Improvements in lupus miliaris disseminatus faciei after three-color (blue, red, and infrared) light-emitting diode monotherapy

Yusuke Yoshizawa, MD, PhD

Key words: LED; LMDF; therapy; three-color; treatment.

INTRODUCTION

Lupus miliaris disseminatus faciei (LMDF) is an idiopathic granulomatous disease characterized by symmetrical, monomorphic, reddish-brown papules on the face.[1] Despite controversy regarding the concept of LMDF, most researchers agree that LMDF is a distinct and independent entity that is clearly distinguishable from other granulomatous diseases.[1] Although various therapies have been proposed for the treatment of LMDF,[1-3] standardized therapies have not been established. However, increased tumor necrosis factor (TNF) pathway activity in lesional LMDF skin was recently reported by Alexanian et al[4]; those authors also demonstrated the robust efficacy of TNF inhibitor therapy for LMDF, as presumed evidence-based medicine.

The usefulness of red and/or infrared light-emitting diode (LED) irradiation in wound healing arises partly from its anti-inflammatory effects, which inhibit the expression of proinflammatory cytokines (eg, TNF-α).[5,6] This report describes a patient with LMDF who improved after receipt of three-color LED monotherapy.

Abbreviations used:

LED:	light-emitting diode
LMDF:	lupus miliaris disseminatus faciei
P. acnes:	Propionibacterium acnes
TNF:	tumor necrosis factor
TNF-α:	tumor necrosis factor alpha

CASE REPORT

A 48-year-old woman presented with asymptomatic papules on the face, which had persisted for 2 months. The lesions had not responded to 1 month of topical metronidazole. Dermatological examination revealed the presence of multiple reddish-brown, dome-shaped papules measuring 3 mm to 4 mm, densely distributed on the center of the patient's face (including the upper and lower eyelids) (Fig 1, *A* and *B*). Blood test results were within normal limits. Chest X-ray scans showed no active lesions. Skin biopsy from the left nasolabial fold showed epithelioid cell granulomas in the upper dermis, as well as central caseous necrosis containing neutrophils with nuclear dust surrounded by a lymphohistiocytic infiltrate (Fig 2). No mycobacterial or fungal components were detected in dermal tissues by Ziehl–Neelsen staining or periodic acid–Schiff staining. The patient was diagnosed with LMDF and prescribed oral doxycycline 100 mg/day for 3 weeks. Doxycycline therapy was ineffective; second-line treatment comprised LED irradiation monotherapy once weekly for 20 minutes. Simultaneous irradiation with blue (405-415 nm), red (620-630 nm), and infrared (850 nm) LEDs was achieved using an N-LED 5000DK (Aderans Medical Research Co, Ltd, Tokyo, Japan) at the following LED integrated intensities: blue, 4.72 J/cm^2; red, 2.63 J/cm^2; and infrared, 6.61 J/cm^2.

After 4 weeks of LED therapy, a therapeutic response was observed as lesion flattening and fading, particularly in the perioral lesions (Fig 3, *A*). After 12 weeks of LED therapy, considerable improvements were observed in all skin lesions except those on the eyelids; pitting scars were visible on the nose and between the eyebrows (Fig 3, *B-1* and *B-2*). At 12 weeks, skin biopsy was repeated adjacent to the first biopsy site. Compared with the first biopsy

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Correspondence to: Yusuke Yoshizawa, MD, PhD, Yoshizawa Dermatology Research Clinic, KS Bill 2F 342-3 Katakura-Cho, Hachioji, Tokyo 192-0914, Japan. E-mail: yclinic@nifty.com.

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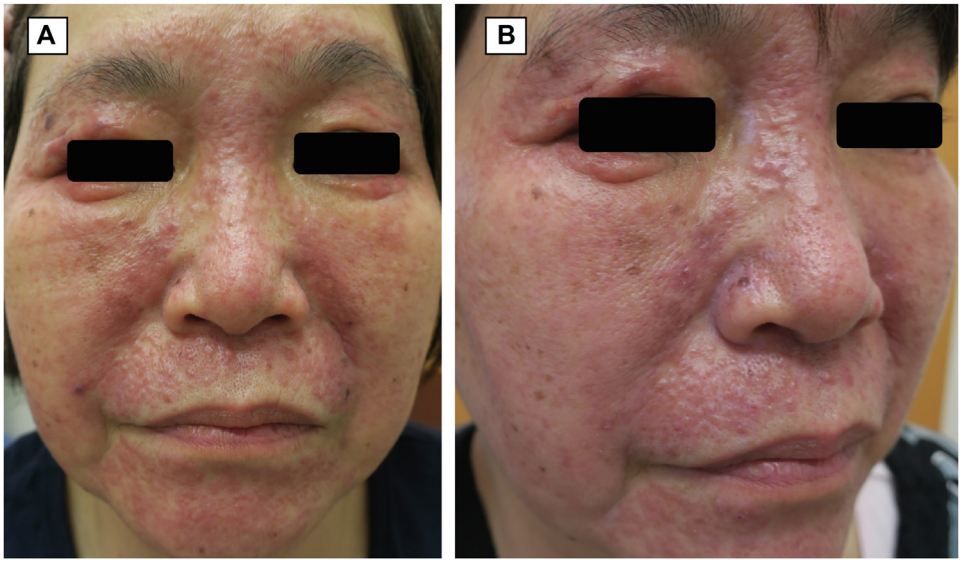

Fig 1. Lupus miliaris disseminatus faciei; clinical findings. **A** and **B,** Before LED irradiation. Multiple *reddish-brown*, dome-shaped papules are densely distributed on the central face, including the *upper* and *lower* eyelids. *LED*, Light-emitting diode.

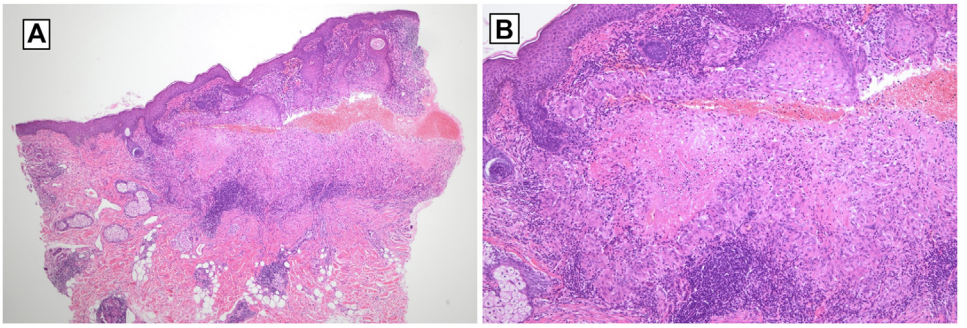

Fig 2. Lupus miliaris disseminatus faciei; histological findings of the first skin biopsy. **A,** Low-power view (hematoxylin and eosin [HE] staining, original magnification ×40). **B,** High-power view (HE staining, ×100). Epithelioid cell granulomas were visible, along with central caseation necrosis containing neutrophils with nuclear dust, surrounded by a lymphohistiocytic infiltrate. Granulomas were located in the *upper* dermis adjacent to pilosebaceous follicles. *HE*, Hematoxylin and eosin; *LED*, light-emitting diode.

findings, the second biopsy showed reduced neutrophil infiltration (nuclear dust) and fewer lymphohistiocytes, along with smaller epithelioid cell granulomas (Fig 4). The LED therapy remains well-tolerated and has been continued without signs of LMDF aggravation.

DISCUSSION

LMDF primarily affects facial skin and its etiology remains unknown.[1] Nearly 70% of the granulomas are located in the middle or deep dermis, but some occur in the upper dermis adjacent to pilosebaceous follicles.[1] These granulomas are characterized by a central area of caseation necrosis that contains neutrophils with nuclear dust, surrounded by a lymphohistiocytic infiltrate comprising multinucleated giant cells; mixed perivascular lymphohistiocytic infiltrates occur in the upper dermis.[1]

Although the patient's skin manifestations may not be typical for LMDF and cultures of biopsy material to identify atypical mycobacterium growth were not performed, the clinical and histological findings (ie, negative findings in dermal tissues upon Ziehl–Neelsen and periodic acid–Schiff staining) collectively support a diagnosis of LMDF. LMDF spontaneously resolves within several years but can cause potentially disfiguring scarring[1]; therefore, treatment is often aggressive.

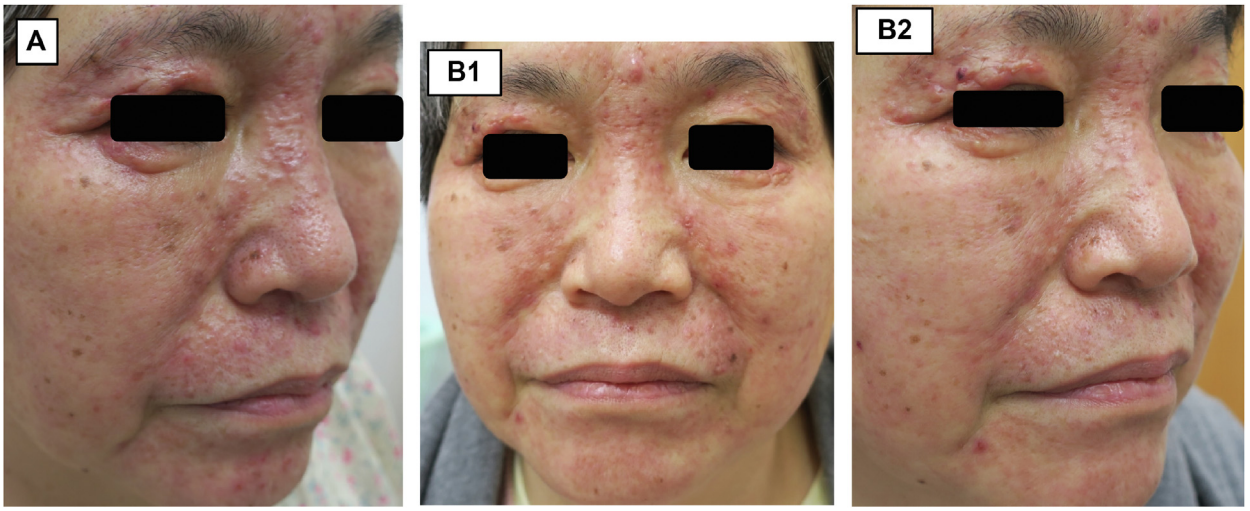

Fig 3. Lupus miliaris disseminatus faciei; clinical findings. **A,** After 4 weeks of LED irradiation, the patient exhibited a response in the form of lesion flattening and fading, particularly in the perioral skin lesions. **B-1** and **B-2,** After 12 weeks of LED irradiation, considerable improvements were observed in all skin lesions except those on the eyelids. Some pitting scars were visible on the nose and between the eyebrows.

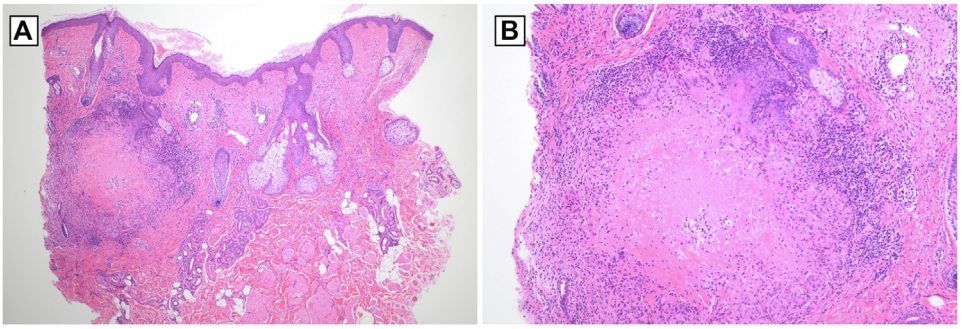

Fig 4. Lupus miliaris disseminatus faciei; histological findings of the second skin biopsy performed at a site adjacent to the first biopsy site, after 12 weeks of LED therapy. **A,** Low-power view (HE staining, original magnification ×40). **B,** High-power view (HE staining, ×100). Compared with findings in the first biopsy, there were reductions in cell infiltration (neutrophils with nuclear dust and lymphohistiocytes) and epithelioid cell granuloma size. *HE*, Hematoxylin and eosin; *LED*, light-emitting diode.

Histological examination before LED irradiation showed that granulomas were located in the upper dermis, in association with pilosebaceous follicles. Nishimoto et al[7] suggested a relationship between LMDF and *Propionibacterium acnes* (*P. acnes*) on the basis of increased levels of *P. acnes* genes in LMDF granulomatous lesions, compared with normal skin. The histological findings in this patient suggest an association between LMDF and *P. acnes*.

In a previous report,[8] treatment of LMDF with nonablative fractional laser resurfacing (1565 nm) was effective, suggesting that wound healing induced by this laser contributes to the resolution of granulomatous inflammation. The LED therapy used in the present patient consisted of 3 colors (blue, red, and infrared) with the expectation that red and infrared LEDs would provide anti-TNF effects[5,6] and blue LED would provide antibacterial efficacy against *P. acnes*.[9] However, little information is available regarding phototherapy for LMDF; the susceptibility of LMDF to reactive oxygen species produced by excessive LED irradiation, which could trigger LMDF exacerbation, is also unclear. Therefore, the most important point in this patient's phototherapy was the avoidance of excessive irradiation.

LED irradiation (880 nm, 7.5 J/cm^2 or 630 nm, 4.2 J/cm^2, respectively) decreased mRNA expression of cytokines in rats with Achilles tendinitis[5] and immunostaining for TNF-α in macrophages in rat muscle after exercise.[6] A review of the combination of blue and red LED therapy for acne vulgaris[10] reported the efficacy of twice weekly LED irradiation (blue: 7.2-48.0 J/cm^2 and red: 9.6-120.0 J/cm^2) or twice daily irradiation (blue: 0.91 J/cm^2 and red: 1.22 J/cm^2). In the current report, the doses of the 3 illuminances were determined with reference to these previous reports; among the 3 output settings, the intermediate output of the N-LED 5000DK was chosen, with duration of 20 minutes.

In summary, the patient showed substantial improvement after three-color LED monotherapy. Future research efforts should explore the treatment of LMDF using LED light sources.

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Conflicts of interest

None disclosed.

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