

## A Case of Widespread Dermatophytosis during Interleukin–17A Inhibitor Treatment in Psoriasis Patient with Tinea Unguium

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Interleukin-17 (IL-17) is secreted by a class of helper T cells called Th17 cells, which stimulates keratinocytes to secrete proinflammatory mediator and to recruit other inflammatory cells in psoriatic skins. IL-17A inhibitor was approved for the management of psoriatic arthritis by FDA. It is the one of the biologics approved as first-line therapy for the management of psoriasis. But several studies show some side effects of IL-17A inhibitor such as upper respiratory infection and fungal infection like *Candida albicans*. Herein we report a widespread dermatophytosis during IL-17A inhibitor treatment. A 66-year-old male patient, with tinea unguium and chronic plaque psoriasis for several decades, presented with multiple erythematous scaly macules and patches for 2 weeks. He medicated IL-17A inhibitor for treating psoriasis total 3 times and last injection was 1 week ago. Dermatological examination revealed the involvement of 20% body surface area in the form of erythematous scaly macules and patches. KOH mount revealed the presence of numerous hyphae. The patient was started on oral terbinafine, topical isoconazole and efinaconazole. His skin lesions were improved after 1 month of anti-fungal therapy. IL-17 plays an important role in mucocutaneous microbial defense. So, fungal infection should be checked in using IL-17A inhibitor patients periodically.

**Key Words:** Dermatophytosis, Interleukin 17, Psoriasis

### INTRODUCTION

Interleukin-17 (IL-17) is a cytokine, secreted by a class of helper T cells called Th17 cells, which stimulates keratinocytes to secrete proinflammatory mediator and recruit other inflammatory cells in human skin. And dysregulation of the IL-17 pathway is associated with the development of diseases like psoriasis<sup>1</sup>.

Interleukin-17A Inhibitor is a recombinant, fully human IgG1 monoclonal antibody which selectively binds and neutralizes Interleukin-17A<sup>2</sup>. It was approved for the treatment of psoriasis by FDA. It is the one of the biologics approved as first-

line therapy for the management of chronic plaque psoriasis. But some kinds of infections like nasopharyngitis and upper respiratory tract infection were most common adverse effect<sup>2</sup>.

And except for candidiasis, only few cases of fungal infection were reported in literature. There were 4 cases of tinea pedis in Japan<sup>3</sup>, 2 cases of tinea cruris<sup>4</sup>, and 1 case of widespread dermatophytosis<sup>2</sup>. But there was no case report with identification of fungal organism.

So, herein we report a case of widespread dermatophytosis caused by *Trichophyton rubrum* during Interleukin 17A inhibitor treatment with chronic plaque psoriasis patient.

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## CASE

A 66-year-old male patient with tinea unguium and chronic plaque psoriasis for several decades, presented with multiple erythematous scaly macules and patches for the last 2 weeks. He was diagnosed as psoriasis by skin biopsy 2 years ago. Because of abnormal liver function test after using oral cyclosporine and methotrexate, he has been prescribed only topical calcipotriol and betamethasone for skin lesion in the

last year. But he had poor compliance with the topical agent due to burning sensation. We then started Interleukin-17A Inhibitor injection for psoriasis on weekly basis. After second injection, the skin lesions showed erythematous scaly macules at lower legs. After the third Interleukin-17A Inhibitor injection, it aggravated and spread to his upper body. Laboratory findings including absolute neutrophil count were within the normal limits. Also there was no other immune-compromising conditions. Dermatological examination revealed involvement



Fig. 1. (A), (B), (C) Erythematous scaly macules and patches at his left chest, axilla and both lower extremities

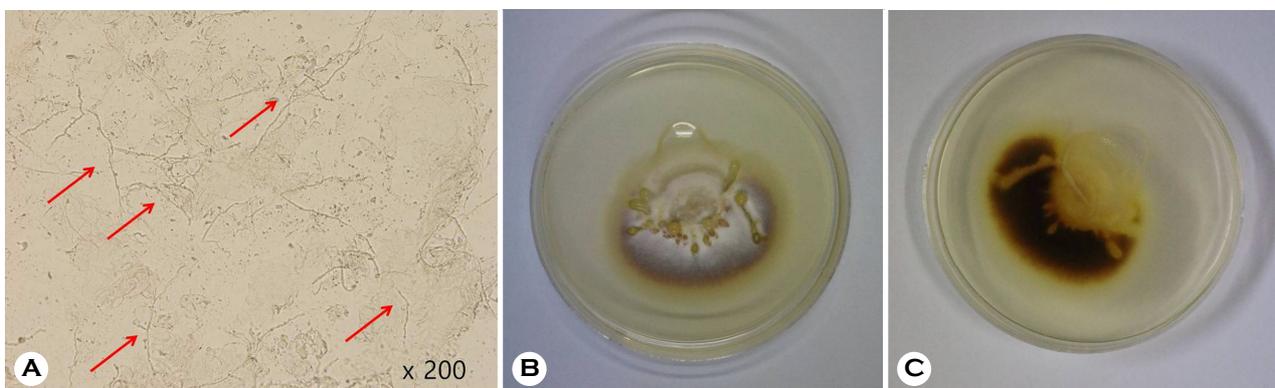


Fig. 2. (A) KOH mount revealed lots of hyphae on specimen. (B) On Sabouraud dextrose agar, colonies matured rapidly and were flat, white colored, and texture ranged from woolly to cottony. (C) The color of the colonies were white initially but darkened to brown with maturity on the reverse side.

about 20% of body surface area in the form of erythematous scaly macules and patches at his left chest, axilla and both lower extremities (Fig. 1A, 1B, 1C).

We performed KOH mount of scale and fungal culture at left chest area. KOH mount revealed lots of hyphae on specimen (Fig. 2A). After incubation at 25°C for 2 weeks on

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Query 1   GACTGACAGCTCTTCAGAGAATTTTTCTTGGTGTCTGTCTCCGGCGGGGCGGTCCGG 60
          |||
Sbjct 208 GACTGACAGCTCTTCAGAGAATTTTTCTTGGTGTCTGTCTCCGGCGGGGCGGTCCGG 149

Query 61  CTCGAGGCTCCAGAAAGGGGCCGCCGGAAGGCTCTCCCTGGCAGGGGGAGCGCGGCCG 120
          |||
Sbjct 148 CTCGAGGCTCCAGAAAGGGGCCGCCGGAAGGCTCTCCCTGGCAGGGGGAGCGCGGCCG 89

Query 121 CCGAGGCAACCGGGTGAGGTAGACAAGAATGGGGCGTACGGCCGGCGCAAGTCTGCTCA 180
          |||
Sbjct 88  CCGAGGCAACCGGGTGAGGTAGACAAGAATGGGGCGTACGGCCGGCGCAAGTCTGCTCA 29

Query 181 CCCCTGATGGAAAGTC 196
          |||
Sbjct 28  CCCCTGATGGAAAGTC 13
    
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Fig. 3. The sequence of ribosomal internal transcribed spacer region was 100% identical with *Trichophyton rubrum*. Basic Local Alignment Search Tool (BLAST) search showed that the most similar species was *T. rubrum*.



Fig. 4. (A), (B), (C) Skin lesions were improved with hyperpigmentation after 1 month of anti-fungal therapy.

Saboraud dextrose agar, colonies matured rapidly and were flat, white colored, and texture ranged from wooly to cottony (Fig. 2B). The color of the colonies was white initially but darkened to brown with maturity on the reverse side (Fig. 2C).

To identify the exact strain of fungus, sequencing was performed with ribosomal internal transcribed spacer region isolated from the colonies. This sequence was 100% identical with *Trichophyton rubrum*. Basic Local Alignment Search Tool (BLAST) search showed that the most similar strain was *Trichophyton rubrum* (Fig. 3). The patient was started on oral terbinafine, topical isoconazole and efinaconazole. His skin lesions were improved with hyperpigmentation after 1 month of anti-fungal therapy (Fig. 4A, 4B, 4C).

## DISCUSSION

IL-17A is a proinflammatory cytokine produced in helper T cells and then combined with IL-17A receptors to over-differentiate the keratinocytes and exacerbate the psoriasis lesions. Thus, IL-17A inhibitor is a drug that can block this process and is widely used to treat psoriasis.

But it affects to human antifungal immunity definitely. Infections like nasopharyngitis and upper respiratory tract infection were most common adverse effect in using IL-17A inhibitors patients. And congenital impairment of IL-17 pathway results in increased susceptibility to fungal infections, such as mucocutaneous candidiasis<sup>5</sup>.

The vast majority of all studies on the protective effects of IL-17 immunity against fungal infections have been focused on *Candida albicans*. However, the mammalian host is exposed to diverse other fungi, including airborne fungi that we inhale and fungi to which our skin is exposed<sup>1</sup>. There was animal model study for the role of IL-17 in immunity against superficial dermatophytosis not caused by *Candida* spp. The study suggested that malfunction of IL-17 pathway results in widespread infection of *Microsporum canis* and weakened T-helper type 1 response. They also observed that mice with wild-type IL-17 develop epidermal thickening on exposure to *M. canis*, while IL-17-deficient mice do not develop this protective barrier function. However, there was no difference in neutrophil accumulation. Recruitment of neutrophils looked irrelevant with this pathway<sup>6</sup>.

There was a research about why patients with psoriasis have fewer skin infections than expected. It proved 200~400 mg of a pure antimicrobial from 50 g samples of psoriatic scales. Amino-acid sequence analysis of this peptide revealed the consensus sequence of beta-defensin<sup>7</sup>. Antimicrobial peptide like beta-defensin is also critical factor of immune

system against antimicrobial organisms in psoriasis patient because IL-17 stimulates production of several antimicrobial peptides including beta-defensin<sup>8</sup>. Absence of innate immune system like epidermis thickening and increased antimicrobial peptide production can be the exact reason for widespread dermatophytosis of patients with using IL-17A inhibitor.

In conclusion, IL-17 aggravates the skin lesion by over-proliferation of keratinocytes in psoriasis patients, but in aspect of fungal infection, it acts as a deterrent against infection through the thickening of epidermis and production of antibacterial peptides. Thus, treatment of 'already existing fungal infection', such as tinea unguium should be preceded before use of IL-17A inhibitor. And physicians always have to keep in mind that fungal infection should be checked in using IL-17A inhibitor patients consistently.

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## CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

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## PATIENT CONSENT STATEMENT

The patient provided written informed consent for the publication and the use of his or her images.

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