Meningitis Caused by *Pseudallescheria boydii* Treated with Voriconazole

Meningitis caused by *Pseudallescheria boydii* is an uncommon infection of the CNS that usually has a poor prognosis and a difficult treatment. We describe a case of chronic meningitis caused by *P. boydii* in an immunocompetent host that was successfully treated with voriconazole, a new antifungal agent.

*Pseudallescheria boydii* (asexual form, *Scedosporium apiospermum*) is a saprophytic fungus frequently isolated from soil and water. Infection of the central nervous system is very uncommon and it is usually associated with immunosuppression, trauma, near drowning, cerebrospinal fluid (CSF) drainage devices, and rachianesthesia. The prognosis is poor (the mortality rate is >75%). Treatment is difficult because of the resistance of the organism to many antifungal agents [1]. We describe a case of chronic meningitis caused by *P. boydii* that responded well to voriconazole therapy. Based on our search of MEDLINE for the period 1996–1999, we believe this is the first report of the use of voriconazole to treat a case of *P. boydii* meningitis.

A 24-year-old man with a normal medical history underwent excision of a pilonidal sinus cyst of the sacrum under rachianesthesia 7 months before admission; there was prolonged healing. One month later, the patient complained of headache and back pain. The CSF showed hypercellularity, an elevated protein level, and a low glucose level. Culture of the CSF was negative. The patient was treated empirically with ceftriaxone and vancomycin. After an initial improvement in his condition, fever appeared again and he was transferred to our hospital.

Upon examination, he was febrile and had papilledema, a stiff neck, 6th nerve paralysis, diminished patellar reflexes, and both ankle jerks were absent; a bilateral Lasegue’s sign was present. His erythrocyte sedimentation rate was 56 mm, and his WBC count was 11,600 cells/mL. Evaluation of a CSF specimen showed a WBC count of 6400 cells/mL (56% neutrophils), a protein level of 496 mg/dL, and a glucose level of 52 mg/dL, with no microbiological growth. A cranial CT was normal. A spinal MRI showed lumbosacral arachnoiditis. A new course of antibiotic therapy with dexamethasone was initiated.

Twenty days later the patient’s condition deteriorated. Evaluation of CSF from a new lumbar puncture revealed purulent liquid and a tangle of septate hyphae that were identified on culture as *Scedosporium apiospermum*. We initiated treatment with voriconazole (Pfizer Central Research, Sandwich, UK) on a compassionate-use basis because we could not obtain an iv formulation of miconazole. Intravenous voriconazole was administered at a dosage of 6 mg/kg/12 h for the first day, then at a dosage of 4 mg/kg/12 h. The patient became afebrile and showed clinical improvement. After 12 days the CSF became sterile. After 4 weeks, treatment was switched to oral voriconazole (200 mg/12 h). No adverse effects were observed, except for a mild and transitory increase of the hepatic enzymes.

We had the in vitro activities of various antifungal drugs tested at the National Center of Microbiology (Madrid, Spain) using a test based on the recommendations of the National Committee for Clinical Laboratory Standards. The following MICs were obtained: amphotericin B, 2 μg/mL; itraconazole, 2 μg/mL; fluconazole, 64 μg/mL; miconazole, 0.12 μg/mL; and voriconazole, 0.5 μg/mL. During oral treatment, voriconazole plasma and CSF levels were 1.92 μg/mL and 0.56 μg/mL, respectively, which exceeded the MICs. After 7 months, CSF evaluation was normal. Treatment was maintained for 12 months. Presently, the patient remains asymptomatic except for mild sciatica.

Meningitis due to *P. boydii* is very uncommon and is usually associated with immunosuppression or near-drowning. It normally follows an acute and fatal course and coexists with cerebral infarcts and/or abscesses [1]. Chronic presentation is rarer, usually appearing in immunocompetent individuals, although its prognosis does not change [2, 3]. In our patient, there were 2 factors that have been associated with CNS infection due to *P. boydii*: the rachianesthesia and the presence of a wound near the CNS [1, 2]. The characteristics of the patient’s CSF were similar to those of previous cases [1–3].

Treatment of such infections is complicated by resistance of the organism to amphotericin B and the fact that other antifungal agents penetrate poorly across the blood-brain barrier. Until now, elective treatment consisted of iv and intrathecal miconazole and surgical excision whenever possible [1, 3]. Voriconazole is a new triazole derivative that has proved to be effective against opportunistic human mycoses. To date, only 1 case of disseminated infection (without CNS involvement) due to *P. boydii* treated with this drug has been described [4]. This case represents the first time that voriconazole has been used to treat CNS infection due to *P. boydii*.

In summary, *P. boydii* must be included as an etiologic agent of chronic meningitis even in immunocompetent hosts, above all if there is any history of trauma or rachianesthesia. Despite the poor prognosis for patients with this infection, voriconazole is a promising antifungal drug for the treatment of the pseudallescheriasis of the CNS because it has good activity in vitro, is available in an iv formulation, has good CSF penetration, and is well tolerated.

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Need for Diagnostic Screening of Herpes Simplex Virus in Patients with Nongonococcal Urethritis

The prevalence of various microorganisms known to cause nongonococcal urethritis, including herpes simplex virus (HSV), was evaluated. The findings suggest that HSV can be a significant etiological agent in nongonococcal urethritis (NGU) and that the necessary laboratory investigations should be performed for all patients with clinical symptoms of NGU.

Nongonococcal urethritis (NGU) ranks as one of the most common sexually transmitted diseases (STDs) in men. It is clinically characterized by mucoid or purulent discharge accompanied with dysuria or itching at the distal end of the urethra. In most clinics, a diagnosis of NGU is confirmed by the absence of gram-negative diplococci on gram-stained preparations, a negative gonococcal culture, and the detection of >5 polymorphonuclear leukocytes on a stained smear of urethral exudate or urinary sediment. The main organisms that are known to cause NGU are Ureaplasma urealyticum, Mycoplasma genitalium, Mycoplasma hominis, and Trichomonas vaginalis. At present, very little is known about the etiological role of HSV in patients with NGU. In our study, we evaluated the prevalence of the various organisms known to cause NGU, including herpes simplex virus (HSV).

An etiologic agent was found for 71 (29.8%) of 238 male patients with symptoms of urethritis who attended our clinic. Neisseria gonorrhoeae was isolated from 3 (4.2%) of the 71 patients, whereas the typical diplococci were not isolated from 68 patients (95.8%). Chlamydia trachomatis was isolated from 35 (51.5%) of the 68 patients; U. urealyticum, 31 (45.6%); M. hominis, 9 (13.2%); and T. vaginalis, 1 (1.5%; figure 1). Antigen detection testing for HSV was performed for only 141 of our patients, whereas serum samples from 202 patients were tested for type-specific antibodies. Antigen detection testing revealed HSV infection in 17 (12%) of the 141 patients, 15 of whom did not have genital lesions. Of the 17 patients, 6 were seropositive for HSV type 1 (HSV-1), 6 were seropositive for HSV type 2 (HSV-2), and 5 were seronegative for HSV-1 and HSV-2. Analysis of serum samples that were tested for type-specific antibodies showed that 25 (12%) of 202 male patients were seropositive for HSV-2. Only 5 (20%) of these patients had a history of genital lesions. One hundred fifty-four (76%) of the 202 male patients were seropositive for type-specific antibodies to HSV-1.

NGU is a common disease in male patients attending STD clinics. In accordance with the current literature [1], we did not find an etiologic agent in most cases. In the cohort of male patients with NGU whom we examined, C. trachomatis and U. urealyticum were the most common pathogens isolated when an etiologic agent could be detected.

Because we found that unrecognized genital infections due to HSV were common among male patients who attended our STD clinic, we included genital HSV detection in our analysis. It has been estimated that about 60% of patients infected with HSV-2 have atypical manifestations of the disease that are unrecognized or underdiagnosed by the physician and the patient [2]. These symptomatic patients with unrecognized disease exhibit shedding of the virus, which can occur with or without genital ulcerations or a history of the classic genital lesions. Therefore, in contrast to what has been previously accepted in the literature, genital lesions are not present in all cases of herpesvirus infection. In our study, antigen detection testing revealed that 17 (12%) of 141 patients with symptoms of NGU who attended our clinic were positive for HSV. Fifteen (88%) of these symptomatic patients did not have genital lesions.