nema pallidum antibody, and a diagnosis of relapsed secondary syphilis was made. Syphilitic hepatitis was suspected on the basis of a 2-fold increase in the level of alkaline phosphatase from previously normal levels, a 2-fold increase in the level of liver enzymes from baseline, a 5-fold increase in total bilirubin to >200 μmol/L, and the exclusion of other etiologies, including viral hepatitis (A and B) and alcohol abuse. Two hours after the patient received intramuscular penicillin V, his temperature increased to 39.0°C. Within 24 h, the AST and ALT levels had increased to 1331 U/L and 328 U/L, respectively, and by 36 h, the patient was encephalopathic, with an international normalized ratio of 2.16, a total bilirubin of 364 mmol/L (direct bilirubin, 197 μmol/L). A diagnosis of Jarisch-Herxheimer reaction was made. Over the next week in the intensive care unit, the patient’s condition and liver status stabilized. Further antibiotic therapy for syphilis was administered without incident. The patient was eventually discharged but died of decompensated liver disease 6 months later.

Syphilitic infection of the liver is well documented [4–6]. This case illustrates the potential for hepatic complications resulting from syphilitic infection and its treatment in cases of HIV-HCV coinfection. Liver injury due to syphilis is thought to be immune mediated, although obstruction of portal lymph nodes by syphilitic adenitis has been proposed. The histological findings are variable and nonspecific and include portal inflammatory infiltrates, hepatocellular necrosis, granuloma, and cholestasis. There is insufficient knowledge of the effects of HIV infection, if any, on the histological manifestations of syphilitic hepatitis.

The Jarisch-Herxheimer reaction is clearly life-threatening in patients with preexisting cirrhosis and limited hepatic synthetic reserve. The rapid lysis of spirochetes releases heat-stable pyrogen, which produces this febrile illness. It is unclear what influence HIV-related immune suppression has on the severity of this reaction. It is noteworthy that among an HIV-seropositive cohort with syphilitic hepatitis (n = 7), no one developed a Jarisch-Herxheimer reaction [7].

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Curtis Cooper, Paul MacPherson, and J. B. Angel
Division of Infectious Disease, The Ottawa Hospital—General Campus, Ottawa, Ontario, Canada

References


Reprints or correspondence: Dr. Curtis Cooper, G12-501 Smyth Rd., The Ottawa Hospital—General Campus, Ottawa, Ontario, Canada. K1H 8L6; ccooper@ottawahospital.on.ca.

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Breakthrough Fusariosis in a Patient with Acute Lymphoblastic Leukemia Receiving Voriconazole Prophylaxis

Sir—Voriconazole is a broad-spectrum triazole antifungal drug with excellent activity against Aspergillus species, most Candida species, and several less-common invasive fungi but with limited activity against pathogenic Zygomycetes. Reports on the successful use of voriconazole therapy for patients with invasive fusariosis [1–3] and in vitro studies showing that the MICs of voriconazole against Fusarium species are usually lower than the MICs of itraconazole and are frequently lower than the MICs of amphotericin B [4, 5] seem to suggest a promising role for voriconazole as a life-saving therapy for immunocompromised hosts with Fusarium infections. For these reasons, the US Food and Drug Administration approved voriconazole for the treatment of Fusarium infection in patients intolerant of or with an infection refractory to other drugs.

Given its broad spectrum and the availability of both oral and intravenous formulations, voriconazole has also been used as antifungal prophylaxis instead of fluconazole, a drug without antimold activity [6–8]. However, the occurrence of breakthrough fungal infections in patients receiving long-term voriconazole therapy has been reported recently. Most of these infections were due to Zygomycetes, but infections with other fungal species have also been observed in these patients [6–8]. Here, we describe a case of breakthrough fusariosis in a patient with acute lymphoblastic leukemia (ALL) receiving long-term voriconazole prophylaxis.

A 22-year-old man received a diagnosis of pre-B cell ALL, and his condition was treated with induction, consolidation, and autologous peripheral blood stem cell transplantation, from February to August 2003. In May 2004, a first leukemia relapse refractory to salvage therapy occurred, and in July 2004, a second chemotherapy course was started. While neutropenic, the patient experienced fever refractory to broad-spectrum antibiotics. A chest CT scan showed a left basal nodular lesion with pleural effusions, making possible a fungal infection, and liposomal amphotericin B (LAmB [Ambisome; Gilead
resistant (e.g., Zygomycetes) or sometimes infection with organisms that are always could be associated with the emergence of most to voriconazole-susceptible fungi, such as these cases, the treatment of infections due apy and immunosuppressive regimens. In patients with a progressive hematological disease who receive multiple chemother-apy and immunosuppressive regimens. In day 23 after the start of chemotherapy, diffuse skin lesions appeared on the left leg. A breakthrough mycosis was suspected, LAmB therapy (3 mg/kg/day) was started instead of voriconazole therapy, and Fusarium species were documented from 3 blood cultures and 1 skin lesion swab. The dose of LAmB was increased to 10 mg/kg, but the patient died 43 days after start of chemotherapy, with disseminated fusariosis. Antifungal susceptibility testing of the isolate performed by the NCCLS M38-A broth microdilution method revealed an MIC and minimum fungicidal concentration (MFC) for amphotericin B of 0.5 and 1 µg/mL, respectively, and an MIC and MFC for voriconazole of 4 and >16 µg/mL, respectively. The MIC for itraconazole was >16 µg/mL.

Although voriconazole is the only licensed antifungal drug with some anti-Fusarium activity besides amphotericin B, several Fusarium isolates demonstrate in vitro resistance to the drug [4, 5]. Therefore, the observation of breakthrough fusariosis during voriconazole prophylaxis is not an unexpected event. As observed by other authors [8], the development of voriconazole-resistant fungal infections may be considered a serious risk for patients with a progressive hematological disease who receive multiple chemotherapy and immunosuppressive regimens. In these cases, the treatment of infections due to voriconazole-susceptible fungi, such as most Candida and Aspergillus species, could be associated with the emergence of infection with organisms that are always resistant (e.g., Zygomyces) or sometimes resistant (e.g., Candida glabrata, Acernon-iun species, and Fusarium species) to the azole. Clinicians should be aware of the potential for breakthrough infections caused by several fungi, including Fusarium species, particularly for patients with severe, prolonged immunosuppression who are receiving long-term voriconazole treatment.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Laura Cudillo,1 Corrado Girmenia,2 Stefania Santilli,2 Alessandra Picardi,1 Teresa Dentamaro,1 Andrea Tendas,1 and Paolo de Fabritiis1

1Department of Hematology, University Tor Vergata, and 2Dipartimento di Biotecnologie Cellulari ed Ematologia, University “La Sapienza,” Rome, Italy

References


Reprints or correspondence: Dr. Laura Cudillo, Dept. of Hematology, University Tor Vergata, Ospedale S. Eugenio, Piazzale Umanesimo 10, 00144 Rome, Italy (cudillo@med.uniroma2.it).

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