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Occam’s Razor Need Not Apply: A Case of Concurrent Cryptococcal Meningitis and Primary Central Nervous System Lymphoma in an Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome Patient

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CLINICAL VIGNETTE

A 28-year-old man with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) (CD4+ cells 4/1%) was diagnosed and treated for cryptococcal meningitis (CM) 3 weeks before admission with a 14-day course of amphotericin and flucytosine and subsequently discharged on oral fluconazole. However, surveillance of cerebrospinal fluid (CSF) cultures collected before discharge later turned positive for Cryptococcus neoformans and he was called back for evaluation.

On admission, the patient reported headache, diplopia, and overall malaise. A head computed tomography showed new enhancing mass lesions in the left and right caudate nuclei with vasogenic edema (Figure 1). Repeat lumbar puncture showed a high opening pressure of 35 mmH2O and C. neoformans detected by antigen and CSF culture. He was resumed on amphotericin and flucytosine induction therapy for presumed relapsed CM with possible cryptococcoma.

A magnetic resonance imaging (MRI) of the brain was obtained and showed 2 different lesions with increased density, restricted diffusion, and low T2 signal relative to normal brain parenchyma, which were most concerning for central nervous system (CNS) lymphoma or toxoplasmosis and less concerning for cryptococcoma by radiographic appearance (Figure 2).

Further CSF studies ruled out toxoplasmosis but showed positive Epstein-Barr virus DNA polymerase chain reaction, again concerning for CNS lymphoma. A brain biopsy could not be obtained due to the location of lesions. Therefore, MRI spectroscopy was performed and showed an increase in the size of both masses suggestive of malignancy (Figure 3) and an elevated choline peak with decreased N-acetylaspartate (NAA) peak, consistent with high-grade CNS lymphoma (Figure 4).

The patient was started on antiretroviral therapy and steroids with initial improvement in symptoms, but he subsequently developed acute neurologic decompensation requiring emergent whole brain radiation therapy, which was complicated by hemodynamic instability and hypothermia. He eventually stabilized and was discharged on oral fluconazole and to complete radiation as an outpatient followed by high-dose methotrexate therapy (Figure 5).

DISCUSSION

Occam’s razor is a principle of diagnostic parsimony that pushes physicians for a unifying diagnosis. However, for patients with advanced HIV/AIDs, the presence of multiple opportunistic infections is not uncommon and parsimony is often impossible. In our patient, Occam’s razor would suggest that cryptococcoma, although rare, would be the most likely diagnosis given recent infection and persistently positive CSF cultures.
However, given advanced immunosuppression, radiographic appearance, and symptom progression despite therapy, the differential diagnosis was broadened.

Diagnosis of CNS lymphoma is difficult and often requires brain biopsy. When location of lesions precludes direct tissue sampling, MRI spectroscopy can be used with enhancement of specific frequencies (eg, elevated choline peak) being highly suggestive [1]. Accurate diagnosis is important, because the treatments of these 2 CNS processes are incongruent. Central nervous system lymphoma is treated with urgent antiretroviral initiation, which could potentiate CM immune reconstitution syndrome [2]. Treatment of both diseases can lead to severe side effects such as pancytopenia from flucytosine, hypothermia, and

![Figure 2](image1.png)  ![Figure 3](image2.png)  ![Figure 4](image3.png)  ![Figure 5](image4.png)
encephalopathy from brain radiation [3] and fever with rigors or renal failure from amphotericin.

Our case illustrates the importance of keeping a broad differential diagnosis in immunocompromised patients, diagnosing CNS lymphoma when tissue sampling is unavailable, and the value of diagnostic accuracy to minimize treatment side effects.

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