Successful Use of Liposomal Amphotericin B in a Case of Amphotericin B–Induced Nephrogenic Diabetes Insipidus

For the past several years, fungi have been responsible for most of the fatal infections in patients with acute leukemias. Therefore, early empiric administration of amphotericin B to patients with persistent granulocytopenia and fever despite therapy with broad-spectrum antibiotics has been proposed for prompt treatment of occult fungal infections [1, 2]. Higher dosages of 1–1.5 mg/(kg · d) of amphotericin B are associated with higher rates of dose-limiting renal toxicity. We describe the clinical course of a patient who developed nephrogenic diabetes insipidus, a very rare type of renal toxicity related to amphotericin B and its management.

A 38-year-old female patient was diagnosed as having acute myelomonocytic leukemia. A chemotherapy regimen with cytarabine, idarubicin, and etoposide was instituted. The patient was neutropenic and became febrile. Despite treatment with broad-spectrum antibiotics, her fever persisted, and, after 6 days, therapy with amphotericin B (1 mg/[kg · d]) was commenced. After receiving amphotericin B for 4 days, the fever resolved; however, the patient was still severely neutropenic. Three days later she developed polydipsia and polyuria (9.4 L/day maximum). After receiving amphotericin B for 10 days, plasma electrolyte levels were as follows: sodium, 148 mmol/L; potassium, 3.5 mmol/L; and calcium, 2.2 mmol/L. Plasma urea level was 27 mg/dL, creatinine level was 0.6 mg/dL, and glucose level was 154 mg/dL. Plasma osmolality was elevated at 318 mosmol/kg with a corresponding urine osmolality of 274 mosmol/kg. Desmopressin, 20 μg, administered intranasally failed to reduce urine output.

The patient’s symptoms together with the laboratory parameters and the failure to respond to exogenous desmopressin suggested the diagnosis of nephrogenic diabetes insipidus resulting from therapy with amphotericin B. Because of the recent defervescence after initiation of antifungal therapy and the worsening features of nephrogenic diabetes insipidus, we continued antifungal treatment with fluconazole (400 mg/d), which resulted in a rapid decrease in urinary output, normalization of plasma electrolyte levels (sodium, 134 mmol/L) and plasma osmolality (284 mosmol/kg).

Meanwhile, the second course of the induction chemotherapy was administered. Three days after the start of fluconazole, however, fever recurred prompting us to readminister amphotericin B. The fever responded again to amphotericin B. When signs of diabetes insipidus recurred, with polydipsia, polyuria, rising plasma sodium levels and plasma osmolality (304 mosmol/kg), and low urine osmolality (264 mosmol/kg), we decided to substitute amphotericin B with 3 mg/(kg · d) liposomal amphotericin B (Ambisome, NeXstar Pharmaceuticals, Braunschweig, Germany). Within 1 day of treatment with liposomal amphotericin B, urinary output decreased from 6.8 L to 3.4 L. Clinical/biochemical features of nephrogenic diabetes insipidus did not recur during the following 16 days while the patient received liposomal amphotericin B, and the patient remained afebrile until hematopoietic regeneration. During the entire clinical course, repeated cultures of blood and urine, as well as imaging studies remained negative.

Nephrogenic diabetes insipidus is characterized by a lack of response of the collecting ducts to circulating antidiuretic hormone, resulting in impairment of the urine concentrating ability and a consecutive loss of free water. The diagnosis of diabetes insipidus is based on a 24-hour urine volume of >30 mL/kg and a urine osmolality of <300 mosmol/kg or a urine

References
specific gravity of $<1010$ [3]. Failure to respond to vasopressin confirms the diagnosis of nephrogenic diabetes insipidus.

A variety of drugs have been reported to cause nephrogenic diabetes insipidus, including amphotericin B [4]. The clinical course in our patient, with prompt resolution of symptoms after cessation of the drug proved that amphotericin B was the underlying cause. The exact mechanism by which amphotericin B causes nephrogenic diabetes insipidus is unclear. Successful use of indomethacin in a similar case suggests that renal prostaglandins and/or modulation of phosphodiesterase activity are involved [5]. Considering the potential adverse effects of indomethacin in a patient with chemotherapy-induced mucosal damage and thrombocytopenia, we favored other treatment options. First, we tried fluconazole, which proved to be a safe and effective substitute in leukemia patients with chronic disseminated candidiasis and serious amphotericin B-related toxicities [6]. Because neutropenic fever recurred during fluconazole therapy we used liposomal amphotericin B, according to a recent report [7], as a second option with success. Our case underscores the value of liposomal amphotericin B as an alternative therapy in amphotericin B–induced nephrogenic diabetes insipidus.

**Septic Shock caused by* Staphylococcus lugdunensis***

Coagulase-negative staphylococci are commensal organisms of the human skin. They have recently been recognized as major nosocomial pathogens. This has prompted more interest in their detailed characterization. We describe a patient who developed septic shock caused by *Staphylococcus lugdunensis* acquired through platelet transfusion.

A 71-year-old man with a history of pancytopenia secondary to myelodyplasia presented to the emergency room complaining of shortness of breath and rectal bleeding of several hours’ duration. He denied cough, fever, or malaise. He also had a history of prostate cancer that had been treated with radiation. During the past year he had had multiple admissions to the hospital because of severe anemia caused by rectal bleeding. He had refused further work-up for the bleeding, which was believed to be related to radiation colitis.

Physical examination on admission was positive for pallor, tachycardia, and rectal bleeding. He did not have an iv catheter at the time of admission. Chest radiography was within normal limits. Laboratory evaluation revealed the following values: WBCs, 900/mm$^3$ with 17% neutrophils; hematocrit, 16%; and platelet count, 8,000/mm$^3$. The patient was admitted to the intensive care unit, and he received platelets and two units of packed red blood cells. While receiving the second unit of red blood cells, he became febrile (temperature, 104°F). Later he become hypotensive and developed respiratory failure. Blood for cultures was obtained; he was intubated, connected to mechanical ventilation, treated with broad-spectrum antibiotics, and supported with vasopressors. The transfused blood was retyped and cultured. The platelet culture yielded *S. lugdunensis* that was susceptible to penicillin. A few days later the patient had recovered, after completion of therapy with vancomycin (due to concern of a penicillin allergy). There was neither evidence of allergic reaction to the blood products nor of any other source of infection. The transfused blood was sterile. There were no reports of any other infected blood products in the blood bank.

Platelet components contaminated with bacteria are an important source of transfusion-associated bacterial sepsis, but the rates are low (0.08%) [1]. Although coagulase-negative staphylococci are usually considered avirulent or usual contaminants of blood cultures, their roles as causes of disease are well established in certain clinical situations, particularly when prosthetic material is present or in profoundly immunocompromised hosts. Wade et al. [2] reported *Staphylococcus epidermidis* as a frequent pathogen in patients with severe granulocytopenia. Winston et al. [3] reported coagulase-negative staphylococci as the most common cause of bacteremia in patients receiving immunosuppressive therapy.

*S. lugdunensis*, first described in 1988, is a coagulase-negative species of the genus *Staphylococcus*, and it may represent up to 10% of the coagulase-negative staphylococci [4]. However, its role as a pathogen has been well established, and, although the majority of clinical isolates represent colonization [4], it can cause serious infections [5]. Indeed, it has been suggested that *S. lugdunensis* may be more pathogenic than other species of coagulase-negative staphylococci [6]. However, this is the first report of *S. lugdunensis* as a cause of septic shock.

Jose G. Castro and Lorraine Dowdy
Division of Infectious Diseases, Jackson Memorial Hospital/University of Miami, Miami, Florida

---

Ernst Späth-Schwalbe, Antje Koschuth, Annett Dietzmann, Julie Schanz, and Kurt Possinger
Charité, Department of Internal Medicine, Medical Oncology and Hematology, Berlin, Germany

**References**