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Phaeohyphomycosis of the Nasal Sinuses Caused by a New Species of *Exserohilum*

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A 27-year-old man with a 6-year history of allergies developed nasal polyps that occluded his nose and prevented visual examination beyond the nasal vestibules. Histological examination of the polyps and bony tissue revealed septate, dematiaceous hyphae invading the bone trabeculae. A dematiaceous fungus was isolated in pure culture from the diseased tissue. Detailed mycological examination of the isolate showed that it produced numerous, distinctive poroconidia from erect, geniculate, sympodial conidiophores. The conidia were straight and cylindroellipsoidal, had 8 to 13 distosepta, and had protruding hila. The outer cell walls of the conidia, which were initially smooth, became unevenly roughened on aging. Comparison with other *Exserohilum* species revealed that the isolate represented an undescribed species; it is named *Exserohilum mcginnisii* sp. nov.

In immunocompromised as well as immunocompetent patients, phaeohyphomycosis may occur as sinusitis, pansinusitis, keratitis, endocarditis, osteomyelitis, cutaneous infections, and meningoencephalitis. Among the various etiologic agents of phaeohyphomycosis, *Bipolaris hawaiiensis* (*Drechslera hawaiiensis*) (2, 8, 23), *B. spicifera* (*D. spicifera*) (2, 7, 19, 22, 24), and *Exserohilum rostratum* (*D. rostrata*) (1, 2) are being recognized with increasing frequency. *B. spicifera* and *E. rostratum* are also known to be opportunistic agents of subcutaneous and systemic phaeohyphomycosis in such lower animals as cats (3, 16), dogs (11), horses (9, 10, 20), and cattle (4, 15, 17, 18). In this report, we describe a phaeohyphomycotic infection of the nasal sinuses caused by a new *Exserohilum* species.

CASE REPORT

A 27-year-old man with a 6-year history of allergies and nasal polyps was admitted to the Veterans Administration Medical Center, Tucson, Ariz., in May 1984. The patient complained of frontal sinus pain and occasional bloody discharges that contained bits of brownish tissue from both nostrils for several months prior to admission. The patient's history included nasal polypectomies in 1982 and 1983. He had had 4 months of desensitization therapy in 1981, with some relief of his allergic symptoms.

On initial physical examination, his nose was found to be occluded by polyps that allowed no visual examination of the nasal cavity. His oral cavity, oropharynx, and neck area were free of infection. Preoperative laboratory data included a leukocyte count of $8.4 \times 10^3/\mu l$ and a hemoglobin concentration of 16.9 g/dl. A preoperative chest roentgenogram was negative for active disease. The maxillary, sphenoidal, and ethmoid sinuses were filled with polyps. Bilateral Caldwell-Luc operations established an excellent airway. His condition improved dramatically postoperatively.

MATERIALS AND METHODS

Materials. A portion of the nasal polyp tissue obtained at surgery was placed in 10% neutral buffered Formalin for histopathological examination. The remainder of the specimen was sent to the microbiology laboratory for bacteriological and fungal cultures.

Methods. The biopsy tissue was homogenized in 0.9% sterile saline, and a portion was mounted in 10% KOH for direct microscopic examination. The rest of the homogenized tissue was streaked on petri plates of Trypticase (BBL Microbiology Systems, Cockeysville, Md.) soy agar with 5% sheep blood (Micro-Bio, Tempe, Ariz.) for isolation of bacterial pathogens on petri plates of Sabouraud dextrose agar (Emmons) containing 0.5 mg of chloramphenicol per ml (Sab+C) and Mycosel (BBL Microbiology Systems) agar for isolation of the fungal pathogens. The Trypticase soy agar plates were incubated at 35°C in 5 to 10% CO_2. The Sab+C and Mycosel agar plates were incubated at 25°C in the dark.

RESULTS

Direct examination. Microscopic examination of a KOH preparation revealed a moderate number of septate, subhyaline to pale-brown hyphal elements.

Bacteriological findings. Cultures on the Trypticase soy agar yielded a group C beta-hemolytic *Streptococcus* sp., *Haemophilus influenzae*, *Staphylococcus aureus*, and several colonies of a dematiaceous fungus. Similar colonies also grew on Sab+C and Mycosel agar, but growth on Mycosel agar was partially inhibited. Microscopic examination of teased mounts of the dematiaceous growth revealed branched, septate, dematiaceous hyphae and a moderate number of long, cylindrical, multicelled conidia with thick septa. The fungus was tentatively identified as a *Drechslera* sp. A subculture of the isolate and histological tissue sections of the polyps and bony tissue were sent to the Division of Mycotic Diseases, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Ga., for study.

Histological findings. Hematoxylin and eosin-stained sections of the polyps from both nostrils revealed fragments of fibromuscular stroma in strips and polypoid configurations surfaced by respiratory epithelium and fragments of bone. Varying degrees of edema, necrosis, and acute and chronic inflammation were noted. The inflammatory cell infiltrate included eosinophils, plasma cells, lymphocytes, macrophages, and focal neutrophils. There were no granulomas. In

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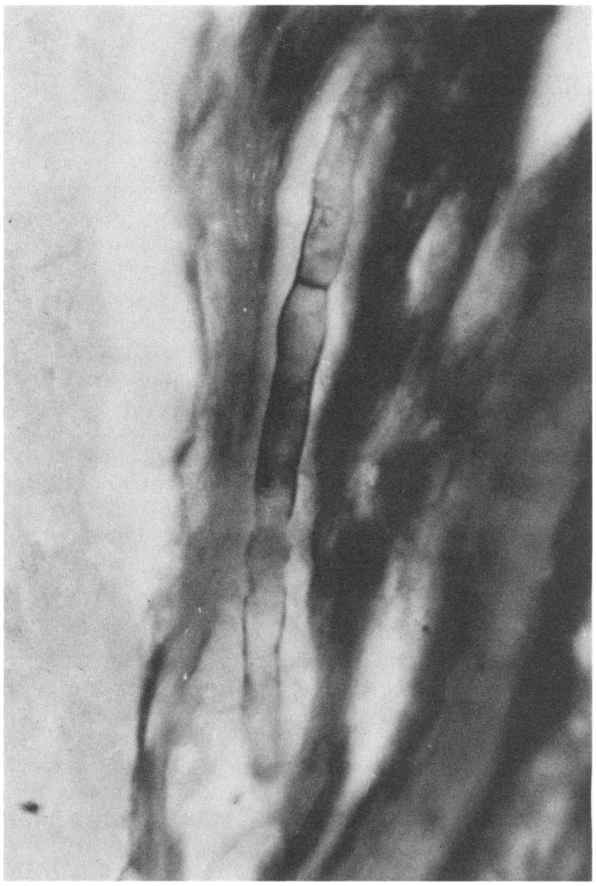

FIG. 1. Septate hypha of *E. mcginnisii* invading the bone trabeculae of the right nostril. Gomori methenamine-silver stain. ×1,100

the tissue stained by the Gomori methenamine-silver procedure, septate hyphae were seen within the bone trabeculae of the right nostril specimen (Fig. 1).

Mycological findings. The fungus was subcultured on Sab+C, Sab+C containing cycloheximide, and potato glucose agar (PGA). After 2 weeks of incubation at 25°C, the colonies on Sab+C and PGA were downy to woolly and raised in the central area. They were deep olivaceous gray to mousey gray (Fig. 2). Growth on Sab+C containing cycloheximide was partially inhibited. The isolate grew well at 37°C (25 to 27 mm in diameter after 2 weeks), but growth at 40°C was very slow (5 to 6 mm in diameter after 2 weeks).

Examination of slide culture preparations on PGA revealed hyphae that were septate, subhyaline to pale to mid brown, and 3.5 to 5.0 μm in diameter. The conidiophores were simple, erect or flexuous (wavy), and sympodial. Their upper portions were fertile and geniculate. The conidia were straight and cylindrical to cylindroellipsoidal, had rounded apices, measured 64 to 100 by 10 to 15 μm, and had 8 to 13 distosepta (having the individual cells each surrounded by a sac-like wall distinct from the outer wall) (Fig. 3). The pale end cells of the conidia were not separated from the intercalary golden-brown cells by thick-walled distosepta. The outer walls of the young conidia were smooth, later becoming unevenly roughened in 3-week-old cultures (Fig. 4). The hila of the conidia were black and distinctly protuberant (Fig. 5). Germination of the conidia was bipolar.

On the basis of Ellis' key (5), the isolate was tentatively identified as *D. halodes*, a fungus that has been shown to be conspecific as *E. rostratum* (12). The isolate resembles *E. gedarefense* (6) with respect to the shape of the conidia. It superficially resembles *E. rostratum* in the number of distosepta produced by the conidia. The conidia of *E. gedarefense* are slipper shaped, have four to six distosepta, and are smooth walled. The conidia of *E. rostratum* are

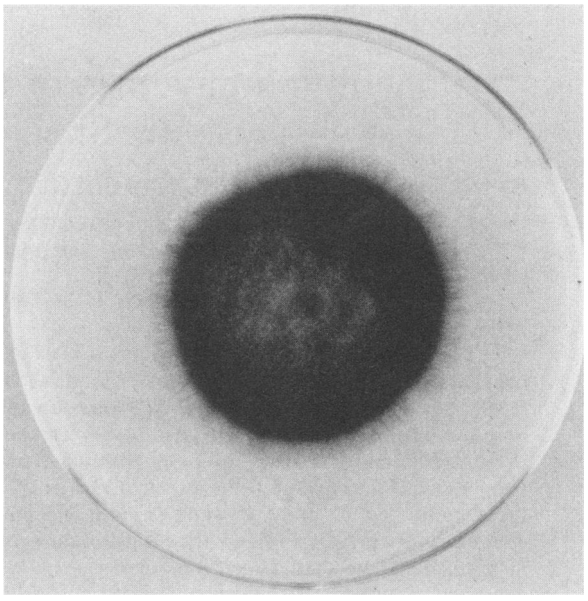

FIG. 2. Two-week-old colony of *E. mcginnisii* on PGA at 25°C.

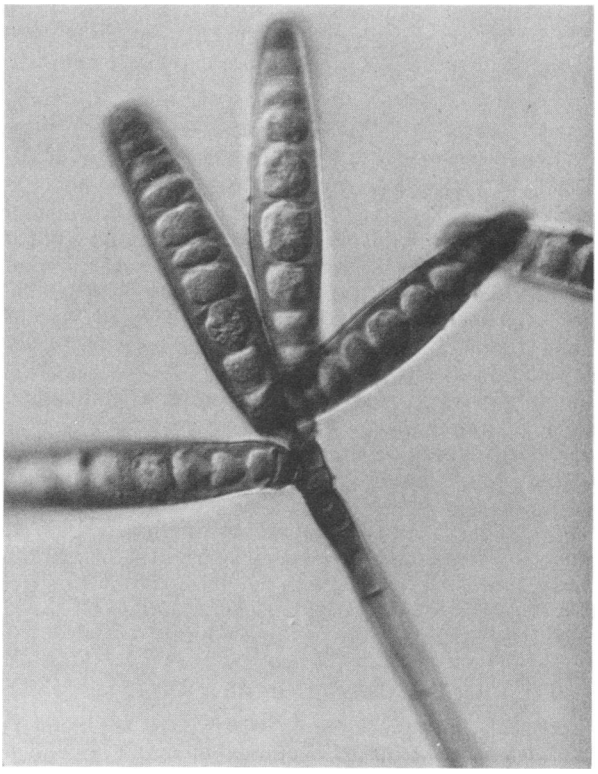

FIG. 3. Erect, sympodial conidiophore and cylindroellipsoidal conidia of *E. mcginnisii*. ×900

slightly curved or cylindrical to ellipsoidal to rostrate, have 6 to 16 distosepta, and are smooth walled. In both *E. gedarefense* and *E. rostratum*, the conidia have a thick, dark distoseptum at each end that separates the pale end cells from the golden-brown intermediate cells. The Arizona isolate produces conidia that are cylindroellipsoidal and smooth when young but becoming unevenly roughened with age. They conspicuously lack dark, thick-walled distosepta that separate the pale end cells from the other cells composing the conidia.

Because of these differences, the Arizona isolate was sent to the Commonwealth Mycological Institute, Kew, Surrey, England. There it was examined by A. Sivanesan. It was found to be distinctively different from all of the known *Exserohilum* species. The Arizona isolate, accordingly, is described as a new *Exserohilum* species. It is named in honor of Michael R. McGinnis, a friend and colleague, for his many taxonomic contributions, in particular in the area of the dematiaceous fungi pathogenic for humans and animals.

***Exserohilum mcginnisii* Padhye et Ajello, sp. nov.** Colonia in agaro cum tuberibus Solani tuberosi et dextroso composito lanuginosa vel lanata, elongata, area centrali erumpenti, sature olivaceo grisea vel sature murina (Ridgway Pl. LI), die decimo quinto crescens sub calore 25°C 35-37 mm diametro, 37°C 25-27 mm, 40°C 5-6 mm. Hyphae ramosae, septatae, pallidae vel modice brunneae, 3.5-5.0 μm diametro. Conidiophora simplicia, singillatim orta, erecta vel flexuosa, parte superiore geniculata, brunnea vel modice brunnea. Conidia recta, cylindrica vel cylindroellipsoidalia, pars media latissima, apicibus rotundatis, 64-100 (media 82.6) × 10-15 (medio 8) μm, octies as tredecies distoseptata, laevigata vel inaequaliter aspera. Hilum distincte prominens. Germinatio bipolaris.

Holotypus: Colonia exsiccata sub numero B-4030D conservata; e polypis nasalibus isolata de aegro in Valetudinario pro Militibus Veteranis Administrationis, Tucson, Arizona.

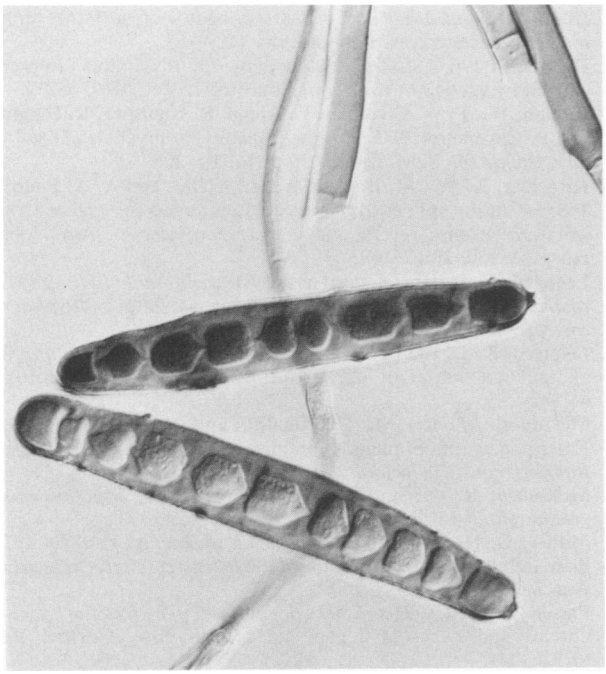

FIG. 4. Conidia of *E. mcginnisii* showing unevenly roughened outer walls and protruding hila. ×1,440

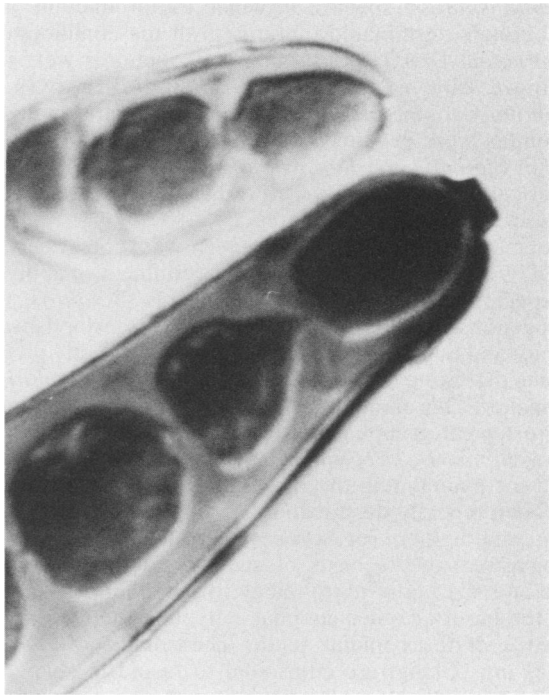

FIG. 5. Basal portion of a conidium showing a protruding hilum. ×2,440.

***Exserohilum mcginnisii* Padhye and Ajello, sp. nov.** Colonies on PGA downy to woolly, raised, erumpent in the central area, deep olive gray (Ridgway Plate LI) to deep mouse gray, and 35 to 37 mm in diameter at 25°C, 25 to 27 mm at 37°C, and 5 to 6 mm at 40°C after 2 weeks of incubation. Hyphae branched, septate, pale to mid brown, and 3.5 to 5.0 μm in diameter. Conidiophores simple, arising singly, erect or flexuous, upper part geniculate, brown to mid brown. Conidia straight, cylindrical to ellipsoidal, broadest in the middle with rounded apices, 64 to 100 (average, 8.26) by 10 to 15 (average, 8.0) μm, 8 to 13 distosepta, walls smooth to unevenly rough. Hilum distinctly protuberant. Germination bipolar.

Holotype, Colonia exsiccata B-4030D conservata. Deposited in the culture collection of the Division of Mycotic Diseases, Center for Infectious Diseases, Centers for Disease Control.

Habitat, Isolated from nasal polyps of a patient at the Veterans Administration Medical Center, Tucson, Ariz.

Living cultures derived from the isolate used to prepare the permanently preserved holotype (B-4030D) have been deposited in the culture collection of the Division of Mycotic Diseases, Center for Infectious Diseases, Centers for Disease Control, under accession number B-4030. Subcultures of B-4030 have also been deposited at the North Carolina Memorial Hospital, Chapel Hill (NCMH 2445), and at the American Type Culture Collection, Rockville, Md. (ATCC 60408).

DISCUSSION

In 1959, some species classified in the genus *Helminthosporium* were segregated and reclassified as *Bipolaris* and *Drechslera* species by Shoemaker (21) because, unlike

Helminthosporium species, in which the production of the apical conidia terminated the growth of the conidiophores, *Bipolaris* and *Drechslera* species conidiophores were indeterminate and extended by sympodial growth. In *Helminthosporium* species, the large, obclavate, multiseptate conidia were produced apically or laterally in verticils, while in *Bipolaris* and *Drechslera* species, the conidia were cylindrical to fusoid and were produced sympodially at the apical area of the conidiophores.

Shoemaker's treatment, however, was not widely accepted by many mycologists, as it was difficult to apply and the species classified under the genus *Bipolaris* were heterogenous. The genus *Exserohilum* was established by Leonard and Suggs (13) for species having distinctly protruding hila that were classified under the genus *Bipolaris* by Shoemaker. This eliminated the inconsistency and permitted a more logical grouping of species into three anamorphic genera, *Bipolaris*, *Drechslera*, and *Exserohilum*. The justification for maintaining the three genera and their concepts have been recently described at length by Alcorn (2).

The genera *Bipolaris*, *Drechslera*, and *Exserohilum* are distinguished on the basis of such characters as conidial shape and size, hilar morphology, origin of the germ tubes from the basal or other conidial cells, and the location and sequence of the conidial septa. The conidia of *Bipolaris* species are oblong, are ellipsoidal to fusoid in shape, and possess hila which are continuous with the conidial wall, with only a slight protrusion and truncated bases. The conidia germinate by germ tubes from one or both of the end cells. In *Drechslera* species, the conidia are cylindrical and do not have protruding hila. The conidia germinate by germ tubes which originate from any or all of the conidial cells. The conidia of *Exserohilum* species are ellipsoidal to fusoid and have distinctly protruding hila with truncated bases. The conidia germinate by germ tubes originating from either one or both of the end cells or other intermediate cells (2). The validity of this taxonomic treatment of the three anamorphic genera is further strengthened by their distinct teleomorphic states, namely, *Cochliobolus* (anamorph *Bipolaris*), *Pyrenophora* (anamorph *Drechslera*), and *Setosphaeria* (anamorph *Exserohilum*).

The distinguishing features of the species pathogenic for humans and lower animals of the two anamorphic genera *Bipolaris* and *Exserohilum* were studied in detail by McGinnis et al. (14). They did a careful study of numerous isolates that had been originally identified as *Drechslera* species and described in the literature as etiologic agents of phaeohyphomycosis. This revealed, in fact, that the isolates were *Bipolaris* and *Exserohilum* species. According to their findings, none of the *Drechslera* species have caused phaeohyphomycosis. Since 1936, when a *Helminthosporium* species was first reported to have caused nasal granulomas in cattle (4), numerous cases of phaeohyphomycosis caused by *Bipolaris* and *Exserohilum* species have been described, often with obsolete names. At present, two *Bipolaris* species (*B. hawaiiensis* and *B. spicifera*) are recognized as being pathogenic for humans and animals. Recently, a third species, *B. australiensis* (M. R. McGinnis, personal communication), has been identified as the causal agent of subcutaneous phaeohyphomycosis. The only *Exserohilum* species known to be etiologic agents of phaeohyphomycosis in humans and animals are *E. rostratum*, *E. longirostratum*, and *E. mcginnisii*.

In 1985, Rolston et al. (19) described a phaeohyphomycotic pansinusitis infection caused by *B. spicifera* in a 19-year-old woman. They also reviewed 10 published human infections caused by *Bipolaris* and *Exserohilum* species. They pointed out that the species classified in these genera were able to cause infections in apparently healthy hosts. Involvement of the paranasal sinuses, central nervous system, and other tissues was common and potentially life threatening. The ability of the above-mentioned species to grow at 40°C indicates their potential to be neurotropic pathogens. In the present study, *E. mcginnisii* was found to be thermotolerant.

It is recommended that when *Bipolaris* or *Exserohilum* species are isolated from clinical specimens, such isolates should not be regarded simply as contaminants; appropriate studies should be carried out to determine if they play an etiologic role.

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