Morphea secondary to interferon beta1b injection: a case and review of the literature

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Abstract

Interferon beta (IFNβ) is a drug used successfully in the treatment of multiple sclerosis (MS). Although IFNβ is a safe and well-tolerated drug, dermatological side effects are common. The most common dermatological adverse effect is a local reaction at the injection site. It may also cause inflammatory and immune-mediated dermatological side effects. However, morphea induced by IFNβ1b injection is very rare.

Keywords: interferon beta, morphea, side effects

Introduction

Morphea is a disease characterized by fibrosis of the skin and subcutaneous tissues [1]. Systemically used drugs can rarely trigger morphea; however, certain injected medications may cause morphea [2]. Interferon β (IFNβ) preparations can be administered as a subcutaneous, intramuscularly-approved treatment for multiple sclerosis (MS), [3]. We report a case in which subcutaneous IFNβ1b was used for MS leading to the development of morphea.

Case Synopsis

A 60-year-old man presented to our clinic with erythematous, infiltrated plaques for one year. He was being followed for a diagnosis of MS for the last 20 years, and has been receiving subcutaneous IFNβ1b injections, 0.25mg/ml (8 million international units), every 2 days for 10 years. Dermatological examination revealed diffuse, hard, slightly erythematous plaques of pink-brownish color with irregular borders and variable dimensions, scattered around the umbilicus and confined to the injection sites (**Figure 1**). The patient's systemic examination, family history, other medication and laboratory tests were unremarkable. Histopathologic evaluation revealed epidermal atrophy, thickening and hyalinization of collagen bundles, atrophy of adnexal structures, and atrophy of fatty tissue around hair follicles and skin appendages in the dermis (**Figures 2, 3**). The patient was diagnosed with morphea secondary to subcutaneous IFNβ1b injection. It was recommended that the injection treatment be changed to another drug. The patient was advised to change the injection site. He was started on topical calcipotriol and clobetasol propionate 0.05% cream treatment once a day. His old lesions significantly

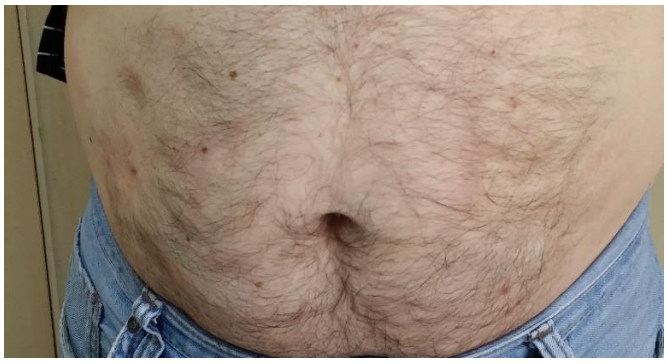

Figure 1. *Diffuse, hard, slightly erythematous plaque lesions of pink-brownish color with irregular borders around the umbilicus.*

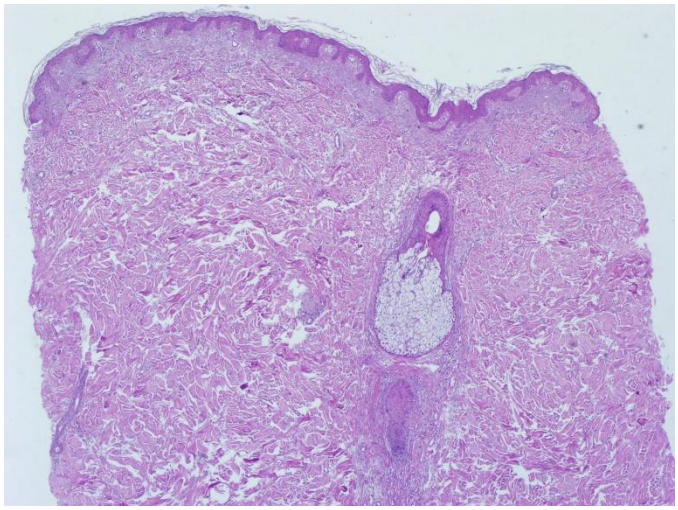

Figure 2. *Epidermal atrophy, thickening and hyalinization of collagen bundles, atrophy of fatty tissue around hair follicle and skin appendages in dermis (H&E, 4×).*

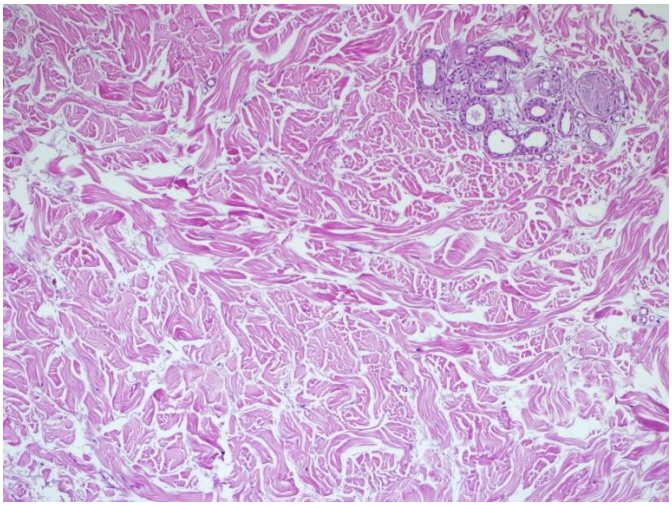

Figure 3. *Thickening of collagen bundles, atrophy of adnexal structures, atrophy of fatty tissue around skin appendages (H&E, 10×).*

regressed with treatment in 6 months, but new lesions occurred in new injection areas.

Case Discussion

Morphea is an inflammatory disease characterized by fibrosis, which causes a thickening of the skin and subcutaneous tissues [4]. Many drugs have been associated with morphea. Bleomycin, dopaminergic drugs, and beta-blockers have been suggested to trigger morphea by increasing collagen synthesis and/or fibroblast growth [2]. Tumor necrosis factor inhibitors have also been implicated in the development of morphea [5].

IFNβ is successfully used in the treatment of MS. Injection site reactions can be as high as 90% in subcutaneous applications and are only 33% in intramuscular applications [3]. Systemic sclerosis has been reported in three patients using IFNβ because of MS.; However, our patient was diagnosed with plaque morphea limited to the injection sites [5]. Recently, morphea has been reported in a patient in which IFNβ1a was used because of MS [4]. Deep morphea has been reported in a 60-year-old patient taking IFNβ1b [1], (**Table 1**). Dysregulation of the Th1/Th2 cytokine balance, recurrent trauma, or both may be responsible for the pathogenesis of morphea in IFNβ injection sites [4]. The initiation of symptoms in our case after 9 years of IFNβ1b treatment suggests that recurrent trauma might play an important role.

Conclusion

In conclusion, our case emphasizes the risk for chronic and severe side effects from IFNβ1b. Several medications administered through injection, such as vitamins B12 and K, are known to induce morphea and the adverse effects of IFNβ1b should be kept in mind when encountering patients with sclerosing skin disorders.

Potential conflicts of interest

The authors declare no conflicts of interests.

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***Table 1**: Demographic characteristics of interferon induced morphea patients in literature.*

Reported By	Age	Gender	Duration of IFN	Reason for IFN	Type of IFN	Injection location	Onset of morphea (after starting IFN)	Treatment	Response to treatment
Lee et al. [1]	60 years	Male	5 years	Multiple sclerosis	IFNβ1b	Anterior thigh	Unknown	Oral prednisone and systemic methotrexate	Near complete remission
Bezalel et al. [4]	52 years	Female	5 years	Multiple sclerosis	IFNβ1a	Anterior thigh	After 6 months	Topical steroid, topical calcitriol and systemic methotrexate	Unknown
Ozlu et al. (present case)	60 years	Male	10 years	Multiple sclerosis	IFNβ1b	Abdomen	After 9 years	Topical calcipotriol and clobetasol propionate 0.05% cream	Old lesions significantly regressed, but new lesions were occurred