

Long-Term Follow-Up of Refractory Mycosis Fungoides Which Achieved Remission with the Addition of Isotretinoin to Methotrexate and Psoralen Plus Ultraviolet A Therapy

Yu Ri Woo, Hae Min Lee, Joong Sun Lee, Dae Won Koo

Department of Dermatology, Eulji University Hospital, Daejeon, Korea

Dear Editor:

Mycosis fungoides (MF) is the most common cutaneous T cell lymphoma. Many therapies are considered based on the patient's individual presentation¹. Early stage MF is known to be easily responsive to conventional therapy. However, there is some early stage MF refractory to conventional therapy and thus need other treatment modalities². A 38-year-old man was presented with a 3-year history of asymptomatic multiple erythematous to dusky red edematous patches over his trunk, legs, neck

and face (Fig. 1A). The skin involvement measured about 45% of total body surface. Skin biopsy specimens from the leg showed clustered epidermotropic atypical lymphocytes in the epidermis with a band-like dense lymphocytic infiltrate in the dermis (Fig. 2A). In immunohistochemical staining, lymphocytes were positive for CD3 and CD4. A T-cell receptor-gamma gene rearrangement revealed the monoclonality in the polymerase chain reaction (PCR) analysis (Fig. 2B). The biopsy finding on the left palpable inguinal lymph node was dermatopathic

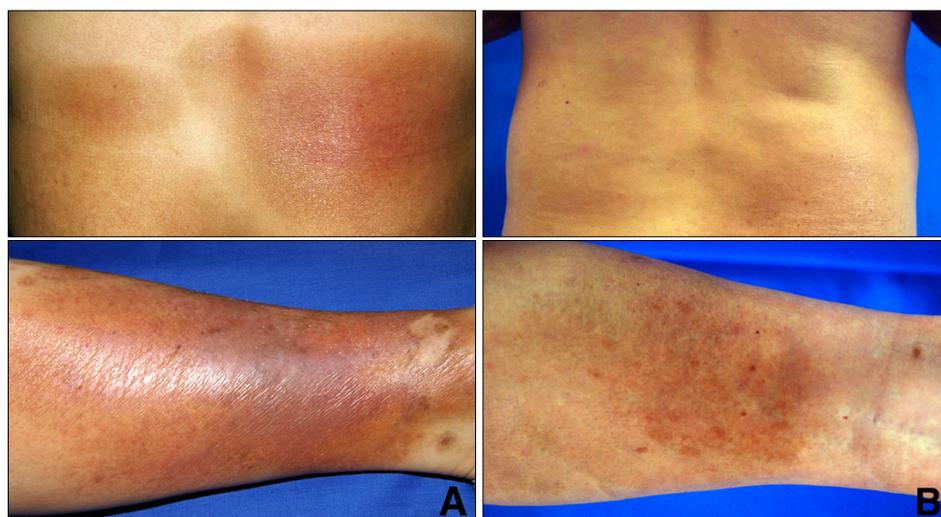


Fig. 1. (A) Edematous dusky red to erythematous patches on the back and the left leg before treatment. (B) Remission on the back and left leg with addition of isotretinoin to methotrexate and psoralen plus ultraviolet A therapy.

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Corresponding author: Dae Won Koo, Department of Dermatology, Eulji University Hospital, 95 Dunsanseong-ro, Seo-gu 302-799, Korea. Tel: 82-42-611-3035, Fax: 82-42-259-1111, E-mail: dwkoo@eulji.ac.kr

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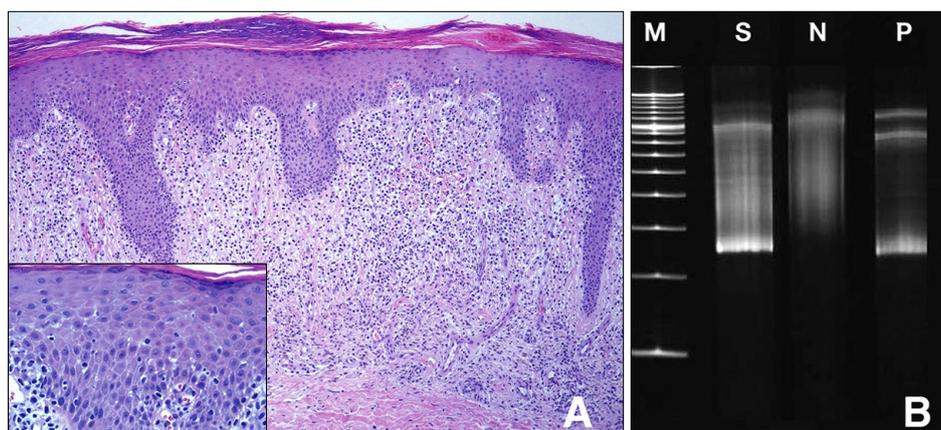


Fig. 2. (A) Epidermotropism with clustered atypical lymphocytes in the epidermis and dense lymphocytic infiltrate with hyperchromatic nuclei in the dermis (H&E, $\times 40$; inset: H&E, $\times 200$). (B) The result of T-cell receptor-gamma gene rearrangement showed the monoclonality in polymerase chain reaction-heteroduplex analysis. Marker (lane M), specimen (lane S), negative control (lane N), positive control (lane P).

lymphadenitis. According to TMNB staging, the patient was diagnosed as MF stage IIA (T2N1M0B0). Initially, he was treated with low-dose methotrexate (7.5 mg/wk) and psoralen plus ultraviolet A (PUVA) twice a week, with maximum doses of 1.3 J/m^2 . However, the disease showed no response during the 5 weeks of therapy. As first generation retinoids, such as isotretinoin, have been shown to be effective in early stage MF for a long period of time¹, isotretinoin (20 mg/day) was newly added to his treatment regimen for the following 6 weeks; consequently, the lesions showed remission (Fig. 1B). According to a recent study, many conventional treatments become ineffective when the skin involvement is over 10%, even in early stage MF². Likewise, although the patient was diagnosed as an early stage MF in this case, the skin lesions were refractory to the initial treatment. Eventually, after the addition of isotretinoin, the skin lesions showed a dramatic improvement without relapse for 2 years. Retinoids are the so-called biological response modifiers with different mechanisms of action than traditional cytotoxic chemotherapies. The biological effects of retinoids in MF are related to its boosting immune function by inducing anti-tumor responses and leading to the apoptosis of tumor cells³. When the retinoid is combined with methotrexate or PUVA, it strengthens the effectiveness of treatment by exhibiting combined actions of each agent and decreasing the side effects by lowering the doses of total UVA irradiation⁴. Nowadays, many studies have focused on retinoid X receptor-selective retinoid, bexarotene. However, the efficacy of

bexarotene compared to traditional retinoids, such as isotretinoin, has yet to be determined³. Thomsen et al.⁵ reported the effectiveness of isotretinoin on MF. However, no study has yet reported about the effectiveness of isotretinoin as a component of this combination therapy for refractory early stage MF. As we observed the dramatic therapeutic effect with the addition of isotretinoin for refractory MF, we suggest that isotretinoin could still be a type of effectual therapeutic option for combination therapy of early stage MF, particularly when the skin involvement is over 10% or refractory to the conventional treatment.

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