

DIAGNOSTIC CHALLENGES AND OUTCOMES OF EMPIRICAL THERAPY FOR NEUROCYSTICERCOSIS IN AN UNTREATED HIV PATIENT

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ABSTRACT

This case report describes a 35-year-old woman, Jane Doe (JD), who recently immigrated to Miami, Florida from Latin America and presented to the emergency department after a witnessed seizure. She reported one prior seizure seven years earlier in her home country, for which she did not receive anti-seizure therapy. JD also disclosed a 16-year history of human immunodeficiency virus (HIV) infection and had been off treatment for the past five years.

An extensive workup for potential infectious etiologies—including tuberculosis, syphilis, toxoplasmosis, cytomegalovirus, herpes simplex virus, strongyloidiasis, and hepatitis—was negative. Magnetic resonance imaging revealed multiple calcified supra- and infratentorial lesions with vasogenic edema and internal septations. Given these findings and JD's history of HIV infection and residence in an endemic region prior to immigration, the differential diagnosis

included central nervous system (CNS) lymphoma, toxoplasmosis, and neurocysticercosis (NCC). Diagnosis was complicated by her advanced HIV disease, negative serologic testing, and the broad differential diagnosis for multiple ring-enhancing lesions in immunocompromised patients.

JD's presentation met Infectious Diseases Society of America criteria for NCC. She was started on a 14-day course of albendazole and praziquantel, as well as levetiracetam for seizure prevention and Bictarvy and Bactrim for HIV management. She was discharged after 12 days with plans for outpatient follow-up. This case underscores the importance of considering NCC in patients with untreated HIV infection and relevant epidemiologic exposures, even when serologic testing is negative.

Keywords: neurocysticercosis, HIV, case report

INTRODUCTION

Neurocysticercosis (NCC) is a parasitic infection of the central nervous system caused by the larval stage of *Taenia solium*. The parasite is endemic in many parts of the world, including Latin America, Southeast Asia, and sub-Saharan Africa. In these regions, NCC accounts for approximately 30% of epilepsy cases and is a leading cause of new-onset seizures in adults [1]. Although not endemic in the United States (US), NCC has become increasingly prevalent with rising immigration from affected areas.

Transmission occurs through ingestion of *T. solium* eggs shed in human feces. Clinical manifestations vary widely depending on the number, stage, and location of cysts, as well as the host immune response. Patients most commonly present with seizures, headaches, or signs of elevated intracranial pressure. NCC can easily be mistaken for other infectious or structural brain lesions. Diagnosis typically relies on neuroimaging, supported by epidemiologic factors and serologic testing. The enzyme-linked immunoelectrotransfer blot (EITB) is the preferred serologic assay due to its high sensitivity and specificity in patients with multiple cysts, while ELISA may yield false-negative results and complicate diagnosis [2]. Diagnostic uncertainty is further amplified in individuals with untreated HIV, whose differential diagnosis or new neurologic symptoms includes a wide range of opportunistic infections and neoplasms [3].

Here, we describe the case of a 35-year-old woman with untreated HIV infection who presented with new-onset

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seizures and multifocal parenchymal lesions consistent with NCC. Her case underscores the challenges of distinguishing NCC from other HIV-associated CNS diseases and highlights the importance of considering NCC in patients with relevant epidemiologic exposures.

CASE PRESENTATION

The patient is a 35-year-old woman with a history of HIV diagnosed in Cuba in 2006 who has not taken antiretroviral therapy for the past five years due to religious beliefs. She was brought to the emergency department by EMS on 12/9/22 after a witnessed seizure. According to a family member, she had been lying on a sofa when she suddenly became unresponsive and developed generalized shaking movements lasting “about 20 minutes.” This was followed by a brief postictal period during which she “fell asleep for a few minutes” and then awoke drowsy and disoriented. Neither the patient nor the family reported urinary or fecal incontinence, head trauma, or tongue biting. On evaluation, the patient denied headache, visual changes, limb weakness or numbness, shortness of breath, or diarrhea.

She reported a remote history of a single seizure many years earlier in Cuba, which she attributed to stress. She denied alcohol or illicit drug use. She endorsed symptoms of anxiety and depression related to family stress but denied suicidal ideation or plan.

She reported maintaining adequate oral intake but noted an unintentional weight loss of approximately 50 pounds over the past year. From an epidemiological perspective, the patient’s prolonged residence in a region where *Taenia solium* is endemic supported consideration of neurocysticercosis, as infection can occur through fecal–oral ingestion of parasite eggs independently of pork consumption.

Admission laboratory studies (**Table 1**) were notable for normocytic anemia, leukopenia, an ESR of 71, and a lactate level of 3.4. A non-contrast head CT (**Figure 1**) demonstrated multiple calcified parenchymal lesions with areas of vasogenic edema. Her EKG showed normal sinus rhythm. The CT findings raised concern for an HIV/AIDS-related central nervous system infection or lymphoma, prompting admission to the inpatient service with early neurology and infectious disease consultation.

The patient was started on levetiracetam 500 mg twice daily. Although she tested positive for parainfluenza on admission, she remained asymptomatic without respiratory complaints. Brain MRI (**Figure 2**) revealed numerous—at least 20—supra and infratentorial lesions, several of which demonstrated calcification, peripheral enhancement, and internal septations. Vasogenic edema was also present. Given the multiplicity and characteristics of these lesions, neurocysticercosis was strongly suspected.

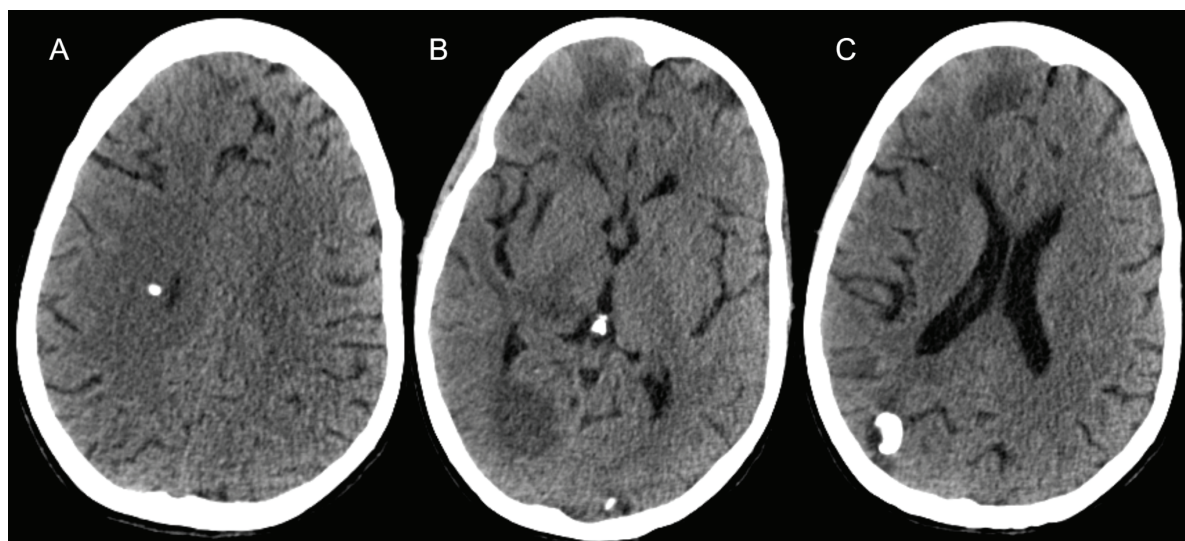


Figure 1. Brain CT without Contrast

CT Brain findings of intracranial lesions at admission. (A, B) Axial Brain CT without contrast images demonstrate numerous calcified parenchymal lesions and regions of vasogenic edema. (D) Largest lesion measuring to 18 mm on long axis.

Table 1. Admission Biochemistry Findings

| Biochemistry | Reference range | Day 1 |
|---|-----------------|----------|
| CBC with differential | | |
| WBC ($\times 10^3/\mu\text{L}$) | 3.40–11.0 | 4.01 |
| RBC ($\times 10^6/\mu\text{L}$) | 3.80–5.20 | 3.21 (L) |
| Hemoglobin (g/dL) | 12.0–15.0 | 8.0 (L) |
| MCV ($\times 10^{-15}\text{L}$) | 80–100 | 80.4 |
| Hematocrit (%) | 35.0–45.0 | 25.8 (L) |
| Platelets ($\times 10^3/\mu\text{L}$) | 130–360 | 191 |
| Metabolic panel | | |
| Sodium (mEq/L) | 136–145 | 137 |
| Potassium (mEq/L) | 3.5–5.1 | 4.2 |
| Chloride (mEq/L) | 98–107 | 104 |
| Bicarbonate (mEq/L) | 21–32 | 26 |
| Calcium (mg/dL) | 8.5–10.1 | 8.6 |
| Glucose (mg/dL) | 70–126 | 101 |
| Liver function | | |
| ALT (U/L) | 16–65 | 18 |
| AST (U/L) | 8–37 | 22 |
| Total bilirubin (mg/dL) | 0.2–1.0 | 0.1 (L) |
| Kidney function | | |
| Creatinine (mg/dL) | 0.55–1.02 | 0.68 |
| BUN (mg/dL) | 7–18 | 19 (H) |
| BUN/Cr ratio | 12.0–20.0 | 27.9 (H) |
| Lactic acid (mmol/L) | 0.5–2.2 | 3.4 (H) |
| Other | | |
| ESR (mm/hr) | 0–20 | 71 |

CBC = complete blood count; WBC = white blood cell; RBC = red blood cell; MCV = mean corpuscular volume; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; Cr = creatinine; ESR = erythrocyte sedimentation rate

The EEG performed on 12/12 was unremarkable. Given the patient’s low CD4 count, she was started on trimethoprim-sulfamethoxazole SS daily for Pneumocystis jirovecii pneumonia (PJP) prophylaxis per Infectious Disease (ID). Due to significant cerebral edema, corticosteroid therapy was initiated on 12/15. As recommended by ID, steroids were to be administered for at least 24–48 hours before starting antiparasitic treatment for neurocysticercosis. Because several lesions were not fully calcified and were suspected to represent viable cysts, treatment for active neurocysticercosis was planned. The recommended regimen included albendazole (15 mg/kg/day, max 800 mg/day) and praziquantel (50 mg/kg/day) for 14 days, in conjunction with steroids. Ophthalmology was consulted prior to therapy initiation; the baseline exam was normal, and no papilledema was observed. Neurosurgery was consulted regarding a potential

transfer to Baptist Main. However, the patient’s neurological examinations remained stable throughout hospitalization, and repeat imaging showed no interval changes. After detailed discussion, neurosurgical evaluation was deemed unnecessary. The patient was transferred to the stepdown unit at WKBH for initiation of albendazole and praziquantel, with neurochecks ordered every two hours. Initial serologic testing for neurocysticercosis was performed using an ELISA and returned negative. Infectious Disease consultants documented that ELISA testing has limited diagnostic utility for neurocysticercosis and therefore ordered confirmatory EITB testing. The EITB subsequently resulted as negative for cysticercus IgG antibodies. As noted by the performing laboratory, a negative EITB result does not exclude the diagnosis of neurocysticercosis. In the setting of advanced HIV infection with severe immunosuppres-

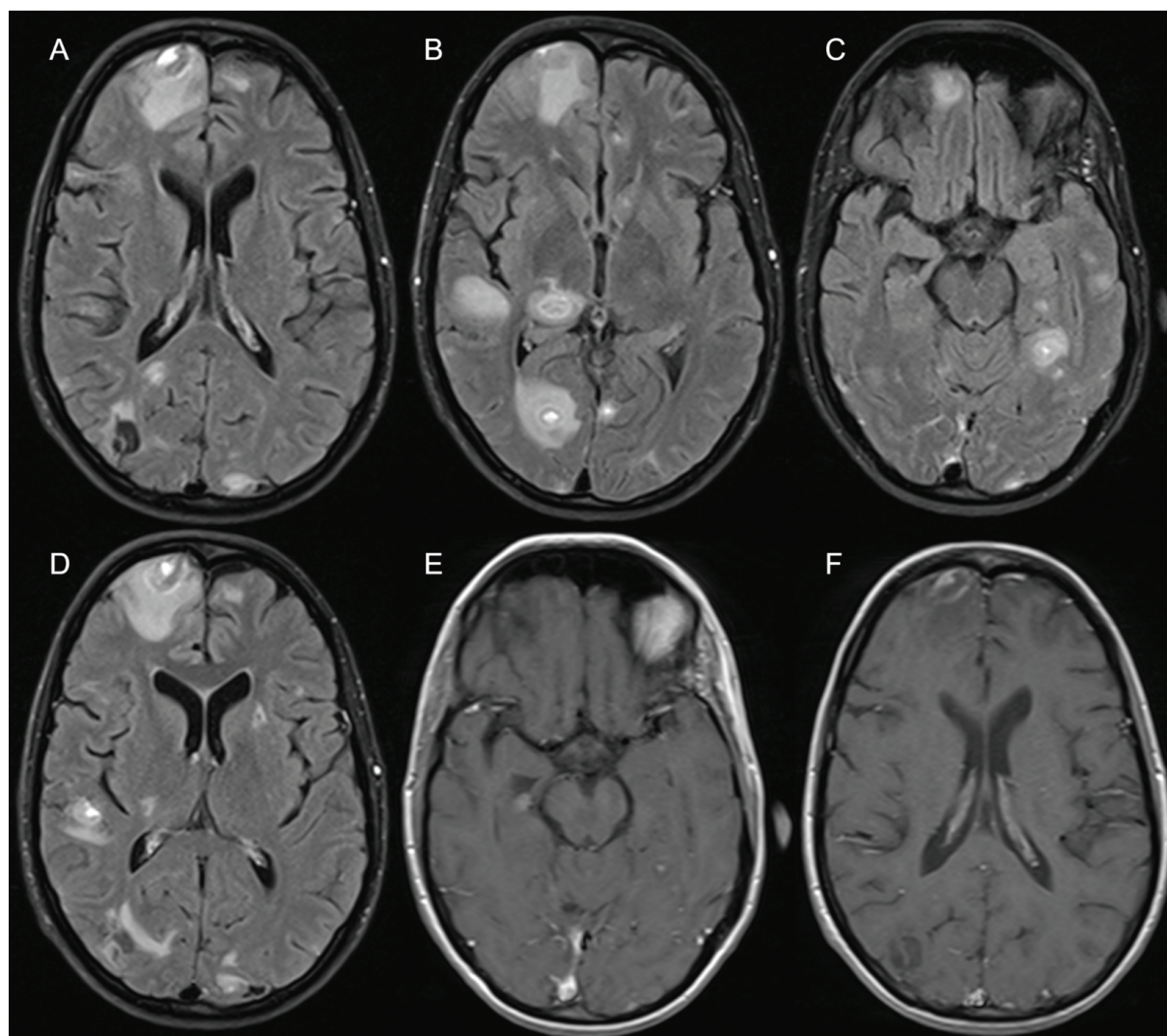


Figure 2. Brain MRI with and without Contrast

MRI findings of intracranial lesions at admission, Images demonstrate multiple supra- and infra-tentorial lesions. (A, B, C, D) Axial T2/FLAIR images show numerous lesions with classic “hole-with-dot” appearance consisting of peripheral enhancement, and eccentric scolex enhancement. Some lesions demonstrate associated calcification and internal septation as well. Vasogenic edema is associated with most of the lesions. (E, F) Axial T1 Post redemonstrates the “hole-with-dot” lesions.

sion (CD4 count 16 cells/ μ L), false-negative serologic results have been well described. The patient will require close outpatient follow-up with Infectious Diseases specialist. She has an appointment scheduled for next week, at which time ID will repeat a CBC and comprehensive metabolic panel. She will also need outpatient neurology follow-up; due to insurance requirements, a referral from her primary care provider will be necessary. These details, along with the importance of medication adherence, were reviewed with the patient, who verbalized understanding. At discharge, the patient was prescribed albendazole and praziquantel to complete a 14-day treatment

course, along with a Medrol Dosepak and famotidine for gastrointestinal prophylaxis during steroid therapy. She was also continued on levetiracetam 500 mg twice daily pending neurology evaluation and maintained on trimethoprim-sulfamethoxazole for PJP prophylaxis. A discharge CT scan of the brain (**Figure 3**) showed findings similar to admission, with multiple calcified lesions and modest improvement in vasogenic edema, though some edema persisted. Imaging did not show evidence of an immediate change in the viable cysts, as none of the lesions had resolved or decreased in size or number, despite initiation of antiparasitic and steroid therapy multiple days prior to her discharge.

Table 2. Infectious Panel

| Infectious Panel | Day 1 |
|----------------------------------|--------------|
| Hepatitis B Surface Antigen | Non Reactive |
| Hepatitis B Core IgM Antibody | Non Reactive |
| Hepatitis A IgM Antibody | Non Reactive |
| Hepatitis C IgM Antibody | Non Reactive |
| QuantiFERON | Negative |
| Strongyloides IgG Antibody | Negative |
| Toxoplasma gondii IgG | Positive |
| Toxoplasma gondii IgM | Equivocal |
| Cytomegalovirus IgG | Positive |
| Cytomegalovirus IgM | Negative |
| Herpes Simplex Virus 1 IgG | Positive |
| Herpes Simplex Virus 2 IgG | Negative |
| Herpes Simplex Virus 1 and 2 IgM | Negative |
| EBV Capsid IgM | Negative |
| Histoplasma Antibody H Band | Negative |
| HIV Viral Load | 992,000 |
| CD 4 Count (/uL) | 16 |

EBV = Epstein-Barr Virus;
 HIV = Human Immunodeficiency Virus

Images

Brain CT without Contrast – 12/10

Impression: There are multiple calcified parenchymal lesions and regions of vasogenic edema. There is no midline shift or acute intracranial hemorrhage.

Brain MRI With and Without Contrast – 12/10 Impression: There are multifocal supra- and infratentorial lesions (at least 20). Several of these lesions show calcification, peripheral enhancement, and/or internal septations. Most are associated with vasogenic edema. The leading consideration is neurocysticercosis. A superimposed or previously treated toxoplasmosis infection could present with a similar appearance. Correlation with CD4 count is recommended. Short-term follow-up and comparison with any prior outside imaging, if available, are suggested.

Brain CT Without Contrast – 12/21 Impression: In this patient with HIV, multiple areas of vasogenic edema are again observed, some of which remain associated with calcified lesions. Superimposed areas of encephalomalacia are also again noted. No new findings.

DISCUSSION

Neurocysticercosis (NCC) is a leading cause of acquired epilepsy and the most common parasitic infection of the CNS worldwide [1]. However, its presentation in patients with untreated HIV remains poorly understood, complicating diagnosis and management. Clinical manifestations arise from degeneration of *Taenia solium* cysts within the CNS and de-

pend on cyst number, size, and location, as well as the host immune response [1]. Reported presentations of NCC in individuals with HIV include epileptic seizures, such as in our patient, as well as headaches, focal neurological deficits, hemiparesis, and signs of increased intracranial pressure [4]. A case report of a patient with NCC presenting with symptoms of cauda equina compression, including acute urinary retention and lower extremity pain and weakness, has also been described [5]. Seizure presentation of NCC appears more likely in patients with lower CD4 counts compared with those who are HIV-negative or have higher CD4 levels [4], which may explain our patient’s atypical clinical picture.

Patients with NCC and HIV may also have concomitant CNS infections at presentation, including toxoplasmosis and tuberculosis [6]. The most common HIV-associated CNS opportunistic infections globally include cerebral toxoplasmosis (including toxoplasmic encephalitis), progressive multifocal leukoencephalopathy, primary CNS lymphoma, cytomegalovirus encephalitis, cryptococcal meningitis, tuberculous meningitis, and herpes simplex virus encephalitis [7]. In patients from non-high-income settings, cerebral malaria, Chagas disease, and NCC should also be considered [7]. This wide differential, combined with HIV-related neurological complications, makes timely diagnosis of NCC challenging, especially in the context of concurrent HIV opportunistic CNS infections. Diagnostic confirmation can be difficult. Serologic tests, including ELISA, lack sufficient reliability, and negative results are particularly common in patients with low CD4 counts [4]. Although EITB is considered the preferred serologic assay for neurocysticercosis, negative results do not exclude the diagnosis, particularly in patients with advanced immunosuppression. Clinical practice guidelines and prior studies have demonstrated reduced sensitivity of serologic testing in individuals with severe HIV-associated CD4 lymphopenia and emphasize that diagnosis may rely primarily on characteristic neuroimaging findings and epidemiologic exposure in such cases [3,4].

Imaging may show vesicular, colloidal, calcified, or racemose cysts. Most cysts are intraparenchymal, although extra-parenchymal, spinal, and subretinal lesions have been reported [4]. Multiple parenchymal lesions are the most frequent finding [8]. These imaging patterns are thought to reflect uncontrolled parasitic proliferation and blunted inflammatory re-

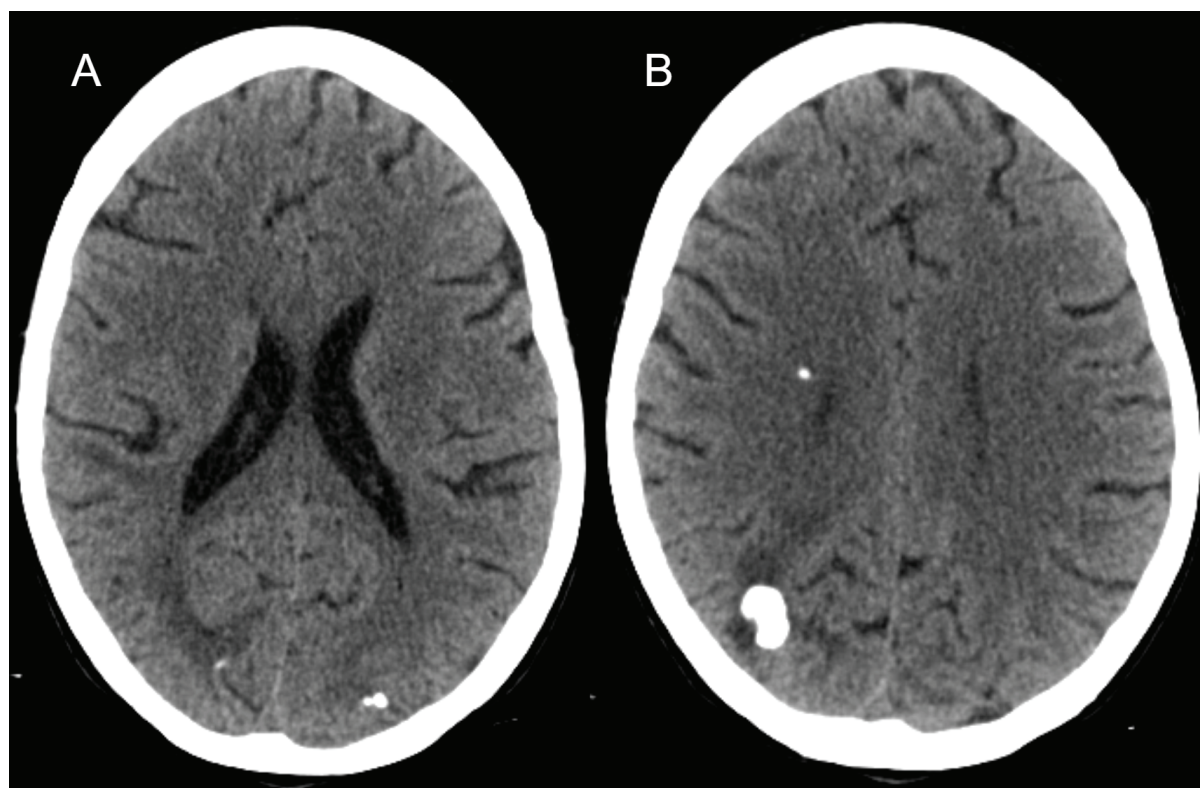


Figure 3: Brain CT without Contrast

CT Brain findings of intracranial lesions at discharge, eleven days after admission. (A, B) Axial Brain CT without contrast images demonstrate numerous calcified lesions with modest improvement of associated vasogenic edema.

sponses due to HIV-related immunosuppression [8]. Atypical lesions, such as racemose cysts, occur more frequently in individuals with CD4 counts below 500 cells/mm³ [8], which may further delay diagnosis.

Management of NCC often involves a combination of medical and surgical therapy. Reported treatments include surgery plus albendazole, surgery alone, albendazole alone, praziquantel alone, or no anthelmintic therapy [4]. Surgical interventions are typically performed for cyst removal (via craniotomy or spinal laminectomy) or for managing elevated intracranial pressure (e.g., ventriculoperitoneal shunt placement) [4]. Some patients receive adjunctive corticosteroids—most commonly dexamethasone or prednisolone [4]. The most frequently used and effective regimen is albendazole 15 mg/kg/day for 14–28 days combined with corticosteroids [4]. Combination therapy with albendazole plus praziquantel has been shown to improve cyst resolution and to increase destruction of viable parenchymal cysticerci for patients with three or more cysts [3,4]. For this reason, our patient was treated with both agents. A

methylprednisolone dose pack was added to the regimen to mitigate exacerbation of symptoms secondary to inflammation from parasite death as a result of the antiparasitic medications [3]. Though our patient did not have complete cyst resolution at the time of discharge, there was some improvement noted in the vasogenic edema surrounding the lesions. The viable cysts did not seem to decrease in number or size at the time of discharge, which is logical considering the patient had just been initiated on antiparasitic treatment and had yet to complete the recommended course, and additionally cyst resolution has been shown to take months to occur. Studies have found that antiparasitic treatment destroys 60% to 80% of viable intraparenchymal cysts and complete cyst resolution occurs in less than 40% of patients [11]. Therefore, an absence of an immediate change in the viable cysts at discharge does not necessarily indicate a lack of efficacy of the treatment regimen.

Among patients presenting with seizures, only a subset received antiepileptic drugs (AEDs) [4]. Some individuals were already on antiretroviral therapy

(ART) at the time of NCC diagnosis, while others began ART concurrently with anthelmintic treatment [4]. This was true for our patient, who experienced a witnessed seizure and was initiated on Biktarvy in addition to albendazole and praziquantel. A known concern when initiating ART is the risk of immune reconstitution inflammatory syndrome (IRIS), which can convert subclinical NCC into symptomatic disease [4]. Nonetheless, anthelmintic therapy is recommended because it reduces recurrent seizure frequency and the risk of chronic epilepsy [9,10].

A further consideration is potential drug–drug interactions among AEDs, ART, and anthelmintics; an area that remains under-studied [4]. Newer AEDs, which have simpler side-effect profiles, are preferred when ART regimens include protease inhibitors [9], although older AEDs may also be effective in controlling seizures in NCC [9]. Although Biktarvy does not contain a protease inhibitor, our patient was started on levetiracetam due to its favorable safety profile and better tolerability.

CONCLUSION

Neurocysticercosis (NCC) is a rare but increasingly recognized cause of adult-onset seizures in the United States, particularly challenging to diagnose in patients with advanced, untreated HIV. Our patient's negative serology, likely due to a CD4 count of 16 cells/mm³, did not exclude NCC. Diagnosis was supported by epidemiologic history, imaging findings, and clinical course, and confirmed by improvement with antiparasitic therapy and corticosteroids. Coordinated treatment alongside re-initiation of antiretroviral therapy minimized the risk of immune reconstitution inflammatory syndrome. This case highlights the importance of detailed travel and exposure histories, timely recognition of NCC, and early intervention to prevent seizure recurrence and long-term neurological complications in immunocompromised patients.

REFERENCES

- Garcia HH, Gonzalez AE, Gilman RH. Taenia solium Cysticercosis and Its Impact in Neurological Disease. *Clin Microbiol Rev.* 2020;33(3):e00085-19. Published 2020 May 27. <https://doi.org/10.1128/CMR.00085-19>
- Del Brutto OH, Nash TE, White AC Jr, et al. Revised diagnostic criteria for neurocysticercosis. *J Neurol Sci.* 2017;372:202-210. <https://doi.org/10.1016/j.jns.2016.11.045>
- White AC Jr, Coyle CM, Rajshekhar V, et al. Diagnosis and Treatment of Neurocysticercosis: 2017 Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH). *Clin Infect Dis.* 2018;66(8):e49-e75. <https://doi.org/10.1093/cid/cix1084>
- Jewell PD, Abraham A, Schmidt V, et al. Neurocysticercosis and HIV/AIDS co-infection: A scoping review. *Trop Med Int Health.* 2021;26(10):1140-1152. <https://doi.org/10.1111/tmi.13652>
- Delobel P, Signate A, El Guedj M, et al. Unusual form of neurocysticercosis associated with HIV infection. *Eur J Neurol.* 2004;11(1):55-58. <https://doi.org/10.1046/j.1351-5101.2003.00696.x>
- Serpa JA, Moran A, Goodman JC, Giordano TP, White AC Jr. Neurocysticercosis in the HIV era: a case report and review of the literature. *Am J Trop Med Hyg.* 2007;77(1):113-117.
- Tan IL, Smith BR, von Geldern G, Mateen FJ, McArthur JC. HIV-associated opportunistic infections of the CNS. *Lancet Neurol.* 2012;11(7):605-617. [https://doi.org/10.1016/S1474-4422\(12\)70098-4](https://doi.org/10.1016/S1474-4422(12)70098-4)
- Kuehnast M, Andronikou S, Hlabangana LT, Menezes CN. Imaging of neurocysticercosis and the influence of the human immunodeficiency virus. *Clin Radiol.* 2020;75(1):77.e1-77.e13. <https://doi.org/10.1016/j.crad.2019.08.001>
- Bhigjee AI, Rosemberg S. Optimizing therapy of seizures in patients with HIV and cysticercosis. *Neurology.* 2006;67(12 Suppl 4):S19-S22. https://doi.org/10.1212/wnl.67.12_suppl_4.s19
- Prasad S, MacGregor RR, Tebas P, Rodriguez LB, Bustos JA, White AC Jr. Management of potential neurocysticercosis in patients with HIV infection. *Clin Infect Dis.* 2006;42(4):e30-e34. <https://doi.org/10.1086/499359>
- Garcia HH, Nash TE, Del Brutto OH. Clinical symptoms, diagnosis, and treatment of neurocysticercosis. *Lancet Neurol.* 2014;13(12):1202-1215. doi:10.1016/S1474-4422(14)70094-8