CASE REPORT

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Markedly clinical improvement of papulopustular rosacea with multimodality therapeutic approach: a case report

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ABSTRACT

Introduction: Rosacea is a chronic inflammatory skin disease that mainly affects the central area of the face. There are four subtypes, and they may progress between subtypes or span multiple subtypes. Due to its long course of the disease, optimum treatments are needed to control the disease progression.
Case: We reported rapid improvement of combining topical metronidazole, doxycycline, and light emitting diode for treating a patient with papulopustular rosacea in a 44-years-old woman, a week from the initial therapy.
Discussion: Therapeutic approaches to rosacea mainly focus on controlling the symptoms with anti-inflammatory agents. More recently, photodynamic therapy, especially light-emitting diodes, has been introduced as a valid alternative or an adjuvant therapy to conventional treatment through their synergic mechanism between therapeutic modalities.
Conclusions: This combination treatment may be effective for treating papulopustular rosacea without any side effects.

Keywords: *Rosacea, papulopustular, metronidazole, doxycycline, light-emitting-diode*.
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INTRODUCTION

Rosacea, typically characterized by flushing, non-transient erythema, papules/pustules, telangiectasia, phymatous change, or a combination, is a chronic inflammatory skin disease mainly affects the central face.[1,2] Based on the classification and staging of rosacea by the National Rosacea Society (NRS), there are four subtypes: erythematotelangiectatic, papulopustular, phymatous, and ocular, recognized based based on different clinical characteristics and may progress between subtypes or span multiple subtypes.[3] Patients with rosacea also often present subjective symptoms, including itching, burning, or stinging sensation.[1]

Rosacea is reported to affect approximately 10% of the population in the United States. The prevalence is higher in women; the most common onset is around the fourth decade of life. Although it isn't life-threatening, rosacea is greatly related to lower psychosocial quality.[4] The pathogenesis and pathophysiology of rosacea are not fully determined, but dysregulation of the innate and adaptive immune system, *Demodex*, ultraviolet exposure, and other trigger factors may contribute.[3] In these past years, treatments option for managing rosacea has expanded, including several topical therapies, oral therapies, light devices, skincare, and modification of lifestyle, but it remains a challenge to achieve satisfactory result both for the doctor and the patients.[1]

CASE

A 44-year-old woman presented to our cosmetic dermatology clinic with a history of pink to reddish eruption on her face since 2 months ago. She reported that the eruption initially appeared on the right cheek, then extended to the other part of the face and reddened over time (Figure 1A). In the previous 2 months, the patient had been treated with fluocinolone acetonide cream at 0.025% and clindamycin gel at 1.25% with no improvement. The eruptions increased a week before the visit. The patient mentioned the appearance of multiple papules and pustules over the reddish eruption with whitish fine scales in some other parts. A burning and stinging sensation were also reported. The patient admitted to being pressured at the workplace these past few weeks. The eruption also appeared reddened after exposure to ultraviolet radiation while leaving for work. There was no previous history of using sunscreen or other skin care products. There was no similar medical condition within the family.

From the physical examination, multiple erythematous macules, papules, plaques, and pustules spread over the upper part of the nose, bilateral cheeks predominantly on the right mandibular region, and chin. There was no ocular abnormality and no periorbita edema. On dermoscopy evaluation, we observed multiple telangiectasia and white scales on a dark red colored background (Figure 1B). Wet mount examination from the skin scrapping did not show signs of *Demodex sp*.

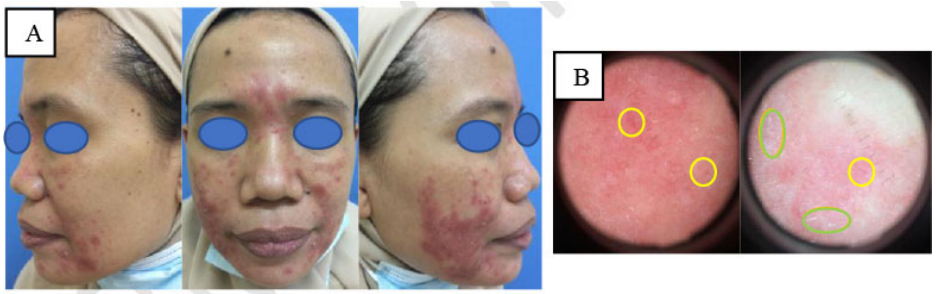

Figure 1A. Papulopustular rosacea with erythema, telangiectasia, papules, and pustules in the patient at the first visit (Patient consent was obtained); **1B.** Dermoscopy from the lesion showed dark red background, multiple vessels (yellow) and white scales (green).

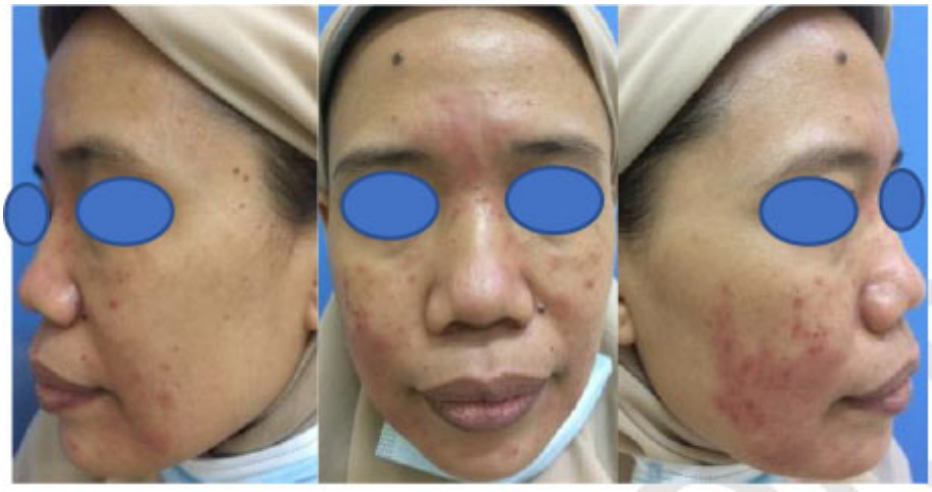

Figure 2. Markedly improved in erythema, papules, and clearance of pustules a week after initial therapy (Patient consent was obtained).

Based on the course of the disease and physical examination, the patient was diagnosed as papulopustular rosacea subtype, moderate grade, according to the classification and grading by NRS. The patient was treated orally with doxycycline 50 mg twice daily and topical 1% metronidazole in 20 g of hypoallergenic amphiphilic cream twice daily. The patient also received light-emitting-diode (LED) therapy once a week with a combination of blue and red light for 15 minutes. In the following week, markedly improvement was seen (Figure 2). A reduction of erythema and papules was observed, and no pustules were seen after only a week following the therapy. The patient was extremely satisfied by the good response, especially with the disappearance of burning and stinging sensations. There was no side effect reported. The patient submitted for another LED therapy maintained by topical metronidazole 1%. Further improvement was observed after 2 weeks.

DISCUSSION

Choosing the best treatment regimens for rosacea has to be based on the subtype and considering the main clinical manifestation when the patient comes. Recently, optimizing topical or physical therapy has been preferred to minimize oral therapy, so the side effects would be less and improve treatment safety.[2] The therapeutic approach explained in this report aims at reporting the dramatically improvement of papulopustular rosacea a week from the initial treatment by combining topical, systemic, and physical therapy. Combination therapy should be considered for managing moderate to severe papulopustular rosacea.[1] Fortunately, there is no contraindication to concomitant therapy and no drug interactions between the medications that are FDA approved for rosacea.[4]

For topical treatments, ivermectin, azelaic acid, and metronidazole are considered first-line agents for papules and pustules.[4] To this patient, we gave 1% metronidazole in 20 g of hypoallergenic amphiphilic cream due to the unavailability of topical metronidazole preparation in Indonesia, as it could be as effective for rosacea treatment in the previous report.[5] Topical metronidazole has shown the ability to decrease both the erythematotelangiectatic subtype's redness and the number of papules and pustules. Metronidazole is both antibacterial and antiprotozoal, but its effectiveness in treating rosacea is credited more with anti-inflammatory and antioxidant properties. It also likely acts by decreasing reactive oxygen species (ROS).[6]

Oral tetracycline antibiotics (e.g., doxycycline) have anti-inflammatory and antiangiogenic activities. Antimicrobial doses of doxycycline at 50–200 mg daily are highly effective in treating papulopustular rosacea.[4] The anti-inflammatory effect is achieved by inhibiting white cell movement during inflammation, lymphocytic proliferation, arachidonic acid (AA) production, and proteolysis mediated by matrix metalloproteinase (MMP). Doxycycline also inhibits gelatinases A and B that promote the integrity of the capillary wall, reduces sensitivity to vasodilatory stimuli, prevents capillary leakage, improves the integrity of connective tissue, and downregulates proinflammatory cytokines that assist in erythema and inflammation associated with rosacea. Doxycycline inhibits MMPs, nitric oxide (NO) synthetase, and extracellular matrix synthesis for angiogenesis impairment.[7] In this case, using doxycycline 100 mg in a divided dose of 50 mg twice daily resulted in significant improvement, with fewer side effects. This is in line with the study from Del Rosso et al. that reported the mean change in the inflammatory lesion and erythema score with a conventional dose of doxycycline (100 mg) and explained the effectiveness for moderate to severe rosacea.[8]

The usefulness of LED therapy combining blue and red light showed benefits and efficacy for treating patients with rosacea.[2] Moreover, an in vitro study on rosacea-like mouse skin reported the efficacy of LED at 630 and 940 nm on the

down-regulation of key inflammatory mediators of rosacea, such as cathelicidin (LL-37), toll-like receptors 2 (TLR2), and kallikreins (KLKs).[9] Treatment with LEDs may also interact with skin microbiome, which could significantly impact the etiopathogenesis of rosacea as on immune response modulation.[2] We submitted the patient to LED therapy and showed a beneficial result that may achieve through several mechanisms explained.

CONCLUSION

The treatment of patients with rosacea still represents a challenge for dermatovenereologists. Without combination treatment, it would be either ineffective or result in patients' dissatisfaction due to the need for continuous treatment. Although rosacea is not a life-threatening disease, the treatment should be targeted as early as possible using multimodality therapeutic options to improve significantly in line with patient satisfaction, including the absence of side effects.

ETHICS IN PUBLICATION

We mentioned patient approval in each of the figures included in this paper.

CONFLICT OF INTEREST

There is no conflict of interest regarding the publication of this paper.

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AUTHORS CONTRIBUTIONS

Each author made a substantial contribution to this paper. MH Priyanto, under the supervision of LS Suseno, examined and followed up with the patient, wrote the initial draft, revised the content, and was responsible for communication with the editorial team during the submission of this paper. AN Wardani assisted in examining the patient and the paper preparation. L Legiawati and IBS Sitohang revised this paper for intellectual content.

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