## Adverse Cutaneous Reactions to Interferon Alfa-2b Plus Ribavirin Therapy in Patients with Chronic Hepatitis C Virus

## Sir,

Chronic hepatitis C virus (HCV) is a highly prevalent disease and represents a serious public health problem. Combination therapy with interferon alfa-2b (IFN- $\alpha$ 2b) plus ribavirin is currently considered the treatment of choice because it has demonstrated higher sustained viral response rates than interferon monotherapy (1). Published studies on large series of patients have shown a significant increase in adverse skin reactions with combined therapy as compared to interferon monotherapy (2-4), without having explained the mechanism by which this increase in secondary cutaneous effects occurs. Increased incidences of pruritus, and skin lesions merely defined as "rash" are reported. Only one study with a limited series of patients lists the types of dermatoses observed in detail (5). The present contribution presents our experience of adverse skin effects observed in patients with HCV receiving treatment with IFN-a2b plus ribavirin.

Between June 1998 and September 2000 we studied 210 patients with HCV undergoing treatment with subcutaneous IFN- $\alpha$ 2b (3 million units three times a week) plus oral ribavirin (1,200 mg per day) over a 12-month period. None of the patients had a previous dermatological history. During treatment, the majority of patients showed varying degrees of dry skin and mucous membranes, and pruritus. In 27 cases (13%; 24 males, three females; age range 24-54 years) we observed skin lesions that began to manifest on average 3.2 months after beginning treatment, with a range of 0.5-8 months (the data are summarized in Table I). Among patients with lesions, 16 (59%) presented eczematous lesions (mostly localized) to the legs, arms or trunk, although two had generalized lesions. Histopathological studies were performed in seven of these patients and all had superficial perivascular dermatitis with spongiosis. We also observed disseminated prurigo-type lesions, lichenoid eruption, seborrheic dermatitis and maculopapular exanthem. One patient developed thoracic herpes zoster 6 months after beginning treatment. All patients showed noticeable clinical improvement with symptomatic treatment (moisturizing creams, antihistamines and/or topical cortisone), and when treatment with IFN-a2b plus ribavirin was terminated the lesions showed complete regression. No patient abandoned treatment and no dose adjustment was required due to cutaneous manifestations.

When comparing our results with those of previous studies, higher incidences of pruritus (2–4) and dry skin (3) were observed. Concerning skin lesions, the high frequency of eczema (59%) among the subjects in our study should be

Table I. Nature of cutaneous lesions observed in 27 out of a total of 210 patients receiving  $IFN-\alpha 2b$  plus ribavirin treatment

Skin lesion	n (%)
Eczema	16 (7.6)
Prurigo	4 (1.9)
Lichenoid eruption	2 (1.0)
Seborrheic dermatisis	2 (1.0)
Maculopapular exanthem	2 (1.0)
Herpes zoster	1 (0.5)

noted. This percentage is significantly higher than that in the only detailed study known to us (5). Finally, given the lack of existing publications concerning the different dermatoses caused by IFN- $\alpha$ 2b plus ribavirin treatment in HCV, we feel that there is a need for a study of this type involving a larger series of patients in order to produce a proper information source that would allow for a correct dermatological approach to these patients.

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