

Rosacea Presents With Erythematous Facial Papules and Pustules

In this case, the authors provide an overview of the condition and steps for diagnosis and treatment.

Arvin Ighani and Benjamin Barankin, MD, FRCPC, FAAD

A 37-year-old Caucasian woman presented with a 3-year history of erythematous facial papules and pustules, predominantly affecting the cheeks, with minor involvement of the chin and nose (Figure). There were no comedones on exam. The patient reported that her skin was sensitive to many topical skin products and that her facial skin felt dry. There are no similar lesions on other parts of the body, including the chest, back, or shoulders. The rest of the physical examination was unremarkable.

Overview and Categorization

Rosacea is a chronic inflammatory skin condition classically characterized by facial signs, including erythema, telangiectasia, and pustules or papules.¹ It tends to present in individuals typically after 30 years of age and is associated with a negative impact on patient quality of life.²⁻⁴ Previously, rosacea was classified into 4 specific subtypes: (1) phymatous rosacea; (2) erythematotelangiectatic rosacea; (3) papulopustular rosacea; and (4) ocular rosacea.⁵ Although this classification system was didactically successful, it led some to overlook the fact that rosacea can simultaneously encompass signs and symptoms from multiple subtypes or even progress from one subtype to another in clinical practice.⁶

Consequently, the National Rosacea Society (NRS) Expert Committee updated its classification system in 2017 such that it is now based on phenotypic manifestations, rather than distinct subtypes.^{1,7} Using these new criteria, it is recommended that rosacea be characterized in updated terms which reflect the pathophysiology of the underlying groupings of signs and symptoms, including: neurovascular, inflammatory, phymatous, and ocular rosacea.¹



Photo courtesy—Benjamin Barankin, MD, FRCPC, FAAD

Figure. A woman presented with a 3-year history of erythematous facial papules and pustules, predominantly affecting the cheeks, with minor involvement of the chin and nose.

Diagnosis

The updated phenotypic criteria proposed by the NRS are separated into 3 categories: (1) diagnostic; (2) major; and (3) secondary. The formal diagnosis of rosacea requires at least 1 diagnostic or 2 major phenotypic criteria.¹ Diagnostic criteria include: fixed centrofacial erythema in a characteristic pattern that can transiently intensify and phymatous changes. Major phenotypic criteria include: flushing, papules and pustules, telangiectasia, and ocular manifestations. Specific ocular manifestations comprise telangiectasia of the lid margin, interpalpebral conjunctival injection, spade-shaped corneal infiltrates, scleritis, and sclerokeratitis. Secondary phenotypic criteria, although nondiagnostic, can be used to further characterize the rosacea and include the following manifestations: burning sensation, stinging

sensation, edema, dryness, and ocular manifestations. Specific ocular symptoms for secondary phenotypic criteria are lid margin irregularities, evaporative tear dysfunction, and “honey crust” accumulations at the base of lashes with collarette. Importantly, a thorough history is required for diagnosis, as many of these clinical features can be transient in nature but should still be considered during assessment.

Pathogenesis

The pathogenesis of rosacea is multifactorial, involving both genetic and environmental components. From a genetic standpoint, no single aberrant gene is associated with rosacea, but patients have increased expression of genes that modulate immune defenses.⁸ Furthermore, there is a predilection for individuals of Celtic and northern European descent to

develop rosacea, further supporting the genetic role of the disease.⁹ From an environmental standpoint, chronic sun exposure increases reactive oxygen species in dermal tissue, leading to modulation of inflammatory pathways through toll-like receptor 2 and kallikrein 5, which are implicated in the development of rosacea.^{10,11} Environmental triggers, like heat, modulate neurogenic signalling cascades involving the vanilloid and ankyrin receptors of cation channels that can lead to the flushing or burning sensations reported in patients with rosacea.^{9,12}

Aberrant vascular and inflammatory responses are also implicated in the pathophysiology of rosacea. High concentrations of antimicrobial pathway components, like cathelicidins, kallikrein 5, toll-like receptor 2, and matrix metalloproteinases, result from microorganism exposure in rosacea patients.^{8,9,13} Additionally, poor barrier function of the skin leads to dehydration and increased water loss, leading to high serine protease levels and exacerbating rosacea.¹⁴

Treatment

Treatment for rosacea can be divided into 2 major categories: nonpharmacologic interventions and pharmacologic interventions.

Nonpharmacologic Interventions

Patient education about triggers is paramount to successful control of rosacea. Individuals should aim to minimize known triggers, including: sun exposure, emotional stress, hot weather, wind, arduous exercise, alcohol, hot baths, cold weather, spicy foods, humidity, and irritating skin care products.¹⁵ Given the poor transepidermal water retention associated with rosacea, appropriate skin care with moisturizers and gentle cleansing can help control disease manifestations.¹⁴ Sun blocks with an SPF of 30 or above are also recommended to protect against UV rays that can lead to production of reactive oxygen species which can ultimately exacerbate rosacea;¹⁶ for those with sensitive skin, physical sun blocks may be preferred.

Pharmacologic Interventions

Topical medications: A variety of approved and off-label topical medi-

cations are used for the treatment of rosacea. Topical ivermectin cream 1%, metronidazole (0.75% or 1% formulation), azelaic acid (15% or 20% formulation), sodium sulfacetamide (10% sodium sulfacetamide with 5% sulfur lotion), and α -adrenergic agonists, like brimonidine tartrate gel 0.5% or oxymetazoline 1% cream, have all been approved for the treatment of rosacea.¹⁷ Off-label use of topical retinoids, topical calcineurin inhibitors, topical macrolides, benzoyl peroxide, or topical permethrin cream 5% can also help with management of rosacea.¹⁷

Systemic medications: Tetracyclines, like doxycycline, have been shown to treat rosacea (including ocular rosacea) by reducing vasodilation, matrix metalloproteinases, and reactive oxygen species.¹⁷⁻¹⁹ Sub-antimicrobial dose doxycycline is commonly used to minimize side effects and prevent antibiotic resistance. Nonselective β -blockers can also be used to reduce flushing and erythema through vasoconstriction, but patients should be advised of adverse events like hypotension and bradycardia.^{20,21} Low-dose isotretinoin can also be effective for treating rosacea.^{22,23} Counselling patients about lab monitoring and potential teratogenic effects of isotretinoin should always be considered at initiation of treatment. ■

Mr Ighani is a MD candidate Year 3 at University of Toronto in Toronto, Ontario, Canada.

Dr Barankin is a dermatologist in Toronto, Ontario, Canada.

References

- Gallo RL, Granstein RD, Kang S, et al. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol.* 2018;78(1):148-155.
- Aksoy B, Altaykan-Hapa A, Egemen D, Karagöz F, Atakan N. The impact of rosacea on quality of life: effects of demographic and clinical characteristics and various treatment modalities. *Br J Dermatol.* 2010;163(4):719-725.
- Buechner SA. Rosacea: an update. *Dermatology.* 2005;210(2):100-108.
- Berg M, Lidén S. An epidemiological study of rosacea. *Acta Derm Venereol.* 1989;69(5):419-423.
- Wilkin J, Dahl M, Detmar M, et al. Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the Clas-

- sification and Staging of Rosacea. *J Am Acad Dermatol.* 2002;46(4):584-587.
- Holmes AD, Steinhoff M. Integrative concepts of rosacea pathophysiology, clinical presentation and new therapeutics. *Exp Dermatol.* 2017;26(8):659-667.
- Tan J, Almeida LMC, Bewley A, et al. Updating the diagnosis, classification and assessment of rosacea: recommendations from the global ROSacea COnsensus (ROSCO) panel. *Br J Dermatol.* 2017;176(2):431-438.
- Yamasaki K, Di Nardo A, Bardan A, et al. Increased serine protease activity and cathelicidin promotes skin inflammation in rosacea. *Nat Med.* 2007;13(8):975-980.
- Two AM, Wu W, Gallo RL, Hata TR. Rosacea: part I. Introduction, categorization, histology, pathogenesis, and risk factors. *J Am Acad Dermatol.* 2015;72(5):749-758.
- Yamasaki K, Gallo RL. The molecular pathology of rosacea. *J Dermatol Sci.* 2009;55(2):77-81.
- Jones D. Reactive oxygen species and rosacea. *Cutis.* 2004;74(3 suppl):17-20, 32-34.
- Pecze L, Szabó K, Széll M, et al. Human keratinocytes are vanilloid resistant. *PLoS One.* 2008;3(10):e3419. doi:10.1371/journal.pone.0003419
- Jang YH, Sim JH, Kang HY, Kim YC, Lee E-S. Immunohistochemical expression of matrix metalloproteinases in the granulomatous rosacea compared with the non-granulomatous rosacea. *J Eur Acad Dermatol Venereol.* 2011;25(5):544-548.
- Dirschka T, Tronnier H, Fölster-Holst R. Epithelial barrier function and atopic diathesis in rosacea and perioral dermatitis. *Br J Dermatol.* 2004;150(6):1136-1141.
- Pelle MT, Crawford GH, James WD. Rosacea: II. Therapy. *J Am Acad Dermatol.* 2004;51(4):499-512.
- Del Rosso JQ, Baldwin H, Webster G; American Acne & Rosacea Society. American Acne & Rosacea Society rosacea medical management guidelines. *J Drugs Dermatol.* 2008;7(6):531-533.
- Two AM, Wu W, Gallo RL, Hata TR. Rosacea: Part II. Topical and systemic therapies in the treatment of rosacea. *J Am Acad Dermatol.* 2015;72(5):761-770.
- Alexis AF, Webster G, Preston NJ, Caveney SW, Gottschalk RW. Effectiveness and safety of once-daily doxycycline capsules as monotherapy in patients with rosacea: an analysis by Fitzpatrick skin type. *J Drugs Dermatol.* 2012;11(10):1219-1222.
- Korting HC, Schöllmann C. Tetracycline actions relevant to rosacea treatment. *Skin Pharmacol Physiol.* 2009;22(6):287-294.
- Hsu CC, Lee JY. Pronounced facial flushing and persistent erythema of rosacea effectively treated by carvedilol, a nonselective α -adrenergic blocker. *J Am Acad Dermatol.* 2012;67(3):491-493.
- Craige H, Cohen JB. Symptomatic treatment of idiopathic and rosacea-associated cutaneous flushing with propranolol. *J Am Acad Dermatol.* 2005;53(5):881-884.
- Park H, Del Rosso JQ. Use of oral isotretinoin in the management of rosacea. *J Clin Aesthetic Dermatol.* 2011;4(9):54-61.
- Kennedy Carney C, Cantrell W, Elewski BE. Rosacea: a review of current topical, systemic and light-based therapies. *G Ital Dermatol Venereol.* 2009;144(6):673-688.