Respiratory distress of unknown etiology in a transplant recipient: think toxoplasmosis!

Ameer Hamza, Ian Jacob Anderson, Basim Al-Khafaji

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ABSTRACT

Disseminated toxoplasmosis is a life-threatening disease in immunocompromised individuals. Infection is contracted from handling contaminated soil, cat litter, or through the consumption of contaminated water or food. It is the third most common lethal foodborne infection in the United States. In transplant patients, most cases occur as a result of reactivation of a latent infection resulting from immunosuppression. We present a case of disseminated toxoplasmosis diagnosed at the time of autopsy. This case emphasizes the importance of maintaining a high index of clinical suspicion and active disease surveillance in this era of sophisticated diagnostic testing.

Keywords: Autopsy; Allografts; Immunosuppression; Opportunistic infections; Kidney transplantation; Toxoplasmosis.

INTRODUCTION

Toxoplasmosis is caused by the protozoan parasite *Toxoplasma gondii*. It is a zoonotic disease with worldwide distribution and an opportunistic pathogen primarily infecting immunocompromised individuals. Global prevalence is 10-80%, but clinically significant disease is uncommon. In the United States, approximately 225,000 cases of toxoplasmosis are reported annually, resulting in 750 deaths, which makes *T. gondii* the third most common cause of lethal foodborne infection in the United States.

In organ transplant recipients, toxoplasmosis most commonly results from reactivation of latent infection; however, donor-transmitted infection or de novo infection are known to occur. In these patients, the most common presentations are retinochoroiditis, cerebritis, pneumonitis, myocarditis, and disseminated disease. We describe the autopsy findings in a renal transplant recipient with disseminated toxoplasmosis diagnosed at autopsy.

CASE REPORT

A 49-year-old Caucasian male with a past medical history of end stage renal disease secondary to diabetes mellitus, status post deceased-donor kidney allograft and on immunosuppression with prednisone, tacrolimus and mycophenolate mofetil; hypertension, obesity, peripheral vascular disease, and anemia presented to the emergency department 6 weeks post-transplantation procedure with dehiscence of his right lower quadrant surgical wound. Upon admission, the patient was noted to be acidicotic, hypovolemic, hyperkalemic, and in respiratory distress, necessitating intubation. He was urgently taken to the operating room for debridement and closure of the wound which he tolerated well; however, during the course of his hospital stay he exhibited altered mental status with continued respiratory distress. Despite receiving high flow supplemental oxygen, oxygen saturations were continually in the low 90% range. He also exhibited marked leukocytosis with a white blood cell count of 26,400/mm³
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Blood and urine cultures yielded no growth. CMV serology by PCR was negative with quantitative CMV DNA less than 250 CPY/ml (NR: < 250 CPY/ml). Toxoplasma serology was not ordered and was not done as a pre-transplant work up. His arterial partial oxygen pressure became critically low at 35.4 mmHg (NR: 80-100 mmHg) and he was intubated, however, there was no improvement of the respiratory status, and the patient experienced cardiorespiratory arrest. Resuscitative efforts were unsuccessful and the patient was pronounced deceased with a postmortem examination requested and subsequently performed.

**AUTOPSY FINDINGS**

Most significant finding at the autopsy was disseminated toxoplasmosis with *T. gondii* identified within the bilateral lungs, heart, liver, pancreas, bilateral native kidneys, transplanted kidney, spleen, bone marrow, and central nervous system (Figure 1 and 2).

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**Figure 1.** Photomicrographs of the heart showing the *T. gondii* cyst (arrowhead and inset) (**A** – H&E, 400X; **B** – *T. gondii* stain 1000X).

**Figure 2.** Photomicrographs of the brain showing the *T. gondii* cysts in the Midbrain (**A** – H&E, 400X) and the Brainstem (**B** – H&E, 400X).
Additional findings included cardiomegaly with left ventricular hypertrophy and moderate calcific atherosclerotic coronary artery disease; bilateral, multifocal necrotizing bronchopneumonia secondary to *T. gondii* (Figure 3); and hepatosplenomegaly.

Immediate cause of death was cardiopulmonary arrest secondary to respiratory distress. Underlying cause was disseminated toxoplasmosis as a consequence of medical immunosuppression. Manner of death was natural.

**DISCUSSION**

*T. gondii* infection in renal transplant patients is rare, but can be rapidly progressive and life threatening. Missed diagnosis is one of the causes of high mortality. Wulf et al.\(^3\) found that 43% of cases were diagnosed at autopsy. Recent data in this regard are not available; however, our case indicates that clinically missed toxoplasmosis in the setting of post-transplant immunosuppression remains a concern today.
T. gondii has two distinct life cycles. The sexual cycle occurs only in cats which are the definitive host. The asexual cycle occurs in other mammals, including humans and some avian species. In humans, infection occurs by ingestion of oocysts from handling contaminated soil or cat litter or through the consumption of contaminated water or undercooked meat of infected animals. Our patient, in fact, did own a cat.

Clinical presentation is nonspecific. Fever occurs frequently, followed by flu-like symptoms, lymphadenopathy, visual changes, pneumonia, and neurologic manifestations such as headache, seizures, altered mental status, and focal neurologic deficits. Our patient exhibited altered mental status and severe respiratory distress which correlated with the autopsy findings of bilateral, multifocal necrotizing bronchopneumonia and central nervous system involvement.

Diagnosis is confirmed by serology, tissue biopsy, or PCR assay for the presence of T. gondii DNA. Serology is of limited value in the setting of reactivation of a latent infection. Moreover, interpretation of serologic tests in immunocompromised patients is not straightforward and absence of specific antibodies does not exclude active disease. The duration for which T. gondii can be detected in blood is not clear. Additionally, T. gondii is only present intermittently in cerebrospinal fluid for unknown reasons, which limits the use of PCR assay. However, it is found to be useful in acute primary infection. Tissue biopsy is not only an invasive procedure, but is also limited by sampling artifact. Maintaining a high index of clinical suspicion is therefore the cornerstone of proper diagnosis. Toxoplasmosis should be high on the list of differential diagnoses in a post-transplant patient with respiratory distress and culture negative sepsis.

Imaging studies are valuable in cerebral and pulmonary toxoplasmosis. MRI is superior to CT scan in cerebral toxoplasmosis. Toxoplasma lesions on MRI appear as high-signal abnormalities on T2-weighted studies and demonstrate a rim of enhancement surrounding the edema on T1-weighted, contrast-enhanced images. CT scans show multiple bilateral cerebral lesions. Chest radiographs in toxoplasma pneumonia usually demonstrate interstitial infiltrate. In our patient, a CT of the head showed asymmetric decreased attenuation in left frontal lobe white matter suggestive of microangiopathy or encephalomalacia. No acute intracranial abnormality or evidence pointing to T. gondii was noted. Chest x-ray showed mild to moderate prominence of the pulmonary vessels, interstitial infiltrates, and changes consistent with atelectasis.

For more prevalent infections, such as HIV, HBV and HCV there is general agreement with respect to pre-transplant screening guidelines. Regarding screening for other infectious agents, including T. gondii, each transplant center follows different protocols. Many transplant centers screen both donors and recipients for anti-Toxoplasma antibody, especially in cases of heart transplant. Screening of donors and recipients for anti-Toxoplasma antibody is not routinely performed for noncardiac transplants, but is part of the screening panel at some transplant centers. Seropositivity is not a contraindication to transplantation but allows for administration of appropriate prophylaxis. Our transplant center does not perform toxoplasma screening routinely.

Moreover, trimethoprim-sulfamethoxazole prophylaxis against Pneumocystis jiroveci is thought to be effective in preventing toxoplasmosis. For these reasons routine pre-transplant screening for T. gondii is not recommended in kidney transplant donors and recipients, especially in low prevalence areas. Toxoplasma serology was neither performed on our patient nor the donor. The patient was initially started on trimethoprim-sulfamethoxazole prophylaxis; however, it was discontinued due to resultant hyperkalemia.

Pyrimethamine is the mainstay of treatment. The most effective available therapeutic combination is pyrimethamine plus sulfadiazine or trisulfapyrimidines. Unfortunately, our patient expired before treatment could be initiated.

This case emphasizes the importance of maintaining a high index of clinical suspicion and active disease surveillance in this era of sophisticated diagnostic testing.

The manuscript is in accordance with St. John Hospital and Medical Center review board’s recommendations.
REFERENCES

1. Papas G, Roussos N, Falagas ME. Toxoplasmosis snapshots: global status of Toxoplasma gondii seroprevalence and implications for pregnancy and congenital toxoplasmosis. Int J Parasitol. 2009;39(12):1385-94. PMid:19433092. http://dx.doi.org/10.1016/j.ijpara.2009.04.003.

2. Hökelek M. Toxoplasmosis. 2017 [cited 2017 Oct 11]. Available from: http://emedicine.medscape.com/article/229969-overview

3. Wulf MW, van Crevel R, Portier R, et al. Toxoplasmosis after renal transplantation: implications of a missed diagnosis. J Clin Microbiol. 2005;43(7):3544-7. PMid:16000502. http://dx.doi.org/10.1128/JCM.43.7.3544-3547.2005.

4. Schoondermark-van de Ven E, Galama J, Kraaijeveld C, van Druten J, Meuwissen J, Melchers W. Value of the polymerase chain reaction for the detection of Toxoplasma gondii in cerebrospinal fluid of patients with AIDS. Clin Infect Dis. 1993;16(5):661-6. PMid:8507757. http://dx.doi.org/10.1093/clinids/16.5.661.

5. Fischer SA, Lu K. Screening of donor and recipient in solid organ transplantation. Am J Transplant. 2013;13(Suppl 4):9-21. PMid:23464994. http://dx.doi.org/10.1111/ajt.12094.

6. Gourishankar S, Doucette K, Fenton J, Purych D, Kowalewska-Grochowska K, Preiksaitis J. The use of donor and recipient screening for toxoplasma in the era of universal trimethoprim sulfamethoxazole prophylaxis. Transplant. 2008;85(7):980-5. PMid:18408578. http://dx.doi.org/10.1097/TP.0b013e318169bebd.

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Correspondence
Ameer Hamza
Department of Pathology - St John Hospital and Medical Center
22101 Moross Road – Detroit/MI – USA
48236
Phone: +1 (313) 613-7511 / Fax: +1 (313) 343-8318
ameerhamza7@hotmail.com