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To the Editor:

Interferon-α (IFN-α) is a group of cytokines with antiviral and antiproliferative effects, used for the treatment of chronic hepatitis C infection and various malignancies. Immunomodulatory effects of IFN may lead to the induction or exacerbation of autoimmune diseases such as psoriasis, systemic lupus erythematosus, and rarely, rheumatoid arthritis (RA). Covalent attachment of a polyethylene glycol (PEG) moiety (pegylation) to IFN-α results in a significantly higher sustained virological response rate in patients with chronic hepatitis C compared to conventional IFN-α. Pegylation also reduces the immunogenicity of IFN-α. We describe the first case of a patient who developed anticyclic citrullinated peptide antibody (anti-CCP)-positive RA following treatment of chronic hepatitis C infection with pegylated IFN-α2a.

A 54-year-old Chinese man with chronic hepatitis C (genotype 2a) infection was placed on a 24-week course of PEG-IFN-α2a 180 µg weekly and ribavirin 400 mg BID. His hepatitis C virus (HCV) RNA became undetectable at Week 12 and remained undetectable throughout his treatment. With no history of arthritis, he developed a diffuse pain syndrome 18 weeks into antiviral treatment. Initially this was attributed to myalgias or possible myositis, but creatine phosphokinase (CPK) and aldolase levels were normal. Treatment with ibuprofen 200 mg every 6 h, celecoxib 200 g/day, and tramadol 100 mg every 6 h provided only minimal relief. Upon completion of a 24-week course of antiviral therapy he developed a sustained virological response as evidenced by persistent undetectable HCV RNA and normal aminotransferase activities. However, he developed a puzzling pain syndrome that was falling loosely into 2 subsets. One subset, associated with mixed cryoglobulinemia, was noted by the absence of anti-CCP titers. HCV-related arthritis often improves despite discontinuation of IFN therapy.

Introduction of peglated formulations of IFN has been hypothesized to minimize the risk for autoimmune induction by reducing immunogenicity. Only 2 cases of RA associated with PEG-IFN treatment for hepatitis C have been reported in the English literature. Although anti-CCP can be used to distinguish HCV-related arthritis from RA, the presence of anti-CCP has not been reported in IFN-associated RA. Anti-CCP has been found to be predictive of more severe joint destruction in RA. Unlike the 2 reported patients with PEG-IFN-associated RA, our patient demonstrated severe erosive disease.

The possibility of pegylated IFN inducing or exacerbating RA in previously predisposed individuals should be considered in patients with hepatitis C who develop arthritis. Screening for RF and anti-CCP may be considered before treating with IFN. Detection of anti-CCP, the presence of nodules, and erosive disease help distinguish RA from HCV-related arthritis, but these characteristics are not always found in patients who develop RA with IFN treatment. The prognosis of patients with PEG-IFN-associated RA remains unclear because of the small number of cases reported. If the symptoms of RA do not resolve after discontinuing PEG-IFN, these patients may require treatment with disease-modifying antirheumatic drugs.

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