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CASE REPORT

Severe papulopustular rosacea with demodicosis in a 47-year-old Filipino female: A case report

Aira Monica R. Abella, MD,[1] Johannes F. Dayrit, MD, FPDS, FDSP[1]

ABSTRACT

INTRODUCTION Rosacea is a chronic relapsing inflammatory facial dermatosis often characterized by flare-ups and remissions exclusively affecting the centrofacial skin.

CASE REPORT This is a case of multiple symmetric intensely erythematous papules, pustules, and plaques over both cheeks in a 47-year-old Filipino female. Dermoscopy showed brown-yellowish structureless areas, straight vessels in a polygonal pattern, dilated follicles, follicular plugs, ill-defined white rosettes, and non-specific scales. Skin punch biopsy showed spongiosis of the epidermis and demodex folliculorum within the follicular infundibulum. The dermis revealed telangiectasia of blood vessels and dense inflammatory infiltrates. Hypertrophy of sebaceous lobules was also seen. The patient was initially treated with oral lymecycline 300mg twice a day for 2 weeks without improvement. Due to the persistence of centrofacial erythema, papules and pustules, the patient was given prednisone 10mg once a day for 1 month and low dose isotretinoin 10mg once a day for 8 months which resulted in significant decrease in erythema and number of existing lesions. To further decrease the inflammation contributed by demodex mites, permethrin 5% cream twice a day for 1 month was applied. Long-pulsed Neodymium-doped yttrium aluminum garnet (Nd:YAG) 1064 nm laser for a total of 10 sessions together with Isotretinoin 10 mg every other day effectively maintained remission for 1 year and 5 months. Gentle skin care measures, sunscreen, metronidazole 0.75% cream once a day, and desonide 0.05% cream twice a day for 1 week in cases of acute flares were maintained during the treatment course.

CONCLUSION An armamentarium of topical and oral antibiotics, corticosteroids, isotretinoin and non-ablative long-pulsed Nd:YAG 1064 nm laser showed significant improvement in the inflammatory papules, pustules, and centrofacial erythema of rosacea and proves to be beneficial in the maintenance of its long-term remission.

KEYWORDS Papulopustular rosacea, Isotretinoin, lymecycline, long-pulsed Nd:YAG laser

INTRODUCTION

Rosacea is a prevalent condition affecting more than 20 million people worldwide.[1] It is frequently diagnosed in women whose onset is seen in ages 35-45 years old.[1,2] Rosacea affects all segments of the population and all skin types.[1] It is primarily diagnosed clinically based on patient's self-reported history, observations, triggers, and overlapping symptoms.[1,3,4] Additionally, the use of a dermatoscope and histopathology may reveal other characteristics of rosacea that can help guide the diagnosis. Current guidelines from the 2018 classification by the National Rosacea Society recommends a phenotype driven approach in the diagnosis and treatment.[1,4] The following features represent independent diagnostic criteria of rosacea: fixed centrofacial erythema or phymatous changes.[1,4] In their absence, diagnosis can also be established by two or more major features: papules/pustules, flushing, telangiectasia, or ocular manifestations.[1,4] While secondary features may occur, burning, stinging, edema, or dry appearance, are not generally considered diagnostic.[1,4] Several studies have shown success in addressing the papules and pustules as well as centrofacial erythema utilizing topical, systemic and/or physical interventions.[5-10]

CASE REPORT

A 47-year-old female Filipino, presented to our clinic with a 5-year history of on and off appearance of intense red papules, pustules and plaques on both cheeks. The lesions were exacerbated by sun exposure, heat, hot weather, and intense emotions. She had never experienced ocular signs or symptoms. A previous dermatologist managed her case as rosacea and was prescribed brimonidine 0.33% gel which resulted in transient improvement of the lesions, but was followed by an exacerbation of the lesions, hence consult at our clinic. Clinical examination revealed multiple, symmetric, well-defined,

[1]Department of Dermatology, Research Institute for Tropical Medicine, Muntinlupa City

Corresponding author
Aira Monica R. Abella, MD

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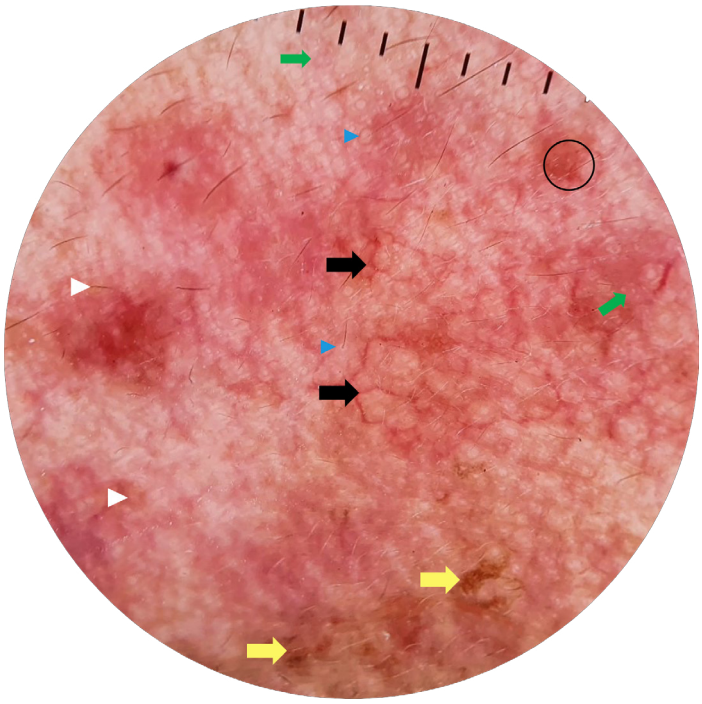

Figure 1. Dermoscopy on initial consult showed, brown-yellowish structureless areas (yellow arrows), straight vessels in a polygonal pattern sometimes called honeycomb pattern (black arrows), dilated follicles (blue arrowheads), follicular plugs (white arrowheads), ill-defined white rosettes (green arrows) and non-specific scales (black ovals).

irregularly-shaped, erythematous, edematous, macules, papules, pustules, and plaques with telangiectasias on the central cheeks and some on the glabella, nose, and chin. Dermoscopy showed brown-yellowish structureless areas, straight vessels in a polygonal pattern, dilated follicles, follicular plugs, ill-defined white rosettes, and non-specific scales (Figure 1). A 4-mm skin punch biopsy was taken from a pustule on the left cheek. Histopathologic examination using Hematoxylin and Eosin stain revealed spongiosis of the epidermis, exocytosis of lymphocytes and demodex folliculorum within the follicular infundibulum. The dermis revealed telangiectasia of blood vessels, and a dense perivascular, interstitial and periadnexal inflammatory infiltrate of lymphocytes, plasma cells and neutrophils. Hypertrophy of sebaceous lobules was seen (Figure 2A-B).

With the clinical, dermoscopic, and histopathologic findings, a diagnosis of papulopustular rosacea with *Demodex folliculorum* was made. The patient was initially treated with oral lymecycline 300 mg twice a day for 2 weeks without significant improvement. Patient was then given prednisone (10 mg once a day for 1 month) in combination with oral isotretinoin (10mg once a day for 4 months then 10 mg every other day for 8 months) to strongly address the inflammatory component of rosacea. Additionally, the patient was instructed to apply permethrin 5% cream twice a day for 1 month. This led to the significant decrease of centrofacial erythema, papules and pustules (Figure 3A-D). Immediately after, the first session of long-pulsed Nd:YAG 1064nm laser toning was performed monthly for a total of 10 sessions while still maintained on low dose isotretinoin 10mg every other day as a way to control flares and decrease vascu-

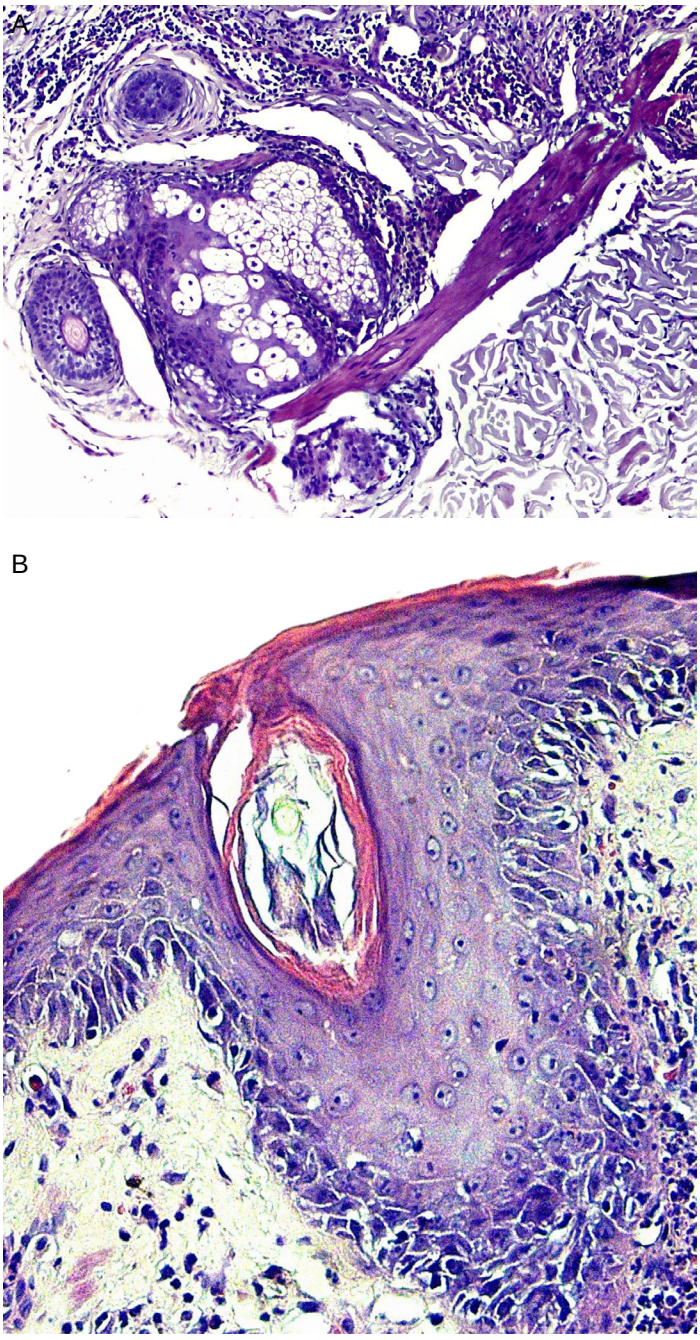

Figure 2. A. Hypertrophy of sebaceous lobules (H&E, 10x); **B.** Demodex folliculorum within the follicular infundibulum (H&E, 20x).

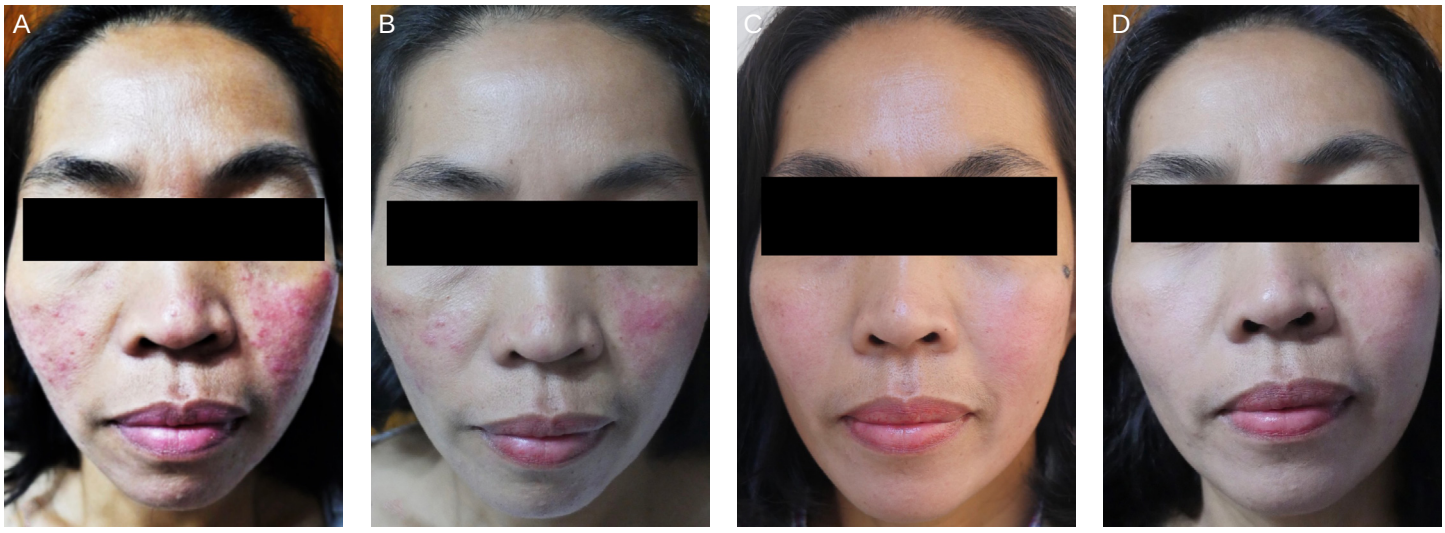

Figure 3. Baseline and follow-up photos while on low dose isotretinoin. **A.** Initial consult **B.** Four (4) months of Isotretinoin 10 mg per day **C.** Three (3) months of Isotretinoin 10mg every other day **D.** Five (5) months of Isotretinoin 10mg every other day.

larity. The vascular probe in genesis (GN) mode was delivered with the following parameters: fluence of 7.1 J/cm^2, 6mm spot size, and frequency of 6Hz for the first pass followed by Top Hat (TH) beam profile with 1.4 J/cm^2, 6 mm spot size, and frequency of 6Hz. Post-laser sessions, patient was advised to apply a moisturizer twice a day for 3 days only. Isotretinoin in combination with long-pulsed Nd:YAG 1064 nm laser showed complete clearing of papules and pustules and significant reduction in erythema and telangiectasia. The patient was in complete remission for 1 year and 5 months. She did not experience flares of flushing nor episodes of persistent erythema. However, there was a recurrence of few erythematous papules and pustules. Isotretinoin (10mg twice a week) was resumed, metronidazole cream 0.75% cream twice a day, sunscreen, and gentle skincare was continued to maintain remission. Occasional flares were treated with desonide cream (twice daily for 1 week). To maintain remissions, isotretinoin (10 mg once to twice weekly) in combination with metronidazole 0.75% cream (once daily), short term desonide cream (twice a day for 1 week) in cases of acute flares, and gentle skincare practices.

DISCUSSION

Rosacea is characterized by multifactorial, inflammatory events and often requires a multidisciplinary approach including adequate skincare, topical and/or systemic therapy as well as physical modalities to treat the various symptoms in an appropriate and targeted manner.[1,3] Initially, our patient was prescribed with topical brimonidine, indicated for persistent facial erythema of rosacea. Topical brimonidine 0.33% gel appears to be well tolerated, however, patients must be advised about the occurrence of severe transient rebound erythema several hours after application and the occurrence of persistent erythema in skin adjacent to the site of long-term brimonidine application.[5] In our patient, brimonidine showed minimal to no improvement owing to poor adherence and since brimonidine only addresses the vascular problem of rosacea.

Demodex folliculorum mites are commensals in the human skin and was found particularly increased in the papules and pustules of rosacea.[4] Eliminating these mites with topical permethrin successfully reduces the inflammatory papules and pustules and was found to be as effective as metronidazole 0.75% gel, however the safety of long-term permethrin use is still unknown for it to be supported as a maintenance regimen.[6] Topical metronidazole was used as add-on therapy and as a maintenance regimen. It is most effective for the treatment of inflammatory papules and pustules, but may also contribute to improvement in erythema by exerting anti-inflammatory effect affecting neutrophil migration and chemotaxis.[7]

Due to the recurrent inflammatory papules, pustules, and centrofacial erythema, combined topical and systemic therapies is a rational approach in this case.[1,3] The patient is a good candidate for oral tetracyclines, considered as first-line therapy for severe papulopustular rosacea.[2] Lymecycline is approved for restricted use in the treatment of severe papulopustular rosacea and severe ocular rosacea in adults.[11] In this case, lymecycline 300 mg twice a day for 2 weeks, was given to our patient owing to its good safety profile and is generally well-tolerated, occasionally causing transient mild gastrointestinal disturbances, and rare allergic reactions.

Despite the use of topical and oral antimicrobials, our

patient showed very minimal reduction in the inflammatory papules, pustules, and centrofacial erythema. However, there was significant improvement when topical antimicrobials were used in conjunction with isotretinoin. Due to its lacking approval, isotretinoin can only be used "off-label" for rosacea.[10] Low-dose isotretinoin is an effective therapeutic option for difficult-to-treat papulopustular rosacea and to maintain remissions.[10] However, relapse was still observed within a median duration of 15 weeks.[10] Long-term therapy of isotretinoin is hence required to achieve optimum response.[10] Isotretinoin in combination with metronidazole 5% cream was done to optimize therapeutic benefit. To date an evidence-based clinical study on the most suitable dose and therapy duration for treatment of rosacea with Isotretinoin is still lacking.[10]

Finally, laser and light-based therapies, which have been used extensively for the treatment of a variety of vascular lesions, have also been used for the vascular features of rosacea, especially telangiectasias.[1,3,10] These modalities do not cure rosacea, and periodic treatments to maintain improvement are often required.[10] Non-ablative long-pulsed Nd:YAG addresses these facets of the disease well and has an important place in rosacea treatment both improving vascular clearance and decreasing the amount of scarring.[1,3,10]

CONCLUSION

The complex condition of rosacea implies that there is a need for a tailored multimodal approach for treatment success. Patient education, skincare, and different therapeutic options such as those in our patient are necessary for the control of rosacea but must be reiterated that none of these is curative. Our patient's presentation demonstrates how rosacea is a chronic, difficult-to-treat disease entity. Standardization of treatment algorithm is needed to help guide physicians, dermatologists, and patients alike.

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