A Case of Amphotericin and Fluconazole Resistant Cryptococcal Meningitis in Advanced HIV Patient

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This is a case of 38-year-old male with G6PD deficiency, schizophrenia, asthma, advanced HIV non-adherent to antiretroviral therapy (ART), with a prolonged history of incompletely treated cryptococcal meningitis and fungemia, who presented in January 2026 after being found down at home. Admission blood cultures were positive for Cryptococcus neoformans var gatti. Lumbar puncture (LP) was performed, and CSF cultures grew Cryptococcus neoformans var gattii. Induction therapy was initiated with amphotericin B 4 mg/kg daily and flucytosine 25 mg/kg every 6 hours. Initial MRI brain revealed signal abnormality in bilateral caudate heads, anterior ganglio-capsular regions that was most compatible with cryptococcal meningitis. Although the blood cultures cleared within 3 days, due to frequent change in mental status, the patient underwent weekly LPs over the next 3 months with CSF cultures persistently positive for Cryptococcus with opening pressures between 14-33 cm H2O. ART with DRV/c-FTC-TAF (darunavir/cobistat-emtricitabine-tenofovir alafenamide) and DTG (dolutegravir) was started after completion of 5 weeks of induction therapy. The patient's HIV viral load decreased drastically from 884,169 to 1,050 copies/mL after 2 weeks. His CSF culture was sent for resistance testing, which indicated that amphotericin B and fluconazole were consistent with epidemiological cutoff values (ECVs) observed with acquired resistance. Amphotericin B was discontinued, and voriconazole 4 mg/kg twice a day was initiated after 9 weeks. Repeat MRI brain revealed a significant increase in previously described signal abnormalities with worsening mass effect and progressive effacement of frontal horns of lateral ventricles, reflecting progressive worsening cryptococcal meningitis. After 5 weeks, dexamethasone was started and ART was discontinued due to concern for IRIS (Immune Reconstitution Inflammatory Syndrome. After discussion with experts in the field of Cryptococcus, amphotericin B was restarted at a higher dose of 6 mg/kg to overcome the high ECV, in addition to treatment with voriconazole and flucytosine. ART was also resumed. Patient developed pancytopenia and renal dysfunction, likely secondary to antifungal therapy. Blood cultures cleared 3 days after amphotericin B was restarted. Unfortunately, his mental status continued to decline, and he was eventually transitioned to hospice in April 2026.