

CASE REPORT

Repeated Paradoxical Aggravation of Preexisting Psoriasis during Infliximab Treatment for Crohn's Disease

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As more rheumatologists and dermatologists have begun to use biological agents such as TNF- α blocker, they have confronted an unexpected complication: psoriasis was paradoxically aggravated or induced by the TNF- α blocker. Although it is not a common complication of TNF- α blocker, this aggravation may be more common than previously thought. To our knowledge, most reports about TNF- α blocker-induced psoriasis have been limited to western countries while only a few cases have been reported in Korea and Japan. In addition, new onset of pustular psoriasis by TNF- α blocker has been reported more commonly than worsening of preexisting psoriasis. Now we report a patient whose preexisting psoriasis vulgaris was aggravated repeatedly after using the TNF- α blocker, infliximab, to control Crohn's disease, which is a rare rheumatologic disease in Korea. (*Ann Dermatol (Seoul)* 21(1) 60~62, 2009)

-Keywords-

Aggravation, Crohn's disease, Psoriasis, TNF- α blocker

INTRODUCTION

Tumor necrosis factor- α (TNF- α) may concurrently contribute to the pathology of both psoriasis and Crohn's disease (CD); thus TNF- α inhibitor was expected to successfully and simultaneously control both psoriasis and CD¹. However, during the clinical application of TNF- α blocker for the treatment of CD, psoriasis was paradoxically

induced or aggravated^{2,3}. In general, aggravation or new onset of psoriasis induced by TNF- α blocker was uncommon and such a paradoxical event was often reported as an incomprehensive or unexpected complication^{4,5}. To our knowledge, most reports about TNF- α blocker-induced psoriasis were limited to western countries until new onset or aggravation of pustular psoriasis by TNF- α blocker was recently reported in Korea and Japan^{3,6}. Incidentally, aggravation of preexisting psoriasis vulgaris due to TNF- α blocker has been reported relatively less frequently than new onset of pustular psoriasis induced by TNF- α blocker⁷.

Herein, we report a patient whose preexisting psoriasis vulgaris was aggravated repeatedly following TNF- α blocker (infliximab) treatment to control CD, which is a rare rheumatologic disease in Korea.

CASE REPORT

A 29-year-old woman was referred to our dermatologic outpatient clinic for evaluation and treatment of her repeatedly aggravated psoriatic skin lesions after infliximab treatment for CD.

In her past medical history, she was diagnosed with psoriasis vulgaris on skin biopsy in June 1999 and with CD in October 2005. With only these two underlying diseases, she had been in relatively good health without any medical problems and her psoriasis had been well controlled with topical steroids for several years.

She was treated with infliximab (5 mg/kg, intravenously) every 6 weeks for CD beginning in December 2006. During the first through third intravenous infusions of infliximab, she did not experience any skin problems and her CD was well controlled. Her psoriasis eventually became aggravated 6 days after the fourth infusion of infliximab. She thought this first aggravation of psoriasis

Received June 18, 2008, Accepted for publication August 5, 2008

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Fig. 1. The patient had almost recovered from her aggravated psoriasis with UVB phototherapy and topical steroid before the sixth infliximab treatment.



Fig. 2. Multiple pruritic erythematous papules and scales developed again and aggravated on her face and extremities after 5 days of the sixth infusion of infliximab.

was unrelated to infliximab at that time and her psoriasis subsided with massive topical steroids. However, similar aggravation of her psoriasis again developed 5 days after the fifth infusion of infliximab and she was referred to our dermatologic clinic with diffuse pruritic erythematous papules and weeping, silvery scales on her face and extremities. She was treated with a combination of UVB phototherapy and topical steroid and her skin lesion cleared (Fig. 1). Each subsequent infusion of infliximab again aggravated her psoriasis (Fig. 2). Finally, she decided not to be treated with infliximab and her psoriasis has been well controlled with UVB phototherapy plus topical steroid without aggravation.

DISCUSSION

As more rheumatologists and dermatologists have begun to use biological agents such as TNF- α blocker, they have been confronted with an unexpected complication: psoriasis was paradoxically aggravated or induced by the TNF- α blocker (Table 1). This paradoxical onset or aggravation of psoriasis is both interesting and embarrassing because TNF- α blocker is considered a drug that controls psoriasis. Aggravation, as in this case, can develop regardless of the type of TNF- α blocker and, among the subtypes of psoriasis, palmoplantar pustulosis develops most commonly⁸.

Although the exact mechanism of this paradoxical skin condition has not yet been determined, several theories

Table 1. Case reports of new onset or exacerbation of preexisting psoriasis following treatment with anti-TNF α therapy (6; our case)

Pt	Age	Sex	Underlying disease & duration (yr)	Time from anti-TNF initiation to psoriasis (mon)	Anti-TNF	Dosage	Con-comitant medication	Previous history of psoriasis	Type of psoriasis	Extent/severity	Outcome	Anti-TNF stopped
1	22	F	SpA (1)	1	Adalimumab	40 mg/15 d	0	Yes	PPP		Stable	No
2	49	M	AS (20)	3	Etanercept	50 mg/wk	NSAID	No	Plaque	Moderate	Stable	No
3	62	M	PsA (15)	15	Infliximab	5 mg/kg	0	Yes	Plaque		Flares	No
4	49	M	AS (30)	6	Infliximab	5 mg/kg	NSAID	No	Plaque	Severe	Improved	Yes
5	38	F	CD (5)	3	Infliximab	5 mg/kg	0	No	PP	Severe	Flares	Yes
6	29	F	CD (3)	6	Infliximab	5 mg/kg	0	Yes	PP	Severe	Improved	No

F: female, M: male, SpA: spondyloarthritis, AS: ankylosing spondylitis, CD: crohn's disease, NSAIDs: nonsteroidal anti-inflammatory drugs, PPP: palmoplantar pustulosis, PP: pustular psoriasis

have been proposed. First, TNF- α blocker activates the auto-reactive T-cells causing autoimmune-related tissue destruction⁹. Second, TNF- α blocker induces IFN- α over-expression in the tissue, which could also cause psoriasis⁷. Third, considering the heterogeneity of psoriasis, TNF- α blocker reduces some plaque types of psoriasis while pustular psoriasis appears to be induced by TNF- α blocker^{2,9}. Fourth, antibody formation against infliximab contributes to development or aggravation of psoriasis³.

In this case, the deterioration of psoriasis cannot simply be explained as an association with the underlying CD or its disease activity, although the prevalence of psoriasis with CD is three times more than that in the general population¹. In this patient, there was no flare up of CD during the treatment with infliximab and some laboratory data, including erythrocyte sediment rate or C-reactive protein, remained within the normal range. In addition, it was not until the fourth infusion of infliximab that her psoriasis became aggravated, which could be explained by the fact that T-cells generally reactivate after prolonged repeated use of TNF- α blocker³. Lastly, withdrawal of infliximab reduced her psoriasis while infusion of infliximab worsened her psoriasis repeatedly.

We report a case in which preexisting psoriasis vulgaris was repeatedly aggravated during treatment with infliximab for CD, which is a rare rheumatologic disease in Korea. Most previously reported cases were confined to new onset of pustular psoriasis induced by TNF- α blocker for underlying rheumatologic disease.

New onset or aggravation of TNF- α blocker-induced psoriasis is regarded as a more common phenomenon than previously recognized and users of TNF- α blockers should pay attention to complications in such cases.

ACKNOWLEDGEMENT

We sincerely thank Eun-So Lee, M.D. (Department of Dermatology, Ajou University Hospital) for critical reading and comments on this manuscript.

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