Maxillary Sinusitis Caused by *Actinomucor elegans*

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We report the first case of maxillary sinusitis caused by *Actinomucor elegans* in an 11-year-old patient. Histopathological and mycological examinations of surgical maxillary sinuses samples showed coenocytic hyphae characteristic of mucoraceous fungi. The fungi recovered had stolons and rhizoids, nonapophysal and globose sporangia, and whorled branched sporangiophores and was identified as *A. elegans*. After surgical cleaning and chemotherapy with amphotericin B administered intravenously and by irrigation, the patient became asymptomatic and the mycological study results were negative.

An 11-year-old female patient, being neither diabetic nor human immunodeficiency virus positive, without evident underlying disease, but with slight leukopenia, was brought to a specialist about left-eye epiphora. On physical examination, the patient reported serosanguinous nasal discharge and decreased sinus ventilation lasting 2 months. A magnetic resonance imaging (MRI) study revealed left pansinusitis, and non-specific treatment was initiated. One month after the first clinical examination, the patient spontaneously expelled seromucous material during a cough. The presence of coenocytic hyphae in a direct examination of this sample, culturing of mucoraceous fungi, and opacification of the left maxillary sinus observed by MRI dictated the need for surgical cleaning of the paranasal sinuses. All the surgical specimens were sent to laboratories for mycological and histopathological studies. Direct microscopy of KOH preparations and tissue sections of the left maxillary sinus showed broad hyphae, typically coenocytic, characteristic of mucoraceous fungi. No evidence of osseous tissue invasion or eosinophils was observed.

The results of histopathological and mycological examinations of the surgical specimens from ethmoid, sphenoid, and frontal sinuses were negative for fungi. The same fungus was isolated from the seromucous material and from the maxillary sinus. The fungus was isolated as a single microorganism from both samples.

In addition to the surgical cleaning, the patient was treated with amphotericin B administered intravenously (1 mg/kg of body weight/day) and by irrigation of the maxillary antrum (5 mg/day), both for 42 days.

The patient was monitored bimonthly by MRI for 6 months after surgery. Although persistence of the opacity in the left maxillary sinus was observed, monthly clinical studies to date have shown an asymptomatic patient with negative mycological study results.

**Mycological findings.** The spontaneously expelled seromucous material and a portion of each tissue biopsy from the paranasal sinuses were inoculated on Sabouraud glucose agar with 5% (vol/vol) blood and Sabouraud glucose-honey agar supplemented with chloramphenicol and 0.5% (wt/vol) yeast extract and incubated at 28 and 37°C.

In both samples, several cottony, white colonies were evident after 48 h of incubation, and microscopic examination showed that they consisted of coenocytic, branched hyphae of variable widths (10 to 25 μm), characteristic of mucoraceous fungi. After 7 days, the same colonies developed globose to subglobose sporangia. The colonies were more exuberant on Sabouraud glucose agar with 5% blood.

The fungus was sent to Departamento Mycologia, INEI, ANLIS “Dr. Carlos G. Malbrán,” Buenos Aires, Argentina, for identification. Subcultures on potato dextrose agar (PDA), Sabouraud glucose agar, 2% malt extract agar, Czapek’s solution agar (Cz), and oatmeal agar were incubated at 25 to 28°C in darkness. Subcultures were examined at 4, 7, and 14 days.

Cultures on PDA yielded fast-growing, cottony, almost white colonies. After 4 days, the colonies measured 75 mm in diameter and became olive-buff, with an abundant aerial mycelium over 1 cm in height and a colorless reverse. Under a dissecting microscope, the colonies showed whorled branched sporangiophores, originating at a short distance below the terminal sporangia and bearing secondary sporangia subtended by cross walls (Fig. 1). The sporangiophores arose opposite from the branched rhizoids. Branched stolons were also present. The microscopic examination showed that all of the sporangia were spherical, 16 to 72 μm in diameter, and slightly colored (cream to buff), had many spores, and were slightly spinous, with elongate-oval (4 to 6 by 30 to 34 μm) columellae but without apophyses. The branched sporangiophores were slightly cream to buff, septate, smooth walled, and 4 to 18 μm in diameter. Stolons and rhizoids were septate, smooth walled, and colorless.

In old cultures, chlamydospores were present. The sporangiospores were globose and smooth walled and showed high size variability in different culture media. We randomly measured the diameters of 52 sporangiospores from a 14-day PDA culture; the values ranged between 4 and 12 μm, the arithmetic mean and standard deviation was 7.33 ± 0.16 μm, and the mode was 7.6 μm.

Subcultures on the other culture media, incubated at 25 to
28°C in darkness, grew very fast and luxuriantly, as on PDA, except that Cz that did not support good growth. On PDA, the fungus grew at 37°C but not at 40°C. Based on these morphological characteristics, we identified the isolate as *Actinomucor elegans* (1, 2). This identification was confirmed by E. Piontelli, Facultad de Medicina, Universidad de Valparaíso, Valparaíso, Chile, and J. D. David, CABI Bioscience, Egham, United Kingdom. This isolate has been preserved in IMI and Universidad de Valparaíso herbaria under the designations IMI383277 and CMUV.171, respectively.

The in vitro susceptibility of the isolate to amphotericin B and fluconazole was evaluated by use of the National Committee for Clinical Laboratory Standards reference method for antifungal susceptibility testing of conidium-forming filamentous fungi (4). The MICs obtained were 2 μg/ml for amphotericin B and 1 μg/ml for itraconazole.

Mucoraceous fungi are the most common group of fungi of the *Zygomycetes* and are an ever-expanding group of organisms capable of causing human diseases. The main categories of infections caused by mucoraceous fungi are sinusitis and rhinocerebral, pulmonary, cutaneous or subcutaneous, gastrointestinal, and disseminated zygomycoses (3, 5).

The incidence of fungal sinusitis, particularly in immunocompetent patients, appears to be increasing. Parasinal sinus mucormycosis usually has been reported for patients with diabetes mellitus but also has been detected in patients without any evident underlying disease. Most of the cases are caused by species of *Rhizopus, Absidia, Rhizomucor*, and *Mucor*. Infections due to other genera of the *Mucoraceae* are less frequent (3, 5). We report the first case of maxillary sinusitis due to *A. elegans* in a young female patient without evident underlying disease but with slight leukopenia. To our knowledge, this fungus has never been isolated from a human source.

*Actinomucor*, one of several genera of the family *Mucoraceae*, was originally described by Schostakowish in 1898 (1). This genus differs from the other mucoraceous fungal genera, except for *Rhizomucor, Rhizopus*, and *Absidia*, in having branched stolons that give rise to rhizoids and sporangiophores. *Actinomucor* is further separated from *Rhizopus* and *Absidia*, two other stoloniferous genera, because of differences in the formation of collumellae and sporangiophores and the limited growth of the stolons. Although *Actinomucor* resembles *Rhizomucor*, it differs from that genus by having hyaline to faintly colored sporangia and by temperature requirements for growth. At present, the genus *Actinomucor* includes two species: *A. taiwanensis*, which is used in the manufacture of sufu, a traditional oriental food made from soybean milk, and *A. elegans*, the type species of the genus *Actinomucor*, which is found in soil and other natural substrata from different countries but which has never been isolated from a human source (1, 2).

These two species are very similar, but the major difference

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**FIG. 1.** Slide cultures (4 days old) on PDA at 25 to 28°C in darkness. The specimen was stained with cotton blue. (A) Whorled branched sporangiophore, originating at a short distance below the terminal sporangium and bearing secondary sporangia subtended by cross walls. Magnification, ×120. (B) Stolons and rhizoids, repeatedly branched. Magnification, ×60. Phase-contrast microscopy was used.
between them is the sporangiospore size; A. elegans has smaller sporangiospores (6 to 8 μm) than A. taiwanensis (7 to 15 μm, even up to 20 μm). Although our isolate had some spores larger than those described for A. elegans, the mean and the mode for the spore sizes are included in the spore size range of this species. Jong and Yuan (2) described other different characteristics, such as maximum growth temperatures and the ability to grow on Cz. According to these authors, A. elegans shows better growth on Cz than does A. taiwanensis; on the other hand, the maximum growth temperature for A. taiwanensis is 37°C, while A. elegans does not grow at this temperature. Under these criteria, our isolate may be identified as A. taiwanensis because it grows at 37°C and develops less on Cz than on PDA. However, Benjamin and Hesseltine (1), who have studied a larger number of strains, observed that several isolates of A. elegans showed smaller amounts of growth on Cz than on PDA and that the maximum temperature of growth was approximately 32°C; however, their results were not conclusive. It is evident that more strains are needed to evaluate these characteristics in order to compare these two species. Based on spore size, which seems to be a major taxonomic criterion, our isolate was identified as A. elegans. We considered that this isolate, with intermediate characteristics, could be a more mesophilic ecotype of A. elegans with some pathogenic properties. Molecular data are required to determine if these two species represent distinct taxons or could be recognized at an appropriate infraspecific rank.

Fungal sinusitis has been broadly divided into four categories: the acute fulminant form, the indolent form, the mycetoma form, and the allergic form (3). In this case, as the patient was immunocompetent, with chronic noninvasive colonization of a maxillary sinus by a fungus and without an eosinophilic reaction, this clinical presentation was diagnosed as the indolent form.

Within the expanding group of susceptible hosts, new fungal opportunists are increasing in number; therefore, diagnosis and management of the infections that they cause can be difficult and will require a greater understanding of mycological details. As an aid to the laboratory identification of this fungus, the most relevant characteristics are as follows. The genus Actinomucor resembles Rhizomucor in having rhizoids, stolons, and spherical sporangia with columellae but without apophyses. Actinomucor has projections of whorls of short branches below the terminal sporangia of the sporangiophores, which are absent in Rhizomucor; a lighter pigmentation of sporangiospores; and a lack of growth at 40°C.

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REFERENCES