The Implications of Low Absolute CD4 Counts in Patients With Cirrhosis and Human Immunodeficiency Virus

To the Editor—In their recent study, Baranoski et al [1] describe a high rate of liver disease progression in patients with human immunodeficiency virus (HIV)-hepatitis B virus coinfection and CD4 counts <200 cells/mm^3. The authors suggest that more advanced immunosuppression in these patients may lead to accelerated liver fibrosis. Because only 50% of the HIV-infected patients were taking antiretroviral therapy at study entry and 78% had detectable HIV viremia, this is a reasonable explanation for the progression of liver disease in these patients with acquired immune deficiency syndrome.

However, another possible explanation is that a low absolute CD4 count may be an independent marker of liver dysfunction, even in patients without HIV. For example, a 2007 study of 60 HIV-negative patients with cirrhosis found that 43% had CD4 counts <350 cells/mm^3 and 7% had CD4 counts <200 cells/mm^3 [2]. Yet although low absolute CD4 counts were common in this study, 95% of these patients had normal CD4 cell percentages. Likewise, several studies of patients with HIV and liver disease have found an association between advanced liver disease and discordant absolute CD4 counts and CD4 percentages [3, 4].

One hypothesis is that liver dysfunction and portal hypertension may lead to splenic sequestration of CD4$^+$ T cells and a low absolute CD4 count, even as the CD4 percentage remains relatively intact [5, 6]. In these patients, the low absolute CD4 count may be a sign of advanced liver disease as opposed to advanced immunosuppression. The clinical and immunologic implications of a low absolute CD4 count but normal percentage in patients with HIV and cirrhosis remain unclear.

In the study by Baranoski et al [1], it is possible that CD4 counts <200 cells/mm^3 were more likely to occur in patients with hepatic fibrosis or splenomegaly, and therefore progression of liver disease was more likely among these patients as well. However, whether or not immunosuppression itself contributed to this progression merits further investigation. In this regard, it would be helpful to know the rates of low CD4 percentages in this study, and whether low percentages were also associated with worsening liver disease in these patients. A link between low CD4 percentage and liver disease progression would support the authors' arguments regarding immunosuppression promoting hepatic fibrosis, whereas lack of association might support consideration of other causes.

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