CASE REPORTS

Timely Diagnosis of Disseminated Toxoplasmosis by Sputum Examination

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Received 19 July 2005/Returned for modification 28 September 2005/Accepted 7 November 2005

The diagnosis of disseminated toxoplasmosis in a 14-year-old allogeneic bone marrow recipient with graft-versus-host disease was determined by the detection of Toxoplasma gondii tachyzoites in sputum smears. Sputum analysis is a valuable alternative in the clinical assessment of pulmonary toxoplasmosis, especially when conventional invasive techniques are not practicable.

CASE REPORT

A 14-year-old girl had been transplanted with human lymphocyte antigen-identical allogeneic hematopoietic stem cells from an unrelated donor because of a T-cell lymphoma. Her pretransplant serological tests were positive for Toxoplasma gondii (immunoglobulin G [IgG] = 60 IU/ml, IgM negative). The donor’s Toxoplasma serology was negative. The recipient received polyclonal immunoglobulin for passive immunoprophylaxis and cyclosporine and mycophenolate mofetil for graft-versus-host disease (GvHD) prophylaxis. She developed acute GvHD, and mycophenolate mofetil was added to her previous therapy on day 97 posttransplantation. On day 113, she presented with fever, cough, dyspnea, pancytopenia, and elevated levels of C-reactive protein. There were interstitial infiltrates in both lungs seen in chest computed tomography images (CT). All diagnostic tests for cytomegalovirus, adenovirus, and Pneumocystis, Aspergillus, and Legionella spp. were negative. The patient’s condition worsened despite probabilistic anti-infective treatment with ceftiraxone, teicoplanin, and caspofungin. A central tricytopenia prompted repeated transfusions. On day 123, she developed headache and vomiting. The fundus examination was normal. The brain CT showed a hypodense area on the right side of the thalamus. Her respiratory status deteriorated with severe hypoxemia requiring oxygen therapy.

Diff-Quick-stained cytospin-prepared sputum smears (Microscopy Hemacolor MERCK catalog no. 65044-93) showed tachyzoites suggestive of Toxoplasma gondii (Fig. 1). T. gondii was detected with specific direct immunofluorescence tests on both bone marrow and sputum specimens. Real-time PCR targeting a repetitive 529-bp DNA fragment of T. gondii (GenBank accession no. AF487550) was positive in both blood and sputum samples.

A treatment combining pyrimethamine (50 mg daily after a 100-mg loading dose) and sulfadiazine (1,250 mg four times daily) was initiated, and the patient steadily improved. Blood and sputum specimen collected after 14 days of treatment were negative for T. gondii PCR. There was progressive hematological reconstruction (as evidenced by blood numeration) and a reduction in size of the brain lesion on the CT. The girl was discharged from hospital after 20 days of pyrimethamine-sulfadiazine treatment.

Toxoplasma gondii is a protozoan parasite of cats and other Felidae. Humans and other homeotherm animals serve as intermediate hosts (15). In immunocompetent hosts, the acute phase is usually asymptomatic. In any case, bradyzoites remain trapped within tissues inside cysts, which can persist in the brain, heart, liver, kidney, and muscles. The immune system controls cyst disruption. As cyst disruption occurs, the released bradyzoites rapidly convert to tachyzoites. Tachyzoites are seen in primary or reactivated infection; their detection is the hallmark of active infection (4).

Disseminated toxoplasmosis is a rare but often fatal opportunistic infection of immunodeficient patients, albeit it has infrequently been reported in immunocompetent patients (2). It can occur in patients with AIDS or in recipients of solid organ or bone marrow transplants (BMT). It usually develops as a primo-infection in seronegative solid organ transplant recipients when the donor was seropositive; i.e., the infection results from the reactivation of Toxoplasma cysts enclosed within a contaminated transplanted organ (10). On the other hand, toxoplasmosis after BMT usually occurs in seropositive recipients and is more common when the donor is seronegative, the donor’s naive immune system apparently contributing to the reactivation of toxoplasmosis in BMT recipients. However, a few cases in BMT have been reported in patients with negative pretransplant serology for Toxoplasma, suggesting a transmission of infection via donor marrow and blood products (3). In addition to positive toxoplasmosis serology before

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of this high sensitivity is that the clinical interpretation of a positive PCR is not always straightforward, since it might be due to a controlled toxoplasmosis reactivation in asymptomatic patients (1). Quantitative real-time PCR might be useful in differentiating between infection and disease. The data from Martino et al. suggest that preemptive therapy based on the results of quantitative real-time PCR might be effective in preventing death associated to T. gondii infections in BMT patients (6).

To our knowledge, this is the first report where the diagnosis of disseminated toxoplasmosis was based on the visualization of T. gondii tachyzoites in sputum smears. This diagnosis led to the prompt initiation of adequate treatment, with complete recovery of the patient. Pretransplant Toxoplasma serology should be tested in both recipient and donor to identify patients at risk of infection. Chemoprophylaxis should be considered in patients with risk factors of disseminated toxoplasmosis reactivation such as positive pretransplant serology, allogeneic transplant, and GvHD and its treatment. Prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMZ) in AIDS patients has proven effective against T. gondii reactivation (12) and can be used after allo-BMT. A high dosage of TMP-SMZ appears to be more effective for the prevention of toxoplasmosis than a low one (13). In part because TMP-SMZ might reduce hematopoiesis, prophylactic treatment against Toxoplasma in BMT recipients is rarely used nowadays even in high-risk patients, and no evidence-based data support this practice (5, 13, 16). Nevertheless, the empirical observation that patients who do not receive chemoprophylaxis developed disseminated toxoplasmosis is in keeping with the AIDS data (6). Thus, systematic chemoprophylaxis targeted at high-risk patients would effectively prevent reactivation of toxoplasmosis in BMT recipients (8). The use of sputum examination should be advocated as an additional diagnosis technique of pulmonary toxoplasmosis since the occurrence of T. gondii tachyzoites in sputum allows early diagnosis and instigation of therapy.

We thank Michel Thuriaux for helpful comments and for checking the English of the manuscript.

REFERENCES