might differ if HCV coinfection is present. Although this piece of data is difficult to gather, efforts should be made to obtain it, because it would throw some light on the issue.

Finally, we agree with the authors [1] and the editorial commentators [5] that a longer duration of follow-up is needed to find significant differences in survival rates between the 2 cohorts. Liver complications might take a longer time to appear in the HIV-HCV–coinfected group, given that only a minority of the patients in this group seem to be in advanced stages of liver disease. In that regard, recent studies with long follow-up times show increased mortality rates due to liver disease among HIV-HCV–coinfected patients [6].

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References

Reply

Sir—Núñez et al. [1] are correct in their comment that the HIV-HCV–coinfected group in our analysis [2] had lower CD4 cell counts and a shorter observation time than the HIV-monoinfected cohort. Although these factors could potentially bias the rate of survival we observed, we did adjust for the number of weeks a patient had been receiving HAART, as well as for CD4 cell count. HCV infection, per se, was not a significant predictor of survival.

We modeled the original analysis using the length of time a patient had been HIV-positive as the duration of survival. If we redo the analysis using survival outcome (death, yes/no) together with the length of time a patient had been HIV-positive and do not use baseline CD4 cell count, then HCV infection is still not a significant factor in predicting survival outcome. The patient’s age and number of weeks receiving HAART remain significant factors in the re-analysis (P = .0012 and P < .0001, respectively).

The dynamics of viral coinfection as it impacts decline in CD4 cell counts, response to antiretroviral therapy, and survival will require ongoing investigation, especially as anti-HCV therapy is used increasingly in clinical practice. We are certain that other mortality analyses for HIV-HCV coinfection will continue to be performed; age, other comorbid conditions, and emerging complications of therapy may impact rates of survival.

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References

Evaluation of Current Immunodiagnostic Criteria for Diagnosis of Neurocysticercosis

Sir—In their recent article, Kojic and White [1] reported an interesting finding concerning false-positive results of the serum enzyme-linked immunoelectrotransfer blot (EITB) assay for diagnosis of neurocysticercosis (NCC), and they emphasized the need for revision of current diagnostic criteria.

I wish to make the following comments on immunodiagnostic criteria for NCC and on the performance of immunoenzymoassays in diagnosis of NCC. In response to a published report on “revised diagnostic criteria” [2], I made the suggestion that it would be appropriate if the second of the 4 major criteria given in the article (see table 2 in [2]) were interchanged with the third minor criterion [3]. In my opinion, it is still logical to apply sensitive immunodiagnostic methods for detection of both specific antibody response and cysticercal antigens in samples of CSF or of CSF and serum, rather than in serum samples alone, because de novo synthesis of anticysticercal antibodies intrathecally has been documented [4]. Drawbacks of using detection of anticysticercal antibody response in serum as a diagnostic criterion are that there could be a possibility of cross-reactions with other phylogenetically related parasites that infest different areas of endemicity, resulting in false-positive reactions [5]. Anticysticercal antibodies detected in CSF samples also produced...
false-positive reactions for patients with chronic infections of the CNS, such as tuberculous meningitis and polyradiculopathy [6]. Therefore, detection of cysticercal antigen would be a better diagnostic criterion because cysticercal antigen would be released as a consequence of an immune response, anticysticercal drug therapeutic response, or by elaboration of excretory/secretory antigen by live cysticerci. Thus, detection of cysticercal antigen would indicate the status of the disease. However, detection of both cysticercal antigen and anticysticercal antibody response in CSF samples would certainly enhance diagnostic accuracy. It is important to keep in mind that enzyme- or erythrocyte-based immunoassays, such as ELISA or hemagglutination assay (HA), may not be able to detect cysticercal antigen in CSF or serum samples when the antigen is completely masked by a specific antibody because of the host’s strong antibody response. This may result in a false-negative result; immunoblot assays, in contrast, can give consistent results [3, 7].

If Kojic and White [1] had tested for both antibody response and cysticercal antigen in CSF samples, the EITB assay results would probably have been negative. Although serum EITB assays have been extensively tested [8], it is advisable to test CSF samples for anticysticercal antibody, antigen, or both to make a definitive diagnosis of NCC. I concur with the views of Kojic and White [1] that the second criterion for diagnosis listed by Del Brutto et al. [3] requires modification and could be revised to read as follows: “Positive results of either enzyme- or erythrocyte-based immunological tests, such as EITB, ELISA, dot-immunobinding assay (DIA), or passive HA, for detection of anticysticercal antibodies, and positive results of tests, such as EITB, tandem-ELISA, capture-DIA, or reverse passive HA, for detection of cysticercal antigen in samples of CSF or of CSF and serum and not in serum samples alone.”

References

Reply
Sir—The letter by Katti [1] comments on the recent report of a false-positive result of an enzyme-linked immunoelectrotransfer blot (EITB) assay for anticysticercal antibody [2] and on the proposed diagnostic criteria for neurocysticercosis (NCC) that were previously published [3]. Dr. Katti suggests that detection of antibody in CSF samples by ELISA or other means be substituted for the serum immunoblot assay as the major form of immunological diagnosis for NCC. The proposed criteria were developed by a group of experts with broad experience working with clinical and laboratory aspects of cysticercosis. Serodiagnosis has proven highly problematic for some patients with neurocysticercosis. This problem stems in part from the biology of the parasites, which actively bind antibody. In fact, some experts have stated that parasite molecules actually function as Fc receptors [4]. As a result, all assays employing unfractionated antigens (including ELISA, hemagglutination assay, and dot-immunoassay, all mentioned by Dr. Katti [1]) are prone to false-positive reactions [5]. Although the frequency of this problem can be decreased by using higher cutoff values, doing so also results in a decrease in the assay’s sensitivity. CSF samples may provide more accurate results than serum samples when used for antibody ELISA assays. Nevertheless, false-positive reactions remain a significant problem.

Tsang et al. [6] have largely overcome this problem by developing an immunoblot assay that uses lentil lectin–purified glycoproteins. Binding to several of the diagnostic bands is characteristically present among patients with neurocysticercosis. The resulting EITB assay has a remarkable specificity, which has allowed for lower cutoff values and improved sensitivity. The false-positive reaction reported by Kojic and White [2] is remarkable precisely because of the generally excellent specificity of the test. The excellent specificity of the EITB assay has allowed serum to be used as a diagnostic specimen. Actual performance data suggests that the predictive value of the EITB assay for neurocysticercosis is even greater with serum samples than with CSF samples [7]. This observation has been confirmed by other investigators [5]. Thus, Dr. Katti’s comments [1] about ELISA with CSF samples are not supported by the results of actual comparative studies. There may be reasons to reconsider whether a single band at 50 kDa in the EITB assay should be considered a definitely positive finding; however, over-