European Journal of Ophthalmology / Vol. 13 no. 4, 2003 / pp. 351-359

Impression cytology and ocular characteristics in ocular rosacea

A.G. KOÇAK-ALTINTAS[1,2], I. KOCAK-MIDILLIOĞLU[1], U. GÜL[3], B. BILEZIKCI[4], O. ISIKSAÇAN[4], S. DUMAN[1]

[1]Department of Ophthalmology, S.B. Ankara Training and Research Hospital, Ankara
[2]Department of Ophthalmology S.B. First Aid and Traumatology Training and Research Hospital, Ankara
[3]Department of Dermatology, S.B. Ankara Training and Research Hospital, Ankara
[4]Department of Pathology, S.B. Ankara Training and Research Hospital, Ankara - Turkey

PURPOSE. *To examine clinical findings and histologic changes on the conjunctival surface in ocular rosacea.*

METHODS. *Thirty-five patients with ocular rosacea and 30 normal subjects underwent dermatologic and ocular examinations. Tear film break-up time, Schirmer tests with and without topical anesthesia, and conjunctival impression cytology were done. Patients were divided into the following groups according to quantity of ocular signs: mild (Group 1), moderate (Group 2), and severe (Group 3). Impression cytology was performed on both upper-bulbar and intrapalpebral inferonasal-bulbar conjunctiva.*

RESULTS. *Patients had significant cell alteration on the conjunctival surface compared with normal eyes. The most frequent ocular signs and symptoms were feelings of dryness and blepharitis. Average tear break-up times for patients with ocular rosacea were 8.2 seconds in Group 1, 5.69 seconds in Group 2, and 5 seconds in Group 3 (17.2 seconds in normal subjects). Schirmer test results with anesthesia were 11.5 mm, 7.6 mm, and 5.0 mm, and without anesthesia were 14.8 mm, 13.6 mm, and 7.0 mm, in Groups 1, 2, and 3, respectively. These results were 18.7 mm with anesthesia and 24.7 mm without anesthesia in normal controls. Schirmer tests and tear film break-up time were significantly lower in patients with ocular rosacea than in normal controls ($p<0.05$). Impression cytology showed that both upper bulbar and inferonasal interpalpebral bulbar ocular surface had significant cell alterations compared with those obtained from normal subjects.*

CONCLUSIONS. *Patients with ocular rosacea not only had decreased tear production but also tear instability. Ocular surface epithelium had significant degeneration in patients compared with normal subjects. (Eur J Ophthalmol 2003; 13: 351-9)*

KEY WORDS. *Impression cytology, Ocular rosacea*

Accepted: November 25, 2002

INTRODUCTION

Acne rosacea is a common chronic skin disease that affects up to 10% of the population. It is characterized by persistent erythema, telangiectasia, papules, and pustules in the flush areas of the cheeks, nose, chin, forehead, and neck (1-3). The classic rhinophyma caused by sebaceous gland hypertrophy is a typical feature of the advanced stage of the disease (4).

Ocular involvement (ocular rosacea) is reported in

3 to 58% of patients depending on gender. The most frequent ocular manifestations are blepharitis, meibomitis, inflamed eyelid margins, scales and crusts of the eyelids, sties, chalazia, blood shot eyes, punctate epithelial erosions, corneal infiltrates, neovascularization, opacity, and perforation (1, 3, 5-7). It has been suggested that all of the ocular findings in rosacea are secondary to eyelid involvement (8). The most common symptoms of ocular rosacea are nonspecific and include burning, stinging, tearing, and foreign body sensation (5).

Many patients with rosacea have decreased tear production and tear instability, which leads to inconsistent ocular surface wetting (6). Patients with dry eye have been reported to have histologic changes of the conjunctiva (9). Conjunctival impression cytology is nonsurgical and is a relatively simple method for obtaining ocular surface cells (9). Twenty percent of patients with rosacea have ocular manifestations initially and these ocular manifestations are nonspecific (10).

The purpose of this study was to evaluate the presenting signs and symptoms, tear film secretion by Schirmer's test, and tear break-up time, as well as their correlation with cell content of the surface conjunctival epithelium by conjunctival impression cytology, in patients with rosacea. The results were compared with those obtained from normal subjects.

PATIENTS AND METHODS

The patients were initially seen for a dermatologic history and examination. The diagnosis of rosacea was based on the presence of telangiectasia of the nose or face, hypertrophic sebaceous glands, papules, pustules, and erythema of the flush areas of the face (6, 11). To support the clinical diagnosis, histopathologic assessments of specimens from affected tissues of patients with rosacea were performed. Thirty-five patients (9 men, 26 women) with ocular rosacea and 30 normal subjects (9 men, 21 women) were studied. All subjects in both groups were white. The mean age of the patients was 48.4 years (range 28–73 years) and mean age of the controls was 42.8 years (range 22–-75 years).

A complete ophthalmologic examination was carried out, including best-corrected visual acuity and slit-lamp biomicroscopy, both with sodium-fluorescein drops, and ophthalmoscopy. Slit-lamp biomicroscopic examination was used to assess irregularity of the posterior lid margin, lid margin vascular injection or telangiectasia, meibomian gland orifice squamous metaplasia, bulbar and palpebral conjunctival hyperemia, papillary hypertrophy on the tarsal conjunctiva, tear film changes such as debris or mucus strands in the preocular tear film, corneal adherent mucus, and other signs (Tab. I). Fluorescein dye staining was performed for evaluation of epithelial changes such as presence of corneal punctate erosions and corneal ulcer. Meibomian gland dysfunction is defined as orifice squamous metaplasia, as evidenced by the presence of white, keratinized plugs, poor to no meibum expression, and lack of active inflammation. Ocular signs were analyzed quantitatively as follows: mild, two or fewer findings (Group 1); moderate, three to four findings (Group 2); and severe, five or more findings (Group 3).

Tear film break-up time (TBUT) was measured using one drop of preservative-free 2% sodium fluorescein. The patient was asked to blink several times to distribute the dye and then to look straight ahead. The examiner observed the tear film with cobalt blue light for development of the first randomly distributed dry spot in the precorneal tear film. The TBUT is recorded as the time between the last blink and the random appearance of the first dry spot. This was repeated three times and then the average TBUT was taken for that eye (1, 12). Fluorescein staining or dry spots on the same area of the corneal surface after every blink or more rapid tear film thinning than elsewhere were considered as a disruption of the ocular surface or manifestation of epithelial cell damage, which excluded them from TBUT evaluation (1, 12).

The Schirmer test was performed without the use of a local anesthetic to estimate physiologic level of tear secretion. The test was repeated with a drop of topical anesthetic to abolish sensory input from corneal and conjunctival epithelium. To exclude excessive reflex tearing, the Schirmer test was always performed without direct light stimuli and nasal stimulation. A standardized Schirmer strip was placed in the outer one third of the inferior cul-de-sac and the patient was allowed to blink at will. Mainly aqueous tear production was measured by the extent of tear uptake into the paper strip in millimeters at the end of 5 minutes. A result of over 5 mm was considered normal (1, 2, 10, 12).

TABLE I - SIGNS OF PATIENTS

Signs	Group 1	Group 2	Group 3	Total
Blepharitis	7 (20.0%)	16 (45.7%)	4 (11.4%)	27 (77.1%)
Papillary hypertrophy	5 (14.3%)	11 (31.4%)	4 (11.4%)	20 (57.1%)
Meibomian gland dysfunction	2 (5.7%)	10 (28.6%)	5 (14. 3%)	17 (48.6%)
Conjunctival hyperemia	1 (2.8%)	10 (28.6%)	5 (14.3%)	16 (45.7%)
Punctate epithelial erosions	1 (2.9%)	8 (22.9%)	4 (11.4%)	13 (37.2%)
Erythema-telangiectasia of lid margin	2 (5.7%)	6 (17.1%)	3 (8.6%)	11 (31.4%)
Pterygium	-	3 (8.6%)	4 (11.4%)	7 (20.0%)
Lithiasis	1 (2.9%)	3 (8.6%)	1 (2.9%)	5 (14.3%)
Corneal vascularization	-	-	2 (5.7%)	2 (5.7%)
Sty-chalazia	-	1 (2.9%)	-	1 (2.9%)
Corneal ulcer	-	1 (2.9%)	-	1 (2.9%)

Ocular surface cells were obtained according to non-invasive and nondestructive conjunctival impression cytology methods (13). Specimens were obtained from the upper bulbar and intrapalpebral inferonasal bulbar conjunctiva using topical anesthesia that did not alter the morphologic appearance of the specimens. Cellulose acetate filter material (Millipore) was cut into pieces measuring approximately 5 x 5 mm. A smooth, toothless forceps was used to grasp one end of the filter and was gently pressed onto the conjunctiva. The filter was left in place for several seconds and then gently removed with a lifting motion. After the specimens were obtained, they were placed in a fixative solution containing 95% ethanol, and stained with periodic acid–Schiff (PAS). The specimens were examined according to Nelson et al's classification of morphologic appearance of conjunctival epithelial and goblet cells (13), as described in the following.

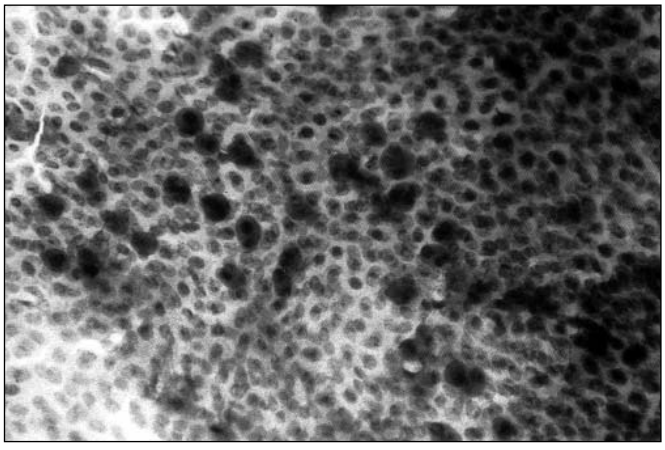

Fig. 1 - *Impression cytology of Grade 0 (periodic acid–Schiff stain, x200 magnification).*

Grade 0: The epithelial cells are small and round with eosinophilic staining cytoplasm. The nuclei are basophilic and large with a nucleocytoplasmic ratio (N/C) of 1:2. The goblet cells are abundant, plump, and oval and have an intensely PAS-positive cytoplasm (Fig. 1).

Grade 1: The epithelial cells are slightly larger and more polygonal and have eosinophilic-staining cytoplasm. The nuclei are smaller (N/C of 1/3). Although the goblet cells are decreased in number, they still have plump, oval shape with an intensely PAS-positive cytoplasm (Fig. 2).

Grade 2: The epithelial cells are large and polygonal and have variable staining cytoplasm. The nuclei are smaller (N/C of 1/4 to 1/5) and some epithelial cells are multinucleated. The goblet cells are markedly decreased in number and are smaller and less intensely PAS-positive with poorly defined cellular borders (Fig. 3).

Grade 3: The epithelial cells are large and polygonal with basophilic-staining cytoplasm. The nuclei are small and pycnotic and, in many cells, absent. N/C is greater than 1/6. The goblet cells are absent (Fig. 4).

As required dy this grading system specimens were graded in blind fashion by the same pathologists (B.B., D.I.). None of the patients used topical or systemic agents at the time of examination. For statistical evaluation, the chi-square test was used.

RESULTS

The ages of the patients with rosacea and subjects in the control group were similar. All the patients with acne rosacea had subjective symptoms included in our study. The most frequent ocular symptoms were dryness, foreign body sensation, irritation, itching, and tearing. Ocular symptoms of patients are presented in Table II. All of the patients showed signs of ocular disease. The grading for ocular signs of the patients was as follows: Group 1 (mild signs), 11 patients (31.4%); Group 2 (moderate signs), 18 patients (51.4%); and Group 3 (severe signs), 6 patients (17.1%). The ocular findings of patients are listed in Table I. Control subjects with objective ocular signs were excluded from this study.

Eight patients (72.7%) with mild ocular signs had an abnormal TBUT (<10.0 seconds), as did 11 patients (61.1%) in Group 2 and all 6 patients in Group 3 with severe ocular rosacea. The mean TBUT was 6.2 seconds in all patients with ocular rosacea (8.2 seconds in Group 1, 5.7 seconds in Group 2, and 5.0 seconds in severely affected Group 3). Mean TBUT was 17.2 seconds in normal subjects. TBUT was significantly reduced in patients with acne rosacea, mainly with severe ocular rosacea (Group 3) ($p<0.05$).

Schirmer test with anesthesia showed an average of 11.5 mm of wetting at baseline secretion for patients in Group 1, 7.6 mm in moderately affected Group 2, 5.0 mm in Group 3, and 18.7 mm in normal subjects. The differences among the patients and control subjects were statistically significant ($p<0.05$). Conversely, patients with fewer ocular symptoms had increased Schirmer values. Schirmer test results without anesthesia showed that the average values were 14.8 mm in patients with mild ocular signs, 13.6 mm in moderately and 7.0 mm in severely affected Group 3, and 24.7 mm in normal controls. The difference was statistically significant between normal subjects and patients ($p<0.05$).

Impression cytology was performed on 24 patients. According to epithelial and goblet cell morphologic features of upper bulbar conjunctiva of Group 1, 6 patients (25%) showed Grade 0, 2 patients (8.3%) showed Grade 1, 1 patient (4.1%) showed Grade 2, and no patient showed Grade 3 differentiation. After analyzing the inferonasal bulbar conjunctiva in the mild ocular signs group (Group 1), 3 patients (12.5%) demonstrated Grade 0, 3 patients (12.5%) Grade 1, and 3 patients (12.5%) Grade 2 differentiation.

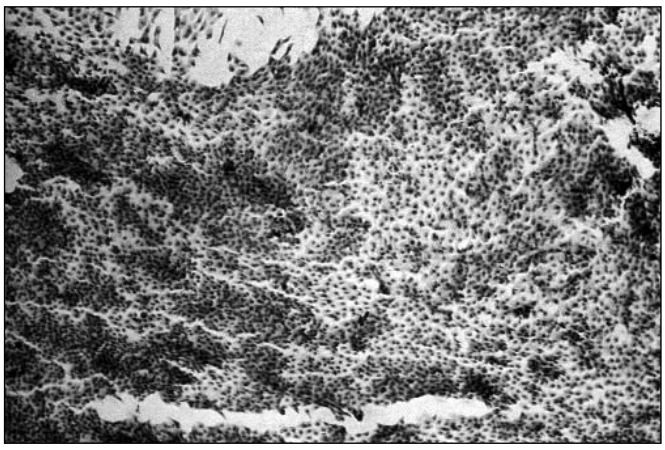

Fig. 2 - *Impression cytology of Grade 1 (periodic acid–Schiff stain, x50 magnification).*

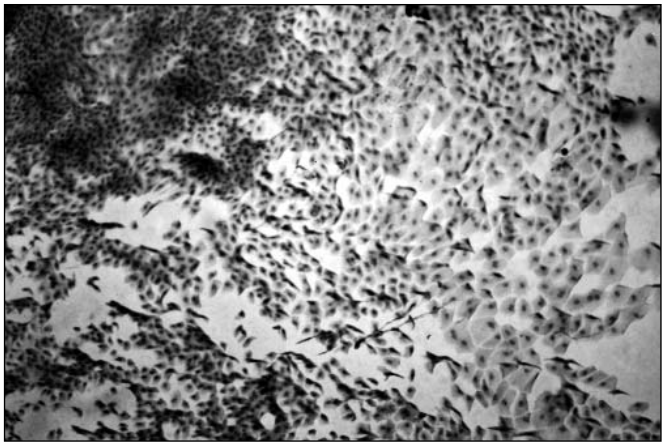

Fig. 3 - *Impression cytology of Grade 2 (periodic acid–Schiff stain, x100 magnification).*

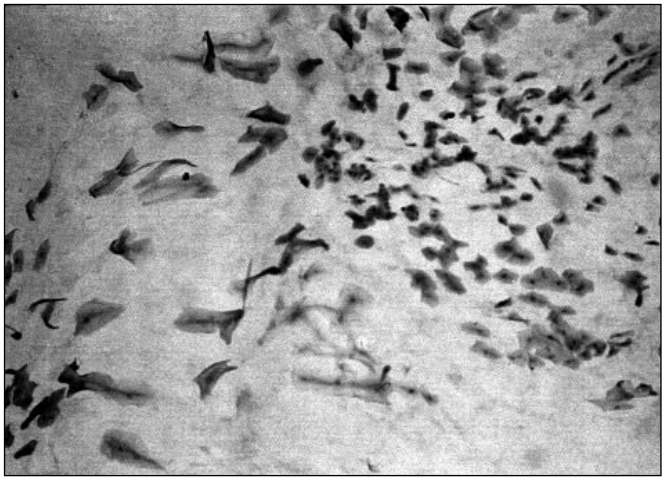

Fig. 4 - *Impression cytology of Grade 3 (periodic acid–Schiff stain, x100 magnification).*

TABLE II - SYMPTOMS OF PATIENTS

Symptoms	Group 1	Group 2	Group 3	Total (%)
Dryness	11 (31.4%)	11 (31.4%)	4 (11.4%)	26 (74.3%)
Irritation	8 (22.9%)	10 (28.6%)	5 (14.3%)	23 (65.7%)
Foreign body sensation	6 (17.1%)	12 (34.3%)	5 (14.3%)	23 (65.7%)
Itching	7 (20.0%)	9 (25.7%)	4 (11.4%)	20 (57.1%)
Tearing	6 (17.1%)	4 (11.4%)	1 (2.9%)	11 (31.4%)
Redness	3 (8.6%)	4 (11.4%)	1 (2.9%)	8 (22.9%)
Lid rusting	-	4 (11.4%)	-	4 (11.4%)
Stinging	-	3 (8.6%)	-	3 (8.6%)
Photosensitivity	-	2 (5.7%)	-	2 (5.7%)
Swelling	-	1 (2.9%)	-	1 (2.9%)

TABLE III - IMPRESSION CYTOLOGY RESULTS OF PATIENTS

	Group 1		Group 2		Group 3		Total	
Grade	UB	IN	UB	IN	UB	IN	UB	IN
Grade 0	6 (25%)	3 (12.5%)	3 (12.5%)	0 (0%)	2 (8.3%)	2 (8.3%)	11 (45.8%)	5 (20.8%)
Grade 1	2 (8.3%)	3 (12.5%)	5 (20.8%)	5 (20.8%)	2 (8.3%)	2 (8.3%)	9 (37./%)	10 (41.7%)
Grade 2	1 (4.2%)	3 (12.5%)	2 (8.3%)	3 (12.5%)	1 (4.2%)	0 (0%)	4 (16.7%)	6 (25%)
Grade 3	0 (0%)	0 (0%)	0 (0%)	2 (8.3%)	0 (0%)	1 (4.2%)	0 (0%)	3 (12.5%)

UP = Upper bulbar; IN = Inferonasal bulbar.

In Group 2 with moderate ocular signs, 3 patients (12.5%) had Grade 0, 5 patients (20.8%) had Grade 1, 2 patients (8.3%) had Grade 2, and no patient had Grade 3 differentiation on upper bulbar conjunctiva and 5 patients (20.8%) had Grade 1, 3 patients (12.5%) had Grade 2, 2 patients (8.3%) had Grade 3, and no patient had Grade 0 differentiation on inferonasal interpalpebral conjunctiva.

Of the patients with severe ocular signs, 2 (8.3%) showed Grade 0, 2 (8.3%) had Grade 1, 1 (4.2%) had Grade 2, and none had Grade 3 differentiation on upper bulbar conjunctiva. In this group, 2 patients (8.3%) had Grade 0, 2 (8.3%) had Grade 1, none had Grade 2, and 1 (4.1%) had Grade 3 differentiation on inferonasal conjunctiva (Tab. III).

A total of 11 patients (45.8%) had normal conjunctival cytology (Grade 0), 9 patients (37.1%) had Grade 1 and 4 patients (16.7%) had Grade 2 cell alteration on specimens obtained from upper bulbar conjunctiva, and none had Grade 3 changes. Five cases (20.8%) had normal cell structure but 10 cases (41.7%) had Grade 1, 6 cases (25%) had Grade 2, and 3 cases (12.5%) had Grade 3 changes on inferonasal conjunctiva. Thirteen (54.2%) specimens from upper bulbar and 19 (79.2%) specimens obtained from interpalpebral inferonasal conjunctiva had a different grade of cell alterations from normal structure.

The upper bulbar and inferonasal interpalpebral ocular surfaces of eyes from normal controls were Grade 0 except in two normal subjects who had Grade 1 differentiation on both sides of conjunctiva.

There was a statistically significant difference in the grading of both upper bulbar and inferonasal interpalpebral impressions between patients with ocular rosacea and normal controls ($p<0.05$). The difference was more prominent in inferonasal interpalpebral impressions in all groups. Statistical analysis was not performed between groups according to localization of impression cytology owing to insufficient numbers in each subgroup.

DISCUSSION

Although ocular rosacea is common, because of highly variable ocular signs and symptoms, it is frequently undiagnosed (1, 14). Because no specific histopathologic pattern has been identified, diagnosis of patients in whom ocular problems develop initially is difficult. Ocular involvement is usually seen between the third and fifth decades (15, 16). In our study the mean age was 48.4 years, and the youngest patient was 28 years.

Most patients with acne rosacea are adult white women. Rosacea without ocular involvement affects women two to three times as often as men (17). Cases with ocular manifestations are about evenly divided between the sexes and ocular complications may be more severe in men (2, 3, 6). In our study, there was a female preponderance. In addition, all of our patients applied initially to the dermatology clinic and then were referred to the ophthalmology department. Dermatologic examination showed that all of them had cutaneous rosacea and all patients had ocular manifestations as well.

The most common ocular symptoms of rosacea are nonspecific and include dryness, foreign-body sensation, burning, tearing, and redness. Dryness (74.3%), foreign-body sensation, and irritation (65.7%) were the most frequent ocular symptoms in our patients. Frucht-Pery and associates (6) reported that foreign body sensation was the most common symptom, occurring in 18 of 24 patients; dryness and itching (52.0%) were the most frequent symptoms in the series of Quarterman et al (1).

The ocular manifestations of rosacea range from minor problems such as blepharitis to sight-threatening problems such as corneal neovascularization, thinning, and perforation. Meibomian gland disease is recognized as a common cause of ocular irritation, which has been reported to occur in 50 to 93% of patients with rosacea (18, 19). Akpek et al (2) observed lid margin telangiectasia in 81%, meibomian gland dysfunction in 78%, and blepharitis in 65% of patients in their study. Among the ocular signs, 94% of the patients had erythema and telangiectasia of the eyelids as the most common ocular sign and meibomian gland dysfunction was the second most common finding in the Quarterman et al series (1). Hope-Ross et al (12) observed meibomian gland dysfunction in all of their patients. The most frequent findings in our study were blepharitis in 27 patients (77.1%), papillary hypertrophy in 20 patients (57.1%), and meibomian gland dysfunction in 17 patients (48.6%).

Keratoconjunctivitis sicca has been described in patients with ocular rosacea (2, 21-25). Gudmundsa et al (22) observed an abnormal Schirmer test in 56% of patients with rosacea. Akpek et al (2) observed keratoconjunctivitis sicca in 34 of 131 patients confirmed by Schirmer test with topical anesthesia. The same test result with anesthesia was normal in the Quarterman et al series (1). Barton et al (25) found 14 mm of wetting in Schirmer test without topical anesthesia, which was lower than the age-matched control subjects' 20 mm and 22 mm. We performed Schirmer test without anesthesia to measure physiologic level of tear secretion and the use of anesthesia to exclude corneal and conjunctival reflex stimulation to estimate mainly basal secretion. The Schirmer test results were found to be decreased in our patients compared to the controls. The decrease in Schirmer test with anesthesia was more reminder than that without anesthesia. Even the test with anesthesia has been shown to reduce tear flow to lower levels than physiologic levels and to abolish excessive reflex tearing due to increased corneal and conjunctival irritation, which is common in patients with epithelial surface problems such as ocular rosacea; therefore, it is a better reflection of the aqueous tear component. Quarterman et al (1) were able to demonstrate a short TBUT of a mean 5.7 seconds in 94% of their patients. Barton et al (25) observed decreased TBUT of 4 seconds, which was significantly shorter than that of age-matched or control subjects. The mean TBUT was 6.24 seconds in our study and it was significantly reduced compared to control subjects. The TBUT may be considered a test of tear function in which stability of the tear film is examined. Meibum lipids, which constitute the superficial tear layer, stabilize the tear film and prevent aqueous tear evaporation. Meibomian gland dysfunction results in deficiency in the lipid component of tear fluid with increased tear evaporation and changes of such tear functions as TBUT (23, 24).

Barton et al (25) found a significant reduction in tear turnover in patients with rosacea. Afonso et al (18) also reported delayed tear clearance rate in patients with rosacea – a feature of aqueous tear defi-

ciency and increased evaporative tear loss due to meibomian gland disease. Delayed tear clearance has been reported to be associated with increased activity of proteolytic enzymes in tear fluid, including plasmin, neutrophil-derived elastase, neutrophil chemotactic factors such as complement components, inflammatory cytokine interleukin 1α (IL-1α), and gelatinase-B. One explanation for the elevated concentration and activity of these mediators in ocular rosacea is increased production or release by epithelial cells on the ocular surface. Another possibility is delayed clearance of these factors from the ocular surface because of reduced tear turnover. Barton et al (25) observed significantly elevated proinflammatory cytokines of tumor necrosis factor-α (TNF-α), which is not normally present at the ocular surface, supporting the theory that elevation of tear inflammatory mediators is largely related to delayed tear turnover. The inverse correlation between IL-1α concentration and Schirmer test suggests that reduced tear turnover may be the main reason for the elevated IL-1α level in patients with rosacea (23). IL-1α is known to increase the production and activity of certain enzymes of the matrix metalloproteinase (MMP) family, including collagenase and gelatinases that degrade extracellular matrix and could contribute to the development of the eyelid and ocular surface destruction in rosacea (18, 23, 25, 26). Epidermal growth factor is a reparative cytokine secreted by the lacrimal gland that is a normal component of tear film. Epidermal growth factor concentration in patients with rosacea is increased in response to chronic ocular surface disease (23, 27, 28). These elevations are believed to be mostly the result of reduced tear turnover, possibly an important cause of ocular surface disease in patients with rosacea (23, 27, 28). Both Schirmer test and TBUT were inversely related to the degree of ocular involvement in our patients: the lower the Schirmer tests scores and the more reduced the TBUT, the greater the number of ocular signs.

Ocular surface epithelial changes can be evaluated by brush cytology, excisional biopsy, or noninvasive methods of impression cytology (our preference). To compare the two extreme sides of conjunctiva, where one side is less exposed to environmental conditions such as drying effect and meibomian glands, and the other side is more exposed to those factors. We prefer to obtain conjunctival samples from the superior bulbar conjunctiva, which is covered by the upper eyelid, and from the infranasal interpalpebral conjunctiva, which is in direct contact with meibomian glands and inferior eyelid margin. The results of impression cytology show that both upper bulbar and inferonasal interpalpebral bulbar ocular surfaces have significant cell alteration, with decreased, abnormal, and absent goblet cells. Although goblet cells are predominantly located in inferonasal bulbar conjunctiva near the limbus, the conjunctival degeneration were more advanced in inferonasal bulbar conjunctiva with decreased or absent goblet cells compared with upper bulbar conjunctiva. Epithelial and goblet cell abnormalities were more significant in interpalpebral bulbar conjunctiva in comparison with upper bulbar ocular surface. This may be explained by the protective effect of the upper lid on the upper bulbar conjunctiva. Additionally, environmental drying effects and closer opposition with meibomian glands may be responsible for the abnormalities in interpalpebral bulbar conjunctiva.

Meibomian gland dysfunction gives rise to qualitative differences in meibum lipid composition. Lee et al (24) found squamous metaplasia in the eyelid margin and in the tarsal conjunctiva in the inferior tarsal site. They also found evidence suggesting that the pathologic process of the meibomian gland dysfunction can spread to the orifice, the surrounding eyelid margin, and even the tarsal conjunctiva in patients with lipid tear deficiency (24).

Tseng (23) postulated that the pathogenesis of conjunctival epithelial alteration may be due to vascular pathology and intense inflammation, which may introduce different factors to facilitate the epithelial metaplasia. Hoong-Xuan et al (4) observed perivasculitis in the conjunctival substantia propria of 62.5% and granulomatous inflammation in half of the patients with acne rosacea on histopathologic study of conjunctiva. They stated that derangement of the conjunctival epithelium, presence of inflammatory cells within it, and subepithelial infiltrates might suggest an exogenous contact stimulus as the cause of the conjunctival inflammation (4). Abnormal meibomian gland secretions in the tear film could act as irritants and contribute to the secondary degeneration. We did not take excisional biopsy, therefore we could not evaluate the extension of inflammatory process as a perivasculitis that are seen in substantia pro-

pria deeper layer of conjunctive but epithelial metaplasia and decrease of goblet cells were observed as superficial cell changes. In our study, this was seen more prominently in the interpalpebral area with close contact to meibomian glands. According to our impression cytology, which shows decreased or absent goblet cells in inferonasal interpalpebral conjunctiva, aqueous tear deficiency and lipid tear deficiency are accompanied by mucin deficiency in patients with ocular rosacea.

In conclusion, although there is no diagnostic test for acne rosacea and none of the findings of the disease are specific, the histologic appearance of the conjunctival surface seems to correlate with both the rate and the content of tear production; tear film abnormality may be caused by an abnormal lipid composition due to meibomian gland dysfunction. Clinical signs, tear film functions, and histologic findings must be evaluated together for correct diagnosis of acne rosacea.

Reprint requests to:
Ayse Gül Kocak Altıntas, MD
Kenedi cad No 72/12
Kavaklıdere
Ankara 06660, Turkey
inci@softhome.net

REFERENCES

1. Quaterman MJ, Johnson DW, Abele DC, Lesher JL, Hull DS, Davis LS. Ocular rosacea signs, symptoms, and tear studies before and after treatment with doxycycline. Arch Ophthalmol 1997; 133: 49-54.
2. Akpek EK, Merchant A, Pınar V, Foster CS. Ocular rosacea patient characteristics and follow-up. Ophthalmology 1997; 104: 1863-7.
3. Barnhorst DA, Foster JA, Chern KC, Meisler DM. The efficacy of topical metronidazole in the treatment of ocular rosacea. Ophthalmology 1996; 103: 1880-3.
4. Hoang-Xuan T, Rodriguez A, Zaltas MM, Rice BA, Foster CS. Ocular rosacea. a histologic and immunopathologic study. Ophthalmology 1990; 97: 1468-75.
5. Knox CM, Smoljn G. Rosacea. Int Ophthalmol Clin 1997; 37: 29-40.
6. Frucht-Pery J, Sagi E, Hemo I, Ever-Modani P. Efficacy of doxycycline and tetracycline in ocular rosacea. Am J Ophthalmol 1993; 116: 88-92.
7. Wilkin JK. Rosacea pathophysiology and treatment. Arch Dermatol 1994; 130: 359-62.
8. Hoang-Xuan T, Rodriguez A, Zaltas MM, et al. Ocular rosacea. A histologic and immunopathologic study. Ophthalmology 1990; 97: 1468-75.
9. Nelson JD, Havener VR, Cameron JD. Cellulose acetate impressions of the ocular surface. Arch Ophthalmol 1983; 104: 1869-72.
10. Browning DJ. Tears studies in ocular rosacea. Am J Ophthalmol 1983; 99: 530-3.
11. Jenkins MS, Brown SI, Lempert SL, Wemberg RJ. Ocular rosacea. Am J Ophthalmol 1979; 88: 618-22.
12. Hope-Ross MW, Chell PB, Kervick GN, Mc Donnell PJ. Recurrent corneal erosion: clinical features. Eye 1994; 8: 373-7.
13. Nelson JD, Havener VR, Cameron JD. Cellulose acetate impression of the ocular surface-dry eye state. Arch Ophthalmol 1983; 104: 1869-972.
14. Browning DJ, Rosenwasser G, Lugo M. Ocular rosacea in blacks. Am J Ophthalmol 1986; 101: 441-4.
15. Erzurum SA, Feder RS, Greenwald MJ. Acne rosacea with keratitis in childhood. Arch Ophthalmol 1993; 111: 228-30.
16. Browning DJ, Proia AD. Ocular rosacea. Surv Ophthalmol 1986; 31: 145-58.
17. Berg B, Liden S. An epidemiological study of rosacea. Acta Derm Venereal 1989; 69: 419-23.
18. Afonsa AA, Sabrin L, Manroy DC, Selzer M, Lukeshwar B, Pflugfelder SC. Tear fluid gelatinase B activity correlates with IL-1α concentration and fluorescein clearance in ocular rosacea. Invest Ophthalmol Vis Sci 1999; 40: 2506-12.
19. Afonsa A, Manroy D, Tseng SCG, Stern M, Pflugfelder SC. Diagnostic sensitivity and specificity of Schirmer test and fluorescein clearance test for ocular irritation. Ophthalmology 1999; 106: 803-10.
20. Hope-Ross MW, Chell PB, Kervick GN, Mc Donnell PJ. Oral tetracycline in the treatment of recurrent corneal erosions. Eye 1994; 8: 384-8.
21. Lemp MA, Mahmood MA, Weiler HH. Association of rosacea and keratoconjunctivitis sicca. Arch Ophthalmol 1984; 102: 556-7.

22. Gudmundsen KJ, O'Donnel BF, Powel FC. Schirmer testing for dry eyes in patients with rosacea. J Am Acad Dermatol 1992; 26: 211-4.
23. Tseng SCG. Staging of conjunctival squamous metaplasia by impression cytology. Ophthalmology 1985; 92: 728-33.
24. Lee SH, Tseng SCG. Rose Bengal staining and cytologic characteristics associated with lipid tear deficiency. Am J Ophthalmol 1997; 124: 736-50.
25. Barton K, Monroy DC, Nava A, Pfugfelder S.C. Inflammatory cytokines in the tears of patients with ocular rosacea. Ophthalmology 1997; 104: 1868-74.