

Pegylated interferon, but not conventional interferon therapy induced severe skin lesions

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Dear Editor:

Pegylation is an important technique that has greatly improved the pharmacologic profile of interferon. Compared with conventional interferon(IFN)- α injections, pegylated interferon (PEG-IFN) has a longer half-life allowing for once-weekly injections and superior antiviral efficacy in the treatment of hepatitis C when used in combination with ribavirin.¹ However, cutaneous side effects had been reported more frequent with PEG-IFN.¹ We present a patient with chronic hepatitis C (CHC) in whom PEG-IFN, but not conventional interferon therapy induced severe skin lesions at the sites of injection.

A 47-year-old woman was diagnosed as CHC on August 2007 and received conventional IFN- α -2b (3MU, every other day) and ribavirin (800 mg daily) for 12 months, and subsequently became negative for HCV RNA. She visited our hospital on June 2009 for generalized malaise and fatigue. She had a history of blood transfusion during uterine-incision delivery 22 years previously. Laboratory parameters at initial evaluation showed alanine aminotransferase (ALT) 187 IU/L, aspartate aminotransferase (AST) 102 IU/L, HCV RNA by polymerase chain reaction was 2,360,000 IU/mL, and genotype was 1b. Liver biopsy prior to second course antiviral therapy showed moderate necroinflammation with portoportal fibrosis (METAVIR Score A2, F3). She was administered PEG-IFN- α -2b (1.5 μ g/kg body weight, weekly) and ribavirin (800 mg daily). About 28

hours after the fourth injection of PEG-IFN, she started to develop pruritic papular erythematous eruption at injection site on the right abdomen. The patient was advised to change of injection site, but the same skin lesions, worsening after each injection, developed on the left abdomen and the dorsal surfaces of bilateral upper arm. After dermatologic consultation, she was started on mizolostine 10 mg daily and on topical corticosteroids, but this did partially relieve the symptoms.

After 48 weeks of treatment, physical examination revealed scaly, pigmented and thickened plaques on bilateral upper arm (Figure 1A, 1B), and eczematous dermatitis with mild lichenification on the abdomen (Figure 1C). Upon completion of the combination therapy, skin symptoms showed complete regression. She maintained normal aminotransferases and undetectable HCV RNA, as well as complete regression of skin lesions, after 12 months follow up.

In this case, it seems highly likely that PEG-IFN- α -2b was responsible for the onset of skin lesions. Since the skin reactions to PEG-IFN are common; the same skin lesions occurred at different injection sites; skin symptoms and lesions showed complete regression after the cessation of medication; and ribavirin had been included in antiviral therapy previously without skin reactions. We used the causal criteria from the World Health Organization to show the probability of adverse drug reaction.²

Antihistamines, emollients and topical corticosteroid had been described to administer cutaneous side effects during interferon therapy.³⁻⁶ Although De-reure, *et al.*³ reported 50% of the patients had to interrupt the antiviral treatment because of cutaneous side-effects, no patients needed to interrupt the antiviral combination regimen in another study.⁴ Also, some patients need to receive systemic corticosteroid and/or switch to non-pegylated IFN to continue treatment.^{5,6}

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Figure 1. Scaly, pigmented and thickened plaques on the right (A) and left (B) upper arm. Eczematous dermatitis with mild lichenification on the abdomen at the end of antiviral therapy (C).

Our patient with genotype 1b had an experience of virus relapse after treating with the conventional IFN plus ribavirin and had a high baseline virus load, which are correlated with a lesser chance to eradicate virus. The patient with advance liver fibrosis had a high risk of progressing to cirrhosis. In addition, the patient refused to receive systemic corticosteroid therapy and/or switch to conventional IFN. Taking these factors into consideration, the combination therapy had been continued and the PEG-IFN- α -2b and ribavirin was maintained in the same dose. Therefore, pruritus continued throughout the treatment process and severe skin lesions were notable at end of treatment.

The clinician should be aware of this relatively common adverse reaction to PEG-IFN injection and it does not always necessitate alteration or discontinuation of therapy. Each case should be individually examined, the successful clinical outcome of this case reinforces the importance of a close interdisciplinary follow-up in order to avoid premature treatment withdrawal.

ABBREVIATIONS

- **IFN:** interferon.
- **PEG-IFN:** pegylated interferon.
- **CHC:** chronic hepatitis C.

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CONFLICTS OF INTEREST

The authors have no conflict of interest to declare.

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REFERENCES

1. Reddy KR, Wright TL, Pockros PJ, Shiffman M, Everson G, Reindollar R, Fried MW, et al. Efficacy and safety of pegylated (40-kd) interferon alpha-2a compared with interferon alpha-2a in noncirrhotic patients with chronic hepatitis C. *Hepatology* 2001; 33: 433-8.
2. Edwards IR, Aronson JK. Adverse drugs reactions: definitions, diagnosis, and management. *Lancet* 2000; 356: 1255-9.
3. Dereure O, Raison-Peyron N, Larrey D, Blanc F, Guilhou JJ. Diffuse inflammatory lesions in patients treated with interferon alfa and ribavirin for hepatitis C: a series of 20 patients. *Br J Dermatol* 2002; 147: 1142-6.
4. Lübke J, Kerl K, Negro F, Saurat JH. Clinical and immunological features of hepatitis C treatment associated dermatitis in 36 prospective cases. *Br J Dermatol* 2005; 153: 1088-90.
5. Hashimoto Y, Kanto H, Itoh M. Adverse skin reactions due to pegylated interferon alpha 2b plus ribavirin combination therapy in a patient with chronic hepatitis C virus. *J Dermatol* 2007; 34: 577-82.
6. Veldt BJ, Schalm SW, Janssen HL. Severe allergic eczema due to pegylated alfa interferon may abate after switching to daily conventional alfa-interferon. *J Clin Gastroenterol* 2007; 41: 432.