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Case 22-2019: A 65-Year-Old Woman with Myopathy

TO THE EDITOR: The case reported by Freeman et al. (July 18 issue) contains conclusions that may perpetuate misconceptions. The patient had acute rhabdomyolysis and necrotizing autoimmune myositis, but the connection with statins is unlikely.

In this patient, myopathy started 2 weeks after coryza and cough; this suggests a preceding viral infection, which is a more likely trigger of necrotizing autoimmune myositis than atorvastatin, which had been initiated 6 months previously. Statins can rarely lead to acute myotoxicity, but the contention that they induce autoimmune myositis is now the most common inflammatory myopathy and that 25% of patients with paraneoplastic, viral, or other forms of necrotizing autoimmune myositis have no known exposure to statins.

Some of these patients have anti-HMGCR–associated autoimmunity that responds to treatment.3 Anti-HMGCR autoantibodies are not statin-specific and do not induce myotubular necrosis and do not explain pathogenicity.3 Most important, anti-HMGCR autoantibodies are not statin-specific because they are most frequently seen in patients with paraneoplastic, viral, or other forms of necrotizing autoimmune myositis who have not received statins.6

In the few patients in whom necrotizing autoimmune myositis does develop after receipt of statins for years, the association is more of a chance phenomenon, considering that necrotizing autoimmune myositis is now the most common inflammatory myopathy and that 25% of Americans older than 40 years of age take statins. The authors’ conclusions could deprive the patient, as well as others with a similar presentation, of a helpful drug.
traindicated in patients with statin-associated autoimmune myopathy. However, the use of proprotein convertase subtilisin–kexin type 9 (PCSK9) inhibitors appears to be safe in this patient population and may be considered in patients with clinically significant cardiovascular risk factors.1

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THE DISCUSSANTS REPLY: Dalakas raises an important point about the relationship between statin use and necrotizing autoimmune myopathy. There is considerable epidemiologic evidence of an association between statin use and necrotizing autoimmune myopathy; however, data to establish statins as causal agents of the illness are lacking. In a large series involving 1947 patients with suspected myopathy who were evaluated at the Johns Hopkins Myositis Center, 104 (5.3%) were positive for anti-HMGCR autoantibodies.1 Of these 104 patients, 75% had a history of statin use. Widespread use of statins, as seen in the United States, can lead to ascertainment bias, linking a rare myopathy with a commonly used drug class. Nevertheless, in the Johns Hopkins cohort, there was a strong association between antibodies and statin use. However, 25% of the patients with anti-HMGCR autoantibodies did not have a history of statin use; thus, necrotizing autoimmune myopathy can occur in the absence of statin exposure. As Dalakas suggests, anti-HMGCR autoantibodies may not necessarily be pathogenic, but they could be biomarkers of the immune-mediated process. Although viral illness is a potential trigger, we did not find compelling literature linking viral illness with anti-HMGCR autoantibodies. Although the duration of statin use before anti-HMGCR myopathy is variable, 2 or more years of exposure is frequently reported. Thus, the time course in this patient is consistent with a statin-associated event.2,3

We agree that Koch’s postulates for causality are not satisfied with regard to the role of statins or HMGCR autoantibodies in causing necrotizing autoimmune myopathy; until there is stronger evidence, it may be better to view the condition as statin-associated rather than statin-induced. We do not agree, however, with rechallenging patients with statins; this perspective was supported in a recent review article stating that all five patients who were rechallenged had adverse effects.4 In our opinion, rechallenging a patient with a statin would require conclusive proof that a statin was not implicated in the disorder. Given the very refractory nature of necrotizing autoimmune myopathy, we think alternative cholesterol-lowering therapy with the use of PCSK9 antibodies or ezetimibe should be the recommended treatment for a patient after the development of a statin-associated anti-HMGCR myopathy.

We thank Pinal-Fernandez and Mammen for their comments. These letters raise important issues in understanding this rare immune-mediated myopathy.

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