Leukocytoclastic Vasculitis Associated with Interferon β-1b Treatment in a Patient with Multiple Sclerosis

**ABSTRACT** Multiple sclerosis (MS) is a chronic, inflammatory and autoimmune disease of the central nervous system. Interferon (IFN) beta-1b is used to prevent progression and exacerbation of the disease, in MS treatment. IFN therapy has many side effects on the skin. However, IFN-associated vasculitic skin lesions are quite rare. I wanted to draw attention to this issue with this case report.

**Keywords:** Interferon treatment; leukocytoclastic vasculitis; multiple sclerosis

**CASE REPORT**

A 47-year-old woman referred to the rheumatology polyclinic because of red rash on her legs. This complaint has been around for 6 years, but the frequency has increased recently. She has been receiving IFN-β-1b therapy in our neurology clinic for about 13 years. Because of this rash, she had been referred to dermatology clinics several times and oral or superficial steroid therapy was recommended. The patient used oral steroids rarely in the beginning, but she has been using it continuously at doses of prednisolone 10-15 mg/day recently. However, skin lesions persisted continuously. There was no rheumatologic feature except the rash in the patient’s history. On physical examination, there were no features other than purpuric rash which showed widespread and convergent tendency in her both lower ex-
tremities. In laboratory tests, anti-nuclear antibody, extractable nuclear antigens, rheumatoid factor, anti-neutrophil cytoplasmic antibodies were negative. C3 and C4 levels were normal. C-reactive protein was 30.1 mg/L and erythrocyte sedimentation rate was 70 mm/h. Complete blood cell count, serum creatinine, fecal occult blood, complete urine test, HBsAg. Anti-HCV were either normal or negative. The result of the skin biopsy was reported consistent with leukocytoclastic vasculitis. The patient was evaluated together with the neurology clinic and neurologically, interferon therapy should be continued. For this reason, it was decided to start immunosuppressive treatment in addition to steroid for the patient’s rashes. Concomitant use of interferon with azathioprine has not been recommended due to the risk of side effects, so methotrexate therapy has been started. The Patient has been on follow-up for about 3 years and still uses methotrexate 20 mg/week and prednisolone 2.5 mg/day. During this time, the rash frequency and prevalence decreased significantly. The pre- and post-treatment status are shown in Figures 1 and 2, respectively.

DISCUSSION

Multiple sclerosis (MS) is an autoimmune, chronic, inflammatory disease of the central nervous system and usually affects young adults.4 It is characterized by recurrent neurological deficits, which are caused by T-cell mediated autoimmunity against central nervous system tissues.5 Immunomodulatory therapies such as IFN-beta have been used to control the progression and activity of MS and to reduce the frequency of exacerbations.4

Interferons (IFN) are natural glycoproteins with functions such as immunoregulatory, antiviral, antiproliferative, antiangiogenesis and oncogen inhibition. Interferons have classes such as alpha, beta, gamma, omega and tau.2,4 IFN alpha and beta are used worldwide in the treatment of many diseases, including MS. Generally all IFN beta forms are well tolerated. However, they also have some side effect risks.4 The most common complications of these side effects are flu-like syndrome and injection site reactions.1,2,4 Injection site reactions are usually mild, manageable and self-limiting. However, in rare cases, more severe reactions may develop, such as necrotic ulcerations that sometimes limit treatment.4 Many reports of cutaneous side effects (such as erythema, swelling, ulceration, and panniculitis) have been published.1 However, the number of articles related to IFN associated cutaneous vasculitis is rare. Szilasova et al. presented with a case of cutaneous lymphocytic vasculitis using IFN-β-1b therapy due to MS. In this case, IFN therapy had to be discontinued and steroids were given for the lesions.1 In another case report; presented with local leucocytoclastic vasculitis at the injection site during interferon gamma therapy. Steroids and colchicine were used in the treatment of lesions of this patient and IFN treatment was continued. The vasculitis did not recur after the injection site was changed, the steroid and colchicine were
stopped. In addition, there are four cases in the literature with IFN-induced leukocytoclastic vasculitis at the injection site. Three of them using IFN alpha and the other using IFN beta. IFN therapy was discontinued in all of these cases and local or systemic steroid therapy was given.

The vasculitic involvement in our case was not related to the site of injection, but showed a more widespread distribution involving both lower extremities (Figure 1). This type of involvement differs from the other case presentations mentioned. IFN beta-1b therapy in the presented patient could not be discontinued due to primary disease. Methotrexate was added to the current treatment because the vasculitis recurred when the steroid was reduced. The steroid dose the patient was using could be significantly reduced. The patient’s complaints also improved significantly and the routine control of the patient still continues in our rheumatology outpatient clinic.

Physicians who follow their patients with IFN therapy should be aware of that serious cutaneous reactions and vasculitic involvement may be associated with this therapy, although this is uncommon. These patients must be referred to a rheumatologist. A treatment that can be started without wasting time after an appropriate search can be a life-saving treatment. It can also allow the continued use of IFN therapy for the primary disease with close follow-up.

Source of Finance
During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest
No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions
This study is entirely author’s own work and no other author contribution.

REFERENCES