A Cryptogenic Cause of Hypokalemia in a Patient with Cryptococcal Meningitis

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Case Presentation

A 39-year-old man with a past medical history of HIV/AIDS (on Biktarvy, CD4 282, VL 90), recurrent cryptococcal meningitis, right basal ganglia CVA in 2022 with residual LLE weakness, hypertension, and polysubstance abuse (cocaine, amphetamines, THC, tobacco) presented to the emergency department with back pain after a mechanical fall due to lower extremity weakness. Initial labs revealed severe hypokalemia and acute kidney injury, with a potassium level of 2.3 despite home supplementation and creatinine of 1.7 mg/dL (baseline 1.1-1.2 mg/dL). He had a blood pressure of 137/84. The patient was diagnosed with HIV/AIDS and cryptococcal meningitis initially in September 2021. He was prescribed a 14-day course of amphotericin B and flucytosine followed by oral fluconazole maintenance therapy. He was noted to have hypokalemia at the time, but it was attributed to the amphotericin B and normalized before discharge with inpatient supplementation. Throughout the following four years, the patient has had multiple recurrences of cryptococcal meningitis with identical treatments, which included fluconazole ranging from 400 to 800mg in addition to varying amounts of potassium chloride supplementation. At the time of the current admission, the patient was taking 600mg fluconazole daily with daily potassium chloride supplementation. While inpatient, the patient's potassium levels were as low as 2.0 despite supplementation of 200 mEq/day, and nephrology was consulted. His workup revealed very low renin and aldosterone levels, with elevated serum bicarbonate and persistent hypertension. He denied licorice ingestion. A diagnosis of apparent mineralocorticoid excess was suspected, and the patient was started on spironolactone. His hypokalemia resolved with this therapy, and he was able to discontinue potassium supplementation prior to discharge.

Discussion

The global guideline established by the European Confederation of Medical Mycology, International Society for Human and Animal Mycology, along with the American Society for Microbiology, outlines induction, consolidation, and maintenance therapy for the treatment of cryptococcal meningitis. Recommended treatment includes amphotericin B-based regimens and flucytosine followed by fluconazole for consolidation and long-term suppression. However, azole antifungal therapy has adverse effects including disruption of adrenal and gonadal steroid synthesis, specifically by inhibiting 11-beta-hydroxysteroid dehydrogenase, which can lead to clinical syndromes such as AME. AME is characterized by hypertension, hypokalemia, and metabolic alkalosis with suppressed levels of renin and aldosterone. Posoconazole and itraconazole show the strongest association with dose-dependent drug-induced AME due to structural similarities, and guidelines recommend transitioning to fluconazole when this condition develops. This case emphasizes the importance of monitoring blood pressure and electrolytes in patients receiving azole antifungals and highlights that AME can develop with any azole drug. In patients that require long-term azole antifungals, the combination of spironolactone and potassium supplementation may be beneficial in mitigating these effects.