

A CASE OF PERIPHERAL ULCERATIVE KERATITIS ASSOCIATED WITH OCULAR ROSACEA

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ABSTRACT

Rosacea is a common, chronic skin disorder characterized by persistent erythema, telangiectasias, papules and pustules in the flush areas of the face and neck. The pathogenesis is not yet clear but the mechanism involved resembles a type IV hypersensitivity reaction. Although it is a common disease, it is usually underdiagnosed by ophthalmologists. The severity of ocular signs ranges from mild blepharoconjunctivitis to vision-impairing corneal involvement such as neovascularization, thinning and in rare instances perforation. Here we discuss the evaluation and management of a patient with rosacea who presented with peripheral ulcerative keratitis.

INTRODUCTION

Under normal conditions the corneal epithelium is firmly attached to the Bowman's membrane by special attachment complexes. They are composed of the hemidesmosomes between the basal epithelial cells, anchoring plaques in Bowman's layer and type VII collagen containing anchoring filaments extending between them (1,2). Consequently any disturbance at this level can predispose to defective epithelial adhesion and repetitive break-down of epithelial cell layer. In the case of further ocular surface compromise by inflammation, denervation, tear deficiency or stromal scarring, the associated failure in epithelial cell migration and proliferation may lead to persistent epithelial defect.

Regardless of the underlying etiology, non-infected corneal ulcers typically begin with a persistent epithelial defect followed by progressive, sometimes rapid corneal thinning. By definition these ulcers develop without microbial invasion, although superinfection is not uncommon and poses considerable risk in these corneas which are already compromised.

Non-infected corneal ulcers can occur in association with a large and heterogeneous group of ocular and systemic diseases (Table I). Therefore it is important to examine the eyelids, tears, corneal sensation in addition to overall general inspection of the patient.

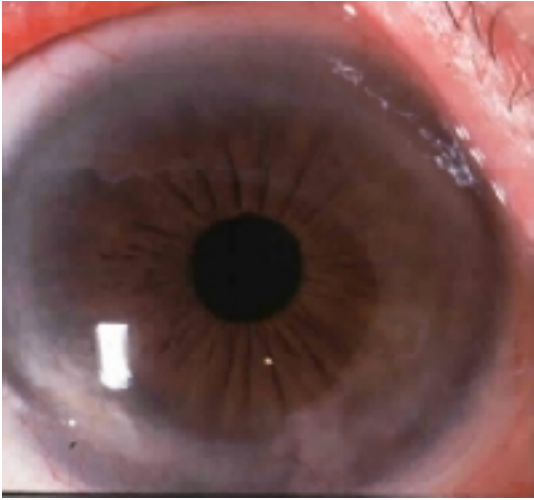
CASE REPORT

A 69 year old white male was referred on March 30, 1995 from the emergency ward at the same hospital with the complaints of redness, pain and tearing in his left eye for two weeks.

Past medical history revealed a cardiac by-pass surgery, cholecystectomy and a hemorrhoidectomy done several years ago.

He also was found to have a corneal ulcer 5 years ago, right upper lid chalazion which was operated 2 years ago, and chronic blepharitis for many years.

On the day of presentation the ophthalmologic examination revealed vision of 20/25 OD, and 20/30 OS. Intraocular pressures were 16 and 17 mmHg right and left eyes respectively. Dilated fundus examination was normal except mild arteriolar attenuation. Slit lamp examination of the right eye revealed arcus senilis, and a 2 + nuclear sclerosis (Figure 1).



The left eye had 3 + conjunctival injection, a peripheral corneal ulcer measuring 4 mm by 8 mm, located inferonasal, and conjunctival pannus adjacent to it (Figure II).



He also had 3 + meibomian gland dysfunction and blepharitis, bilaterally. Upon external examination he was noted to have telangiectasias, papules, erythema on his forehead, cheeks, and chin. He also had sebaceous gland hypertrophy of his nose (Figure III).



He was diagnosed as peripheral ulcerative keratitis secondary to rosacea. The corneal cultures were taken and the patient was started on hourly topical ciprofloxacin 0.3 %, and oral doxycycline 100 mg, qd. On the next day the patient was noted getting better. Few days later, Staph aureus was grown on the cultures, which was sensitive to ciprofloxacin, besides other antibiotics. On April 4, 1995, he also was started on Inflamase 1 % qid, due to the delayed healing of the ulcer. Approximately 2 weeks after the presentation, the ulcer was completely epithelized with a 10-20 % corneal stromal thinning. Thus the patient was asked to return to the clinic in 3 weeks on oral doxycycline and lid hygiene with warm compresses. But he was lost to follow-up till December 20, 1996, when he presented with a peripheral corneal ulcer, this time on his right eye. He had discontinued the oral doxycycline and was not doing the lid hygiene with warm compresses. Again the corneal cultures were taken and he was immediately started on topical ciprofloxacin this time with the topical steroid, Inflamase 1 % qid. Three days later, in the follow-up visit the corneal ulcer was completely epithelized and the patient was comfortable. There was no growth on the cultures. He was asked to continue taking the oral doxycycline and doing lid hygiene with warm compresses.

DISCUSSION

Acne rosacea is a chronic, hyperemic disease of the skin affecting the forehead, nose and the cheeks, characterized by erythema, telangiectasia, papules, pustules, and hypertrophic sebaceous glands (3). The most advanced form of the disease is rhinophyma. The disease is more common in women and although it may begin as early as 2 years of age, usually seen between the ages of 30 and 50 (4). It is common in people of Northern European ancestry. It has been reported in blacks (5) and Japanese (6).

The pathogenesis of rosacea is still unclear. Some authors attribute the lesions to a cell mediated immune response to *Demodex folliculorum* because inflammatory infiltrates including T helper cells can be found around the mites (7). Histopathologic study of conjunctiva in rosacea shows attenuation and infiltration by inflammatory cells, mainly helper-inducer T cells (CD 4), phagocytic cells, and antigen presenting (CD 14 Mac-1) cells. The substantia propria contains large subepithelial infiltrates of inflammatory cells and sometimes granulomas. The mechanisms involved resembles a type IV hypersensitivity reaction (8).

It is known that branched chain fatty acids are present in the meibomian gland secretions in twice the concentration reported for sebaceous secretion. These fatty acids have lower melting points and are important in spreading of tears. Patients with rosacea have smaller fractions of this type of fatty acids. Therefore the abnormal meibum is the possible explanation for the tear film instability in these patients (9). In addition certain fatty acids for example those with 12 carbon backbone are more irritant than others. The burning symptom out of proportion to the clinical

signs in these patients could possibly be explained by this factor (10).

The most common symptoms of ocular rosacea are non-specific and include foreign body, gritty or dry sensation, burning, tearing, or the redness. Frequently the symptoms are out of proportion to the minimal eye findings.

Telangiectasia of the lid margins, meibomian gland dysfunction, and blepharitis are the common forms of lid involvement (11). Lempert reported that 57 % of all patients over age 19 scheduled for chalazion excision had rosacea (12).

Conjunctival involvement in ocular rosacea is usually in the form of a mild bulbar conjunctival hyperemia. Cicatrizing conjunctivitis, conjunctival granuloma, and phlyctenular conjunctivitis are less common conjunctival manifestations (13).

The most common form of corneal involvement is in the form of a superficial punctate keratopathy which usually occurs in the lower 1/3 of the cornea. Peripheral epithelial nodular elevations, recurrent epithelial erosion syndrome, corneal neovascularization with peripheral thinning, and corneal ulcer are the other forms of corneal involvement (13).

Episcleritis, scleritis and vitritis can also be associated with rosacea.

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Episcleritis, scleritis and vitritis can also be associated with rosacea (14)

Decreased tear secretion has also been reported. Lemp using Schirmer I test as a measure of aqueous tear secretion, found a significantly greater prevalence of dry eye in patients with ocular rosacea than in normal controls (15). Zengin et al also reported that oral tetracyclines do not help decreased tear secretion in these patients but improve the tear film break-up time(16).

Duke-Elder stated that rosacea is a common disease that is frequently underdiagnosed (17).

Usually the ophthalmologists fail to inspect the entire face of the patients when performing an ophthalmologic examination. The skin lesions required to confirm a suspicion of ocular rosacea need not be severe. Minor erythema, few papules or pustules may help a questionable diagnosis. Twenty percent of the patients present with the non-specific ocular problems of rosacea, but have not yet developed the skin lesions. In these cases there is no specific test to distinguish rosacea from other diseases causing the same signs and symptoms. Also consultation from a dermatologist is useless (18).

Browning and Proia suggested a set of criteria for the diagnosis of rosacea based on the dermatological and ocular findings (14). They also pointed that the response to a clinical trial of oral tetracyclines may be helpful in confirming a tentative diagnosis.

Treatment of rosacea is multifaceted. Lid hygiene with warm compresses is important to reduce the oil and blepharitic scales around the eyelashes. Here the point should be made to the patient that, the goal is to clean the bases of the lashes and the lid margins, not just the eyelid skin.

Antibiotic ointments effective against Staph such as bacitracin and erythromycin can be used to control the more acute bacterial overgrowth. The patient who wear eye make-up should replace their products on a regular basis to reduce the likelihood of reinoculation.

Aggressive treatment of dry eye is important in relieving the burning symptom. If the artificial tears fail to control patients' symptoms, punctal occlusion should be considered.

Tetracycline is an antibiotic with a broad spectrum of activity (19). Doxycycline and minocycline are the longer acting derivatives. Tetracycline decreases the production of lipase in sensitive and resistant strains of Staph. Lipases act on wax and sterol esters to release free fatty acids that can affect the solubility of other lipids in the tear film or contribute to ocular inflammation (20).

Tetracyclines can also inhibit collagenase by binding to Zn in corneal collagenase (21). They have a favorable effect in the adhesion of healing corneal epithelium. They should be cautiously used in pregnant or lactating women or children under 8 years, because it accumulates in the growing bone and teeth (22). The use of outdated tetracycline causes damage to renal tubules, resulting in Fanconi's syndrome (23). The main side effects are GI and dose related. Allergic reactions include urticaria, fixed drug eruptions, periorbital edema, and morbilliform rash.

Photosensitivity is a toxic reaction.

Metronidazole is broad spectrum antibiotic and antiparasitic which is highly effective in treating dermatologic findings (24). It is not currently available in ophthalmic preparation and therefore cannot be used directly on the lids.

Topical steroids can be useful in managing the keratitis, episcleritis of rosacea, until tetracyclines takes effect. Close follow-up and the lowest concentration of steroid that is effective are recommended. Because the patients with rosacea are prone to rapid corneal melting with higher corticosteroid concentrations (25).

Finally rosacea patients who require penetrating keratoplasty are more prone to graft rejection than other patients not only because their corneas are well vascularized but also the presence of tear film abnormalities.

Table I Etiology of Non-Infected Corneal Ulcers

Local, Not Immune-mediated

Post infectious

Traumatic: chemical burn, thermal burn, radiation burn

Post-surgical: diabetes, keratorefractive procedure

Abnormalities of the eyelids or eyelashes: entropion, ectropion, cicatricial exposure, trichiasis, lagophthalmos, idiopathic incomplete blink, floppy eyelid syndrome

Neurologic disorders: neurotrophic keratitis, neuroparalytic keratitis

Dermatologic disorders: acne rosacea, psoriasis

Local, Immune-mediated

Vernal conjunctivitis

Mooren's ulcer

Staphylococcal marginal ulcer

Post surgical: virgin suture reaction, allograft rejection

Systemic, Not Immune-mediated

Nutritional disorders

Leukemia

Systemic, Immune-mediated

Lacrimal disorders: primary keratoconjunctivitis sicca, Sjogren's syndrome, graft versus host disease

Collagen vascular disorders: relapsing polychondritis, rheumatoid arthritis, systemic lupus erythematosus, periarteritis nodosa, Wegener's granulomatosis

Stevens-Johnson's Syndrome, cicatricial pemphigoid

Allergic disorders: atopic keratoconjunctivitis

(Principles and Practice of Ophthalmology Albert DM, Jacobiec FA, eds. Clinical Practice Chapter 11, p225)

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Review Questions for Rosacea and PUK

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1. Which is a feature of acne rosacea?
 - a. Comedon
 - b. Papulesc.
 - c. Telangiectasia
 - d. Erythema
 - e. Pustules

2. What type of collagen is present in hemidesmosomes?
 - a. I
 - b. II
 - c. III
 - d. IV
 - e. V
 - f. VI
 - g. VII

3. What is/are the most common finding/s of rosacea?
 - a. Telangiectasia
 - b. Meibomian gland dysfunction
 - c. Irregular lid margin
 - d. Chalazia
 - e. All of the above

4. Which is not a finding of rosacea? a. Cicatrizing conjunctivitis b. Peripheral ulcerative keratitis c. Keratoconjunctivitis sicca d. Glaucoma e. Scleritis

5. What is the best treatment for ocular rosacea? a. Warm compress and lid massage b. Oral tetracycline c. Anti-Staphylococcal eye ointment d. Artificial tears e. All of the above

Answers: 1. A (ref. 3) 2. E (ref. 1) 3. E (ref 11) 4. D (ref 13) 5. E (ref 13)