diabetes in HIV-infected persons [1]. Although most isolates show in vitro susceptibility to commonly used antifungal agents, fluconazole-resistant strains have been recovered from oropharyngeal specimens from HIV-infected persons. In vitro studies have proven that fluconazole-resistant strains can be generated from susceptible isolates by exposure to fluconazole [2]. There are increasing reports of C. dubliniensis fungemia in immunocompromised hosts [3–5]. To date, all of the isolates from such cases were fluconazole susceptible. In addition, there have been no documented cases of death attributed to C. dubliniensis infection. I describe a patient with acquired immunodeficiency syndrome (AIDS) who is, to my knowledge, the sentinel case of mortality attributable to C. dubliniensis infection.

A 33-year-old man with AIDS (CD4 cell count, 100 cells/mL; viral load, 309,000 copies/mL) presented with a 3-day history of fever, abdominal pain, jaundice, and decreasing urine output. His medical history was notable for multiple episodes of oral candidiasis, which had been treated successfully with fluconazole. Three weeks before presentation, the patient had been hospitalized at our institution with methicillin-susceptible Staphylococcus aureus bacteremia and tricuspid valve endocarditis, secondary to intravenous drug use. A peripherally inserted central catheter (PICC) had been placed, and the patient had been transferred to a subacute care facility to complete a 4-week course of vancomycin therapy. He was not treated with any antiretroviral medications.

At admission, the patient’s medications included vancomycin. Allergies included a rash caused by penicillin. The patient’s temperature was 39.2°C, blood pressure was 100/50 mm Hg, heart rate was 112 beats/min, and respiratory rate was 24 breaths/min. Physical examination revealed icteric sclerae and skin, a harsh systolic murmur, diffuse abdominal tenderness, and an intact PICC. The WBC count was 8200 cells/mm³ (83% neutrophils), the hemoglobin level was 7.6 g/dL, the platelet count was 53,000 platelets/mm³, the blood urea nitrogen level was 46 mg/dL, the creatinine level was 5.7 mg/dL, and the bilirubin level was 6.1 mg/dL. Cultures of blood obtained at admission both from a peripheral vein and from the PICC grew germs tube–producing yeast. The PICC was removed and fluconazole (400 mg/day) was added to the patient’s treatment regimen on day 2 of hospitalization. Vancomycin therapy was continued.

The patient’s multiorgan dysfunction progressed, reflected by worsening anemia and thrombocytopenia, disseminated intravascular coagulation, anuric renal failure, deteriorating hepatic function, severe metabolic acidosis, and protracted hypotension. Multiple blood cultures grew germ tube–producing yeast. Results of a fluorescent in situ hybridization assay indicated that the yeast isolates were not Candida albicans. Serum samples tested negative for cryptococcal antigen. An echocardiogram showed no new valvular vegetations. Fluconazole was changed to caspofungin on day 3 of hospitalization.

The yeast was C. dubliniensis. In vitro drug-susceptibility studies showed that the isolates were susceptible to fluconazole (MIC, 0.5 μg/mL). The patient died on day 8 of multi-organ failure due to C. dubliniensis septicemia. Autopsy findings confirmed disseminated C. dubliniensis infection with hepatic, renal, peritoneal, and bone marrow involvement.

To my knowledge, this is the first reported fatality due to C. dubliniensis fungemia. Clinical vigilance, aggressive and early diagnosis, and appropriate therapy are essential to guard against this emerging pathogen. Prior azole exposure and the ability of C. dubliniensis to develop induced fluconazole resistance should also be considered when choosing antimicrobial treatment for C. dubliniensis fungemia in immunocompromised patients.

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References


Gatifloxacin Therapy Associated with Hypoglycemia

Sir—Sporadic published case reports [1, 2] and anecdotal reports to the US Food and Drug Administration MedWatch system have linked administration of fluoroquinolone antibiotics (FQAs), in particular gatifloxacin, with early-onset hypoglycemia in patients with diabetes. Most reported patients were aged ≥65 years and were concomitantly receiving a sulfonylurea class drug. FQAs have been demonstrated to augment insulin release in a dose-dependent manner from isolated pancreatic islet cells [3] and to increase insulin levels in patients with type 2 diabetes mellitus who are not receiving medication [4], actions similar to those of sul-
fonyureas. In consideration of the data indicating that the background rate of hypoglycemia in sick elderly persons who require hospital admission may be ~5% [5], we examined whether gatifloxacin therapy is associated with a higher incidence of hypoglycemia than therapy with non-FQA drugs in this group of patients.

We prospectively studied a convenience sample of patients aged ≥65 years who were admitted to our urban municipal hospital and who initiated antibiotic therapy. We defined hypoglycemia to be a blood sugar level of ≤60 mg/dL within 48 h after the first dose of antibiotic. The gatifloxacin cohort comprised any patient receiving gatifloxacin, and patients receiving non-FQA drugs were part of the control cohort. Exclusion criteria included admission to the intensive care unit; the use of any antibiotic within 48 h of hospital admission; a blood sugar level that is unknown or that is ≤60 mg/dL prior to the initial antibiotic dose; the receipt of pentamidine, quinidine, octreotide, or corticosteroids (≥20 mg/day of prednisone); and a known or suspected adrenal insufficiency or insulin-secreting tumor. Capillary blood sugar levels were measured 4 times daily for patients with diabetes, and abnormal readings were confirmed by blood glucose determinations. Patients without diabetes had their blood sugar levels measured at least once per day and if symptomatic.

The results from 5 (10%) of 50 patients receiving gatifloxacin and 1 (1.1%) of 89 patients receiving non-FQA drugs met the definition of hypoglycemia (P = .041, by z test). Of the first 5 patients in the gatifloxacin cohort, 16 (32%) were diabetic, compared with 34 (38%) of the patients in the control cohort. Of the 6 patients who developed hypoglycemia, 5 were diabetic, and only 2 were receiving oral hypoglycemic medication. In the gatifloxacin cohort, hypoglycemia developed in 4 (25%) of 16 patients with diabetes, compared with 1 (3%) of 34 patients without diabetes (P = .055, by z test). Of the 5 patients with hypoglycemia in the gatifloxacin cohort, 2 had elevated serum creatinine levels.

This small prospective cohort study supports the relationship between gatifloxacin therapy and the development of hypoglycemia within 48 h of the initial dose of this antibiotic in patients aged ≥65 years, especially if they have diabetes. Concomitant administration of oral hypoglycemic therapy is not necessary. Clinicians should be aware of this association, and, because of the possible dose dependency of this effect, they should ensure an appropriate dose modification of gatifloxacin therapy in patients with renal insufficiency, including age-related decrease in creatinine clearance. We did not examine the relationship between the administration of other FQAs and early-onset hypoglycemia.

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