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Short Communication

A Case of Oral Geotrichosis Caused by *Geotrichum capitatum* in an Old Patient

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SUMMARY: Geotrichosis is an uncommon fungal infection. *Geotrichum capitatum* is commonly acknowledged as an opportunistic fungal pathogen that causes systemic geotrichosis in immunocompromised patients, especially patients with acute leukemia and severe neutropenia. Here, we report a case of oral geotrichosis caused by *G. capitatum* in an old patient with no hematological malignancies. Fungal cells were detected in clinical specimens obtained with oral swabs using the KOH technique. Yeast colonies with peripheral hairs were exclusively isolated as fungi from the oral mucosa and feces of the patient. The isolates were identified as *G. capitatum* by morphological findings, sugar-assimilation tests, and the nucleotide sequences of the ITS regions of the rDNA. Effective treatment of the patient was achieved with amphotericin B syrup in accord with the results of in vitro susceptibility tests. *G. capitatum* should be recognized as a fungal pathogen involved in superficial infections of older persons, as should *Candida* spp., even in the absence of hematological malignancies.

Geotrichosis is an uncommon fungal infection. *Geotrichum capitatum*, an anamorph of *Dipodascus capitatus*, is commonly acknowledged as an etiologic species causing invasive and disseminated geotrichosis in immunocompromised patients with hematological malignancies such as acute leukemia and severe neutropenia (1). In the present paper, we describe a rare case of oral geotrichosis caused by *G. capitatum* in an old patient with no hematological malignancies.

A patient was a 92-year-old male and resided in a geriatric health services facility. He had hypertension, cardiac insufficiency, multiple cerebral infarctions, and dementia, and had not received any immunosuppressive drugs. Laboratory findings on February 27, 2004, were as follows: serum albumin, 3.4 g/dl; cholinesterase, 3,838 IU/l; AST, 18 IU/l; ALT, 12 IU/l; creatinine, 0.9 mg/dl; blood sugar, 97 mg/dl; WBC, 3.2 $\times 10^3/\mu$l; RBC, 272 $\times 10^4/\mu$l. On February 28, 2004, the patient was temporarily treated with amphotericin B (AMPH) syrup due to the presence of a black, hairy tongue. On June 22, 2004, the patient had a slightly mossy, flared, and swollen tongue, in which slightly clavate fungal cells were observed in scratch samples of tongue treated with a solution containing 15% potassium hydroxide and 40% dimethyl sulfoxide (KOH technique). Following administration of AMPH syrup for 1 month (3 times/day), the fungal cells disappeared from the tongue in the KOH specimen. On September 28, 2004, the tongue was again observed as mossy, flared, and swollen, and fungal cells with similar morphological features to those on June 22, 2004 were observed in a scratch sample from the tongue. The infection was cured by a second administration of AMPH syrup for 1 month. The patient died of acute bronchitis on April 26, 2005.

On June 22 and September 28, 2004, clinical specimens were obtained from the tongue and feces in order to isolate of fungal cells by scratching the area with sterilized swabs. The samples were then cultured at 30°C for 72 h on chromogenic agar plates (CHROMagar™ Candida; BD Co., Tokyo, Japan). A few green colonies were generated on the chromogenic agar from a fecal specimen obtained on June 22 and from a tongue specimen obtained on September 28, and these colonies were identified as *Candida albicans* by PCR targeting of the DNA topoisomerase II gene (2). White-pink colonies with peripheral hairs were generated from all the clinical specimens. Microscopy of this fungus revealed a clavate form and septate hyphae, which were similar morphological characteristics to those of the fungus observed by direct examination using the KOH technique. Therefore, we identified this fungus as an etiologic agent in this patient and we attempted to further characterize it.

For identification of the fungus, slide cultures using potato dextrose agar (PDA; Difco Laboratories, Detroit, Mich., USA), sugar assimilation tests using API 20C AUX (Bio Merieux SA, Lyon, France), and nucleotide sequencing of the internal transcribed spacer (ITS) regions of the rDNA were performed. In the slide cultures, sympodial conidia were observed at the apices of branches, and annelloconidia were also found. These microscopic features of the isolates are compatible with those of *G. capitatum* (3). In the sugar assimilation tests, the isolates assimilated glucose and glycerol, and their ability to assimilate sugars coincided with that of *G. capitatum*. For more specific identification of the isolates, the ITS-1 and ITS-2 regions of the isolates were sequenced. Genomic DNAs of the isolates were purified using a DNA purification kit (FirstDNA kit; Qbiogene Inc., Carlsbad, Calif., USA) and then amplified using ITS-specific primers (4). The PCR products were purified using a MinElute™ PCR purification kit (QIAGEN GmbH, Hilden, Germany), processed according to the protocol of an ABI PRISM BigDye™ Terminator Cycler Sequencing Ready Reaction Kit (PE Applied Biosystems, Foster City, Calif., USA), and sequenced with a DNA sequencer (ABI PRISM™ 310 Genetic Analyzer; PE Applied Biosystems). The sequence data were analyzed

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using the Basic Local Alignment Search Tool (BLAST) system. The sequences of the isolates completely coincided with that of *G. capitatum* (GenBank accession no. AF455443). These morphological and genetic results verified that the isolates were *G. capitatum*.

As described above, characteristic clavate cells were directly observed in this case using KOH specimens from a symptomatic tongue, and *G. capitatum* was exclusively isolated twice from clinical specimens from two different sources. In contrast, only a few colonies of *C. albicans*, which is recognized as a pathogenic species, were present. These findings indicate that *G. capitatum* was the etiologic agent leading to superficial geotrichosis on the tongue of this patient. Unfortunately, we were unable to define the cause of the acute bronchitis in this patient. *G. capitatum* is frequently isolated from human skin, respiratory tract, and digestive tract samples (5). However, infection by this fungus is not common. *G. capitatum* has been reported to cause disseminated infections in patients with hematological malignancies such as acute leukemia and severe neutropenia (1), as well as in rarer cases concomitant with other diseases (6,7). It is accepted that the risk factors for systemic infection with *G. capitatum* are prolonged neutropenia, aggressive chemotherapy, administration of broad-spectrum antibacterial agents, and an alteration of local defenses by the obstruction or deterioration of skin and mucosa (5). In the present case, the patient had hypertension, cardiac insufficiency, multiple cerebral infarctions, and dementia; however, the clinical findings did not reveal a remarkable immunocompromised status, except for the normal decline in immunity seen with advanced age. These findings suggest that *G. capitatum* is an etiologic agent, not only in opportunistic systemic infections in immunocompromised individuals, but also in superficial infections in older persons, similar to *Candida* spp.

When AMPH syrup was used as chemotherapy in this patient, fungal cells temporarily disappeared from the tongue. The results of in vitro susceptibility tests using ASTY (Kyokuto Pharmaceutical Industrial Co., Tokyo, Japan) revealed that the isolated *G. capitatum* showed sensitivity to AMPH (MIC, 0.5 μg/ml) and flucytosine (MIC, 0.125 μg/ml); intermediate sensitivity to fluconazole (MIC, 8 μg/ml), itraconazole (MIC, 0.25 - 0.5 μg/ml), and miconazole (MIC, 1 - 2 μg/ml); and low susceptibility to micafungin (MIC, >16 μg/ml). These findings are consistent with those of a previous report describing the variable sensitivity of *G. capitatum* to flucytosine and sensitivity to AMPH, miconazole, and ketoconazole (3). Furthermore, Christakis et al. reported varying in vitro susceptibility of *G. capitatum* to flucytosine, itraconazole, and fluconazole (8). These results suggest that AMPH is a suitable antifungal agent, and that AMPH syrup is effective at preventing systemic development in patients with oral geotrichosis. In this case, *G. capitatum* was exclusively isolated again from the tongue of a patient who had previously been cured by the administration of AMPH syrup. Oral geotrichosis by *G. capitatum* is an uncommon infectious disease. In this case, the administration of AMPH syrup for 1 month does not appear to be a sufficient chemotherapeutic treatment for oral geotrichosis; it is likely that remaining microorganisms were the cause of a second infection.

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