Correspondence

Early-Onset Liver Fibrosis Due to Primary Hepatitis C Virus Infection Is Higher Over Time in HIV-Infected Men

To the Editor—We were pleased to read the recent report by Vogel et al [1] of their study undertaken in response to our findings of rapid onset fibrosis during primary hepatitis C virus (HCV) infection in human immunodeficiency virus (HIV)–infected men [2]. Their study, plus the recent publication of the liver biopsy results of Bottieau et al [3], seems to cement that this unexpected outcome is a true consequence of primary HCV infection in HIV-infected men. We disagree, however, that their results using transient elastography demonstrate a sharp decrease in the fibrosis progression rate (FPR) to a clinically unimportant level soon after the primary HCV infection period has waned.

Transient elastography measures liver stiffness, not fibrosis per se. In patients with new viral hepatitis [4] and in patients with chronic HCV infection [5], inflammation contributes significantly to the liver stiffness score. Patients with biopsies showing as little as stage 0–1 fibrosis but with higher alanine transaminase (ALT) levels had a high rate of spuriously attributed cirrhosis (stage 4) [5]. Because Vogel et al did not have liver biopsies of these patients, they could not adjust for this effect, and they thereby vastly overestimated the stage of fibrosis (and therefore the FPR) during early primary HCV infection. Then, when they calculated FPR in the subgroup of just 5 patients who were assessed at later times when inflammation and ALT were much lower, they found a much lower FPR.

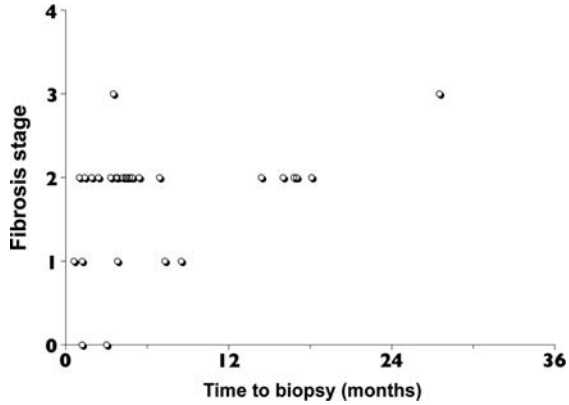

Figure 1 Liver fibrosis stage as a function of time to liver biopsy from primary hepatitis C virus (HCV) diagnosis. Fibrosis was scored from biopsy specimens using the criteria of Scheuer (stage 0–4) [2]. The time to biopsy was calculated from the date of first-noted alanine transaminase elevation (>90% of cases), antibody seroconversion, or new HCV viremia, in months.

To better address this issue, in continuation of our previously reported study, we performed a total of 29 liver biopsies of HIV-infected men with primary HCV infection (including the 11 reported previously [2]). Figure 1 shows a plot of histological stage against the time from first-noted ALT elevation (which coincided with the clinical presentation in >90% of cases). The results of this analysis show that higher histopathological stage of fibrosis was associated with increasing length of HCV infection (regression analysis, $P = .04$). These data further reinforce that in HIV-infected men there is rapid onset of fibrosis in the first 1–2 years after primary HCV infection that does not appear to resolve. Due to the same short time of follow-up as in the Vogel et al study, we cannot determine from these data the rate at which this fibrosis does or does not continue to accumulate. What happens in the subsequent 2–5 years will determine how clinically meaningful these findings end up being. But with a baseline of stage 2 fibrosis in most men immediately following the primary HCV infection, even a relatively low FPR would lead to cirrhosis more rapidly than in most clinical settings. We are optimistic that with the continued development of new HCV treatments we may be able cure nearly everyone with HCV infection within 5–10 years—but that may be too long for some of these patients. We therefore encourage Vogel and colleagues to perform long-term follow-up of their enrolled patients as we plan to do with ours so we can directly monitor liver disease progression in these patients.

Note

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References

1. Vogel M, Page E, Boesecke C, et al. Liver fibrosis progression after acute hepatitis C virus infection in HIV-positive individuals. Clin Infect Dis **2012**; 54:556–9.
2. Fierer DS, Uriel AJ, Carriero DC, et al. Liver fibrosis during an outbreak of acute hepatitis C virus infection in HIV-infected men: a prospective cohort study. J Infect Dis **2008**; 198:683–6.
3. Bottieau E, Apers L, Van Esbroeck M, Vandenbruaene M, Florence E. Hepatitis C virus infection in HIV-infected men who have sex with men: sustained rising incidence in Antwerp, Belgium, 2001–2009. Euro Surveill **2010**; 15:19673.
4. Arena U, Vizzutti F, Corti G, et al. Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology **2008**; 47:380–4.
5. Tapper EB, Cohen EB, Patel K, et al. Levels of alanine aminotransferase confound use of transient elastography to diagnose fibrosis in patients with chronic hepatitis C virus infection. Clin Gastroenterol Hepatol **2012**.

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