New-Onset Psoriasis Following Treatment with Pegylated Interferon-Alpha 2b and Ribavirin for Chronic Hepatitis C

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Hepatitis C virus infection, a major global health problem with an estimated 170 million individuals with chronic infection around the world, is the leading cause of chronic liver disease. The importance of treating HCV infection is to prevent hepatocellular carcinoma and liver cirrhosis, the leading causes of liver transplantation in the United States and Western Europe.

Interferon-alpha, a known treatment for HCV infection, works by modulating immune function through action on natural killer cells and enhancement of the CD8+ cytotoxic T cell response by up-regulation of the expression of major histocompatibility complex class I molecules on cells surface (including hepatic cells) [1]. It also disrupts replication of HCV by induction of antiviral protein synthesis in responsive cells, thus lowering the viral load. Pegylated IFNα is more effective than standard IFNα due to its increased serum half-life, which results in higher peak levels and more sustained exposure to the drug.

Ribavirin is an oral nucleoside analog with activity against several RNA viruses. It lowers aminotransferase levels in chronic hepatitis C. Combination therapy with IFNα 2b and ribavirin is the most effective treatment available for chronic hepatitis C and is considered to be more effective than treatment with IFNα 2b alone.

We present a patient with new-onset psoriasis, most likely a dermatological side effect of IFNα 2b and ribavirin treatment for chronic hepatitis C.

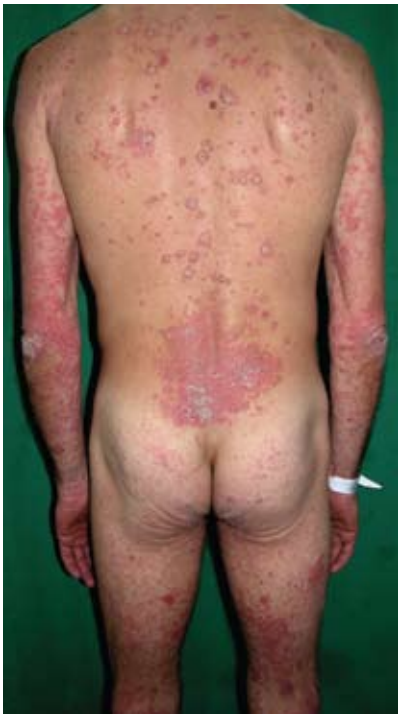
HCV = hepatitis C virus
IFNα = interferon-alpha

PATIENT DESCRIPTION

The patient, a 40 year old white man with a prior history of drug abuse, was diagnosed with HCV infection based on the presence of serum antibodies against HCV and HCV RNA. His history and family history were negative for skin diseases including psoriasis. Six months after the diagnosis of HCV infection, treatment with pegylated IFNα 2b and ribavirin was initiated. Three weeks after institution of therapy, an extensive, symmetrical papulosquamous rash, consistent clinically with plaque-type psoriasis, appeared [Figure]. The rash was located on the face, scalp, trunk and extremities, including palms and soles, with a predilection for the extensor surfaces. It consisted of erythematous papules and plaques covered with silvery scales, with a positive Auspitz sign. Twelve percent of the total body surface area was involved, and the calculated PASI score (Psoriasis Area and Severity Index) was 14. Nail involvement was manifested by onycholysis. There was no joint involvement.

A biopsy from an erythematous scaly papule on the back revealed histological findings characteristic of psoriasis, including parakeratosis with the presence of Munro micro-abscesses, absence of the granular layer, acanthosis with elongated rete ridges, and capillary dilatation in the papillary dermis. Physical examination was unremarkable. There was no fever. Laboratory tests for erythrocyte sedimentation rate, blood count, blood chemistry including transaminase levels, serologic tests for syphilis, urine analysis, and chest X-ray were normal or negative. Serum HCV RNA was negative at this time.

A generalized, symmetrical papulosquamous eruption consistent with the diagnosis of plaque-type psoriasis.



Despite topical treatment with steroids and emollients, there was a marked worsening of the psoriatic rash and new lesions appeared. Drug-induced psoriasis was suspected and

treatment with both pegylated IFNα 2b and ribavirin was stopped a month after the appearance of the rash. Drug withdrawal resulted in a rapid and marked improvement, with almost complete clearance within 14 days.

COMMENT

Various cutaneous adverse reactions during treatment with IFNα were reported previously. The most commonly reported adverse effect is injection-site reaction, occurring in approximately 60% of the patients. Other cutaneous adverse reactions include alopecia, lichen planus, vitiligo, hypopigmented atrophic plaques, facial erythema, eosinophilic pustular folliculitis, erythema and purpura [2].

Psoriasis associated with IFNα treatment for chronic hepatitis C was first reported in the English-language medical literature in 1993. To our knowledge, nine case reports have been published in the English literature, linking the development or the exacerbation of psoriasis to treatment of HCV infection with IFNα, either pegylated or non-pegylated and either as monotherapy or combined with ribavirin.

In the present case, the appearance of extensive psoriasis was most likely induced by the combination therapy of pegylated IFNα 2b and ribavirin. The following data imply the possible role of these drugs as the causative agents:

- the latent period from intake of the drugs until the development of the rash was 3 weeks in our case, a time interval within the range of previously reported cases (1–12 weeks)
- rapid resolution occurred shortly after withdrawal of the offending drugs in our case, as in previously reported cases
- the type of psoriasis that occurred in the present case was the plaque type, as in previously reported cases
- the nail involvement in the present case had been previously reported.

In the present case the possible causative role of HCV in the induction of psoriasis was ruled out in view of the following: firstly, the association between psoriasis and hepatitis C is rare and controversial [3]; secondly, in the present case the marked flare of psoriasis occurred during treatment for hepatitis C at a time when serum HCV RNA was negative.

The possible role of other infections in the induction of psoriasis was less likely in the absence of any evidence of infection (based on clinical, laboratory and imaging data) before or during the psoriatic flare. Furthermore, although new-onset psoriasis might occur in the patient's age group (third to fourth decade), the absence of a family history of psoriasis further supports the assumption of drug-induced psoriasis in this case.

Psoriasis is considered a T cell-mediated disease, with cutaneous and systemic over-expression of various pro-inflammatory cytokines, such as interleukins, interferon-gamma and anti-tumor necrosis factor-alpha [4]. The possible association between IFNα and the development of psoriasis has been suggested, based on the following observations:

- natural IFNα-producing cells (plasmacytoid cells) infiltrated the skin of a patient with psoriasis
- the expression of IFNα in the development of early stages of psoriasis was noted
- the IFNα signaling pathway was activated in psoriatic skin
- increased sensitivity to IFNα has been demonstrated in psoriatic T cells [5].

The exact mechanism by which IFNα may cause induction or exacerbation of psoriasis is not completely understood. Suggested key processes are the enhancement of the CD8+ T cell response, induction of the expression of CXCR3 on those T cells (facilitating homing to the skin), and augmentation of pro-inflammatory cytokine expression and response [1].

In summary, a patient with new-onset plaque-type psoriasis after treatment with pegylated IFNα 2b and ribavirin is described. The etiological role of both drugs in the induction of psoriasis was supported by clinical data, timing and the literature. In view of the worldwide increase in the number of patients treated with the combination of IFNα and ribavirin for HCV infection, increased awareness of the appearance of psoriasis as a drug-induced adverse effect is advised.

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"Nations have recently been led to borrow billions for war; no nation has ever borrowed largely for education. Probably, no nation is rich enough to pay for both war and civilization. We must make our choice; we cannot have both"

Abraham Flexner (1866-1959) U.S. educator