Morbilliform drug eruption due to pegylated α-interferon can show complete regression after switching to non-pegylated interferon

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ABSTRACT

Pegylated or non-pegylated α-interferon are frequently used medications for the treatment of both chronic hepatitis B and chronic hepatitis C. Skin disorders, which are mainly comprised of eczematous dermatitis, are frequently seen during treatment with this drug. However, drug eruption or morbilliform eruptions due to interferons have been rarely reported so far. We herein describe a patient who developed morbilliform drug eruption under treatment with pegylated interferon. She was able to continue treatment after switching from pegylated interferon to conventional interferon.

Key words: α-interferon, chronic hepatitis B, drug eruption, morbilliform, pegylated interferon.

INTRODUCTION

Pegylated interferon (PEG-IFN) along with ribavirin is the current standard of care for the treatment of chronic hepatitis C. Pegylated and non-pegylated forms of IFN-α are also choices of treatment of chronic hepatitis B (CHB).1 However, side-effects of IFN-based treatments are common and remain a major cause of therapy discontinuation and subsequent failure. Alopecia (14–27%) and injection site erythema (6–29%) are the most frequently seen cutaneous side-effects during treatment with PEG-IFN-α.2–4 The incidence of rash, which occurs in approximately 10% of CHB patients treated with PEG-IFN, increases with the introduction of ribavirin to PEG-IFN-based regimens.5 Skin reactions associated with PEG-IFN plus ribavirin treatment mostly comprise eczematous dermatitis.6,7 However, morbilliform drug eruptions caused by IFN have been rarely reported to date. Here, we present a case of drug eruption during therapy with PEG-IFN-α-2a for CHB.

CASE REPORT

A 30-year-old woman with a 2-year history of CHB was referred to an infectious disease clinic. On laboratory examination, she was found to have elevated serum levels of alanine aminotransferase (213 U/L) and aspartate aminotransferase (76 U/L). Her liver biopsy showed features compatible with hepatitis B virus infection with grade 7 inflammatory activity and stage 1 fibrosis (according to Knodell score). She started treatment with PEG-IFN-α-2a 180 μg once weekly, with a diagnosis of hepatitis B e-antigen-negative CHB. After the second dose of PEG-IFN, she started to develop a rash, which was confluent and itchy, which affected the antecubital area, anterior abdominal wall and back. The rash spread to the whole body after the third dose of PEG-IFN and we referred the patient to the dermatology clinic. Physical examination revealed generalized, erythematous, non-squamous, maculopapular exantheme that affected the trunk, back and upper extremities.
with a presumptive diagnosis of drug eruption (Fig. 1). She was commenced on prednisolone 40 mg/day for 3 days and a moderately potent topical steroid, and she omitted one dose of PEG-IFN. As her eruptions improved well within 2 weeks, we reinstated the PEG-IFN therapy. However, after the seventh dose of PEG-IFN-α-2a, the same rash reappeared on her back. We performed skin biopsy to confirm the early diagnosis of morbilliform drug eruption. Histology of the skin specimen revealed vacuolar degeneration of the dermoepidermal junction and a superficial perivascular inflammation with lymphocytes and sparse eosinophils (Fig. 2). These clinicopathological features were consistent with morbilliform drug eruption. We stopped the PEG-IFN treatment and switched to conventional IFN-α-2a three times weekly. Skin lesions showed complete regression within 1 week, and the topical steroid was stopped. Lesions did not reappear under treatment with non-pegylated IFN.

**DISCUSSION**

The most common cutaneous side-effects during PEG-IFN therapy are injection site reaction, alopecia and dermatitis. A limited number of published studies have investigated the type of dermatitis observed during PEG-IFN-based therapy, and the data are generally derived from the PEG-IFN plus ribavirin treatment of chronic hepatitis C (CHC). According to these studies, over 20% of treated patients show skin lesions, of which the most common type is eczematous dermatitis, and the lesions can be controlled by emollients and/or topical steroids without discontinuation of antiviral treatment. In the published work, there are far less data concerning drug eruption as a side-effect of IFN-based therapy, but there are reports that PEG can cause skin reactions.

A study by Manjon-Haces et al. considered 210 patients with CHC under treatment with IFN-α-2b plus ribavirin, and skin lesions appeared in 27 cases. Eczema was the most common type of dermatitis, which was observed in 16 patients (59%). They reported that two patients developed maculopapular exanthema, which could have been similar to our case, but detailed information is not available concerning these lesions.

Veldt et al. have described a patient who developed severe allergic eczema under treatment with PEG-IFN and ribavirin. The patient did not respond to topical steroids and antihistamines, but his eczema abated after switching from PEG-IFN to daily regular IFN. There is a similarity to the present case in that the PEG molecule was the causative agent of skin reactions, and switching to non-pegylated IFN abated the skin lesions, and allowed the patient to continue antiviral therapy.

One of the interesting features of our case is that the patient showed generalized rash, consistent with a diagnosis of drug eruption, within a short period of therapy with PEG-IFN. The recurrence of skin eruption
after the second session of PEG-IFN, as well as remis-
sion of the lesions despite continued treatment with
conventional IFN-α-2a, suggests that the causative
agent responsible for the skin reaction was related to
the PEG component of PEG-IFN and changing PEG-
IFN to IFN was effective in preventing the develop-
ment of this reaction. The limitation of this case study
is the lack of a provocation test, in vitro test or patch
test to confirm the PEG-IFN-induced drug eruption.

Milkiewicz et al.10 have reported a hepatitis B
patient who developed generalized skin lesions dur-
ing treatment with PEG-IFN-α. However, in contrast
to our patient, skin lesions of that patient were consist-
ent with urticaria and the patient responded well to
treatment with topical steroids and antihistamines.

Lubbe et al.6 have reported that the majority of 36
patients with de novo onset of skin symptoms associ-
ated with the introduction of PEG-IFN-α-2a plus riba-
virin developed eczematous dermatitis. However,
they did not observe maculopapular exanthema in
any of their patients. Thus, morbilliform drug eruption
might be a very rare complication of PEG-IFN therapy.

In conclusion, morbilliform drug eruption can be
considered as a side-effect of PEG-IFN-based ther-
apy of chronic viral hepatitis, although it is only seen
rarely. This skin reaction can resolve after switching
to non-pegylated IFN, thus allowing the patient to
continue treatment.

REFERENCES

1 European Association for the Study of the Liver. EASL
Clinical Practice Guidelines: management of chronic

2 Manns MP, McHutchison JG, Gordon SC et al. Peginter-
feron alfa-2b plus ribavirin compared with interferon
alfa-2b plus ribavirin for initial treatment of chronic
965.

3 van Zonneveld M, Flink HJ, Verhey E et al. The safety of
pegylated interferon alpha-2b in the treatment of chronic
hepatitis B: predictive factors for dose reduction and
treatment discontinuation. Aliment Pharmacol Ther

4 Marcellin P, Lau GK, Zeuzem S et al. Comparing
the safety, tolerability and quality of life in patients
with chronic hepatitis B vs chronic hepatitis C treated
485.

5 Lau GK, Piratvisuth T, Luo KX et al. Peginterferon Alfa-
2a, lamivudine, and the combination for HBeAg-positive
2695.

6 Lübke J, Keri K, Negro F, Saurat JH. Clinical and immu-
nological features of hepatitis C treatment-associated

7 Manjón-Haces JA, Vázquez-López F, Gómez-Diez S
et al. Adverse cutaneous reactions to interferon alfa-2b
plus ribavirin therapy in patients with chronic hepatitis C

8 Cottoni F, Bolognini S, Deplano A et al. Skin reaction in
antiviral therapy for chronic hepatitis C: a role for poly-
ethylene glycol interferon? Acta Derm Venereol 2004;
84: 120–123.

9 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.

10 Milkiewicz P, Yim C, Pache I, Heathcote J. Diffuse skin
reaction in patient with hepatitis B, treated with two
different formulations of pegylated interferon. Can J