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# Unmasking Ocular Rosacea: Diagnostic Challenges and Evolving Management

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## Introduction

Ocular rosacea is a chronic inflammatory condition affecting the eyes, and is often associated with cutaneous rosacea. It is a common yet frequently underdiagnosed disorder that can lead to significant ocular morbidity and, in severe cases, vision loss.

## Case Report

A 49-year-old male with a known history of acne rosacea (**Figure 1**) presented with bilateral interstitial keratitis, characterized by subepithelial scarring and neovascularization. A comprehensive workup, including serologic testing for syphilis and a full rheumatologic evaluation, yielded unremarkable findings. During follow-up, the patient experienced a single episode of corneal infectious ulcer, attributed to contact lens wear, which resolved without significant sequelae. Over 15 years of follow-up, his condition has remained stable with ongoing treatment, including oral doxycycline, topical fusidic acid ointment, fluorometholone, and cyclosporine. Imaging studies have demonstrated bilateral irregular astigmatism, corneal thinning, and stromal scarring (**Figure 2**). The patient declined corneal transplantation.

## Discussion

Acne rosacea is a common, chronic skin disorder characterized by telangiectasia, persistent erythema, papules, pustules, and sebaceous gland hypertrophy. It primarily affects the central areas of the face, including the forehead, cheeks, and nose.<sup>1</sup>

Ocular rosacea is estimated to affect up to 75% of patients with acne rosacea, although this

number may be underestimated due to diagnostic challenges.<sup>2</sup> The condition can occur in both adults and children, with a reported age range of 22 months to 85 years.<sup>3,4</sup> Interestingly, ocular symptoms may precede or occur in the absence of cutaneous manifestations in up to 90% of cases, making diagnosis particularly challenging.<sup>2,5</sup>

The pathophysiology of ocular rosacea is complex and not fully understood. Recent research suggests that it involves an interplay of factors, including innate and adaptive immunity, environmental triggers, and neurovascular sensitivity.<sup>2</sup> The role of bacterial lipases, interleukin-1 alpha, and matrix metalloproteinases has been implicated in the development of blepharitis and corneal epitheliopathy associated with the condition.<sup>1</sup> Additionally, variations in the local and systemic microbiome, including *Demodex* infestation, may contribute to the pathogenesis, severity, and different phenotypes of rosacea.<sup>6</sup>

Ocular rosacea presents with a wide spectrum of signs and symptoms, often mimicking other ocular surface disorders. The most common symptoms reported include foreign body sensation and burning.<sup>4</sup> Clinical signs typically involve the eyelids, conjunctiva, and cornea. Frequently observed features include telangiectasia and irregular lid margins, along with meibomian gland dysfunction (MGD).<sup>4</sup> Chronic blepharoconjunctivitis is a hallmark of ocular rosacea, often accompanied by MGD.<sup>7</sup> Corneal involvement, which occurs in approximately one-third of patients, can range from mild punctate epithelial erosions to severe complications such as corneal vascularization, ulceration, scarring, and, in rare cases, perforation.<sup>5,7</sup> These corneal manifestations can lead to decreased visual acuity and, if left untreated, may result in permanent vision loss.<sup>4</sup> A study on pediatric ocular rosacea



**Figure 1. A)** A 49-year-old male with acne rosacea affecting the central facial region, including the forehead, nose, and cheeks **B)** Examination reveals characteristic eyelid involvement, with erythema and telangiectasia; courtesy of Anat Maytal, MD, Johanna Choremis, MD, FRCSC, and Julia C. Talajic, MD, MPH, FRCSC

cases found that 50% of the patients exhibited sterile corneal ulcers.<sup>8</sup> This highlights the importance of early recognition and treatment in the pediatric population to prevent the progression of corneal pathology.

Rosacea has been associated with other systemic disorders, including cardiovascular disease, inflammatory bowel disease, migraines, and depression.<sup>2,6,7</sup> This underscores the need for a comprehensive approach to patient care and potential need for interdisciplinary management.

Diagnosing ocular rosacea is primarily clinical, and is based on the observation of characteristic signs and symptoms.<sup>5</sup> However, the absence of a specific diagnostic test and the variable presentation of the disease can lead to delays in diagnosis, particularly in patients without obvious cutaneous rosacea.<sup>5,6</sup> This is especially true for children, where the condition may be underrecognized.<sup>3,6</sup>

In vivo confocal microscopy has emerged as a valuable tool for analyzing corneal and meibomian gland structures.<sup>9</sup> In patients with rosacea, inflammatory cells can be observed in the corneal tissue. The meibomian glands may appear from hyperreflective to atrophic, and Demodex mites can be observed within the gland follicles. This non-invasive imaging technique can help quantify alterations in the cornea and may aid in the early detection of corneal involvement.

In 2017, the National Rosacea Society Expert Committee established an updated classification

system for rosacea, which includes ocular rosacea as a distinct subgroup.<sup>10</sup> This classification system aids in obtaining more accurate diagnoses and guides treatment strategies.

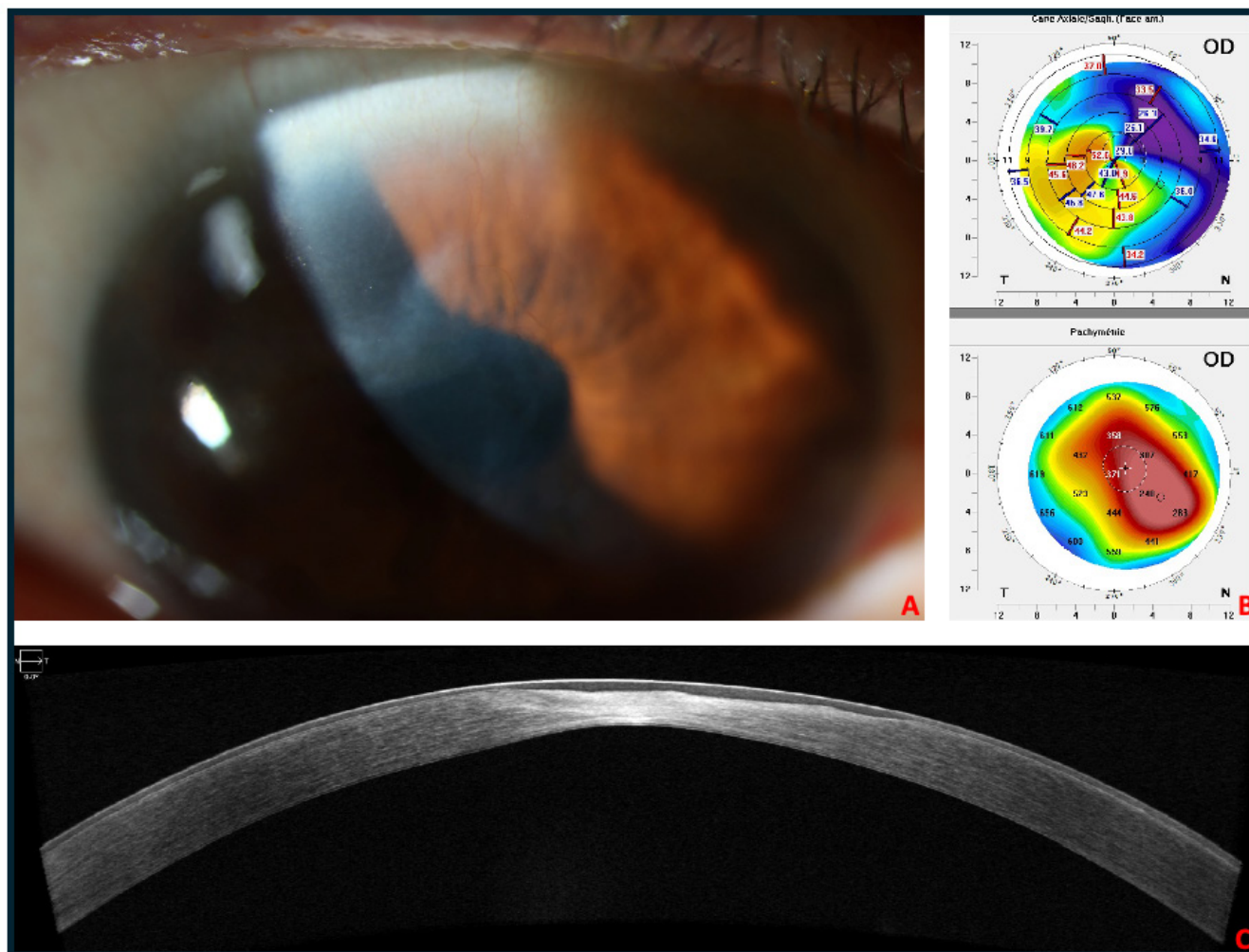
Research has explored diagnostic approaches, such as glycomics analysis of tear fluid. One study demonstrated that tear fluid samples from rosacea patients yielded distinctive oligosaccharide patterns, which could potentially serve as an objective diagnostic marker for the disease.<sup>11</sup> This approach showed promising results, with a reported sensitivity of 100% and specificity of 95.2% in distinguishing ocular rosacea cases from normal controls.

Managing ocular rosacea involves a multifaceted approach, combining patient education, skin care, and pharmacological interventions.

The first-line of defence in managing rosacea is patient education and preventive measures. Patients are advised to avoid specific triggers that can exacerbate symptoms, such as certain foods (including alcohol, caffeine, and spicy foods), environmental factors, and stress. Proper skin care is essential, involving the use of moisturizers to decrease transepidermal water loss and sunscreen to block ultraviolet light.<sup>12</sup>

Pharmacological interventions play a crucial role in managing ocular rosacea, and are typically implemented in a step-wise manner based on the severity of symptoms and clinical findings.<sup>12</sup> Initial therapy often includes supportive





**Figure 2. A)** Corneal involvement is evident, with stromal scarring and neovascularization observed. **B)** Pentacam corneal tomography demonstrates irregular astigmatism and significant thinning. **C)** Anterior segment optical coherence tomography reveals a central hyperreflective area consistent with stromal scarring; courtesy of Anat Maytal, MD, Johanna Choremis, MD, FRCSC, and Julia C. Talajic, MD, MPH, FRCSC

measures such as preservative-free lubricants and warm compresses to improve meibomian gland function.<sup>13,14</sup> Topical antibiotic ointments, particularly erythromycin, are also frequently used to combat the underlying inflammation and bacterial component associated with ocular rosacea.<sup>15</sup> For patients who remain symptomatic despite first-line measures, a short course of low-dose topical corticosteroids, such as loteprednol or fluorometholone, may be introduced and gradually tapered.<sup>16</sup> At this stage, adding immunomodulatory therapy, such as topical cyclosporine, is often considered to address underlying inflammation and support long-term disease control.<sup>17</sup>

For more severe cases, systemic antibiotics, particularly tetracyclines such as doxycycline, are often prescribed.<sup>1,2</sup> These antibiotics not only have

antimicrobial properties but also inhibit matrix metalloproteinases, downregulate cytokines, and suppress angiogenesis, among other anti-inflammatory mechanisms.<sup>18</sup> Even low-dose, slow-release forms of doxycycline have demonstrated significant improvements in ocular symptoms, with effects lasting 6 to 17 months after discontinuing treatment.<sup>19</sup> However, long-term treatment is limited due to side effects involving the gastrointestinal system, photosensitivity, and tooth discoloration in young children.<sup>19</sup> Interestingly, while tetracyclines are widely used, the optimal dosing regimens and treatment efficacy specifically for ocular rosacea have not been rigorously studied.

Recent advancements in understanding the pathogenesis of rosacea have led to new treatment targets. Researchers are exploring

the role of the microbiome, including Demodex infestation, in the development and severity of rosacea, which has led to novel therapeutic approaches.<sup>6</sup> Lotilaner ophthalmic solution 0.25% (XDEMZY®) has emerged as a promising treatment for Demodex blepharitis, receiving FDA approval in July 2023.<sup>20</sup> This novel GABA-Cl inhibitor has demonstrated significant efficacy in eradicating Demodex mites.<sup>21</sup> Clinical trials have shown that lotilaner not only reduces collarette grades and mite density but also improves erythema due to Demodex blepharitis, with effects lasting up to a year after treatment completion.<sup>22,23</sup>

For patients with MGD, intraductal meibomian gland probing has emerged as an effective technique. This procedure has shown significant improvements in symptoms such as discomfort, tearing, and blurred vision, with patients reporting a decreased need for artificial tears and oral medications.<sup>24</sup>

Intense pulsed light (IPL) therapy has emerged as a promising treatment for ocular rosacea, offering relief for patients suffering from associated dry eye disease and MGD.<sup>25,26</sup> This treatment works by delivering high-intensity light pulses to the affected areas, which can help improve the function of meibomian glands and reduce inflammation.<sup>27,28</sup> IPL treatment regimens for ocular rosacea typically involve multiple sessions spaced several weeks apart. A typical protocol begins with three monthly treatments using initial settings of a 560-nm filter, pulse durations of 2.4 and 6.0 ms separated by a 15-ms delay, and a starting fluence of 25 J/cm.<sup>2,29</sup> The optimal treatment parameters may vary depending on the specific IPL system used and the patient's individual characteristics. IPL has also been shown to be effective against Demodex mites. A study observing the real-time effects of IPL on a live Demodex mite demonstrated complete immobilization and destruction of the organism following IPL application.<sup>30</sup>

Radiofrequency (RF) irradiation has also shown promise as a potential treatment for ocular rosacea, particularly in addressing the underlying inflammatory and angiogenic processes.<sup>31</sup> The treatment has been found to reduce keratinocyte proliferation in the epidermis and decrease the expression of pro-inflammatory cytokines and angiogenesis-related factors, including vascular endothelial growth factor (VEGF), a potent angiogenic factor implicated in rosacea pathogenesis. However, the optimal dosing and maintenance protocols for both IPL and RF

treatments have yet to be established to ensure sustained long-term efficacy. Furthermore, the necessity of continuing adjunctive therapies such as tetracyclines, corticosteroids, or cyclosporine remains to be determined.

In cases of corneal complications, which can include vascularization, ulceration, and scarring, more aggressive treatment and close follow-up are usually necessary.<sup>7</sup> Topical treatments may include low-dose steroid preparations and antibiotics to control inflammation and prevent secondary infections. Oral tetracycline derivatives have also shown efficacy in managing corneal manifestations.<sup>3,8</sup> In severe cases, surgical interventions such as corneal transplantation may be necessary.<sup>4</sup>

Ideally, managing ocular rosacea would benefit from a multidisciplinary approach, involving both dermatologists and ophthalmologists.<sup>32</sup> Early recognition and prompt referral for ophthalmologic examination are crucial for preventing permanent eye impairment. Conversely, ophthalmologists should be aware of the potential underlying skin disease when encountering signs suggestive of rosacea.

## Conclusion

In conclusion, ocular rosacea remains a complex and potentially sight-threatening condition that requires early diagnosis and appropriate management. As our understanding of the condition evolves, future research should focus on developing targeted therapies and improving diagnostic criteria. This will help ensure timely intervention and prevent potential vision loss.

NOTE: Specific indications, contraindications, warnings, precautions and safety information exist for these products and therapies. Please consult a clinician and product instructions for use prior to application. Rx only.

As with any case study, the results should not be interpreted as a guarantee or warranty of similar results. Individual results may vary depending on the patient's circumstances and condition.

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## Financial Disclosures

**A.M.:** None declared.

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