

Managing generalized interferon-induced eruptions and the effectiveness of desensitization

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Summary

Background We evaluated the value of skin tests and the efficacy of a 12-step desensitization protocol to pegylated interferon (IFN) in patients with generalized drug eruptions due to IFNs.

Methods A retrospective study (1998–2009) was followed by a cross-sectional clinical study conducted prospectively (2009–2011). All patients received a dermatological clinical examination and skin tests. Twelve-step IFN desensitization was proposed for patient with active hepatitis C and no alternative therapy.

Results Twenty-six patients (13 males, mean age, 53.5 years) had generalized reactions to IFNs; 21 were treated with IFN- α and 5 with IFN- β . Moreover, 21 patients had skin tests. Intradermal tests (IDTs) were positive after an average of 72 h. Cross-reactivity between peg-IFN- α 2a and peg-IFN- α 2b was observed in 5/10 cases in the prospective study. In 16 of 26 cases, IFN treatment was stopped. In 8 of 16 cases of diffuse eczematous drug eruption, treatment was continued. The corticosteroid and antihistamine were sufficient in 4/8 cases. In three other cases, topical tacrolimus was highly effective. In 3 of 16 cases in which treatment were stopped, patients underwent the early resumption of peg-IFN- α . These three patients had positive tests with peg-IFN- α 2a and peg-IFN- α 2b and successfully completed the tolerance induction protocol for peg-IFN- α 2b. Tolerance induction involved a weekly dose of peg-IFN and a gradual increase in the recovery of an antiviral C. Clinical tolerance was excellent, and the patients' viral load C became negative.

Conclusions Our study demonstrates the benefit of allergy testing in cases of generalized drug reactions to IFN, cross-reactivities in a single class of IFNs and the importance of delayed IDT reading. We report for the first time the effectiveness of 12-step desensitization with peg-IFN.

Keywords cutaneous adverse drug reaction, drug allergy, interferon, skin tests, tolerance induction

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Introduction

Interferons (IFN) are glycoproteins made up of three main types: IFN- α (subtypes: 2a, 2b, pegylated or not, con1), whose main indications are chronic hepatitis C and melanoma; IFN- β (subtypes: 1a, 1b), prescribed for multiple sclerosis; and IFN- γ , used as prophylaxis in familial granulomatosis. About 5–12% of side-effects related to IFN treatment involve adverse skin reactions, either localized at the injection site or generalized skin reactions. Some maculopapular exanthemas (MPEs) or generalized urticarias may involve an allergy to

biological agents and thus can be classified as beta-type reactions [1]. When generalized reactions to IFN occur, antihistamines and corticosteroids (CS) are usually proposed. There is only one reported case of a successful desensitization protocol to IFN- α [2]. Twelve-step desensitization protocols have been used to treat systemic, generalized immediate reactions to other biological agents or chemotherapeutic drugs [3], but there are no reported cases of a 12-step protocol for generalized reactions to IFN.

From preliminary results obtained by a retrospective study, we could propose a standardized method for

managing cutaneous adverse drug reactions to IFN. The aim of the study was to determine whether other treatment than topical CS could be useful and assessed the value of drug skin tests, which has been vigorously debated. Secondly, among a few number of patients multisensitized to IFN, we tried to determine the value of a 12-step desensitization protocol for IFN treatment, tolerance and efficiency.

Patients and methods

Study population

A cross-sectional, single-centre clinical study was conducted retrospectively from 1998 to 2009 (study A) and prospectively from 2009 to 2012 (study B) (Table 1). It included patients who had experienced generalized eruptions while receiving IFN treatment. The following information was collected for all patients: age, sex, results of dermatological examination, class of suspected IFN, associated drugs taken and pathology for which the drugs had been prescribed. All patients in study B were examined by the same dermatologist (CP). All patients had a dermatological follow-up, including skin tests in most cases. Associated antiviral drugs were also skin-tested.

Patient management

All patients were examined during their adverse reactions. In cases of non-severe and easily controlled eruptions, only antiviral treatment and symptomatic therapy were initially continued in the form of class IV topical corticosteroids and oral antihistamines. Clinical reassessment was performed every 15 days. Six weeks after the disappearance of the eruption, a dermato-allergological investigation was performed.

In the case of hepatitis, if the eruption could not be controlled by corticosteroids and antihistamines, or if any serious biological disturbances occurred, IFN and antiviral treatments were discontinued. Dermato-allergological tests were scheduled 6 weeks after the disappearance of the eruption. Peg-IFN- α was frequently used with telaprevir, boceprevir or ribavirin. In all cases, these drugs were tested and then reintroduced without IFN.

Drug skin tests were performed at least 6 weeks after the disappearance of the eruption, without antihistamines, topical corticosteroids or systemic corticosteroids. For this, different classes of IFNs were used in study A, whereas different IFNs within only the suspected class were used in study B. Thus, in the case of eruptions suspected to be due to IFN- α , skin tests were routinely performed with IFN- α 2a, IFN- α 2b, pegylated IFN and non-pegylated IFN. When IFN- β was the

suspected agent, IFN- β 1a and IFN- β 1b were used. For each patient, concomitant therapies were also tested. In accordance with European guidelines [4], patch tests were performed with all drugs taken by patients in their commercialized forms diluted at 30% in petrolatum. Drugs were applied to the back using IQ chambers (Chemotechnique, Vellinge, Sweden), then read on days 2 and 4 and 1 week later.

Prick tests using the same drugs at usage concentrations were performed on the forearm. Readings were taken at 20 min and 24 h, and the results were compared to those obtained with a negative control (saline) and a positive control (histamine). Intradermal tests (IDTs) were performed with IFN, and all drugs administered to the patient by injection and only when the results of other skin tests were negative. Briefly, sequential dilutions in saline from 10^{-2} up to the usage concentration were injected at 0.02 mL on the external side of the arm. To standardize the method of IDT with IFN, the mean diameters of all injection papules (wheals) measured following this method are reported in Table 2. Results were considered positive if the diameter of the injection papule measured immediately after ID administration had doubled at 20 min, accompanied by a surrounding erythema (Table 2). For delayed readings at 24 h, results were considered positive if there was an erythema and an infiltration at the injection site.

Tolerance induction

For some patients with active hepatitis C virus (HCV), there was no alternative therapy. If these patients tolerated antiretroviral drugs, they were subjected to a 12-step IFN desensitization treatment under doctors' supervision (Tables 3 and 4); protocol adapted from those for other agents [3, 5–7]. First ribavirin was readministered, with a good tolerance in all cases. In a second time, antiviral drug (telaprevir or boceprevir) was readministered in same conditions. Under antihistamine (desloratadine 5 mg/day) the day before desensitization then 2 days, the desensitization protocol was performed weekly. Patients were discharged 5 h after the end of the desensitization protocol if no side-effects occurred.

Results

A total of 26 patients (13 women, 13 men; mean age 53 years; age range 33–81 years) were included in this study (Table 1 and Figure 1). All underwent dermatological examination and later immunological investigations. 21 were treated with IFN- α : 16 for active hepatitis C, three for melanoma, one for chronic myeloid leukaemia and one for polycythemia vera. The other five received IFN- β for multiple sclerosis. Clinical

Table 1. Results of the retrospective and prospective studies

Case	Sex	Age	Drug adverse reaction	IFN	Associated treatment	Disease	Results Pt	Results pt	Results IDT	Alternative
Retrospective Study A (1998–2009)										
1	F	54	MPE	Peg-IFN- α 2b	Ribavirin	HCV	–	–	Peg-IFN- α 2b + 144 hIFN- α 2b + 144 h	Substitution with Peg-IFN- α 2a (IDT-)
2	F	58	MPE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	–	Lose touch
3	M	38	MPE	Peg-IFN- α 2a	NO	PV	–	–	Peg-IFN- α 2a + 120 h	Substitution with IFN- α 2b (IDT -)
4	M	56	MPE	INF- α 2b	NO	Melanoma	NT	NT	NT	Cessation of treatment
5	F	60	MPE	Peg-IFN- α 2b	Ribavirin	HCV	NT	NT	NT	Anti-H1 + Topical CS insufficient, Cessation of treatment
6	M	42	GEE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	Peg-IFN- α 2a + 24 hIFN- α 2b -	Cessation of treatment
7	F	36	GEE	IFN- β 1a	NO	MS	–	–	IFN- α 2a + 96 hIFN- β 1a + 96 h	Treatment continued with narrow band UVB Topical CS and anti-H1 insufficient
8	F	53	GEE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	–	Lose touch
9	M	56	GEE	IFN- β 1b	NO	MS	–	–	IFN- β 1b + 48 hIFN- α 2a + 48 h	Reintroduction of IFN- β 1b: reactivation of GEE; alternative: IFN- β 1a (IDT-)
10	M	81	GEE	Peg-IFN- α 2b	Ribavirin	HCV	NT	NT	NT	Topical CS and anti-H1
11	F	56	GEE	INF- α 2b	NO	Melanoma	NT	NT	NT	Topical CS and anti-H1
12	M	63	GEE	IFN- α 2b	NO	Melanoma	–	–	IFN- α 2b + 48 h ; IFN- α 2a + 48 h ;	Reintroduction of IFN- α 2b: reactivation of GEE; topical corticosteroid and anti-H1 insufficient. Cessation of treatment
13	M	55	GEE	Peg-IFN- α 2a	Ribavirin	HCV	NT	NT	Peg-IFN- α 2b + 48 h	Topical CS and anti-H1 insufficient; topical tacrolimus effective +++
14	F	33	urticaria	IFN- β 1b	NO	MS	–	–	NT	Cessation of treatment
Prospective Study B (2009–2012)										
15	F	60	MPE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	Peg-IFN- α 2a + 20mns	12-step desensitization with Peg-IFN- α 2b
16	M	61	MPE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	Peg-IFN- α 2b + 48 h	12-step desensitization with Peg-IFN- α 2b
17	M	63	MPE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	Peg-IFN- α 2a + 24 hPeg-IFN- α 2b + 24 hIFN- α 2a + 24 h	12-step desensitization with Peg-IFN- α 2a
18	F	49	MPE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	Peg-IFN- α 2a + 168 hPeg-IFN- α 2b + 168 hIFN- α 2a + 168 h	Cessation of treatment. Topical corticosteroid and anti-H1 insufficient.
19	M	68	MPE	Peg-IFN- α 2a	Ribavirin + telaprevir	HCV	–	–	Peg-IFN- α 2a + 48 hPeg-IFN- α 2b + 48 hIFN- α 2b + 48 h	Cessation of treatment
20	M	51	GEE	Peg-IFN- α 2a	Ribavirin	HCV	–	–	Peg-IFN- α 2a + 24 h	Topical CS and anti-H1 insufficient; topical tacrolimus effective +++

(continued)

Table 1. (continued)

Case	Sex	Age	Drug adverse reaction	IFN	Associated treatment	Disease	Results Pt	Results pt	Results IDT	Alternative
21	F	69	GEE	Peg-IFN- α 2a	Ribavirin + telaprevir	HCV	Peg-IFN- α 2b + 168 hIFN- α 2b + 168 h	–	Peg-IFN- α 2a + 168 h	Treatment continued with topical CS and anti-H1
22	F	50	GEE	Peg-IFN- α 2a	Imatinib	CML	–	IFN- α 2b + 24 h	Peg-IFN- α 2b + 24 hIFN- α 2b + 24 h	Topical CS and anti-H1 insufficient; topical tacrolimus effective +++
23	M	37	Urticaria	Peg-IFN- α 2a	Ribavirin	HCV	IFN- α 2a + 48 hPeg-IFN- α 2a + 96 hPeg-IFN- α 2b + 96 h	–	Peg-IFN- α 2a + 24 hPeg-IFN- α 2b + 24 hIFN- α 2a + 24 h	Cessation of treatment
24	F	56	Lichenoid eruption	Peg-IFN- α 2a	Ribavirin + telaprevir	HCV	–	–	– (0/4 IFN- α tested)	Treatment continued with topical CS and anti-H1
25	F	46	GEE	IFN- β 1a	NO	MS	–	–	– (0/3 IFN- β tested)	Cessation of treatment (glatiramer acetate)
26	M	40	Urticaria	IFN- β 1a	NO	MS	–	–	– (0/3 IFN- β tested)	Cessation of treatment (glatiramer acetate)

F, female; M, male; MPE, maculopapular eruption; IFN, interferon; Peg-IFN- α 2a, PEGASYS[®]; Peg-IFN- α 2b, VIRAFERONPEG[®]; IFN- α 2a, ROFERON[®]; IFN- α 2b, INTRONA[®]; HCV, hepatitis C virus; CML, chronic myeloid leukaemia; GEE, generalized eczematous eruption; NO, none; MS, multiple sclerosis; Pt, patch tests; pt, prick tests; IDT, intradermal tests; CS, corticosteroids; anti-H1, antihistamines; PV, polycythemia vera.

Table 2. Mean diameter of injection papule (Pi) with 0.02 mL injected volume, measured just after injection

Dilution	Mean diameter of Pi with 0.02 mL		
	10-2	10-1	Pure
peg-IFN- α 2a (concentration)	4.9 mm (3.6 μ g/mL) σ = 0.5 mm	4.9 mm (36 μ g/mL) σ = 0.7 mm	4.7 mm (360 μ g/mL) σ = 0.6 mm
Peg-IFN- α 2b (concentration)	4.6 mm (0.001 mg/mL) σ = 0.7 mm	5.1 mm (0.01 mg/mL) σ = 0.7 mm	4.3 mm (0.1 mg/mL) σ = 1 mm
IFN- α 2a (concentration)	4.6 mm (0.03 MUI/mL) σ = 0.7 mm	5 mm (0.3 MUI/mL) σ = 0.8 mm	4.8 mm (3 MUI/mL) σ = 0.33 mm
IFN- α 2b (concentration)	5.1 mm (0.06 MUI/mL) σ = 0.6 mm	4.6 mm (0.6 MUI/mL) σ = 0.5 mm	4.3 mm (6 MUI/mL) σ = 0.7 mm

MUI, mega international units; σ = SD (standard deviation).

Table 3. Tolerance induction protocol for peg-IFN- α 2b (Viraferon-peg[®])

Step	Time (min)	Dose (mg)	Cumulated dosage (mg)
1	15	0.0012	0.0012
2	15	0.012	0.0132
3	15	0.12	0.1332
4	15	1.2	1.3332
5	15	1.2	2.5332
6	15	1.2	3.7332
7	15	12	15.7332
8	15	12	27.7332
9	15	12	39.7332
10	15	26.75	66.2332
11	15	26.75	92.7332
12	240	26.75	120

Table 4. Tolerance induction protocol for peg-IFN- α 2a (Pegasys[®])

Step	Time (min)	Dose (mg)	Cumulated dosage (mg)
1	15	0.0018	0.0018
2	15	0.018	0.0198
3	15	0.18	0.1998
4	15	1.8	1.9998
5	15	1.8	3.7998
6	15	1.8	5.5998
7	15	18	23.5998
8	15	18	41.5998
9	15	18	59.5998
10	15	40.13	99.7332
11	15	40.13	139.86
12	240	40.13	180

features (Figure 1) were generalized eczematous eruption (GEE) (12 cases), MPE (10 cases), generalized urticaria (three cases) and lichenoid eruption (one case). In our hospital in 2011, generalized side-effects occurred in 10 of 200 patients (5%) treated with IFN for hepatitis C. Drug skin tests were performed for 21 patients. Indeed, five patients had no skin tests in retrospective study (A). Patch tests were negative in 19 of 21 cases. Prick tests were positive in only one case. IDTs performed with the suspected IFN were positive in 16

of 21 cases. Injection papule sizes after injecting 0.02 mL IFN are reported in Table 2. The delay in the occurrence of positive results on IDT ranged from 20 min to 6 days, with an average of 72 h (Figure 2). Three patients (#9, 12, 15) with delayed positive results had a subcutaneous readministration of the IFN that had led to the positive IDT. These readministrations were followed by a relapse of the systemic adverse reaction, reactivating an MPE in one case (Figure 3) and GEE in the two other cases. Among the 16 patients tested for several IFNs, cross-reactivities were observed in 10 cases (62, 5%) in the same IFN class and between different classes; Peg-IFN- α 2a and peg-IFN- α 2b had cross-reactivities in 50% of cases.

Among 14 cases due to IFN- α , 13 had positive IDTs with the suspected IFN. In one case of lichenoid drug eruption (#24) due to IFN- α , both patch tests, prick tests and IDTs were negative. In six cases of GEE due to IFN- α , the IDTs with the IFN involved were positive in all cases. In eight cases of an MPE due to IFN- α , the IDTs with IFN involved were positive in 7/8 cases. In one case of urticaria due to IFN- α (#23), IDT was positive.

The delay in the occurrence of adverse reactions to IFN- α was from 1 week to 9 months (average, 11 weeks). In 4 of 26 cases, patients had been exposed to IFN in a previous line of treatment. In 16 of 26 cases, treatment with IFN had to be discontinued (Figure 1) due to MPE associated with severe pruritus with insomnia resistant to topical corticosteroid (nine cases), urticaria (three cases) and GEE in 4 of 12 cases. In 3 (#1, 3, 9) of these 16 cases, another IFN for which the IDT was negative was introduced, with good tolerance and, in two cases, IFN was discontinued because we found an alternative treatment (#25, 26). In the seven remaining cases with GEE, IFN treatment with ribavirin or antiprotease could be continued. Three (#10, 11, 21) saw sufficient improvement taking antihistamines and topical corticosteroids. Of the other four patients, 1 (#7) saw an improvement in eczematous lesions by continuing IFN under narrowband ultraviolet B (UVB) phototherapy, and three another showed a spectacular

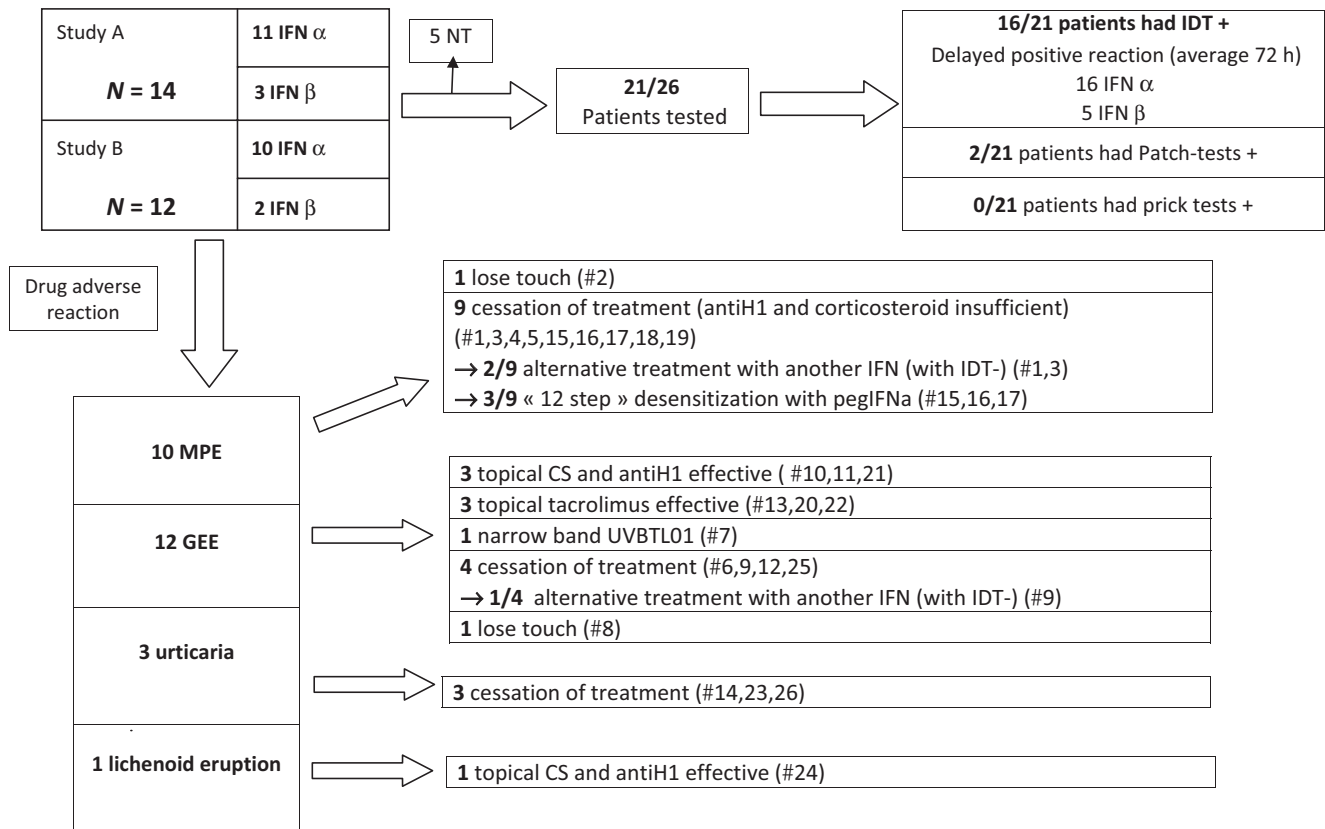


Fig. 1. Scheme of study.



Fig. 2. Importance of delayed reading of intradermal tests for interferons (Table 1 Study A Case 3).

Fig. 3. Reactivation of a generalized fixed drug reaction after resumption of peg-IFN- α 2a without tolerance induction in patient 15.

improvement after the application of topical tacrolimus (#13, 20, 22); topical CS were ineffective. In these four cases with hepatitis C (#10, 13, 20, 21), the therapeutic

response to IFN was good, and the viral load (VL) became undetectable.

Of the 16 patients in whom treatment was discontinued, 3 (#15, 16, 17) had a very noxious evolution of



Fig. 4. Slight pruritic and macular lesions on the proximal area of the legs with a 12-step desensitization protocol to peg-IFN- α 2b in patient 15.

their hepatitis C with biological criteria for hepatic fibrosis, which mandated the resumption of antiviral treatment (peg-IFN- α with ribavirin and antiprotease). They had (Table 1 Study B) delayed positive IDTs for peg-IFN- α 2a and peg-IFN- α 2b, negative skin tests with ribavirin or antiprotease and well tolerated the reintroduction of those antiviral drug. Therefore, we initiated a 12-step desensitization protocol for IFN, as detailed in Table 5, with good tolerance and effectiveness.

Discussion

Cutaneous side-effects of IFN are not rare; in 2011, they occurred in 5% of all patients treated with peg-IFN- α for active hepatitis C [8]. Here, we report 26 cases of generalized eruptions in which the continuation of treatment would have been compromised in the absence of a specific dermatological and allergological management protocol. We thus proposed and followed guidelines that allowed 7 of 12 of these patients to continue IFN- α therapy (Study B). In the case of adverse reactions to IFN- β , skin tests are not useful because there are two alternative therapeutic protocols for multiple sclerosis.

With IFN- α , the use of topical corticosteroids with antihistamines is proposed. These were effective in 4 of 26 of our cases. If these are not effective, narrowband UVB phototherapy (one case) or topical tacrolimus

(three cases) may be used to treat generalized eczematous rashes, but in our experience they are not effective in managing MPE.

For patients with uncontrolled hepatitis and with positive results on IDTs performed with different IFNs who experience no relief from external therapies, a 12-step desensitizing protocol is valuable. There is only one report of tolerance induction for IFN- α in a 65-year-old patient with active hepatitis C liver fibrosis with a detectable VL who experienced systemic hypersensitivity to IFN- α during a first-line treatment [2]. The patient was administered increasing doses from a 10^{-5} dilution to a cumulative dosage equivalent to the therapeutic dose (that reached under antihistamines in three consecutive days). The treatment continued with a daily injection over 54 weeks. Desensitization was efficient and the patient's HCV VL was undetectable at the end of treatment. According to our hepatologist colleagues, this type of daily administration was not possible for our patients. As peg-IFN- α had to be delivered once a week, we decided to follow a 12-step desensitization procedure as has been proposed for chemotherapies or biological agents [3, 5–7]. We are the first to report the effectiveness of this desensitization protocol in three patients with severe MPE and uncontrolled VL. Although it requires time and money, the protocol allowed for complete control of the VL in these three patients with no alternative choice of therapy. The mechanisms of drug eruptions to IFN are poorly understood. Clinical manifestations such as MPE, GEE, urticaria similar to those observed with xenobiotics, delayed onset and positive skin tests—as observed in 16 of our patients—favour a hypersensitivity mechanism. In our patients, patch tests with IFN had no value. There is one positive report of a patch test performed with IFN- α in a patient with hairy cell leukaemia who developed an eczematous reaction at the injection site [9]. Meller et al. [10] reported one case of an MPE attributed to peg-IFN- α 2b in a patient who had negative patch tests with IFN but delayed (day 3) positive results on IDTs performed with peg-IFN- α 2a and peg-IFN- α 2b (but negative with IFN- α 2b.) Patch tests can be useful for demonstrating the effects of associated antiviral therapies. The present study emphasizes the value of IDTs to this end and also for studying potential cross-reactivities between different IFNs. There are only nine reports of IDTs performed with IFN [11–13]. Dereure et al. [11] reported one case of positive IDTs (undiluted and at 10% in saline) with IFN- α 2b among six patients with eczematous adverse reactions to IFN- α . In one patient with an IFN- β -induced urticaria, IDTs were positive with IFN- β 1b but negative with IFN- β 1a [13]. Berger et al. [12] performed patch tests, prick tests and IDTs with IFN- α with negative results in one case. Therefore, we conclude that the adverse reactions in our patients

Table 5. Clinical course of three patients who had the 12-step protocol

Patient	12-step desensitization	Side-effects to desensitization	Other treatment	Reason for ceasing protocol	Viral load
15	Doses: see Table 3; Duration: weekly for 52 weeks	After the 5th course: maculopapular or macular lesions as in Figure 4 controlled with topical clobetasol. From the 25th to the 52nd courses, no adverse effect.	Desloratadine at the beginning Ribavirin and antiprotease from the 6th to the 52nd course	End of the therapy	Undetectable
16	Doses: see Table 3 Duration: weekly for 32 weeks	The only side-effect was an eczematous reaction at the injection site that was easy to control with corticosteroid. Beginning in the 30th week, we attempted to administer the entire dose without desensitization (120 mg peg-IFN- α 2b). Cutaneous tolerance was good	Desloratadine at the beginning Ribavirin and antiprotease from the 6th to the 32nd course	Haematotoxicity (side-effects of IFN)	Undetectable
17	Doses: see Table 4 Duration: weekly for 22 weeks	13th week, the patient developed an itchy papular eruption on the right arm that was controlled by topical clobetasol and 5 mg desloratadine per day. Following the 17th course, he had an MPE on the trunk. The dose of desloratadine was increased to 10 mg per day, and topical betamethasone was applied to the skin lesions	Desloratadine at the beginning Ribavirin and antiprotease from the 6th to the 22nd course	Haematotoxicity and asthenia (side-effects of IFN)	Undetectable

MPE, maculopapular exanthema.

were due to the immunomodulating action of IFN- α and were dose dependent, and that atopic dermatitis history and dry skin associated with HCV would have been predisposing factors in the development of GEE.

Patch tests have a low value and are not recommended, but our study emphasizes the value of delayed IDT readings in the study of cross-reactivities. IDTs are supposed to always be positive, but we collected 33 negative results among 54 IDTs performed with IFN. The positive predictive value of IDTs is unknown, but it could be good, as three of our patients with positive IDTs had a relapse of their generalized eruption after the reintroduction of IFN- α that had previously given positive results on IDT. We obtained delayed, relevant positive results on IDTs performed with the responsible IFN in 16 of 21 patients tested (76%). IDTs can be useful for studying cross-reactivities and finding an alternative peg-IFN- α . In our patients, IDTs allowed four reintroductions of an alternative IFN with negative IDTs, and these alternative therapeutics were well tolerated in all cases. Allergological investigations are not useful in cases of eruption due to IFN- β . In such cases, IFN- α is not a useful therapeutic alternative. Moreover, patients with multiple sclerosis have two other alternative therapies to choose from. However, in cases of a reaction to peg-IFN- α in patients suffering from hepatitis C, IDTs can help guide the choice of an alternative IFN- α or a desensitization procedure. Indeed, most protocols used for patients with hepatitis C pair peg-IFN with ribavirin or an antiprotease (boceprevir or telaprevir). In cases of more common localized reactions at the injection site, topical corticosteroids with

antihistamines are sufficient for controlling the cutaneous adverse effect with no need for allergological investigations.

This study has some limitations. The sample size was small, and it included only patients with generalized skin reactions.

Conclusion

Intradermal tests with delayed readings can be useful for managing patients with generalized eruptions due to IFN, studying cross-reactivities and guiding the choice of alternative treatments. In the case of GEE, if topical corticosteroids and antihistamines are not sufficient to control the rash, UVB narrowband or topical tacrolimus could be used. In patients who do not tolerate any peg-IFN- α or who have active hepatitis C, a 12-step desensitization protocol to peg-IFN- α could be helpful.

Author's contribution

Claire Poreaux analysed the data and wrote the manuscript. Annick Barbaud conceived and supervised the study. All authors collected data, read and critically revised the final manuscript.

Conflict of interest

None of the authors have a declared conflict of interest.

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