Treatment of Severe Pulmonary Blastomycosis with Oral Itraconazole: Case Report

The recommended treatment of severe blastomycosis in both immunocompromised and normal hosts is amphotericin B [1]. We report a case of life-threatening pulmonary blastomycosis that required treatment with oral itraconazole because of hepatotoxicity associated with amphotericin B [2].

A 26-year-old man was transferred to our hospital with severe community-acquired pneumonia that had progressively worsened over 6 weeks. The diagnosis of blastomycosis was made shortly after transfer, and treatment was commenced with oral itraconazole capsules (Sporanox; Janssen-Ortho, Inc., Toronto, Canada) (200 mg twice daily); however, by day 5 of hospitalization, his condition had further deteriorated, and amphotericin B (Fungizone; Bristol-Meyers Squibb Canada, Inc., Montreal, Canada) was added to his treatment at a dosage escalating to 50 mg intravenously once daily. On day 6, he developed respiratory failure and required intubation and mechanical ventilation. After amphotericin B treatment was started, the patient’s liver transaminase levels progressively increased, and liver biopsy demonstrated histological changes compatible with an adverse drug effect due to amphotericin B and no evidence of blastomycosis. Therefore, administration of amphotericin B was discontinued (total dose, 175 mg), and itraconazole therapy was continued at 200 mg twice daily (Sporanox Oral Solution [Janssen-Ortho], which contains hydroxypropyl-β-cyclodextrin) through a nasogastric tube. Liver enzyme levels subsequently returned to baseline within 6 days of discontinuation of amphotericin B treatment.

The patient was treated in the intensive care unit with mechanical ventilation for a total of 36 days. During this time, he produced copious amounts of thick, purulent, bloody sputum, cultures of which yielded Blastomyces dermatitidis until day 29 of itraconazole treatment. For ~1 month, he was intermittently febrile with temperatures of >38.5°C, developed severe anemia, had white blood cell counts persistently elevated at >15 × 10^9/L, and had chest roentgenograms that demonstrated bilateral areas of consolidation with superimposed adult respiratory distress syndrome. The patient was discharged to home after 49 days of hospitalization and continued treatment with itraconazole capsules (200 mg twice daily) for 6 months. At the end of treatment, there was an area of cavitating lung disease. Am Rev Respir Dis 1981; 123:336–39.


References

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were similar to those for our patient with respect to the severity and duration of their illnesses, although all 10 patients were treated with amphotericin B at dosages of 0.7–1.0 mg/kg daily and survivors received total doses of 1000–3000 mg. In one case, B. dermatitidis was isolated from sputum until the 15th day of therapy, compared with positive cultures for our oral itraconazole–treated patient until day 29. This difference in time to negative cultures possibly may reflect the fungicidal effect and efficacy of amphotericin B, which were found to be more rapid than and superior to, respectively, those of itraconazole and ketoconazole in a murine model of blastomycosis [4] and in a small series of children with pulmonary blastomycosis [5].

Severe blastomycosis is associated with a mortality rate of >50% despite the use of amphotericin B, which should remain the treatment of choice [3]. However, in the rare circumstance that amphotericin B or its lipid preparations are not able to be administered, intravenous or the oral solution of itraconazole may provide the most effective therapeutic alternative.

Ceftriaxone Therapy for Syphilis: Report from the Emerging Infections Network

Alternatives to penicillin for the treatment of syphilis continue to be sought [1]. The Centers for Disease Control and Prevention (CDC) currently recommend that tetracyclines be used when penicillin injections are contraindicated [2]. High-dose amoxicillin [3] and azithromycin [4] have both been recently studied. The third-generation cephalosporin ceftriaxone is active in vitro against Treponema pallidum [5]. Small-scale studies of patients with syphilis have suggested that this agent has clinical efficacy [6–8]. However, there is currently no generally accepted or recommended dose or dosing schedule for this use of ceftriaxone.

During a review of literature on syphilis treatment for the 1998 revision of the CDC Sexually Transmitted Diseases Treatment Guidelines, questions were raised regarding the frequency of ceftriaxone use for the treatment of syphilis in the United States. To address this issue, we enlisted the use of the Infectious Diseases Society of America Emerging Infections Network (EIN), a cooperative agreement program funded by the CDC. In May 1998, the EIN queried 444 infectious diseases consultants who care for adult patients about their use of ceftriaxone for the treatment of patients with early syphilis. Respondents included EIN members from all parts of the continental United States.

EIN members were asked if they had ever used ceftriaxone for the treatment of early-stage (i.e. primary, secondary, or early latent) syphilis and, if so, how often, under what circumstances, at what dose, and with what outcome. Three hundred twelve physicians (70%) responded. Fifty-nine (19%) of these respondents, from all sections of the country, reported using ceftriaxone to treat syphilis in both patients infected with HIV and uninfected patients. Eleven physicians (4%) used ceftriaxone for the treatment of primary syphilis. The number of cases treated varied from 1 to 25 per physician. Most patients received 2 g intravenously or intramuscularly once daily for 2–10 days. Penicillin allergy was the reason most often cited for ceftriaxone use.

Nineteen respondents (6%) used ceftriaxone for the treatment of secondary syphilis. The number of cases treated ranged from 1 to 6 per physician. Doses ranged from 1 to 2 g intravenously and intramuscularly once or twice daily for 3–21 days. The reason most often cited for ceftriaxone use was penicillin allergy. In a few instances, penicillin allergy in pregnancy was identified as the specific situation warranting ceftriaxone use. There was one reported therapeutic failure (clinically and serologically) for a nonpregnant patient.

Forty respondents (13%) reported use of ceftriaxone for the treatment of early latent syphilis. These physicians used ceftriaxone 1 to 5 times. Twenty-eight physicians used a 2 g dose, whereas 9 used a 1 g dose (no data provided by 3 respondents from this field). Most physicians administered ceftriaxone intravenously once daily for 10–21 days. Again, the reason most often given for ceftriaxone use was penicillin allergy. There were 5 reported therapeutic failures, including 2 clinical failures.