

From Pathophysiology of Rosacea to Clinical Care

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ABSTRACT

Rosacea, a dermatologic disorder characterized by persistent facial erythema, papules, and pustules, often accompanied by ocular involvement, poses diagnostic and therapeutic challenges. This review comprehensively explores the clinical presentation, diagnostic criteria, differential diagnosis, and management strategies for rosacea. Emphasizing the multifactorial nature of its pathogenesis, including genetic and immune components, the review underscores the importance of individualized treatment approaches. Specialist referrals, especially for refractory cases, and a diverse range of treatment modalities, from topical medications to laser therapies, contribute to effective management. Regular monitoring and early intervention mitigate complications, ensuring a favorable prognosis. Ongoing research enhances our understanding of rosacea, guiding advancements in its diagnosis and management.

KEYWORDS: rosacea, facial erythema, papulopustular rosacea, ocular rosacea, differential diagnosis, treatment modalities, specialist referral, genetic factors, immune dysregulation, dermatologic disorder.

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INTRODUCTION

Rosacea, a persistent inflammatory condition, is frequently identified in individuals of Celtic descent, potentially influenced by a tendency to diagnose more readily in individuals with lighter skin. This condition typically emerges between the ages of 30 and 50. The diagnosis hinges on the presence of either a fixed reddening of the central face in a distinct pattern that may periodically worsen or the development of phymatous changes. Alternatively, a diagnosis can be established if two or more major features are present, including flushing, papules and pustules, telangiectasia, and ocular symptoms.

Ocular rosacea, affecting about half of patients with skin involvement, is characterized by eyes that appear watery or bloodshot, a feeling of a foreign object, visible blood vessels and redness of the eyelid margin, irregular eyelid margin, and the development of chalazia and styes. The primary diagnostic tools for rosacea are a comprehensive patient history and physical examination.

Tailored treatments focus on the specific clinical features presented by each patient. Brimonidine, a topical α -agonist, effectively reduces overall redness. Laser and intense pulsed light therapies are recommended for minimizing visible blood vessels. For papulopustular disease, topical agents such as azelaic acid, metronidazole, and ivermectin are recommended, with the option of adding low-dose oral

doxycycline if necessary. In more severe cases, low-dose oral isotretinoin is considered a third-line treatment.

Phymatous rosacea may respond to retinoids, either in topical or oral form, although laser or other ablative procedures produce the best outcomes for severe cases. Mild ocular involvement may be managed through good eyelid hygiene and artificial tears, but low-dose oral doxycycline or tetracycline could be effective. For severe ocular disease resistant to other treatments, the use of cyclosporine eye drops is recommended.

It's important to be mindful of potential pitfalls in diagnosis, particularly the tendency to overlook ocular involvement, which occurs in up to 50% of patients with skin-related rosacea. Therefore, thorough screening for ocular symptoms and redness of the conjunctiva or eyelid margin is essential for comprehensive patient care.

CLASSIFICATION

Rosacea, a persistent skin disorder, is identified by distinct major and secondary features, known as phenotypes. The diagnostic criteria involve the presence of at least one of two diagnostic features: fixed centrofacial erythema in a characteristic pattern that may periodically intensify or the development of phymatous changes. Additionally, a diagnosis may be established with the presence of two or

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more major features, including flushing, papules and pustules, telangiectasia, and ocular manifestations.

The ocular manifestations of rosacea encompass various signs such as lid margin telangiectasia, interpalpebral conjunctival injection, spade-shaped infiltrates in the cornea, scleritis, and sclerokeratitis. Secondary features, which may accompany one or more diagnostic or major features, include a burning sensation, stinging sensation, edema, dryness, and the presence of so-called honey crust and collarette accumulation at the base of lashes, irregular lid margin, and evaporative tear dysfunction.

The classification of rosacea is designed to guide treatment approaches. Traditionally, it was categorized into four subtypes based on the main clinical features that commonly presented together: erythematotelangiectatic rosacea (subtype 1), papulopustular rosacea (subtype 2), phymatous rosacea (subtype 3), and ocular rosacea (subtype 4). However, a newer classification introduced in 2016 and officially adopted in 2017 rejects these subtypes. The shift is based on the recognition that an individual may exhibit features from more than one subtype, or they may progress from one subtype to another over time.

This contemporary classification recommends tailoring treatment based on the patient's specific symptoms or signs, referred to as a phenotype. This approach acknowledges the variability and overlapping nature of rosacea features, aiming for a more personalized and effective treatment strategy that aligns with the individual manifestations of the condition.

CLINICAL PRESENTATION

Patients with rosacea often present with persistent redness of the face, intermittent and potentially prolonged facial flushing, and complain of a burning, stinging, or dry appearance of the affected skin. Recurrent skin breakouts, characterized by papules and pustules occurring in the center of the face, are common. Ocular symptoms may include dry eye, a sensation of a foreign body, light sensitivity, or blurred vision. Ocular involvement, estimated to occur in 6% to 50% of patients with cutaneous rosacea, often goes unrecognized. Therefore, it is recommended to screen all patients with cutaneous rosacea for ocular symptoms and hyperemia of the conjunctiva or lid margin. Symptoms tend to progress slowly over years.

On physical examination, patients may exhibit intermittent or persistent central facial erythema, which may extend to the peripheral face, ears, neck, and upper chest. Intermittent facial flushing, telangiectasia, and papules or pustules in a central facial distribution are commonly observed. Edematous facial plaques and thickened skin with irregular surface nodularities (phymatous changes) may also be present. While these changes can occur in any sebaceous facial region, the nose is the most commonly affected site.

Ocular findings associated with rosacea include a watery or bloodshot appearance with conjunctival injection, telangiectasias, and erythema of the lid margin. Irregular lid

margins, periocular erythema, chalazia, and styes are also common signs of ocular rosacea. Overall, the ocular manifestations of rosacea should not be overlooked, as they can have significant consequences, including scleritis, keratitis, and iritis, potentially leading to decreased visual acuity from corneal scarring and surface irregularities. Regular monitoring and screening for ocular symptoms are crucial in the management of rosacea.

PATHOGENESIS

The precise pathogenesis of rosacea remains elusive, although there are indications of a genetic component given its higher incidence in specific ethnic groups. Individuals with rosacea exhibit heightened expression of various genes, resulting in the dysregulation of the innate immune system. Microorganisms like *Demodex folliculorum* and *Staphylococcus epidermidis* may contribute to the development of rosacea by stimulating the innate immune system, while neurogenic dysregulation is implicated in symptoms such as flushing and burning. Moreover, the skin of those with rosacea displays increased transepidermal water loss and reduced epidermal hydration.

Several factors and associations contribute to rosacea development. The disorder is most prevalent in individuals aged 30 to 50, with rhinophyma more common in men over 40. While women are more susceptible to rosacea, men are more likely to progress to advanced stages, especially rhinophyma. A family history of rosacea is present in up to 30% of cases, with a twin study revealing a 50% genetic contribution. However, genome studies have not identified a specific causative gene. Ethnicity and race also play a role, with a higher prevalence in people of Celtic and Northern European descent.

Various environmental factors contribute to rosacea development, including sun damage and exposure. Cold exposure, along with the consumption of alcohol, spicy foods, and hot drinks, serves as triggers for flushing and can exacerbate rosacea symptoms, though they are not considered direct triggers for its development.

Primary diagnostic tools for rosacea include history and clinical examination. Diagnostic criteria encompass fixed centrofacial erythema or phymatous changes, along with major features like flushing, papules and pustules, telangiectasia, and ocular manifestations. Ocular involvement occurs in up to 50% of patients with cutaneous rosacea but often goes unrecognized, underscoring the need to screen all patients for ocular symptoms. Skin biopsy is reserved for cases where the diagnosis is uncertain or when ruling out other conditions is necessary.

DIFFERENTIAL DIAGNOSIS

Lupus Erythematosus:

Yellow-brown papules on the central face, particularly around the periorbital region.

Granulomas with central caseation necrosis in the dermis.

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No flushing or telangiectasia.

Overlap between lupus miliaris disseminatus faciei and rosacea can occur clinically and histologically.

Demodicidosis:

Severe Demodex infection may present with rosacea-like features, especially papules and pustules.

Absence of flushing and telangiectasia.

Suspected in a patient unresponsive to initial rosacea therapy; diagnosed by identifying excess Demodex mites.

Photodermatitis:

Triggered by sun exposure or a combination of sun exposure and phototoxic drugs.

Similar skin changes to rosacea.

Acne Vulgaris:

Oily skin with comedones, larger pustules than in rosacea, nodulocystic lesions, and a tendency to scar.

Comedones are absent in rosacea.

Less erythema compared to rosacea.

Typically affects a younger population than rosacea.

Both rosacea and acne vulgaris may feature telangiectasias.

Perioral Dermatitis:

Presence of micropustules and vesicles around the mouth and sometimes the eyes.

Patient history may reveal the use of topical corticosteroids or fluorinated toothpaste.

Seborrheic Dermatitis:

Scaling and erythema of the scalp, eyebrows, external auditory canals, and retroauricular folds.

Often coexists with rosacea.

Ocular rosacea may be mistaken for blepharitis caused by seborrheic dermatitis.

Steroid-Induced Acne:

Clinical findings similar to acne vulgaris.

Patient history includes corticosteroid use.

Blepharitis:

Inflammation and irregularity of the lid margin with scaling and flaking in isolated blepharitis.

Telangiectasia of the conjunctiva and lid margin may occur but are more likely in ocular rosacea.

Over 50% of ocular rosacea patients exhibit signs of cutaneous rosacea.

TREATMENT

The management of rosacea focuses on reducing inflammation, alleviating symptoms, and improving skin appearance while minimizing exposure to triggers.

Patients inadequately responding to approved treatments should be referred to a dermatologist. Laser or intense pulsed light therapies consideration warrants referral to an experienced dermatologist. Suspected ocular rosacea cases unresponsive to initial treatment should be referred to an ophthalmologist. Referral to an ophthalmologist is also recommended for patients requiring specific ocular treatments or developing complications.

General recommendations include the use of gentle skin care and sunscreens. Specific treatment choices depend on individual characteristics and rosacea severity. Evidenced options include topical brimonidine, azelaic acid, ivermectin, and oral doxycycline. Lower-quality evidence supports topical metronidazole and oral tetracycline. Laser, light-based therapies, and topical cyclosporine are options for ocular rosacea.

Various medications are used based on symptoms and rosacea severity: Brimonidine, oxymetazoline, azelaic acid, ivermectin, metronidazole, sulfacetamide/sulfur, doxycycline, tetracycline, isotretinoin, and cyclosporine.

Recommendations encompass skin moisturizers, sun protection, and trigger avoidance. For ocular rosacea, supportive measures include lid hygiene, warm compresses, and artificial tears.

Procedures like vascular (pulsed dye) laser, short and long-wavelength devices, and intense pulsed light therapy can address unresponsive telangiectasia and erythema. Regular monitoring, especially by an ophthalmologist for ocular rosacea patients, is crucial.

Complications may include progression to phymatous rosacea and ocular issues. However, persistent facial erythema or papulopustular rosacea generally responds well to treatment, with positive outcomes for phymatous rosacea through laser ablation or surgical excision.

CONCLUSION

In conclusion, rosacea is a multifaceted dermatologic condition characterized by persistent facial erythema, papules, and pustules, with potential ocular involvement. The clinical presentation varies, encompassing a spectrum from erythema and telangiectasia to more severe manifestations like phymatous changes. Patients may experience both physical and ocular symptoms, necessitating comprehensive evaluation.

The etiology of rosacea remains elusive, with genetic, immune dysregulation, and microbial factors implicated. A thorough history and physical examination, including ocular assessments, play pivotal roles in diagnosis. Differential diagnosis involves distinguishing rosacea from conditions like acne vulgaris, perioral dermatitis, and lupus erythematosus, emphasizing the importance of recognizing characteristic findings.

Management aims at reducing inflammation, improving skin appearance, and minimizing triggers. Specialist referrals are recommended for cases not responding to standard treatments, highlighting the need for individualized approaches. A range of treatment options, including topical and systemic medications, laser therapies, and supportive care, offers diverse strategies to address the varying presentations of rosacea. Regular monitoring, especially for ocular involvement, ensures effective management and improved patient outcomes.

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While complications such as progression to phymatous rosacea or ocular manifestations may occur, early intervention and appropriate treatment contribute to a favorable prognosis. The evolving understanding of rosacea pathophysiology and advancements in therapeutic modalities underscore the importance of ongoing research and collaborative efforts in optimizing care for individuals affected by this dermatologic condition.

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