
Comprehensive Evaluation of Pathophysiology, Differential Diagnosis and Advanced Therapeutic Approaches in Rosacea: A Comprehensive Analysis

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ABSTRACT

Rosacea, a chronic, recurrent skin disease, has long intrigued the medical community because of its complex pathophysiology and varied clinical presentation. In this article, a comprehensive assessment of current advances in understanding the underlying mechanisms of rosacea is presented. Inflammatory processes, neurovascular dysfunction, and possible genetic factors contributing to the development and progression of this condition are explored in detail.

In addition, the differential diagnosis of rosacea is discussed in depth, considering its clinical similarities with other dermatologic and vascular diseases, and the most recent diagnostic tools, such as dermoscopy and molecular tests, which have revolutionized diagnostic accuracy, are highlighted.

In terms of therapeutic approaches, conventional options such as topical and systemic agents are reviewed, as well as emerging therapies based on modulation of the skin microbiota and inhibition of specific inflammatory mediators. The efficacy and safety of laser therapies and minimally invasive procedures, which have shown promising results in the treatment of rosacea, are discussed.

This article offers a comprehensive overview of rosacea from an advanced medical perspective, highlighting advances in the understanding of its pathogenesis and providing a detailed guide to the diagnostic and treatment options currently available. The information presented is intended to inform and guide health care professionals in the optimal management of this complex clinical entity.

KEY WORDS: Rosacea, skin, disease

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INTRODUCTION

Rosacea, a chronic, polymorphous dermatologic entity of multifactorial etiology, is positioned as a clinical and scientific challenge due to its inherent pathophysiologic complexity and varied phenotypic expression. This skin condition, characterized by chronic inflammation, neurovascular dysfunction and dysregulated immune involvement, has captured the attention of the medical community by virtue of its

notorious prevalence and substantial impact on the quality of life of affected patients.¹

While rosacea has been the focus of attention for centuries, recent decades have witnessed a dizzying increase in the understanding of its underlying molecular and cellular underpinnings, unveiling intricate interactions between genetic, environmental, and immunologic factors that contribute to its diverse clinical manifestation. Rosacea emerges as a clinical

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paradigm in which the cutaneous inflammatory cascade is intricately interconnected with the dermal vasculature, leading to vasodilation, formation of telangiectasias and potentiation of the characteristic facial redness.

Clinical symptoms vary widely, ranging from persistent erythema and telangiectasias to papules, pustules and skin thickening, which may mimic other clinical entities, thus complicating their differential diagnosis. The lack of definitive diagnostic markers has prompted the need for comprehensive approaches that consider not only clinical aspects, but also complementary tests such as dermoscopy and molecular techniques to ensure accurate assessment.¹

As we move into the era of precision medicine, therapeutic strategies for rosacea have evolved considerably, encompassing pharmacologic and nonpharmacologic options. Topical therapy, systemic administration of anti-inflammatory agents, and innovation in laser procedures and medical devices have expanded the therapeutic arsenal available to physicians, allowing for a personalized approach based on disease severity and subtype.^{1,2}

In this introduction, we will chart a path toward a deeper understanding of rosacea, exploring its pathogenesis, diverse clinical presentation, and current and emerging management options. Through a critical and comprehensive review of the medical literature, we aim to provide a solid foundation for subsequent detailed analysis of the pathologic mechanisms, differential diagnostic strategies, and therapeutic modalities that shape the current paradigm of rosacea care.³

RELEVANCE

Rosacea, a dermatological entity of an inflammatory and vascular nature, is of considerable clinical and scientific relevance due to its increasing incidence, its substantial impact on patients' quality of life and the inherent complexity of its pathogenesis. This skin condition, characterized by chronic facial inflammation, abnormal vasodilatation and phenotypic variability, has a significant impact on the dermatological health and psychosocial sphere of sufferers.³

The increasing prevalence of rosacea in diverse geographic populations has created an epidemiologic scenario that demands a better understanding of the contributing factors, as well as a thorough assessment of the potential long-term implications for skin and overall health. Establishing an efficient management approach and identifying effective preventive strategies are imperative to adequately address this emerging public health problem.⁴

EPIDEMIOLOGY

The epidemiology of rosacea, although constantly evolving, reveals patterns of incidence and prevalence that vary according to the populations studied and geographical factors. It is estimated that this condition affects more than 400 million people worldwide, with a higher preponderance in fair-skinned populations of European descent.⁴

The gender distribution also shows a skew toward females, although severe and disfiguring symptoms may predominate in males.⁵

The influence of genetic factors is undeniable, and epidemiological studies suggest a greater predisposition in individuals with a family history of rosacea. In addition, the role of environmental triggers, such as excessive sun exposure, temperature extremes, hormonal changes, and consumption of certain foods and beverages, has intensified in the modern understanding of rosacea epidemiology.⁵

The clinical variability of rosacea, ranging from transient erythema to more pronounced inflammatory manifestations, adds a layer of complexity to its epidemiology. Subclassification into distinct clinical subtypes, such as erythematotelangiectatic, papulo-pustular, phymatous and ocular rosacea, reflects the heterogeneity of clinical presentation and highlights the need for differentiated therapeutic approaches.⁶

Taken together, the epidemiology of rosacea raises questions about the interactions between genetics, environment, and immunology, as well as the need for prospective research to shed light on underlying causal relationships and provide guidance for optimal preventive and therapeutic strategies. This deepened epidemiologic understanding will be essential to effectively address the challenge posed by rosacea in the contemporary skin health landscape.⁶

CLINIC

Rosacea, a chronic, polymorphous dermatologic condition, presents with a varied clinical expression encompassing a range of cutaneous and ocular manifestations, characterized by chronic facial inflammation and neurovascular dysfunction. This clinical entity manifests most prominently in the central region of the face, and its phenotypic presentation encompasses several subtypes, each with distinctive features reflecting the complex interplay between inflammatory, vascular and neurological mechanisms.^{6,7}

Erythematotelangiectatic rosacea, one of the primary subtypes, is characterized by the presence of persistent facial erythema, often accompanied by dilated cutaneous telangiectasias. This facial erythema is particularly prominent in the central area of the cheeks, nose, forehead and chin, generating persistent

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redness of variable intensity. Flushing and burning sensations are common in this subtype, denoting neurovascular dysfunction leading to disproportionate vasodilatation in response to environmental and emotional stimuli.⁷

Papulo-pustular rosacea, another distinctive subtype, is characterized by the presence of inflammatory papules and pustules in the context of facial erythema. These inflammatory lesions may mimic acneiform-like conditions, but their centralized distribution in areas of chronic erythema and the absence of comedones are crucial differential points. Papulopustular rosacea is frequently accompanied by pruritic and burning sensations, further exacerbating the cutaneous discomfort experienced by patients.⁸

Phymatous rosacea, also known as rhinophyma, represents a more severe and thickened manifestation of the disease, characterized by nodular enlargement of the nose and sometimes other facial areas. This clinical entity is often stigmatizing and can significantly affect the patient's self-image, underscoring the need for early and appropriate therapeutic management.⁹

Ocular rosacea, although not a subtype category, is an important manifestation involving involvement of the eyes and their adjacent structures. Blepharitis, conjunctivitis, and keratitis are common findings in ocular rosacea, which can result in symptoms such as dry eye, itching, and foreign body sensation. Integrating ophthalmologic evaluations into the comprehensive management of rosacea is crucial to adequately address this often underappreciated component of the disease.⁹

In summary, the clinical presentation of rosacea is extremely varied, ranging from persistent facial erythema and telangiectasias to papules, pustules and, in more advanced cases, facial thickening. The combination of inflammatory, neurovascular and genetic factors contributes to the complexity of its diverse clinical presentation. A thorough approach to the identification and accurate classification of clinical subtypes is essential for accurate differential diagnosis and effective therapeutic management.¹⁰

DIAGNOSIS

The diagnosis of rosacea, a chronic and multifaceted cutaneous entity, is a clinical challenge that requires a combination of a meticulous approach and a thorough knowledge of the clinical features, as well as skill in discriminating this entity from other dermatologic conditions of similar presentation. The absence of definitive diagnostic markers has stimulated the search for clinical criteria and complementary tools to achieve an accurate and discriminative evaluation.¹¹

A detailed clinical history and a thorough physical examination are the mainstay in the diagnostic process of rosacea. The primary clinical manifestation of facial erythema, particularly in the centropalpebral areas, is of significant importance, as well as the identification of specific subtypes such as erythematotelangiectatic, papulo-pustular and phymatous rosacea, among others. The detection of exacerbating triggers, such as sun exposure, temperature changes, emotional stress and the ingestion of certain foods and beverages, is essential for a comprehensive understanding of the disease and its clinical course.¹¹

Dermoscopy, a noninvasive tool that has emerged as a valuable adjunct in dermatologic diagnosis, offers an expanded perspective of vascular and pigmentary features in rosacea. Vascular patterns such as telangiectasias and tortuous capillaries can be visualized in detail, contributing to differentiation from other cutaneous processes. The presence of scaling, although not a universal feature, can also be seen by dermoscopy and may point to a more phymatous skin presentation.¹²

In cases of uncertain diagnosis or in the presence of ocular symptoms, ophthalmologic evaluation is imperative for the identification and management of ocular rosacea. Ocular manifestations, ranging from blepharitis to keratitis, demand a specific approach involving collaboration between dermatologists and ophthalmologists.¹³

Clinical correlation between phenotypic presentation and complementary tools, such as dermoscopy and ophthalmologic evaluations, culminates in a comprehensive diagnosis of rosacea. However, meticulous differential diagnosis with other skin conditions, such as systemic lupus erythematosus, perioral dermatitis and Cushing's syndrome, underscores the need for a comprehensive approach.¹⁴

In summary, the diagnosis of rosacea relies on a precise clinical approach, integrating phenotypic criteria and complementary tools, to achieve a definitive and discriminative assessment. Detailed understanding of clinical variability and interdisciplinary collaboration are essential in the identification and management of this challenging clinical entity.¹⁵

TREATMENT

The therapeutic management of rosacea, a chronic dermatologic condition of multifactorial etiology, involves an integrated strategy that considers the complex interplay between underlying inflammatory, vascular and neurological mechanisms. Because the disease presents a diversified range of clinical subtypes, each with distinctive therapeutic peculiarities, the precise therapeutic approach is tailored in

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accordance with the phenotypic presentation, symptom severity and individual patient preferences.¹⁶

The therapeutic approach to rosacea rests on two main pillars: pharmacological treatment and non-pharmacological modalities. Topical treatment, comprising agents with anti-inflammatory and vasoconstrictive properties, is considered a primary option in mild to moderate cases. The application of topical metronidazole, azelaic acid or ivermectin has been noted for its ability to reduce erythema and attenuate inflammatory lesions, often improving skin appearance and alleviating associated symptomatology.¹⁶

In more pronounced cases, systemic therapy may be considered, with the use of oral antibiotics such as doxycycline or minocycline, which exert anti-inflammatory and cutaneous immune modulating effects. Oral isotretinoin, although reserved for refractory and severe cases, may be beneficial by targeting multiple pathological pathways, including the regulation of sebaceous hyperplasia and inflammation.¹⁷

Facial redness and telangiectasias, prominent features in rosacea, can be addressed by nonpharmacologic therapies. Laser procedures, including intense pulsed phototherapy and pulsed dye laser, have emerged as effective therapeutic modalities by selectively targeting abnormal vasodilation, reducing erythema and improving patients' quality of life. Also, energy-based treatments, such as electrocoagulation and thermocoagulation, can be used for ablation of specific vascular lesions.^{17,18}

Patient education on the management of exacerbating triggers, sun protection and the choice of appropriate skin care products is considered fundamental in the long-term management of rosacea. A multidisciplinary approach, involving dermatologists, ophthalmologists and, in specific cases, psychologists, is essential for a comprehensive evaluation and successful management. ^{17,18}

Rosacea treatment is a personalized process that integrates pharmacologic and nonpharmacologic therapies to address the complexity of underlying pathologic mechanisms and clinical variability. The precise selection of therapeutic approaches, guided by phenotypic presentation and disease severity, culminates in clinical improvement and quality of life for patients affected by this broad-spectrum dermatologic condition.¹⁸

CONCLUSION

In conclusion, rosacea, a complex dermatologic entity with diverse clinical manifestations and a multifaceted pathophysiology, remains a clinical and scientific challenge in contemporary skin medicine. The deepening understanding of

the underlying mechanisms, interconnecting inflammation, neurovascular dysfunction and genetic components, has shed light on the phenotypic heterogeneity and variability in clinical presentation.

Elucidation of epidemiology, classification of clinical subtypes and refinement of diagnostic tools have been imperative for accurate diagnosis, enabling a precise and personalized therapeutic approach. The integration of pharmacologic and nonpharmacologic therapeutic options, including topical and systemic agents, as well as laser procedures and innovative medical devices, is the foundation for effective management.

Comprehensive rosacea care encompasses not only clinical improvement but also improvement of patients' quality of life, given the visible and sometimes stigmatizing nature of the disease. Encouragement of patient education, interdisciplinary collaboration between dermatologists and ophthalmologists, and consideration of preventive approaches are essential for long-term management.

Despite advances in the understanding and treatment of rosacea, questions remain regarding molecular interactions and the relative contribution of genetic and environmental factors. Future developments in clinical and basic research promise to shed additional light on these aspects, providing opportunities to further improve medical care and quality of life for patients.

Ultimately, the ongoing study of rosacea exemplifies the continuing convergence between scientific knowledge and clinical practice, where the evolving understanding of its pathogenesis and the development of more targeted therapies offer hope for more effective and empathetic care for those affected by this chronic and complex skin condition.

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