Allescheria (Petriellidium) boydii Sinusitis in a Compromised Host

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The first case of *Allescheria (Petriellidium) boydii* sinusitis is reported. The organism was isolated from the maxillary sinus in an elderly, diabetic, chronic alcoholic man on maintenance hemodialysis who developed a syndrome resembling mucormycosis. Infections with *A. boydii* are infrequent and are most commonly limited to Madura foot. In addition, several cases of pulmonary and central nervous system involvement have been described. There is no established therapy for *A. boydii*, since the published data on antimicrobial sensitivity are limited. Our organism was inhibited by 1.25 mg of amphotericin B per ml and 0.15 mg of miconazole per ml.

Reports of infection with *Allescheria (Petriellidium) boydii* are infrequent. The infection with this organism most commonly reported from this country is Madura foot. Occasionally, cases of pulmonary and central nervous system infection have been reported, usually in patients with a possible predisposing underlying condition. Here, we report the isolation of *A. boydii* from the maxillary sinus in an elderly diabetic chronic alcoholic man on hemodialysis who developed a syndrome resembling mucormycosis.

CASE REPORT

A 58-year-old diabetic man on chronic hemodialysis entered the hospital on 28 May 1975 complaining of progressive loss of vision in his right eye over several weeks.

This retired foundry worker with a long history of excessive alcohol intake was treated at the Veterans Administration Hospital (VAH) for the first time in 1962 for a right upper lobe nonspecific lung abscess. He next sought medical care in December 1972 at another hospital where Laennec cirrhosis was documented by liver biopsy, and esophageal varices were demonstrated by arteriography. In early 1974, newly discovered diabetes mellitus was treated with oral hypoglycemic agents. In August 1974, the patient was admitted to the VAH with uncontrolled hypertension, renal failure, and anasarca. An ophthalmologist noted full extraocular movements and 20/20 vision bilaterally. The patient was discharged much improved with a creatinine value of 6 mg/100 ml. In January 1975, because of deteriorating renal function, hemodialysis was begun. In February 1975, he was admitted with severe epistaxis requiring a posterior nasal pack for several days. Between February and May, he entered the VAH on

three separate occasions for hepatic encephalopathy and gastrointestinal bleeding from an undetermined site.

During a routine outpatient hemodialysis on 22 May 1975, he complained of 3 to 4 weeks of painless loss of vision in his right eye. Examination of the left eye was completely normal. Examination of the right eye revealed ptosis, exophthalmos, decreased adduction, and visual acuity limited to light-dark perception. On 28 May 1975, in the ophthalmology clinic, the left eye was normal and the right eye showed edematous lids and extraocular motion limited to less than 5 mm in all directions, with a 15-mm exotropia in the primary position of gaze. Intraocular pressures and slit lamp examination of both eyes were normal. Funduscopy displayed grade II atherosclerotic and grade II hypertensive changes with sharp disks bilaterally. The patient was admitted to the ophthalmology service.

On admission, the temperature was 99.2°F (ca. 37.3°C) rectally, blood pressure, 180/90 mm of Hg, pulse, 90 beats/min, and respirations, 18/min. Positive findings included cardiomegaly with a sustained left ventricular impulse at the anterior axillary line, an S4 gallop, a grade III/VI systolic murmur radiating to the left axilla, a 16-cm firm, non-tender liver palpable 5 cm below the right costal margin, a palpable spleen tip, trace ankle edema, decreased touch and vibratory sensation in a stocking distribution, and a functioning arteriovenous shunt in his right arm. An otolaryngological consultant confirmed a normal ear, nose, and throat exam.

The hemoglobin was 8.8 mg/100 ml; leukocyte count was 10,600/mm³, with 87% neutrophils, 7% lymphocytes, 5% monocytes, and 1% eosinophils. The sodium was 136 meq/liter; glucose, 90 mg/100 ml; blood urea nitrogen, 75 mg/100 ml; creatinine, 13 mg/100 ml; bilirubin 0.6 mg/100 ml; albumin, 3.0 mg/100 ml; and alkaline phosphatase, 134 IU/ml.

Electrocardiogram revealed left ventricular hypertrophy with strain. A chest X-ray displayed cardiomegaly. The urine specific gravity was 1.010, and contained 3+ protein and 20 leukocytes/high-power field. Tomograms revealed opacification of the right maxillary and right ethmoid sinus, as well as mucosal thickening in the sphenoid sinus. Computerized axial tomography showed erosion of the medial wall of the right orbit.

A right Caldwell-Luc procedure was performed on 30 May for diagnosis. Black necrotic tissue completely filled the right maxillary antrum. Gram stain of this tissue completely filled the right maxillary antrum. Gram stain of this tissue revealed many polymorphonuclear leukocytes and occasional gram-positive cocci. A lactophenol cotton blue preparation of this tissue revealed septate hyaline hyphae, branching at right angles. On the basis of these studies, treatment was begun, consisting of amphotericin B, 0.6 mg/kg per day, and cephalothin, 2 g every 6 h. Routine cultures incubated aerobically and anaerobically (GasPak, BBL, Cockeysville, Md.) grew *Staphylococcus aureus* and *Proteus mirabilis*. Specimens for fungal culture were plated on Sabouraud dextrose medium, and isolates were subcultured on brain heart infusion, Eugon broth and agar, and Levine eosin methylene blue. Specimens were also submitted to the pathology laboratory for microscopic examination (Fig. 1). Pathological examination showed chronic sinusitis with a feltwork of branching septate hyphae and many scattered conidia. A mold isolate obtained on Sabouraud dextrose agar and histopathological sections were sent to the Clinical Mycology Section, National Institutes of Health, Bethesda, Md. K. J. Kwon-Chung identified the mold as *A. boydii*. The histopathological specimens were examined by both K. R. Kwon-Chung and John Bennett, who concurred that the hyphae, conidia, and distinctive synnemata in the sinus tissue were entirely consistent with the morphology of the *A. boydii* isolate. Synnemata are a recognized cultural characteristic of this species, but their appearance in tissue may be unique to this case.

On 31 May, after transfer to the medical service, a lumbar puncture showed an opening pressure 260 mm of H₂O; protein, 265 mg/100 ml; glucose, 206 mg/100 ml (simultaneous blood glucose, 120 mg/100 ml); erythrocyte count, 2,905/mm³ (traumatic); and leukocyte count, 9/mm³, all neutrophils. When the procedure was repeated 3 days later, the opening pressure was 180 mm of H₂O; protein, 125 mg/100 ml; glucose, 92 mg/100 ml; erythrocyte count, 15/mm³; and leukocytes, 0. Cerebrospinal fluid cultures on each specimen for bacteria, mycobacteria, and fungi were all negative.

Cephalosporin therapy was continued for 10 days. Amphotericin B therapy was changed to 35 mg three times a week (after each dialysis). Extensive debridement was recommended, but was not performed because of the patient's multiple underlying problems. After 3 weeks, the patient remained afebrile, except for occasional temperature elevations associated with the amphotericin administration. On June 24, ophthalmological examination revealed

increased ability to adduct and elevate the right eye and resolution of the ptosis. Visual acuity remained the same. The left eye now showed a marked decrease in acuity, such that the patient could only count fingers at 6 feet (ca. 180 cm). The remainder of the examination, including funduscopy, was unchanged.

Ophthalmological reevaluation on 28 July, after 1,350 mg of amphotericin B, revealed full extraocular movements in both eyes. The right eye continued to have no light perception and the left eye had improved to 20/200. There was no direct right pupillary response, but a good consensual one was observed. Funduscopy examination was unchanged.

The patient was readmitted to the VAH in September 1975 and shortly thereafter died of unrelated causes. Permission for a postmortem examination was not obtained.

RESULTS AND DISCUSSION

This is the first report of sinusitis due to *A. boydii*. It occurred in an elderly man with multiple, chronic disease processes, each reported to predispose to opportunistic infection. The presentation suggested mucormycosis, but the diagnosis of *A. boydii* was established by microbiological and histological study of specimens obtained at surgery. After a Caldwell-Luc procedure and initiation of amphotericin B treatment, the patient appeared to stabilize. The role of these therapeutic maneuvers is conjectural.

A. boydii is a well-known cause of Madura foot and is the organism most frequently isolated from this condition in the United States and Europe (2, 11). In 1909 this fungus was originally identified in its imperfect form by Tarozzi (23) when isolated from a Sardinian with Madura foot, and, in 1911, was named *Monosporium apiospermum* by Saccardo (1). Boyd and Crutchfield (5), in 1921, isolated a new perfect fungus from a patient with Madura foot which in 1922 was named *Allescheria boydii* by Shear. (In 1970, Malloch [14] proposed the transfer of this species from *Allescheria* to the genus *Petriellidium*.) It was not until 1944 that Emmons (8) demonstrated that these represented different forms of the same organism. *M. apiospermum* represented the asexual or imperfect form of the fungus, and the same culture may at a later stage display cleistothecia and ascospores characteristic of *A. boydii*. This fungus grows rapidly on artificial media at room temperature and at 37°C and forms colonies that are initially white but later become dark grey. *A. boydii* is a soil saprophyte and has a worldwide distribution (1). It usually gains access to the body by cutaneous inoculation; most of the reported infections have been in farmers in tropical and subtropical regions.

FIG. 1. Specimen from maxillary sinus revealing conidia and synnemata of *A. boydii*. (a) $\times 400$; (b) $\times 1,200$ (courtesy of K. J. Kwon-Chung).

A. boydii rarely causes infections in locations other than the cutaneous and subcutaneous tissues of the foot. We have found 13 recorded cases of pulmonary involvement. These generally have occurred in farmers, and most have

had underlying structural pulmonary disease (12, 13, 15, 17, 18, 20, 24; L. I. Lutwick, J. M. Galgiana, R. H. Johnson, and D. A. Stevens, Clin. Res. 24:114A, 1976). Belding and Umanzio (3) isolated the organism from a patient with

otitis externa, and Glassman et al. (10) described a diabetic woman with severe endophthalmitis due to *M. apiospermum* after a cataract extraction. She was treated successfully with amphotericin B eye drops. Central nervous system involvement has been noted on four occasions. Rosen et al. (19) reported systemic dissemination with the formation of thyroid and brain abscesses in a 19-year-old girl with rapidly progressive glomerulonephritis who was being treated with cortisone and azathioprine. Forno and Billingham (9) described thyroid and brain abscesses in a 56-year-old rancher with systemic lupus erythematosus on steroid therapy. Shelby (22) reported a slowly progressive meningitis in a 49-year-old woman, and Benham and Georg (4) reported a case of meningitis developing 4 weeks after spinal anesthesia that was fatal after an 8-month illness. Recently, Lutwick et al. (Clin. Res. 24:114A, 1976) reported four additional cases: brain and thyroid abscesses in a patient with lupus nephritis taking prednisone; endophthalmitis in a patient with lupus nephritis taking prednisone and azathioprine; pulmonary lesions in a patient with lymphoma taking prednisone; and septic arthritis in a patient after open trauma to the knee.

There is no established treatment for *A. boydii* infections, and the antimicrobial sensitivity data for this organism are limited. Reported minimal inhibitory concentrations of amphotericin B for this organism have ranged from 0.9 to 40 $\mu\text{g/ml}$ (7, 16, 22). These are difficult to interpret because of the lack of standardization of this test for fungi. Minimal inhibitory concentrations for the organism isolated in this case report were determined by John Bennett, Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, Bethesda, Md. He reported values of 1.25 $\mu\text{g/ml}$ for amphotericin B and 0.15 $\mu\text{g/ml}$ for miconazole.

We have described *A. boydii* sinusitis which first appeared to be mucormycosis in an elderly man with multiple risk factors. The progression of the disease seemed to be arrested concomitant with amphotericin B administration. This organism should be added to the list of opportunistic pathogens in diabetics and in patients on chronic dialysis.

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