Cryptococcal cerebrospinal fluid shunt infection treated with fluconazole

DANIEL EYMARD, MD, FRANÇOIS LEBEL, MD

D EYMARD, F LEBEL. Cryptococcal cerebrospinal fluid shunt infection treated with fluconazole. Can J Infect Dis 1993;4(4):227-228. A 37-year-old woman with a cadaveric renal allotransplantation required intra-cranial shunting devices after a presumptive episode of tuberculous meningitis. Six months later, she developed a culture-proven cryptococcal meningitis. Without having her ventriculo-auricular shunt removed, she was successfully treated with a short course of amphotericin B (335 mg) and flucytosine (nine days) followed by prolonged therapy with oral fluconazole (400 mg daily for 72 days). Three years post treatment she had no evidence of relapse, and normal renal graft function.

Key Words: Cryptococcus neoformans, Fluconazole, Renal transplant, Shunt infection

Cryptococcus au niveau du liquide céphalorachidien suite à un shunt, traitée par fluconazole

RÉSUMÉ: Une femme de 37 ans ayant subi une allotransplantation rénale a requis l'implantation d'un dispositif de shunt intracrânien après un épisode soupçonné de méningite tuberculuse. Six mois plus tard, elle a développé une méningite à Cryptococcus confirmé par les résultats de culture. Sans que l'on ait eu à extraire le shunt ventriculo-auriculaire, elle a été traitée avec succès grâce à l'administration d'amphotéricine B (335 mg) durant une brève période et de flucytosine (durant neuf jours), suivie d'un traitement prolongé avec fluconazole par voie orale (400 mg par jour durant 72 jours). Trois ans après le traitement, elle ne présentait aucun signe de rechute et la fonction de la greffe rénale était normale.

Current standard therapy for cryptococcal meningitis is amphotericin B, either alone or in combination with flucytosine (1). Treatment with amphotericin B is, however, problematic in clinical scenarios where preservation of renal function is an urgent priority. In renal transplant recipients, although this regimen is effective (2), it may threaten the viability of the renal graft (3). In theory, therefore, fluconazole suggests itself as a favourable alternative to amphotericin B in renal transplant patients who require treatment of cryptococcal meningitis. We report clinical success in a renal transplant patient treated with fluconazole for cryptococcal meningitis.

CASE PRESENTATION

A 37-year-old woman with Alport’s syndrome underwent a cadaveric renal allotransplantation in 1973 and again in 1985. Four months prior to the 1985 graft, therapy with isoniazid and rifampin was initiated for a presumptive diagnosis of tuberculous meningitis. Cerebrospinal fluid (CSF) analysis revealed pleocytosis with a white cell count of 0.035x10⁹/L and a red cell count of 0.015x10⁹/L, elevated protein at 1.2 g/L, and low glucose CSF-to-serum ratio of 0.07. CSF bacterial, fungal, mycobacterial and viral cultures were all negative. Cryptococcal antigen detection (Crypto-La test, International Biologic Labs, New Jer-
The patient’s clinical course remained uneventful for yeasty-like organisms, and glucose CSF-to-serum ratio was negative at that time and the hydrocephalus improved postoperatively. Three years post treatment the patient is doing well, with no evidence of relapse, and normal renal graft function.

**DISCUSSION**

Cryptococcal antigen could not be demonstrated in the patient’s CSF, even though the kit used has previously been shown to be both highly sensitive and specific (4). A false negative result secondary to a protein zone effect was excluded by performing the test at various dilutions. Other investigators have explained similar false negative results by posting a low production of antigen in their isolates (5). In one published series, antigen was not detected in eight of 88 acquired immune deficiency syndrome (AIDS) patients with proven cryptococcal meningitis (6).

Although the present patient received a 19-day course of amphotericin B, it cannot account for her clinical cure. In another published series (7), four of five renal transplant patients with cryptococcal meningitis relapsed after a short course of 28 days of amphotericin B. Therefore, although the amphotericin B and flucytosine may have decreased the burden of cryptococci, the durability of her long term cure must be ascribed to the fluconazole.

Fluconazole already has a well-established clinical role in the treatment of AIDS patients, both as definitive treatment of cryptococcal meningitis in patients at low risk for treatment failure (8), as well as for long term suppression of cryptococcal disease in this population (9). Fluconazole has also been reported to induce a cure in a renal transplant patient with cryptococcal meningitis (10). This is the first report of fluconazole treatment for a fungal CSF shunt infection in an immunocompromised host. Sequential treatment with an initial short course of amphotericin B and flucytosine followed by prolonged fluconazole is an effective regimen for cryptococcal meningitis in patients at high risk for amphotericin-related nephrotoxicity.

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**REFERENCES**


