8. Pathoulas JT, Stoff BK, Lee KC, Farah RS. Ethical outpatient dermatology care during the coronavirus (COVID-19) pandemic. *J Am Acad Dermatol* 2020; 82: 1272-3.

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Effectiveness of combined bexarotene and excimer laser treatment for folliculotropic mycosis fungoides

Folliculotoropic mycosis fungoides (MF) is a variant of MF, that clinically shows acneiform or follicular keratosis-pilaris-like lesions on the head and neck, which histologically shows selective infiltration of atypical lymphocytes in the follicular epithelium. Folliculotropic MF shows a more aggressive clinical course in comparison to classic MF [1]. In a recent study, folliculotropic MF was classified into two distinct patterns: an early variant and an advanced tumour variant. The prognostic implications differ, with the early variant following a more indolent course [2].

In an excimer laser, the dissociation of xenon and chloride gases creates a 308-nm monochromatic light, which suppresses T lymphocyte proliferation via the induction of apoptosis [3]. The effectiveness of excimer laser for classic MF has been reported [4]. We herein report a patient with advanced stage folliculotropic MF, who was successfully treated with a combination of bexarotene and excimer laser therapy.

A 58-year-old Japanese man presented to our hospital with a skin lesion that had persisted for three months. A physical examination revealed several tumours on his head and face (*figure 1A*) and erythema with follicular accentuation on his back, abdomen and upper extremities (*figure 1B)* . A histological examination of a tissue specimen obtained from a head nodule revealed infiltration of atypical small cells around the hair follicles (*figure 1C)* and prominent folloculotropism. (*figure 1 D*). Immunohistochemically, the atypical cells were positive for CD3 and CD4 (*figure 1E)*. Clonal rearrangement of the T-cell receptor gene of lymphocytes that had infiltrated into the skin was detected. Blood test findings were almost within normal limits. No atypical lymphocytes were detected. Soluble interleukin-2 receptor level was not elevated (378 U/mL). HTLV-I antibodies were not detected. No lymph node or internal organ abnormalities were detected on positron emission tomography-computed tomography. No bone marrow involvement was observed. Accordingly, the patient was diagnosed with folliculotropic MF (T3N0M0, Stage-b). The patient was initially treated with topical steroids and bexarotene (300 mg/m^2). Two weeks later, the skin lesions on the trunk showed slight improvement; however, the tumours showed no change. Therefore, irradiation using an excimer laser (XTRAC® velocity7; STRATA Skin Sciences, Inc., PA) was performed for the remaining erythema and tumours on the face, head and trunk (200 mJ/cm^2, three times/week). Thereafter, the skin lesions gradually improved, and completely disappeared at 10 weeks (*figure 1F, G)*. No side effects, except for slight erythema, were observed. The bexaroten and excimer laser treatment (200 mJ/cm^2, twice/month) has been continued as maintenance therapy without signs of relapse.

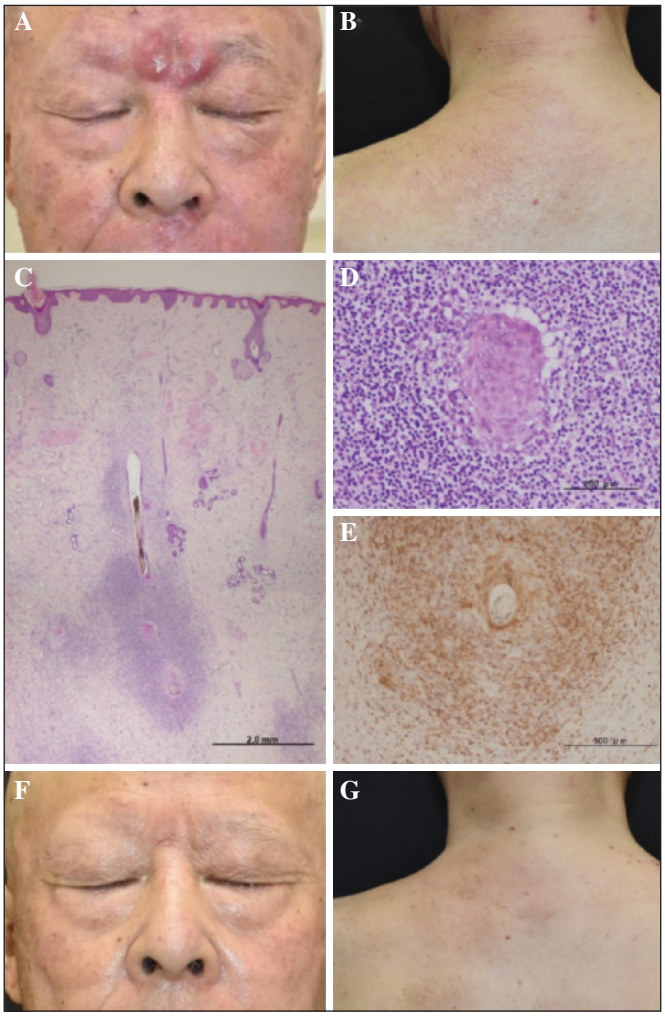

Figure 1. **A**, **B**) Clinical appearance of the forehead (**A**) and upper back (**B**) before treatment. **C**, **D**) Histological examination showing tumour cell infiltration around hair follicles (haematoxylin and eosin staining). **E**) Immunohistochemical examination showing infiltrating tumour cells expressing CD4. **F**, **G**) Clinical appearance of the forehead (**F**) and upper back (**G**) at 10 weeks after irradiation with XTRAC®.

In the present patient, combination therapy with bexarotene and excimer laser treatment was effective for both the erythema on the trunk and the tumour on the face and head. Skin-directed therapy, such as psoralen plus ultraviolet A (PUVA), is recommended for the initial treatment of early-stage folliculotropic MF. Radiotherapy, oral retinoids or systemic chemotherapy are commonly required for the treatment of advanced stage folliculotropic MF [5]. Bexarotene (synthetic retinoid X receptor agonist) is approved for the treatment of cutaneous T cell lymphoma. Single cases in which folliculotropic MF was successfully treated with bexarotene have been reported, mostly involving combination therapy with interferon alpha or radiotherapy [6, 7]. Combination therapy with bexarotene and PUVA was also reported to induce a good response in a case of folliculotropic MF [8]. The XTRAC®

velocity7 excimer laser delivers coherent, monochromatic short-pulse radiation through a hand-held device with a 20 × 20 mm circular spot size. It can emit a high-intensity laser beam (83,000 W/cm^2) by pulsed oscillation. This enables the delivery of higher fluence to deep skin lesions, resulting in the induction of apoptosis of tumour cells [9]. Furthermore, exposure of healthy skin to UV radiation may be avoided by targeted phototherapy using excimer laser [9]. In addition, we hypothesized that combination therapy with bexarotene and excimer laser treatment might have a synergistic effect, as combination therapy with bexarotene and PUVA tended to be more effective for classic MF at an early stage and led to a complete clinical response with fewer PUVA sessions using a lower PUVA dose compared to PUVA monotherapy [10]. Given the above, this combination therapy may be a useful therapeutic option for folliculotropic MF, although further research will be required to clarify the effectiveness of this therapy. ■

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1. Lehman JS, Cook-Norris RH, Weed BR, *et al*. Folliculotropic mycosis fungoides: single-center study and systematic review. *Arch Dermatol* 2010; 146: 607-13.

2. Hodak E, Amitay-Laish I, Atzmony L, *et al*. New insights into folliculotropic mycosis fungoides (FMF): A single-center experience. *J Am Acad Dermatol*. 2016; 75: 347-55.

3. Beggs S, Short J, Rengifo-Pardo M, Ehrlich A. Applications of the excimer laser: a review. *Dermatol Surg*. 2015; 41: 1201-11.

4. Deaver D, Cauthen A, Cohen G, Sokol L, Glass F. Excimer laser in the treatment of mycosis fungoides. *J Am Acad Dermatol* 2014; 70: 1058-60.

5. van Santen S, van Doorn R, Neelis KJ, *et al*. Recommendations for treatment in folliculotropic mycosis fungoides: report of the Dutch cutaneous lymphoma group. *Br J Dermatol* 2017; 177: 223-8.

6. McGinnis KS, Junkins-Hopkins JM, Crawford G, Shapiro M, Rook AH, Vittorio CC. Low-dose oral bexarotene in combination with low-dose interferon alfa in the treatment of cutaneous T-cell lymphoma: clinical synergism and possible immunologic mechanisms. *J Am Acad Dermatol* 2004; 50: 375-9.

7. Apisarnthanarax N, Ha CS, Duvic M. Mycosis fungoides with follicular mucinosis displaying aggressive tumor-stage transformation: successful treatment using radiation therapy plus oral bexarotene combination therapy. *Am J Clin Dermatol* 2003; 4: 429-33.

8. Krönke A, Schlaak M, Arin M, Mauch C, Kurschat P. Successful treatment of a folliculotropic mycosis fungoides with bexarotene and PUVA. *Eur J Dermatol* 2012; 22: 259-60.

9. Kontos AP, Kerr HA, Malick F, Fivenson DP, Lim HW, Wong HK. 308-nm excimer laser for the treatment of lymphomatoid papulosis and stage IA mycosis fungoides. *Photodermatol Photoimmunol Photomed* 2006; 22: 168-71.

10. Whittaker S, Ortiz P, Dummer R, *et al*. Efficacy and safety of bexarotene combined with psoralen-ultraviolet A (PUVA) compared with PUVA treatment alone in stage IB-IIA mycosis fungoides: final results from the EORTC Cutaneous Lymphoma Task Force phase III randomized clinical trial (NCT00056056). *Br J Dermatol* 2012; 167: 678-87.

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COVID-19-associated livedo and purpura: clinical and histopathological findings

Cutaneous manifestations of coronavirus disease 2019 (COVID-19) have been classified as acral areas of erythema with vesicles or pustules (pseudo-chilblain), other vesicular eruptions, urticarial lesions, maculopapular eruptions, and livedo or necrosis [1, 2]. As there have been few reports of COVID-19-related cutaneous manifestations in Japan, it remains unclear whether this classification applies to Japanese patients. We report a case of cutaneous manifestations of severe COVID-19 infection in a Japanese patient, a 60-year-old woman with no significant medical history. She arrived at the referring hospital with a 10-day history of fever, cough, olfactory disturbance, and respiratory distress. A nasopharyngeal swab test for SARS-CoV-2 RNA amplification was positive. She was referred to our hospital, and remdesivir (Day 1: 200 mg/day; Days 2-5: 100 mg/day), ceftriaxone (2 g/day), and methylprednisolone (60 mg/day) were administered. Additionally, continuous hemodiafiltration and endotoxin adsorption therapy were performed. However, her condition worsened, and extracorporeal membrane oxygenation was initiated on the nineth day post-admission. On the eleventh day, livedo racemosa on both knees and elbows and purpura on the fingertips were observed (*figure 1A, B*).

Knee skin biopsy revealed pauci-inflammatory vascular thrombosis with endothelial injury in the superficial dermis, and necrosis of keratinocytes and sweat gland cells (*figure 1C-H*). Finger skin biopsy revealed dilated blood vessels in the superficial dermis, and congested blood vessels with proliferation of vascular endothelial cells in the deeper dermis (*figure 1I-M*). Immunostaining revealed positive staining for C3d (Bioss Antibodies, BJS, CN), SARS-CoV-2 envelope and spike protein (Gene Tex Inc., CA, USA), as well as type I interferon-inducible myxovirus resistance protein A (MXA; Santa Cruz Biotechnology, CA, USA) on vascular endothelial cells (*figure 1N-Q*).

Laboratory tests revealed abnormalities in coagulation/fibrinolysis: 95,000 platelets/μL (normal: 158,000-348,000 platelets/μL), 22.3 μg/mL fibrinogen/fibrin degradation products (normal: ≤ 5.0 μg/mL), and 11.8 μg/mL D-dimer (normal: ≤ 1.0 μg/mL). In addition, monoclonal IgM and cryoglobulin were not detected. The eruptions gradually improved, disappearing on the 29th day post-admission.

COVID-19-related skin manifestations with livedo/necrosis have been reported as relatively rare (6%), occurring transiently, in elderly patients and severe cases [1, 3].