# Photodynamic Therapy for Acne Vulgaris With Topical 5-Aminolevulinic Acid FREE

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# REPORT OF A CASE

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A 24-year-old Japanese woman presented with a 10-year history of intractable acne vulgaris lesion on her face. The lesions coincided with her menstrual cycle, and resisted various treatments including 1% nadifloxacin cream, clindamycin hydrochloride lotion, and chemical peeling with glycolic acid and other agents.

## THERAPEUTIC CHALLENGE

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Our aim was to find an effective and safe treatment for intractable acne vulgaris.

# **SOLUTION**

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After obtaining informed consent, the patient was treated with topical 5-aminolevulinic acid photodynamic therapy (ALA-PDT). Twenty percent ALA (A 7793; Sigma, St Louis, Mo) in an oil-in-water emulsion (Yoshida, Tokyo, Japan) was applied to a  $5 \times 5$ -cm area of the right cheek for 4 hours with a light-shielded dressing. On Wood lamp examination, the affected lesion showed numerous dots of vivid red fluorescence corresponding to pilosebaceous units in a  $5 \times 5$ -cm² square pinkish fluorescence area. The lesion was then exposed to a 635-nm laser light of 5 J/cm² total using a pulsed excimer-dye laser (PDT EDL.1; HAMAMATSU, Hamamatsu-shi, Japan) without anesthesia. The patient tolerated irradiation well.

Immediately after treatment, the affected lesion demonstrated edematous erythema (Figure 1). Four days after the irradiation, the affected lesion showed a very thin crust formation, and was completely healed in 10 days. After healing, full face treatment of 30% to 40% wt/wt glycolic acid chemical peeling was performed every 3 to 4 weeks and 1% nadifloxacin cream was applied. In the lesions not treated by ALA-PDT, acne became aggravated 1 week before each menstrual cycle. However, the affected area did not present any new acne during a follow-up period of 8 months (Figure 2). The ALA-PDT was applied to the entire face at the patient's request.

Figure 1.

Left, A  $5 \times 5$ -cm² area of the right cheek treated with topical 5-aminolevulinic acid (arrows) photodynamic therapy. Two days after the treatment, the affected lesion showed edematous erythema. Right, Photograph of an untreated lesion on the left cheek.



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## Figure 2.

Four days before the expected start of menstruation and 3 months after the photodynamic therapy session. Left, On the treated area (arrows) only acne scars without new acne were seen. In the area not treated with photodynamic therapy, aggravation of acne was observed. Right, Photograph of aggravation of acne in the affected area.



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## COMMENT

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Acne vulgaris is a common disorder of great cosmetic concern to young people. Although a small number of acne lesions is tolerable and easily treated, repeated recalcitrant acne has a tendency to lead to scarring, causing further distress.

Although tretinoin or isotretinoin is extremely effective for intractable acne, there is a potential for teratogenicity. 12 Therefore, its application may be limited; these medications are not available in Japan.

To achieve a good outcome in this patient, we opted for PDT because there is considerable evidence in the literature and in our experience of selective damage to sebaceous glands in patients treated with ALA-PDT.34

Since the study by Kennedy et al, it has been reported that PDT with endogenous protoporphyrin produced from exogenous ALA is useful for treating nonmelanoma skin cancers. 5-Aminolevulinic acid is a compound used with PDT although it is not a sensitizer itself. Its great advantage is that the photosensitizing effects disappear within 24 hours and topical application decreases the chance of side effects. Therefore, PDT coupled with ALA is used not only for treatment but also for diagnosis. This treatment is also effective for benign cutaneous disorders.

Concerning the influence of ALA-PDT on sebaceous glands and hair follicles, Divaris et al3 reported an in vivo study in albino mice. Accumulation of protoporphyrin as fluorescence was marked in sebaceous glands and less evident in hair follicles and epidermis. Irradiation with optimal wavelength light resulted in destruction of sebaceous glands and damage to hair follicles and epidermis. After recovery from this transient damage, a decreased number of pilosebaceous units were observed and normal structure was maintained. Dierickx et al4 reported a case of nevus sebaceous that resolved after repeated ALA-PDT treatments. A specimen obtained from their patient showed sebaceous glands were replaced by fibrosis in the layers treated with ALA-PDT. Also, in our experience with ALA-PDT or ALA- photodynamic diagnosis, dots of fluorescence corresponding to pilosebaceous units are clearly seen, especially in the seborrheic region of the face. From these observations, and from our experience and other studies, it seems that the sebaceous gland is the most sensitive to ALA-PDT in normal skin.

Our case demonstrates the possibility of an effective treatment for intractable acne vulgaris. A single session of 5 J/cm² irradiation prevented the development of new lesions during a follow-up period of 8 months without causing adverse effects. In the affected lesion, old acne scars were noticeable, but these were gradually diminished by repeated glycolic acid chemical peeling treatments.

It was unclear how long the development of new acne could be prevented because the patient requested that ALA-PDT be applied to her entire face. The mechanisms that prevent new lesions are not clear, although reduction of seborrhea in the face is possible. As focal comedo formation has been reported after repeated high-energy doses of radiation with a good supply of oxygen, too large an energy dose carries the risk of the opposite effect. It is necessary to determine the optimal energy dose to maintain a good skin condition for the longest period possible; the 8 months of positive outcome in our case after a single session with 5 J/cm2irradiation may be sufficient. To resolve these issues and determine the optimal treatment settings, larger studies are needed.

Concerning treatment cost, the laser equipment is expensive although ALA alone is not expensive. In PDT for acne vulgaris, incoherent light sources may be more advantageous than lasers because they are cheaper and available for uniform skin surface illumination of large areas.

#### <u>Article</u>

# ARTICLE INFORMATION

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#### **Editorial Comment**

Photodynamic therapy with ALA has finally made PDT a potentially practical treatment option for several dermatologic conditions. The use of ALA-PDT has received Food and Drug Administration approval for the treatment of actinic keratoses. It has shown promise for the treatment of superficial nonmelanoma skin cancers. 5-Aminolevulinic acid's propensity to localize to the pilosebaceous unit has been exploited for the effective removal of unwanted hair, irrespective of hair or skin color. The ability to achieve long-term remission of recalcitrant acne vulgaris after only 1 ALA-PDT treatment, if confirmed in larger trials, would be a major advance in acne therapy. Unfortunately, the high cost of the equipment needed and lack of adequate third-party payer reimbursement may limit the use of ALA-PDT to major teaching institutions for the foreseeable future.—*George J. Hruza, MD* 

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