Letters to the Editors

Successful treatment of a patient with both systemic lupus erythematosus and progressive hepatitis C using immunosuppressive therapy and interferon beta

Sirs,

Systemic lupus erythematosus (SLE) is characterised by loss of tolerance to nuclear antigens and inflammation in multiple organs. SLE patients could also have pulmonary arterial hypertension (PAH). One of the most prominent features of SLE is continuous activation of the type I interferon (IFN) signature (1). This leads us to presume that the administration of type I IFN to SLE patients should be avoided because it can exacerbate SLE. Here we report a patient with both SLE and progressive hepatitis C virus (HCV) infection treated successfully using prednisolone (PSL), cyclophosphamide, IFNβ and ribavirin.

A 28-year-old woman developed excessive bruising due to low platelet count. She had no medical history. She was diagnosed as having idiopathic thrombocytopenic purpura and treated with PSL (unknown dose) and splenectomy at another hospital. Her platelet count was maintained with PSL 5 mg/day.

She developed dyspnea and arthralgia at the age of 34 and visited our hospital. Detailed examination showed low platelet count (147,000/μl), high urine protein level (1.15g/day), pericarditis, positive antinuclear antibody (speckled×1280), high ds-DNA level (72.7IU/ml), and low C3 level (62.5mg/dl). Other autoantibodies were negative. Based on these findings, she was diagnosed as having SLE. Right heart catheterization revealed PAH, with mean pulmonary arterial pressure (mPAP) of 58mmHg. She also had insidious HCV-genotype 1b infection (HCV-RNA, 7.10Meq/mL). After initial treatment with PSL 60mg/day, she achieved remission from SLE-PAH. We did not treat HCV infection because IFN-free therapy with direct-acting antivirals (NS3/4A protease inhibitor, NS5A inhibitor, and NS5B polymerase inhibitor) were not approved in Japan at that time and IFN administration was thought to exacerbate SLE. The dsDNA level in the patient increased at 48 years of age. Because cyclosporine A caused liver damage, 3 mg/day tacrolimus was added to 9 mg/day PSL, which led to the normalisation of the dsDNA level.

At the age of 53, she was admitted to our hospital for flared SLE-PAH (mPAP 46 mmHg). In the course of successful treatment for SLE-PAH with PSL 40 mg/day, one session of intravenous cyclophosphamide 500mg plus endothelin receptor antagonist (tacrolimus was discontinued at the same time), her HCV infection progressed, showing elevated serum alanine aminotransferase (ALT) and HCV-RNA levels. A liver biopsy specimen showed findings compatible with HCV infection. Another cause of hepatic dysfunction was not evident. Two months later, her total bilirubin (3.9 mg/dL) and ALT (226U/L) levels indicated imminent liver failure, so we administered short-acting IFNβ plus ribavirin 600 mg. We avoided polyethylene glycol (PEG)-IFN because a shorter half-life of IFN would be better, and IFNα required PEG attachment. After treatment, both her SLE and HCV infection resolved.

Previous reports showed that treatment with IFNα (2) and IFNβ (3, 4) can lead to drug-induced lupus, and IFNβ can lead to drug-induced pulmonary hypertension (5). These findings indicate administration of not only IFNα, but IFNβ, can exacerbate SLE-PAH. While it has also been reported that 8 SLE patients with HCV reactivation treated with pegylated IFN plus ribavirin did not show exacerbation of SLE (6). The clinical outcome of our case suggested that IFNβ administration does not exacerbate SLE. There exists another possibility that enhanced immunosuppressant drugs partly prevented IFNβ from exacerbating SLE; however, we supposed that ribavirin did not suppress the flare of SLE because ribavirin, having anti-HCV activity, is thought to activate the immune system.

IFNβ would be the treatment of choice for SLE patients who have HCV and cannot use IFN-free therapy due to adverse effects of direct-acting antivirals. In addition, SLE patients with malignant melanoma or glioblastoma may benefit from IFNβ administration. When using IFNβ in patients with SLE or pulmonary hypertension, we need to monitor for exacerbation cautiously. Future studies should address the similarities and differences between IFNα and IFNβ regarding the aetiology of SLE.

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