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CASE REPORT

Extensive Psoriasis Induced by Pegylated Interferon Alfa-2a and Ribavirin in the Treatment of Chronic Hepatitis C

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A 56-year-old man with chronic hepatitis C was treated with pegylated interferon alfa-2a in combination with ribavirin. However, psoriatic lesions appeared and worsened dramatically during therapy. Because of the extensive skin eruptions, he stopped therapy for chronic hepatitis C and subsequently started narrow-band ultraviolet B phototherapy and topical calcipotriol/betamethasone dipropionate ointment. After this, the psoriasis improved in a slow but comprehensive manner. Our case suggests that physicians should keep in mind the possibility of psoriasis as a side effect of interferon treatment for chronic hepatitis C. **(Ann Dermatol 25(4) 479～482, 2013)**

-Keywords-
Hepatitis C, Peginterferon alfa-2a, Psoriasis, Ribavirin

INTRODUCTION

Interferon is a naturally occurring glycoprotein and an immune modulating agent that is used to treat several diseases, including chronic hepatitis B and C[1]. Mild adverse cutaneous reactions, such as, itching, urticaria, dryness, and hair loss, are relatively common during interferon treatment[2]. It is also well known that interferon-alfa can exacerbate pre-existing psoriasis, but new onset psoriasis has rarely been observed. To the best of our knowledge, extensive psoriasis induced by pegylated interferon alfa-2a and ribavirin for chronic hepatitis C has not been previously reported. Herein, we present the case of a patient with chronic hepatitis C who was treated with pegylated interferon-alfa and ribavirin, and developed psoriasis for the first time.

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CASE REPORT

A 56-year-old male patient was referred to our clinic with generalized confluent erythematous scaly plaques of 6 months duration. He had no previous history of cutaneous disease such as psoriasis and presented with sharply circumscribed erythematous plaques with scales on his trunk, buttock, extremities, and scalp (Fig. 1). The skin eruptions were relatively symmetric in distribution and were asymptomatic. In addition, he presented prominent nail pitting, and onycholysis on his finger nails. A histopathological examination revealed marked acanthosis, epidermal hyperplasia, and Munro's microabscess compatible with psoriasis (Fig. 2). According to these clinical and histopathological findings, the patient was diagnosed as having psoriasis.

We then sought to identify the possible triggering factors and found that he had been treated for chronic hepatitis C for 11 months, with a treatment protocol consisting of pegylated interferon alfa-2a 180 μg injected subcutaneously once weekly and ribavirin 1,000 mg daily. While

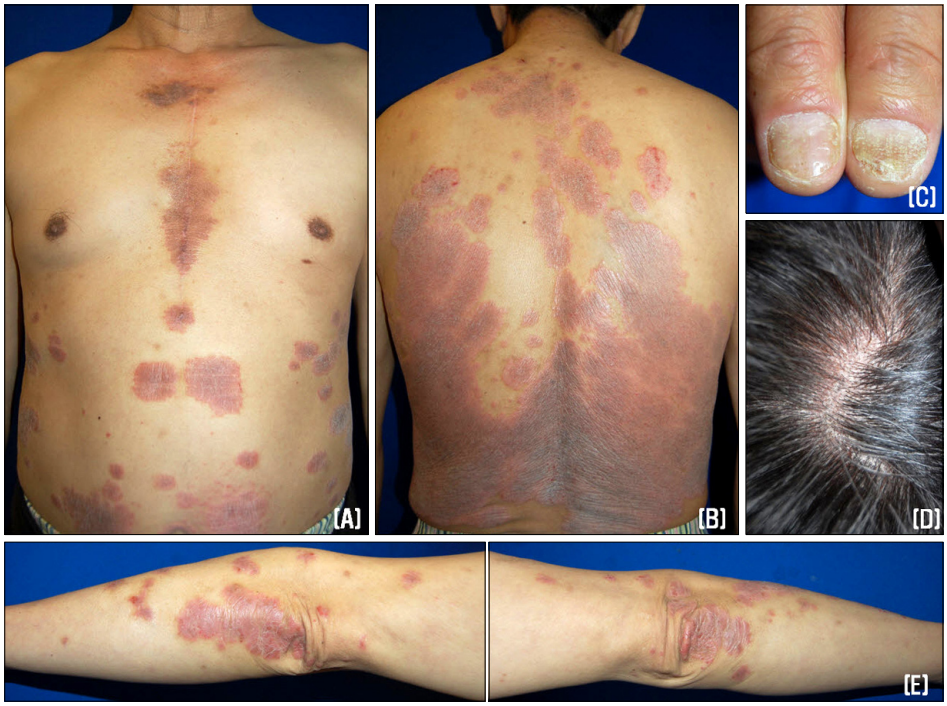

Fig. 1. Multiple sharply demarcated erythematous plaques on the abdomen (A) and back (B) prominent nail pitting (C), scalp involvement (D), and extremities (E).

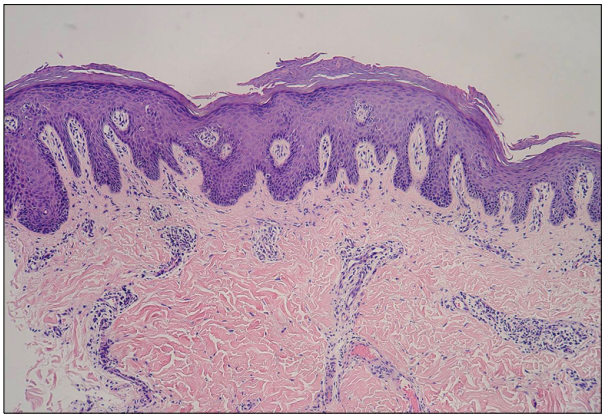

Fig. 2. Histopathologic examination from the skin lesion revealed marked acanthosis, epidermal hyperplasia, and Munro's microabscess (H&E, ×100).

receiving treatment, his transaminase levels (aspartate aminotransferase [AST], alanine aminotransferase [ALT]) decreased to normal and hepatitis C virus RNA became undetectable. However, five months after beginning treatment, psoriatic lesions occurred and gradually worsened during the therapy. Nevertheless, he continued the interferon treatment due to a progressive reduction in transaminase levels and the absence of any uncomfortable symptoms associated with the skin lesions. However, the psoriatic lesions worsened and eventually involved more than 40% of his body surface area. At the time of diagnosis, the interferon treatment was only one month from completion, but considering the severity of the psoriasis, we stopped interferon and started narrow-band ultraviolet B (NB-UVB) phototherapy and topical calcipotriol/betamethasone dipropionate ointment. Subsequently, the psoriasis slowly improved without recurrence.

DISCUSSION

The current standard treatment for chronic hepatitis C is a combination of pegylated interferon-alfa and the antiviral drug ribavirin, which are administered for 24 or 48 weeks according to the genotype of the hepatitis C virus[1]. Pegylated interferon-alfa is synthesized by adding a polyethylene glycol molecule to standard interferon, and in this derivatized form interferon has an extended circulating life and greater stability[2]. The cutaneous adverse effects of pegylated and conventional interferon have been reported to be similar, including transient alopecia, pruritus, vasculitis, cutaneous necrosis, and eczema at injection sites[2]. Rarely, interferon can also induce autoimmune diseases such as autoimmune thyroiditis, systemic lupus-like syndromes, rheumatoid arthritis, and sarcoidosis[2].

Various triggering factors can either induce or exacerbate psoriasis. Some drugs are of major concern, such as, β-blockers, lithium, antimalarial agents, and nonsteroidal anti-inflammatory drugs[3]. However, these triggering factors were absent in our patient. Furthermore, previous studies have reported that when interferon is administrated

by self-injection subcutaneously, psoriasis can be worse around the interferon injections sites. Taylor et al.[4] speculated that this could be the result of either a high local interferon concentration or Koebner phenomenon.

Several mechanisms have been proposed to clarify the close relationship between interferon treatment and the induction of psoriasis. Interferon stimulates Th1 mediated inflammatory response, which has been reported in psoriatic T-cell infiltrates, and could thus be responsible for psoriasis exacerbation[5]. Alternatively, because interferon acts to increase the lymphocytotoxic activity of natural killer lymphocytes and induces keratinocytes to produce interleukin-1, it may trigger and initiate the psoriatic process[6]. On the other hand, not all psoriasis patients develop interferon-alfa induced exacerbation, which probably reflects the heterogeneity in the pathogenesis[7].

In 1993, Garcia-Lora et al.[8] first described a case of psoriasis in a patient receiving interferon alfa for chronic hepatitis. A review of the English literature showed that, including the present study, 11 cases of interferon-associated psoriasis in viral hepatitis have been reported (Table 1). These studies indicate that after the initiation of interferon treatment, the onset of psoriasis may range from 1 week to 5 months. With regard to the development of the disease, new onset psoriasis take longer to emerge that the aggravation of pre-existing disease. In several of the reported cases, interferon was discontinued, either because of the psoriasis or due to nonresponder hepatitis, and psoriasis resolved in these patients within several months. Our case is the first to report on a patient treated with pegylated interferon alfa-2a and ribavirin.

Including the present work, two cases relate to patients who received a combination of interferon alfa and ribavirin or pegylated interferon alfa and ribavirin. Although the exact mechanism underlying the effect of ribavirin on hepatitis C is unknown, a recent study showed that it could also stimulates Th1 responses in T cells *in vitro*[9]. However, no case of psoriasis has been reported after treatment with ribavirin alone.

The appearance of severe psoriasis in a patient with viral hepatitis poses a difficult therapeutic problem[8,10-12]. Oral retinoids and methotrexate are contraindicated in patients with an abnormal liver function, and while topical corticosteroids and NB-UVB therapy are expected to have minimal risk to the liver, psoriatic lesions are usually resistant to the treatment. Many clinicians believe that the onset of psoriasis during interferon therapy is an absolute contraindication to its continuation[13]. In accord with the reported cases[4,7,8,10-15], we believe that interferon-associated psoriasis can be resolved by treatment discontinuation.

Based on the evidence discussed above, we are convinced

Table 1. Reported cases of interferon-associated psoriasis in viral hepatitis

Case No.	Author (year)	Sex/Age (yr)	Underlying disease	Past history of psoriasis	Treatment for hepatitis	Onset (mo)	Cessation of interferon	Treatment for psoriasis	Follow-up (mo)
1	Garcia-Lora et al.[8] (1993)	M/33	Hepatitis C	−	Interferon α-2b	5	+	Emollient	Resolution (6)
2	Georgetson et al.[10] (1993)	M/46	Hepatitis B	+	Interferon α	ND	+	-	Improved (ND)
3	Georgetson et al.[10] (1993)	M/42	Hepatitis C	+	Interferon α	1	+	PUVA	Improved (ND)
4	Erkek et al.[14] (2000)	M/65	Hepatitis C	−	Interferon α-2a	1	−	Acitretin	Resolution (4)
5	Taylor et al.[4] (2000)	M/47	Hepatitis C	−	Interferon α-2a	3	−	Topical steroid, PUVA	Improved (ND)
6	Downs and Dunnill[7] (2000)	M/56	Hepatitis C	+	Interferon α-2b tribavirin	1	−	BB-UVB	Improved (ND)
7	Ketikoglou et al.[12] (2005)	M/32	Hepatitis B	−	Pegylated interferon α-2b	1	+	-	Resolution (1)
8	Kartal et al.[11] (2005)	F/45	Hepatitis C	+	Pegylated interferon α-2b Ribavirin	0.25	+	Topical steroid	Resolution (1)
9	Citro et al.[13] (2007)	F/50	Hepatitis C	−	Interferon α-2b	3	−	-	Improved (ND)
10	Tekin et al.[15] (2010)	M/25	Hepatitis B	−	Pegylated interferon α-2b	ND	−	NB-UVB	Improved (3)
11	Our case	M/56	Hepatitis C	−	Pegylated interferon α-2a Ribavirin	5	+	NB-UVB, Topical steroid/ vitamin D	Resolution (8)

M: male, F: female, ND: not described, PUVA: psoralen plus ultraviolet A, BB-UVB: broad-band ultraviolet B, NB-UVB: narrow-band ultraviolet B.

that interferon was responsible for the development of psoriasis in our patient. Indeed, the close temporal connection between the onset of psoriasis and its subsidence and the interferon treatment suggests a strong connection. Our case cautions that physicians should pay attention to the possibility of adverse effects before starting interferon treatment.

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