ed for intragroup correlation for cluster (hospital).

Furthermore, no significant difference in survival was documented for patients who received flucytosine when stratified by AmB formulation. In patients who received lipid formulations of AmB, survival correlated with fungemia (OR, 0.04; 95% confidence interval [CI], .002–.90; P = .043) but not flucytosine use (OR, 2.3; 95% CI, .29–19.1; P = .415), renal failure at baseline (OR, .88; 95% CI, .08–9.52; P = .91), calcineurin-inhibitor agent use (OR, 3.5; 95% CI, .28–43.3; P = .327), age (OR, 1.05; 95% CI, .94–1.17; P = .35), or the year of diagnosis (OR, 1.12; 95% CI, .70–1.79; P = .614). Although the sample size was suboptimal for evaluating the efficacy of flucytosine in patients who were receiving AmB deoxycholate, when adjusted for the aforementioned variables, survival correlated with renal failure at baseline (OR, .015; P = .04) and fungemia (OR, .003; P = .06) but not flucytosine use (OR, 3.55; P = .48), age (OR, .97; P = .76), calcineurin-inhibitor agent use (OR, 12.7; P = .27), or the year of diagnosis (OR, 1.5; P = .32).

We note that in previous studies, flucytosine’s beneficial effect in patients with cryptococcal meningitis was largely on mycological outcomes, such as cerebrospinal fluid sterilization, and not survival per se [3]. Deaths in transplant recipients with cryptococcosis are rarely due to failure to sterilize cerebrospinal fluid but are due to multiorgan failure, suggesting a role of host immune responses. The difference between survival in our patients who were receiving the lipid formulations of AmB and survival in our patients who were receiving AmB deoxycholate persisted even when controlled for flucytosine use and other potential confounders.

Acknowledgment

Potential conflicts of interest. N.S. has received grant support from Pfizer. H-Y.S.: no conflicts.

References


4. Reprints or correspondence: Dr Nina Singh, VA Pittsburgh Healthcare System, University Dr C, Pittsburgh, PA 15240 (nis5@pitt.edu).

5. Clinical Infectious Diseases 2010;50(11):1544–1545. © 2010 by the Infectious Diseases Society of America. All rights reserved. 1556-4838/2010/5011-0021$15.00 DOI: 10.1086/652715

Should HIV-Infected Patients with Unexplained Chronic Liver Enzyme Elevations Be Tested for Hepatitis E Virus?

To the Editor—We read with interest the report by Kovari et al [1] describing 385 human immunodeficiency virus (HIV)–infected individuals with incident chronic elevations of alanine aminotransferase levels, in the absence of hepatitis C or B virus coinfection. The authors found that chronic alanine aminotransferase elevation in their population was associated with high body mass index, frequent alcohol consumption, and cumulative exposure to combination antiretroviral therapy, especially stavudine.

Despite its many strengths, an important limitation of this study is that they did not exclude hepatitis E virus (HEV) as a potential cause of chronic viral hepatitis in this population. HEV, a significant global agent of viral hepatitis, was first identified in 1980 [2, 3] and is generally believed to only cause acute infections. Recent reports, however, have shown that solid organ transplant recipients receiving immunosuppressive therapy can develop chronic HEV infection, with associated chronic liver enzyme elevations [4, 5]. Two instances of chronic HEV infection in immunocompromised HIV-infected patients, with associated chronic liver enzyme elevations, have also been reported [6, 7].

Whether HIV-infected patients with unexplained chronic liver enzyme elevations should be routinely tested for HEV is an open question. On one hand, a diagnosis of chronic HEV infection could obviate the need for further diagnostic testing. Switching of antiretroviral therapies could also potentially be avoided if HEV infection is detected. Chronic HEV infection should be evaluated by detection of HEV RNA, because seroconversion following HEV infection may be delayed or absent in some immunocompromised patients [4].

On the other hand, there are no data to indicate that HIV-infected individuals are at increased risk of HEV infection, compared with the general population [8, 9]. Clinical hepatitis due to HEV infection is an uncommon disease in industrialized countries. Chronic hepatitis due to HEV infection in immunocompromised patients may also be uncommon. One recent study failed to detect HEV infections among 43 HIV-infected patients with chronic cryptogenic hepatitis [10], but other HIV-infected populations have not been evaluated.

Rather than a general recommendation for HEV testing in all HIV-infected patients with unexplained chronic liver enzyme elevations, we suggest that a subset of patients be given the highest priority for testing. This subset could include HIV-infected patients living or travelling in Asia and Africa, as well as patients living in countries such as the United Kingdom, France, and Germany where autochthonous hepatitis E is increasingly diagnosed [11–13]. Patients who report HEV risk
factors, including exposure to febrally contaminated food or water, direct contact with swine and potentially other animals, and consumption of undercooked mammalian meats, especially organ meats [13], may also be good candidates for HEV testing. Finally, because the evidence to date suggests that only individuals who are immunocompromised develop chronic HEV viremia [4–7], testing could be limited to these patients.

In the absence of HEV data, it is not possible to determine the frequency of chronic alanine aminotransferase elevations in the Swiss HIV Cohort Study attributable to HEV infection. However, both HIV and HEV are ubiquitous global pathogens, and a current research priority is to better understand the frequency and clinical consequences of coinfection with these 2 viruses.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Mark H. Kuniholm,1 Alain B. Labrique,2 and Kenrad E. Nelson3

1Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York; and Departments of 2International Health and 3Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

References


Reprints or correspondence: Dr Mark H. Kuniholm, Dept of Epidemiology and Population Health, Albert Einstein College of Medicine, 1300 Morris Park Ave, Belfer Bldg 1308, Bronx, NY 10461 (mark.kuniholm@einstein.yu.edu).

Clinical Infectious Diseases 2010; 50(11):1545–1546 © 2010 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2010/5011-0022$15.00 DOI: 10.1086/652716

To the Editor—We thank Kuniholm et al [1] for their interest in our study on the incidence and risk factors for chronic elevation of alanine aminotransferase (ALT) levels in human immunodeficiency virus (HIV)–infected persons without hepatitis B or C virus coinfection [2]. They suggest that chronic hepatitis virus E (HEV) infection should be considered in the differential diagnosis in this patient group. We indeed did not look for HEV as a cause for chronic ALT elevation. However, the prevalence of HEV infection is very low in our study population, as reported at the Conference on Retroviruses and Opportunistic Infections by investigators of the Swiss HIV Cohort Study [3]. In this study, Swiss HIV Cohort Study participants with chronic elevated ALT values and no hepatitis B and C infection were screened for positive anti-HEV immunoglobulin G in the latest stored plasma sample. In HEV seropositive subjects, HEV polymerase chain reaction was performed on a plasma sample stored 3 months prior to, at the time of, and 3 months after the first elevated ALT value. Among 735 patients with chronic ALT elevation, 19 (2.6%) were HEV seropositive. At the time of ALT elevation, HEV polymerase chain reaction results were positive in only 1 of these 19 patients.

Whether tests to detect HEV are indicated among HIV–infected persons with chronic ALT elevation in the absence of hepatitis B or C virus coinfection or other causes of chronic hepatitis must depend on the local epidemiology of HEV infection and the travel history of individual patients. Because of its low prevalence in our study population, we do not expect that the omission of HEV serology or molecular tests had a relevant influence on the results of our study.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Helen Kovari, Bruno Ledegerber, and Rainer Weber

Division of Infectious Diseases and Hospital Epidemiology, University Hospital, University of Zurich, Zurich, Switzerland

References