mechanisms (polyclonal B-cell response) are similar between infliximab-induced liver injury and acute and chronic viral hepatitis [1]. We present a new case of FPAs during certolizumab therapy that, in support of Tennant et al, suggests that this may be a class phenomenon.

A 37-year-old healthcare worker with previously normal liver test results was referred for the evaluation of elevated aminotransferase levels, identified during routine follow-up, during receipt of certolizumab therapy for rheumatoid arthritis. The patient was found to have an alanine aminotransferase level of 424 IU/L and an aspartate aminotransferase level of 376 IU/L. The prothrombin time was mildly elevated, at 13.7 seconds. The total bilirubin level and the alkaline phosphatase level were unremarkable, and tests for detection of hepatitis A, B, and C virus were negative. The anti-nuclear antibody titer was positive, at 1:80, the rheumatoid factor level was 1243 IU/mL, and the anti-smooth muscle antibody titer was negative. Interestingly, the patient was found to have a positive herpes simplex virus (HSV) IgM titer, with an OD ratio of 2.57 (normal range, 0–0.9) and a negative HSV immunoglobulin G titer. Given these acute findings in an immunosuppressed patient, intravenous acyclovir therapy was started while awaiting results of confirmatory HSV-specific polymerase chain reaction (PCR). Although acute HSV-associated hepatitis was possible, additional differential diagnoses included DILI and drug-induced autoimmune hepatitis. Given the wide spectrum of differential diagnoses and the associated broad variance in therapies, it was evident that a definitive diagnosis was essential. A liver biopsy specimen was obtained, showing mild lympho-histiocytic and lympho-plasmacytoid portal inflammatory infiltrates, mild interface hepatitis, and focal ballooning degeneration with expansion of the hepatic plates. Immunohistochemistry studies were negative for HSV, and results of 2 HSV-specific PCRs were also negative, suggesting DILI as the etiology. Pathological findings were consistent with previously published reports of DILI due to other monoclonal antibodies to tumor necrosis factor α, such as infliximab, which can produce an autoimmune-like form of DILI [5]. Certolizumab was, thus, discontinued, and on outpatient follow-up, the patient’s liver test results returned to normal within 2 months.

In our case, certolizumab was believed to be the causative factor leading to DILI and FPAs. Similar to the case presented by Tennant et al with infliximab, certolizumab is also a monoclonal antibody to human tumor necrosis factor α, and both are used for their antiinflammatory activity in patients with rheumatoid arthritis and those with inflammatory bowel disease. In both cases, the high rheumatoid factor titer may have been involved in the mechanism of the FPA, which has been described in prior studies, namely a polyclonal B-cell response [6]. We appreciate the case report presented by Tennant et al and suggest that both cases provide a potential window into the understanding of FPAs in DILI, as well as the global phenomenon of FPAs in general.

Regardless of the specific mechanism, it is paramount for clinicians to recognize that FPAs can be seen in any cause of acute or chronic hepatitis, including viral hepatitis, drug-induced hepatitis, and autoimmune hepatitis. FPAs can result in diagnostic errors and a resultant delay in appropriate patient care, with potential catastrophic consequences.

**Notes**

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**Reply to Tennant and Post**

To the Editor—We greatly appreciate the interest in our work by Tennant et al [1]. While our study described the presence false-positive antibodies (FPAs) in acute and chronic viral hepatitis virus infections and observed that this may be as a result of polyclonal B-cell activation [2–4], Tennant et al have described that viral hepatitis FPAs (a hepatitis A virus immunoglobulin M [IgM] FPA in the face of drug-induced liver injury [DILI]) are also possible. Additionally, Tennant et al suggest that the
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