Acetazolamide Therapy and Intracranial Pressure

Sir—We read with interest the article entitled “A Randomized, Double-Blind, Placebo-Controlled Trial of Acetazolamide for the Treatment of Elevated Intracranial Pressure in Cryptococcal Meningitis” by Newton et al. [1], which evaluated the addition of acetazolamide to standard regimens for cryptococcal meningitis. This important study question is frequently raised not only of patients with cryptococcal meningitis, but also of those with CNS coccidioidomycosis. Though their study was ended because of unacceptable electrolyte abnormalities and adverse events, Newton et al. [1] postulated that there may be subsets of patients who would benefit from the use of acetazolamide. We concur that this is likely and report our experience using acetazolamide to treat 2 patients with persistent, symptomatic elevation of intracranial pressure (ICP) following completion of antifungal therapy for fungal meningitis.

One of our patients had meningitis secondary to Cryptococcus neoformans and the other had meningitis due to Coccioidoides immitis. Both patients were immunocompetent and without significant medical conditions. One patient received amphotericin B/flucytosine and the other patient received fluconazole, and both patients underwent serial lumbar punctures. Both continued to have elevated ICP after their initial antifungal treatment course and, despite chronic fluconazole therapy and sterilization of their CSF, both had significant papilledema with visual impairment. For the patient with cryptococcal meningitis, a 2-month course of acetazolamide therapy at a total dose of 500 mg/day was associated with resolution of the papilledema and restoration of visual acuity. The patient with C. immitis meningitis required 4 years of acetazolamide therapy; intermittent discontinuation of acetazolamide resulted in recurrence of headaches and visual disturbances. No significant electrolyte abnormalities or adverse events were observed. The papilledema did not recur after the cessation of therapy.

Chronically elevated ICP may lead to serious sequelae, including visual and hearing loss, systemic hypertension, severe cephalgia, and depressed mentation [2, 3]. Techniques used to decrease intracranial pressure in patients with fungal meningitis include serial lumbar puncture and placement of a lumbar drain or intraperitoneal shunt [2, 4]. Serial lumbar punctures are most often employed, because they pose the least risk and are time-efficient outpatient procedures. A large-volume lumbar puncture not only removes fluid directly but also restores the autoregulatory resorptive function of the arachnoid villi. Unfortunately, this therapeutic modality is impractical for long-term therapy, as scarring eventually occurs. Shunt and drain placement are effective but invasive outpatient procedures that carry the risk of traumatic and infectious complications. Acetazolamide is an attractive adjuvant therapy because it is noninvasive, easily implemented, and has relatively few side effects in patients who are not receiving nephrotoxic agents. Acetazolamide may be used to reverse chronically elevated ICP due to fungal meningitides and deserves further investigation.