CASE REPORT

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

Cem ÖZİŞLER[a]

[a]Clinic of Rheumatology,
University of Health Sciences,
Dışkapı Yıldırım Beyazıt Training and Research Hospital,
Ankara, TURKEY

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Correspondence:
Cem ÖZİŞLER
University of Health Sciences,
Dışkapı Yıldırım Beyazıt Training and Research Hospital,
Clinic of Rheumatology,
Ankara, TURKEY
cemozisler@gmail.com

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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; multipl sclerosis

Interferon beta-1b (IFN-β-1b) is a recombinant human IFN-β. It is used to prevent disease progression and to reduce exacerbations in multiple sclerosis (MS) patients. IFN-β-1b is generally well tolerated. The most common side effects of this treatment are; injection site reaction and flu-like syndrome.[1,2] Autoimmunity can be seen as a long-term side effect of this therapy that can cause significant clinical consequences and even interferon treatment interruption.[3] Many reports of cutaneous side effects (such as erythema, swelling, ulceration, and panniculitis) have been published.[1] However, the number of reports related to isolated cutaneous vasculitis is rare. In this article, leukocytoclastic vasculitis arising in a 47-year-old woman who received IFN beta-1b treatment for MS will be discussed. A written informed consent was obtained from the patient.

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. Complet 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 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.[4,5] 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. Szilasiova 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

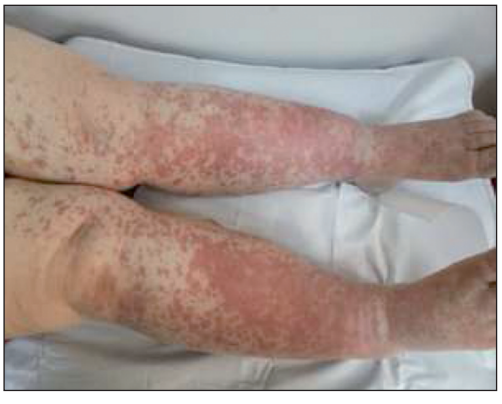

FIGURE 1: Pre-treatment view.

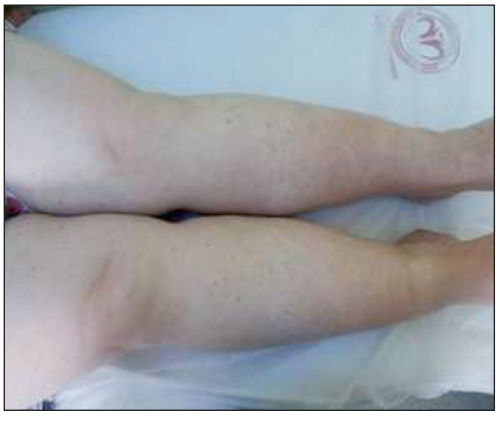

FIGURE 2: Post-treatment view.

stopped.[2] 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.[6-9]

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

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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

1. Szilasiová J, Gdovinová Z, Jautová J, Baloghová J, Ficová M, Bohus P. Cutaneous vasculitis associated with interferon beta-1b treatment for multipl sclerosis. Clin Neuropharmacol 2009;32(5):301-3.
2. Wang F, Liu JH, Zhao YK, Luo DQ. Interferon-gamma-induced local leukocytoclastic vasculitis at the subcutaneous injection site. An Bras Dermatol 2016;91(5 Suppl 1):76-8.
3. Tanrıover MD, Sozen T. [Interferon-α therapy and autoimmunity]. Hacettepe Medical Journal 2007;38:39-44.
4. Faghihi G, Basiri A, Pourazizi M, Abtahi-Naeini B, Saffaei A. Multipl cutaneous necrotic lesions associated with interferon beta-1b injection for multiple sclerosis treatment: a case report and literature review. J Res Pharm Pract 2015;4(2):99-103.
5. Kolb-Mäurer A, Goebeler M, Mäurer M. Cutaneous adverse events associated with interferon-β treatment of multiple sclerosis. Int J Mol Sci 2015;16(7):14951-60.
6. Feldmann R, Löw-Weiser H, Duschet P, Gschnait F. Necrotizing cutaneous lesions caused by interferon beta injections in a patient with multiple sclerosis. Dermatology 1997;195(1):52-3.
7. Christian MM, Diven DG, Sanchez RL, Soloway RD. Injection site vasculitis in a patient receiving interferon alfa for chronic hepatitis C. J Am Acad Dermatol 1997;37(1):118-20.
8. Pinto JM, Marques MS, Correia TE. Lichen planus and leukocytoclastic vasculitis induced by interferon alpha-2b in a subject with HCV-related chronic active hepatitis. J Eur Acad Dermatol Venereol 2003;17(2):193-5.
9. Adişen E, Dizbay M, Hizel K, Ilter N. Leukocytoclastic vasculitis during pegylated interferon and ribavirin treatment of hepatitis C virus infection. Indian J Dermatol Venereol Leprol 2008;74(1):60-2.