Phaeohyphomycosis Caused by *Phaeoacremonium inflatipes*

ARVIND A. PADHYE,†* MIRIAM S. DAVIS,‡ DALE BAER,‡ ANNE REDDICK,‡ KAUSHAL K. SINHA,† AND JULIANA OTT§

Mycotic Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333; South Carolina Department of Health and Environmental Control, Columbia, South Carolina 29202; and Lexington Medical Center, West Columbia, South Carolina 29169

Received 2 March 1998/Returned for modification 8 April 1998/Accepted 1 June 1998

*Phaeoacremonium inflatipes*, one of three species previously classified as strains of *Phialophora parasitica*, was identified as the causal agent of a subcutaneous infection of the left foot of an 83-year-old woman from South Carolina. The patient had a granulomatous growth over the anteromedial aspect of her left foot. It was surgically excised, which led to complete healing without complications. Tissue sections of the excised mass stained with hematoxylin and eosin and Gomori’s methenamine silver strains showed many septate hyphal elements of various lengths, some exhibiting brownish pigment in the cell walls of the hyphae. Portions of the tissue, when cultured, yielded many colonies which were initially glabrous, off white becoming velvety, greyish brown on aging. Microscopically, their hyphae were septate, branched, and phaeoid and bore lateral and terminal, erect, septate conidiophores. The conidiogenous cells (phialides) were terminal or lateral, mostly monophialidic, subcylindrical to spiny in shape, and constricted at their bases and bore funnel-shaped, inconspicuous collarettes at their tips. The conidia were subhyaline, oblong, and ellipsoid to allantoid.

In 1996, Crous et al. (3) proposed the new hyphomycete genus *Phaeoacremonium* with *Phaeoacremonium parasiticum* (= *Phialophora parasitica*) as its type species. Morphologically, the genus *Phaeoacremonium* is intermediate between the genera *Acremonium* and *Phialophora*. It is distinguished from *Acremonium* by its phaeoid vegetative hyphae and conidiophores and from *Phialophora* by its narrow, spinelike (aculeate) conidiogenous cells and inconspicuous collarettes. A detailed study by Crous et al. (3) of a large number of isolates originally identified as *P. parasitica* made it obvious that it represented a cluster of related and morphologically well-defined species producing subcylindric to aculeate phialides with inconspicuous collarettes not at all resembling those of other *Phialophora* species. An earlier analysis of restriction fragment length polymorphism and RNA gene sequence data from isolates of *Phialophora americana*, *P. verrucosa*, *P. richardiae*, and nine isolates of *P. parasitica* by Yan et al. (11) revealed that six of the nine *P. parasitica* isolates belonged to one distinct group. The other three isolates each exhibited a unique restriction map. However, they were closer to *P. parasitica* than to any other species of *Phialophora* studied. Crous et al. (3) proposed to accommodate the isolates that caused human infections, previously grouped under *Phialophora parasitica*, in three species including *Phaeoacremonium parasiticum* and two new species, *P. inflatipes* and *P. rubrigenum*. They also described three additional species (*Phaeoacremonium aleophilum*, *P. angustius*, and *P. chlamydosporum*) that are not known to cause human infections. We report a subcutaneous, granulomatous infection of the left foot of a woman from South Carolina and describe salient features of the causal agent, *P. inflatipes*.

**Case report.** An 83-year-old Caucasian woman reported pain in her left knee, difficulty in walking and weight bearing, and the need to sit down for long periods of time. She also had pain in her left foot with a large lump on its medial side; this lump had been enlarging. On examination, she was found to have fusiform swellings over both knees and had marked patellofemoral crepitation on both sides. However, it was more pronounced on the left than on the right side. There was no ligamentous instability, and she had good neurovascular status in both lower extremities. Examination of the left foot revealed a soft mass over the anteromedial aspect of her foot. It was minimally tender on deep palpation. When surgically excised, the mass looked like a foreign body surrounded by a granuloma. Sections of the excised tissue stained with hematoxylin and eosin, periodic acid-Schiff, and Gomori’s methenamine silver (GMS) stains revealed dense, proliferated, fibrous connective tissue showing an inflammatory reaction composed of proliferated capillary cells. Multinucleated foreign body-type giant cells were present. Epithelioid cells were prominently seen in the reactive process. Sections stained by periodic acid-Schiff and GMS stains demonstrated numerous septate, hyphal fragments of various lengths measuring 2.0 to 3.0 μm in diameter (Fig. 1). Sections stained by hematoxylin and eosin showed a few phaeoid hyphal elements, consistent with the diagnosis of phaeohyphomycosis. As has been the case with many other localized phaeohyphomycotic lesions, in this case, total excision of the granulomatous mass led to complete healing of the lesion without complications or relapse.

Portions of the excised tissue were cultured on Sabouraud glucose agar with chloramphenicol (Sab+c) and Sab+c containing cycloheximide. Morphology was studied on potato dextrose agar (PDA). Cultures were incubated at 25 and 37°C in the dark. Initially, colonies on Sab+c and PDA were glabrous, creamy to off white, and raised, becoming greyish brown after 8 days at both temperatures of incubation. Colonies on Sab+c and PDA at 25°C after 2 weeks were velvety, flat, olivaceous brown to grey, and 26 to 28 mm in diameter. Hyphae were septate, branched, and smooth walled to warty, becoming light brown, and measured 2.0 to 3.0 μm in diameter. Conidiophores were erect, simple or branched, subcylindrical, phaeoid...
in the lower portions, and lighter brown toward the tips. They were smooth, zero- to four-septate, and variable in length. Conidiogenous cells were terminal or lateral, mostly monophialidic, also polyphialidic, smooth walled, hyaline to pale brown, elongated, and subcylindric and were constricted at their bases. Occasionally, percurrent growth of phialides was also observed. At the tips, they bore narrow, cylindric to funnel-shaped, inconspicuous collarettes. Conidia aggregated into slimy heads at the tips of the phialides or slid down along their sides. The conidia were subhyaline and oblong-ellipsoid to allantoid (sausage shaped) and measured 3.0 to 5.0 by 1.5 to 2.5 μm (Fig. 2 and 3). The isolate grew well at 25 and 37°C (8 to 11 mm in 2 weeks) but failed to grow at 40°C. It hydrolyzed gelatin. Based on the inflated phialides with basal constrictions (near the basal septum), the isolate (96-034129 = CDC B-5747) was identified as *P. inflatipes*. It was sent to G. S. de Hoog, Centraalbureau voor Schimmelcultures (CBS), Baarn, The Netherlands, who confirmed our identification. It was deposited in the CBS collection as CBS 729.97.

Three species of *Phaeoacremonium* that cause human infections, namely, *P. parasiticum*, *P. inflatipes*, and *P. rubrigenum*, were formerly recognized under the genus *Phialophora* as strains of *P. parasitica*. The majority of human infections caused by these species that have been described in the literature were in the nature of subcutaneous abscesses, cysts, or chronic or acute arthritis in immunocompromised and immunocompetent hosts (1, 4, 6–9, 12) and were acquired through traumatic inoculation. Systemic infections, fungemia or endocarditis, have been rare (5, 10). In the present case, the host was apparently immunocompetent but did not remember having sustained any obvious trauma to her left foot.

*P. inflatipes* can be distinguished from *P. parasiticum* by its slightly larger conidia and, more importantly, by its inflated phialides, which are constricted at their bases. Those of *P. parasiticum* are more spindelike and not constricted at their bases. *P. inflatipes* has a wide geographic distribution, and it has been isolated from plants such as *Nectandra* sp. in Finland, stems of oak trees (*Quercus virginiana*), *Vitis vinifera* in Costa Rica and the United States, stems and roots of *Sorbus intermedia* in Germany, and soil in Tahiti. It has been isolated from a *Pyracantha* thorn (8) and from synovial fluid from a patient in the United States (3), toenails of a patient from Finland (3), and white granules from a eumycotic mycetoma in a patient from Venezuela (2).

When subcutaneous lesions caused by *P. parasiticum* or *P. inflatipes* were localized and diagnosed early, total surgical excision often led to uncomplicated healing. However, therapy for infections caused by *P. parasiticum*, *P. inflatipes*, and *P. rubrigenum* in immunocompromised hosts is not satisfactory. Antifungal agents such as amphotericin B, 5-fluorocytosine, ketoconazole, and terbinafine have been used in the past with variable success (5, 8, 9). In the present case, surgical excision led to uncomplicated cure of the infection.
REFERENCES