CHARACTERIZATION OF A PREVIOUSLY UNDESCRIBED LAGENIDIUM PATHOGEN ASSOCIATED WITH SOFT TISSUE INFECTION: INITIAL DESCRIPTION OF A NEW HUMAN OOMYCOSIS

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The genus *Lagenidium* in the class *Oomycetes* includes more than 50 species, most of which occur as parasites of algae, fungi, nematodes, crustaceans, or insect larvae. It was first recognized as a medically important genus in 1999, when a previously undescribed species of *Lagenidium* was identified as a cause of subcutaneous and systemic disease in dogs. More recently, the authors have isolated a second pathogenic *Lagenidium* species from tissues obtained from four dogs and one person with chronic subcutaneous infections. The purpose of this report is to characterize this newly recognized pathogen, and to describe for the first time the clinicopathologic features associated with *Lagenidium* sp infection in a human patient.

Clinical findings in both the human and canine patients were characterized by progressive deep cellulitis (often with numerous draining tracts) involving one or more extremities. Amputation was curative in two dogs with lesions limited to a single distal extremity, and repeated aggressive surgical resection combined with longterm itraconazole and terbinafine administration was curative in a dog with multiple recurrent cutaneous lesions. In the human patient, chronic cellulitis involving a single distal lower extremity failed to respond to voriconazole but later showed marked improvement after administration of posaconazole. Histologically, lesions were characterized by granulomatous inflammation centered around broad, infrequently septate hyphae; eosinophilic inflammation, necrosis, and suppuration were variably present. Immunoblot analysis of the serologic response of three affected dogs to soluble mycelial extracts of *L. giganteum* and of the previously described pathogenic *Lagenidium* species was performed, and indicated that each dog's serum recognized a large number of antigens of both *Lagenidium* species.

Culture of affected canine tissues on peptone-yeast-glucose agar at 30C for 3 days yielded growth of a colorless to white mostly submerged colony. The human isolate produced small, restricted, heaped, white to cream-colored colonies approximately 3 to 5 mm in diameter after 10 days incubation at 25C on potato flakes agar. Short hyphal fragments of varying widths (10 - 30 um) were present; however large, globose to oval-shaped cells (to 116 um in diameter) were the prominent feature. Molecular identification of the isolates was performed by amplifying and sequencing the 18s and ITS regions of the ribosomal RNA gene. The 18s region shared 97.3% identity with *Lagenidium giganteum*, 97.3% identity with the previously described pathogenic *Lagenidium* species, 96.2% with *L. myophilum,* and 96.1% with *L. humanum.* In the ITS region, three of the canine isolates were identical, with the fourth canine isolate and the human isolate differing from the other three by 2 bp each. In comparison with other *Lagenidium* species, the ITS region of the clinical isolates shared 65.8% identity with the previously described pathogenic *Lagenidium* species, 65.7% identity with both *L. giganteum* and *L. humanum*, and 60.3% identity with *L. myophilum.* Cladistic analysis supported placement of the clinical isolates in the Family Pythiales.

The discovery of a second mammalian pathogen in the genus *Lagenidium* and the identification for the first time of *Lagenidium* sp infection in a human patient suggest that the oomycetes represent an emerging and possibly underdiagnosed group of medically important pseudofungi.