Fatal Disseminated Acanthamoeba lenticulata Infection in a Heart Transplant Patient

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We report a fatal case of disseminated acanthamelibiasis caused by Acanthamoeba lenticulata (genotype T5) in a 39-year-old heart transplant recipient. The diagnosis was based on skin histopathologic results and confirmed by isolation of the ameba from involved skin and molecular analysis of a partial 18S rRNA gene sequence (DF3).

Acanthamoeba is 1 of 3 genera of free-living amebae that commonly cause disease in humans (1). These protozoa have been implicated in local infections, such as amebic keratitis, mainly in immunocompetent contact lens wearers, and in the mostly fatal, granulomatous amebic encephalitis in immunocompromised patients with HIV/AIDS and immunosuppressant-treated patients, including organ transplant recipients (2–4). Disseminated acanthamelibiasis (DA), which is defined as widespread extracerebral disease, is extremely rare, but its incidence has increased in recent years (5). Among DA reported, only 5 occurred in solid organ (3 lung and 2 kidney) transplant recipients (4). We report a fatal case of DA in a heart transplant recipient and identify Acanthamoeba lenticulata (genotype T5) as the cause of life-threatening disease.

The Case

A 39-year-old man from Martinique had received a second heart transplant in March 2004 because of chronic rejection. He had received his first transplant 14 years earlier because of alcohol-related dilated cardiomyopathy. Skin complications included epidermoid carcinoma on the right leg in 1995 and diffuse viral warts on the trunk in 2003. Maintenance immunosuppression after the second heart transplant in 2004 included cyclosporine (220 mg/day), prednisone (20 mg/day), and mycophenolate mofetil (500 mg/day). The latter drug was withdrawn because of pancytopenia. Postsurgery complications included acute refractory bleeding (aortic anastomosis), cytomegalovirus infection of the gut, bacterial pulmonary infection, and postoperative renal failure that required chronic hemodialysis that prolonged his stay in the intensive care unit (ICU) to 5 months.

In January 2006, after a short visit to Martinique, the patient was transferred to our institution because of fever, dyspnea, and acute costal and back pain, with suspected osteitis underlying cutaneous lesions. Two months earlier, 4 trunk and leg abscesses or carbunclelike skin lesions had developed. Despite oral antistaphylococcal therapy, these lesions spread and became ulcerated and painful. Three ulcerated, violaceous plaques with undermined deep-infiltrated margins were present: 1 on the trunk (largest diameter 5 cm) (Figure, panel A) and 1 on each thigh. Three subcutaneous abscesses were present on the trunk and their puncture yielded a brown liquid. The differential diagnosis included pyoderma gangrenosum, neutrophilic dermatoses, mycobacteriosis, cutaneous bacterial infection, and calciphylaxis (chronic hemodialysis).

The first histologic examination of a periulcerated skin lesion (punch biopsy specimen) showed diffuse dermal and hypodermal neutrophil infiltration and sparse histiocytelike cells (Figure, panel B). No infectious elements were identified. Biologic data indicated an inflammatory syndrome (C-reactive protein 250 mg/L [normal <5 mg/L], procalcitonin 25 ng/mL [normal <1 ng/mL]), with increased elevated circulating neutrophil counts (10.9 × 10⁹ cells/L) and anemia (hemoglobin 7 g/dL). Cultures of blood, abscess fluid, and involved skin were repeatedly negative for bacterial,
mycotic, or parasitic agents. A computed tomographic body scan showed a massive abscess under the left kidney associated with pulmonary nodules without cutaneous calciphylaxis. Positron emission tomography scan confirmed those abnormalities and showed extensive and severe bone osteomyelitis.

Atypical pyoderma gangrenosum with visceral involvement was considered and treated with 3 intravenous prednisolone pulses. After minor initial improvement, the patient’s condition deteriorated, and 10 days later septic osteomyelitis. Those abnormalities and showed extensive and severe bone involvement was considered and treated with 3 intravenous prednisolone pulses. After minor initial improvement, the patient’s condition deteriorated, and 10 days later septic osteomyelitis.

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Table. rDNA sequences of Acanthamoeba isolate (2/533) from the patient, a keratitis isolate (GAK1), 3 environmental T5 subtypes, and 4 other genotypes from persons with nonkeratitis infections

<table>
<thead>
<tr>
<th>Genotype (strain)</th>
<th>DF3 sequence (5′→3′)*</th>
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<tbody>
<tr>
<td>T5 (2/533)</td>
<td>CAAAACACC GGCGTTAATCTCTTCTT----CGGGGTTAAGCGTTGCTGAAAT</td>
</tr>
<tr>
<td>T5 (GAK1)</td>
<td>CAAAACACC GGCGTTAATCTCTT----CGGGGTTAAGCGTTGCTGAAAT</td>
</tr>
<tr>
<td>T5 (7/2)†</td>
<td>CAAAACACC GGCGTTAATCTCTT----CGGGGTTAAGCGTTGCTGAAAT</td>
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<tr>
<td>T5 (PD2S)‡</td>
<td>CAAAACACC GGCGTTAATCTCTT----CGGGGTTAAGCGTTGCTGAAAT</td>
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<tr>
<td>T5 (FLAVIV)§</td>
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</tr>
<tr>
<td>T4</td>
<td>CAAAACACC GGCGTTAATCTCTT----CGGGGTTAAGCGTTGCTGAAAT</td>
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</tr>
<tr>
<td>T12</td>
<td>CAAAACACC GGCGTTAATCTCTT----CGGGGTTAAGCGTTGCTGAAAT</td>
</tr>
</tbody>
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*Sequence differences are shown in boldface.
†Five isolates at European Molecular Biology Laboratory (EMBL).
‡Eight isolates at EMBL.
§One isolate at EMBL.

Conclusions

Protozoan infections are rare in heart transplant recipients, unlike in lung transplant recipients (8,9). To our knowledge, our patient, whose DA involved skin, bones, lungs, intraabdominal organs, and perhaps the brain, represents the first case to be reported in a heart transplant recipient. In a recent review of the literature, Duarte et al. (4) reported 5 cases of DA in lung (60%) or kidney (40%) transplant recipients. DA was difficult to diagnose in the patient, with 60% of the diagnoses made postmortem, which is similar to 74% of the diagnoses in 23 HIV/AIDS patients (2). The patient’s clinical picture was atypical because his lesions were pyodermal ulcers with subcutaneous abscesses, whereas the most frequently reported clinical skin manifestations were painful nodules, purpura, and pustules (10). Furthermore, the first histologic examination did not identify cysts. Acanthamoeba trophozoites with characteristic acanthopodia, cytoplasmic vacuoles, and a prominent nucleolus, especially in dermal vessels, were observed only after staining of the second biopsy specimen with hematoxylin and eosin in a context of strong clinical suspicion of DA. When reexamined retrospectively, the first skin biopsy specimen contained some pathogens, but trophozoites had been misidentified as histiocytelike cells.

Another important finding was the identification of the DA-causative agent as genotype T5, which is commonly
found in the environment (11) and corresponds to *A. lenticulata*. This species has been isolated from nasal mucosa of persons without documented amebic infection (12). Although *A. lenticulata* has been shown to be pathogenic (12), genotype T5 was only recently isolated from a patient with keratitis (13). To our knowledge, our patient has the first case in which genotype T5 is the etiologic agent of a nonkeratitis, life-threatening DA infection.

*Acanthamoeba* spp. are free-living amebae found in soil, water, air, humans, and various animals (14). Depending on the molecular methods used (i.e., nuclear 18S rRNA or 16S rRNA mitochondrial gene amplification), 15 genotype sequences have been identified in environmental and human strains (T1–T15, Table). While genotype T4 is the most prevalent (79% of isolates) (15), only 1 *A. lenticulata* strain isolated from a patient with ocular keratitis had genotype T5 (13).

This case should alert physicians to a rare but life-threatening infection with *A. lenticulata* (genotype T5) in a heart transplant recipient. In organ transplant patients, when sterile cutaneous ulcers or subcutaneous abscesses develop that fail to respond to antibacterial treatments and pulse corticosteroids, histologic analysis should emphasize identifying *Acanthamoeba* spp.

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Dr Barete is a dermatologist at the Hôpital Tenon of the Université Pierre-et-Marie-Curie in Paris. His research interests include infectious complications, mycotic skin infections, Kaposi sarcoma, and Epstein-Barr virus lymphoproliferation in organ transplant recipients.

**References**


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