Successful Use of Voriconazole for Treatment of Coccidioides Meningitis

A 30-year-old Caucasian man developed fever, myalgia, and dry cough that lasted for 3 weeks. He works as a house painter in Phoenix, Ariz. Three months later, he developed right-sided headache, meningismus, and photophobia. A lumbar puncture (LP) revealed normal opening pressure, lymphocytic pleocytosis (340 white blood cells, 96% lymphocytes), elevated cerebrospinal fluid (CSF) total protein (162 mg/dl), and low CSF glucose (25 mg/dl). A cryptococcal antigen test was negative, and bacterial, viral, fungal, and acid-fast bacillus cultures were negative. Titers of anti-Coccidioides antibodies in serum and CSF were 1:16 and 1:2, respectively, as determined by complement fixation (CF). Serum antibodies to Coccidioides were detected by enzyme immunoassay. Evaluation for immunodeficiency, including human immunodeficiency virus serology, was negative.

The patient took oral fluconazole (600 mg/day), but his symptoms persisted. A computed tomography scan of the head was normal, and repeat LP revealed no improvement in CSF parameters. Fluconazole was stopped, and intravenous amphotericin B deoxycholate (AMB-DOC) was begun. Within 72 h, the patient developed acute nonoliguric renal failure. Amphotericin B lipid complex (ABLC) (5 mg/kg of body weight/day) was substituted for AMB-DOC. The patient’s headaches and creatinine improved gradually. ABLC was discontinued, and oral fluconazole (600 mg/day) was begun.

The patient subsequently moved to Chicago, Ill. During the next 6 months he continued to have headaches associated with elevations in both CSF white blood cell count and titers of anti-Coccidioides antibody. Treatment with high doses of liposomal amphotericin B (up to 10 mg/kg/day) or fluconazole (1,200 mg/day) resulted in only partial clinical improvement. An Ommaya reservoir was placed, and escalating daily doses of intraventricular AMB. This was discontinued, and high-dose oral voriconazole (400 mg twice daily) was begun, after which the headaches resolved. The patient initially complained of solar photosensitivity, but this improved with the use of sunblock.

Two months later, evaluation of complaints of low back pain resulted in diagnosis of an intradural abscess at T11. The lesion, suspected to be a coccidioidomycoma, was surgically excised, but stains and cultures were negative. Surgery was complicated by communicating hydrocephalus, requiring ventriculo-peritoneal shunt placement.

After 21/2 years of treatment with voriconazole, the patient’s headaches and back pain have resolved. Follow-up LPs reveal normal CSF cell counts, protein, and glucose. Serum and CSF anti-Coccidioides (by LP) antibodies by CF have remained undetectable (titers of <1:1). This patient’s dose of voriconazole has been reduced to 200 mg twice daily, and lifelong therapy is planned.

Meningitis is a rare complication of infection with the fungus Coccidioides. Since this patient acquired his infection while in Arizona, he was presumed to have been infected with Coccidioides posadasii, which has recently been identified as the etiology of coccidioidomycosis outside of California (3). It is not known whether C. posadasii responds differently to fluconazole therapy than Coccidioides immitis. The treatment of Coccidioides meningitis can be difficult. Untreated infection is associated with nearly 100% mortality. There is doubt as to whether meningeal coccidioidomycosis is curable, and some authorities recommend lifelong antifungal therapy to prevent recurrence (2).

Although not approved for the treatment of the endemic mycoses, voriconazole has in vitro activity against these fungi, including C. immitis (5). Voriconazole has 96% oral bioavailability, low protein binding, and extensive tissue distribution, including penetration into the central nervous system (4). Voriconazole may be effective in patients with refractory coccidioidomycosis (1), including possibly infections due to C. posadasii. Further clinical studies are warranted.

REFERENCES


Laurie A. Proia
Allan R. Tenorio*
Department of Internal Medicine
Section of Infectious Diseases
Rush Medical College
600 South Paulina
Suite 143 Academic Facility
Chicago, IL 60612

*Phone: (312) 942-5865
Fax: (312) 942-8200
E-mail: allan_s_tenorio@rush.edu