rapidly, with the need for ventilatory support. Acute respiratory distress syndrome developed, and the patient died of multiple organ failure.

DISCUSSION

Most patients with pulmonary toxoplasmosis present with dry cough, dyspnea, and fever (1). Due to the infrequency of this clinical entity, diagnosis of pulmonary toxoplasmosis can be easily overlooked. Clinical and radiologic findings are nonspecific and cannot be distinguished from other more common opportunistic infections (6). In spite of morbidity, thoracoscopic or open lung biopsy remain the gold standards for diagnosis. Direct visualization of tachyzoites on Giemsa staining has low sensitivity and depends on the pathologists' skills. In this context, less invasive and more reliable diagnostic techniques are necessary. Although rarely requested in BAL, PCR for *T. gondii* can be a fast and effective diagnostic tool (8-14). A correct diagnosis made in a timely fashion, followed by the administration of pyrimethamine and sulfonamides, assures an excellent survival rate for immunocompetent patients and a 60% survival rate for immunosuppressed patients (1,6).

In the case reported, pulmonary toxoplasmosis was diagnosed by a positive PCR in BAL. The lung is the second most common organ affected in extracerebral toxoplasmosis (4,7). Previous studies of AIDS patients who underwent FOB with BAL found 2-14% of *T. gondii* PCR positivity (9,10,12,13). Despite reports of isolated extracerebral toxoplasmosis in AIDS patients, the most common form of the disease is with central nervous system involvement (7). Our patient's brain CT showed a highly suggestive pattern for neurotoxoplasmosis. However, a negative PCR for *T. gondii* was found on the cerebrospinal fluid (CSF). This could be explained by previous administration of SMT-TMP. Foudrinier et al. found a substantial reduction of *T. gondii* CSF PCR sensitivity, from 60 to 16%, in patients under anti-toxoplasmic treatment or *P. jirovecii* prophylaxis (14).

In immunosuppressed AIDS patients, concomitant opportunistic infections are not uncommon. Cases of pulmonary coinfection of *Pneumocystis jirovecii* and *T. gondii* have been previously reported (15-17). In this case, clinical deterioration with acute respiratory distress syndrome and multiple organ dysfunction syndrome could be explained by either infection (18).

This case illustrates that a high index of suspicion is necessary for diagnosis of pulmonary toxoplasmosis, a potentially fatal condition. Due to high diagnostic performance, PCR in BAL should be included in the evaluation of immunosuppressed patients with nonspecific pulmonary diseases.

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