Management of Potential Neurocysticercosis in Patients with HIV Infection

Sashank Prasad, Rob Roy MacGregor, Pablo Tebas, Lourdes B. Rodriguez, Javier A. Bustos, and A. Clinton White, Jr.

Departments of 1Neurology and 2Infectious Diseases, University of Pennsylvania, Philadelphia; 3Infectious Disease Section, Department of Medicine, Baylor College of Medicine, Houston, Texas; 4Service of Internal Medicine and Infectious Diseases, Hospital Guillermo Almenara, Empresa de Seguros de Salud, and 5Cysticercosis Unit, Instituto de Ciencias Neurologicas, Lima, Peru.

In patients with human immunodeficiency virus, the diagnosis of neurocysticercosis can be complex, and the current diagnostic criteria may not apply. We report 3 cases and suggest including the CD4+ T lymphocyte count as an important factor in the proper diagnosis and treatment of patients with human immunodeficiency virus and potential neurocysticercosis.

Cysticercosis, caused by the pork tapeworm 

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, is endemic in many areas of the world and constitutes the most common helminthic infection of the brain [1]. Immigration has led to increased prevalence in industrialized nations as well; there are ∼1000 cases in the United States annually [2]. The correct diagnosis of neurocysticercosis can be difficult, and it relies on a combination of history of exposure, physical examination, neuroimaging, and serological testing. A recent consensus statement suggests diagnostic criteria (table 1). Because diagnostic certainty (e.g., absolute criteria) is usually not available, diagnosis often relies on a combination of characteristic major, minor, and epidemiologic criteria.

In this report, we discuss the complexities of diagnosing neurocysticercosis in HIV-infected individuals. The current diagnostic scheme is useful in this instance, but must be applied with caution [3]. The presence of HIV infection and the extent of immunocompromise alter the likelihood of various etiologies of CNS lesions. In addition, the clinical significance of cysticercal infection may be affected by HIV coinfection. Therefore, clinicians should take the patient’s HIV status into consideration when making decisions about the treatment of patients and the initiation of therapy.

A positive serum enzyme-linked immunoelectrotransfer blot (EITB) assay result is included among the major criteria for the diagnosis of neurocysticercosis. In this test, glycoproteins are isolated from parasites by lectin affinity chromatography, and the antibody response is analyzed [4]. A result that shows bands corresponding to any of 7 glycoproteins (molecular weights, 13, 14, 18, 21, 24, 39–42, and 50 kd) is considered positive. The test was initially reported to be 98% sensitive and 100% specific [4]. Subsequent studies, however, have demonstrated poor sensitivity in cases with single or calcified lesions [5]. In addition, the exact positive predictive value of the serum EITB assay is unknown in patients from areas of endemicity who may be seropositive without having the disease [6]. Furthermore, some authors recommend interpreting a single 50-kd band as an equivocal finding [7, 8].

Diagnosing neurocysticercosis in patients with HIV can be even more complicated. Because the leading causes of HIV-associated brain masses in persons who do not live in areas of endemicity are Toxoplasma encephalitis and primary CNS lymphoma, stereotactic biopsy is recommended for patients who do not respond to 2 weeks of empirical anti-Toxoplasma therapy [9]. In developing countries, however, there is a significantly greater incidence of CNS mass lesions due to other causes, including tuberculosis and cysticercosis. Therefore, one suggested approach is to begin presumptive therapy for these illnesses without resorting to brain biopsy [10]. Of 32 patients treated in this manner, 28% were presumed to have neurocysticercosis and had good outcomes after receiving empirical therapy [10].

Relatively few cases of presumed HIV and neurocysticercosis coinfection have been reported, even in areas where there is high prevalence of each disease individually [10–15]. For example, a series of 94 autopsies of Mexicans with HIV revealed that only 1.1% had neurocysticercosis, compared with 2.4% in control autopsies [15]. Moreover, the symptomatic manifestation of cysticercosis may be further reduced by interactions between the 2 disease processes [13]. Symptomatic neurocysticercosis largely depends on the host inflammatory response, and decreased cell-mediated immunity characteristic of advanced HIV infection makes cysticercosis more likely to remain asymptomatic [14, 16]. Neurocysticercosis, therefore, may be more likely to present when the CD4+ T lymphocyte count is relatively spared. In the series of Modi et al. [10], for example,
6 patients who had neurocysticercosis had a mean CD4+ T lymphocyte count of 509 cells/mm³ (range, 107–768 cells/mm³). Conversely, other etiologies predominated in patients with substantially lower CD4+ T lymphocyte counts.

HIV status is not a factor in the current recommendations for diagnosing and treating neurocysticercosis [3]. We present 3 cases to illustrate how HIV status may be included as a factor in determining how to approach the diagnosis and treatment of this disease.

Case reports. The first patient was a 51-year-old Indian woman from British Guyana who had immigrated to Pennsylvania 10 years prior to admission. HIV was diagnosed 6 years prior to admission, but had remained asymptomatic, and she had a recent CD4+ T lymphocyte count of 350 cells/mm³. She was not receiving antiretroviral therapy. At another institution, she presented with seizures involving the left arm and leg, without loss of consciousness. An MRI of the brain showed a right, parietal, 14-mm, rim-enhancing lesion with a hyperintense mu-
50, 42–39, 24, 21, 18 and 14-kd bands (figure 2), antihelminthic therapy was not initiated. The patient did well with therapy, but was later lost to follow-up.

The third patient was a 72-year-old man in Lima, Peru, who had been diagnosed with HIV infection 9 months earlier and presented with a 2-month history of lethargy, intermittent headaches, and episodes of ataxia and loss of vision. A recent CD4⁺ T lymphocyte count was 105 cells/mm³, but he had not yet started antiretroviral therapy. At the time of admission, his neurological examination was normal. The sample obtained from lumbar puncture revealed a WBC count of 2 cells/mm³ (100% lymphocytes), a protein level of 112 mg/dL, and a glucose level of 2.2 mmol/L. India ink capsule stain revealed no organisms. MRI revealed numerous intraparenchymal enhancing and nonenhancing lesions, some with a mural nodule consistent with neurocysticercosis (figure 4). The diagnosis was subsequently supported by EITB assay result that was positive for 7 bands (figure 2). He was treated with dexamethasone followed by albendazole. During therapy, he had transient worsening of his mental status and ataxia. However, by day 12, the headaches, altered mental status, visual acuity, and ataxia had improved.

Discussion. Given increasing immigration of people to the United States from areas where cysticercosis is endemic, the approach to a patient with HIV-associated brain lesions should include evaluation for cysticercosis in the appropriate circumstances. For example, a study of Hispanic patients (with or without HIV) who presented with seizures to an emergency
The department found that in 10% the cause was neurocysticercosis [2]. Early consideration of neurocysticercosis in appropriate patients can help avoid unnecessary delay in diagnosis. Moreover, this approach may help avoid unnecessary brain biopsy, a procedure that carries nontrivial morbidity and mortality [17]. In addition to empirical trial treatment with anti-Toxoplasma agents, a rational approach might include early use of the serum EITB assay in patients with known history of exposure.

However, the initially reported high sensitivity and specificity of the EITB assay may be misleading. The sensitivity may be reduced in particular groups of patients and in individuals from areas where cysticercosis has high seroprevalence [7]. Furthermore, the result may be less reliable in patients with AIDS, as has been noted with Toxoplasma serological tests.

In many cases of definite or probable cysticercosis, it may be prudent to institute antihelminthic therapy. Antiparasitic treatment leads to more rapid resolution of lesions, which can help establish the diagnosis and may decrease the frequency of recurrent seizures. The cases reported here demonstrate how HIV can influence the clinical analysis of whether brain lesions are more or less likely to be caused by neurocysticercosis as well as the approach to clinical management. In our first patient, we surmised that a relatively high CD4+ T lymphocyte count indicated the capacity for sufficient inflammation in the case of cysticercal infection, possibly accounting for the patient’s symptoms. At the same time, the initial elevated CD4+ T lymphocyte count made the diagnosis of toxoplasmosis less likely. The initial MRI scan also revealed a cystic lesion with a mural nodule, a radiographic pattern thought to be diagnostic of neurocysticercosis. Although the brain biopsy was consistent with this diagnosis, it did not lead to a firm diagnosis. Even with the single 50-kd band as the only evidence of seropositive neurocysticercosis, the likelihood of symptomatic disease was sufficient to justify treatment. In our second patient, a substantially lower CD4+ T lymphocyte count reduced the likelihood that symptoms were from neurocysticercosis because of an attenuated host immune response. Especially given the ra-

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**Figure 3.** Gadolinium-enhanced axial (left) and coronal (right) MRI of patient 2 showing numerous right temporofrontal, ring-enhancing lesions in the brain.

**Figure 4.** A gadolinium-enhanced, T1-weighted MRI of patient 3 showing numerous intraparenchymal enhancing and nonenhancing lesions, some with a mural nodule consistent with neurocysticercosis.
diagnostic features of the brain masses, other etiologies were more likely, and therapy for neurocysticercosis was withheld despite positive serologic test results. In the third case, MRI revealed numerous hypodense lesions, several of which contained pathognomonic mural nodules. The EITB assay result also corroborated a clinical diagnosis of neurocysticercosis. The diagnosis was further supported by the transient worsening of symptoms that often occurs after antiparasitic therapy. This mild presentation, despite the impressive burden of disease seen on the MRI scan, may have been due to blunting of the inflammatory response because of underlying HIV infection. Although a relatively low CD4+ T lymphocyte count was suggestive of other possible etiologies, anticysticercal therapy was administered with success.

These cases illustrate that the EITB assay result always needs to be interpreted with caution, in consideration with radiographic and clinical data. Importantly, the CD4+ T lymphocyte count may influence the decision to either start therapy or entertain other diagnoses. The CD4+ T lymphocyte count is not currently a consideration in the evaluation of neurocysticercosis. However, in the context of HIV infection, patients with higher CD4+ T lymphocyte counts are more likely to have symptomatic neurocysticercosis that requires treatment. We propose that the treatment of these patients be tailored on the basis of their CD4+ T lymphocyte count (table 2).

It is unknown to what extent antiretroviral therapy, by reconstituting the immune system, can exacerbate a latent, untreated neurocysticercosis coinfection. However, we have noted one case in which symptomatic neurocysticercosis followed immune reconstitution (A.C.W., unpublished observation). Further observations will be necessary to elucidate this point.

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References


Table 2. Proposed treatment for HIV-infected patients with positive cysticercosis serological test results.

<table>
<thead>
<tr>
<th>CD4+ T lymphocyte count, cells/mm³</th>
<th>Probability of neurocysticercosis*</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>&gt;200</td>
<td>Definite or probable</td>
<td>Treat as neurocysticercosis</td>
</tr>
<tr>
<td>&gt;200</td>
<td>Unlikely</td>
<td>Consider other diagnoses</td>
</tr>
<tr>
<td>&lt;200</td>
<td>Definite, probable, or unlikely</td>
<td>Consider other diagnoses</td>
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* Based on the diagnostic scheme proposed by Del Brutto et al. [3].