Clinical Evaluation of Corneal Diseases Associated with Floppy Eyelid Syndrome

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We examined 18 cases of floppy eyelid syndrome, first reported in the Orient, in patients ranging in age from 11 to 55 years (mean 24 years); 16 were men and two were women. In contrast to previous reports in which almost all patients were obese men, only three of our patients were mildly obese. The most common abnormal corneal finding was punctate epithelial keratopathy (five patients - 28%). Keratoconus was detectable in three patients (17%) overall; it was bilateral in one case and unilateral in two. Other miscellaneous corneal findings were corneal astigmatism and corneal opacity. In two cases, we found a familial tendency to skin hyperextensibility and joint hypermobility, and in one case, floppy eyelid syndrome developed after pars plana vitrectomy. The pathogenesis of the syndrome is still unknown, but our findings suggest that the more important pathogenetic risk factors are not obesity and sleeping pattern, but genetic collagen and/or elastin abnormality.

Key words: floppy eyelid syndrome, papillary conjunctivitis, keratoconus, corneal astigmatism, corneal opacity

INTRODUCTION

Floppy eyelid syndrome was first reported by Culbertson and Ostler in 1981. The syndrome is characterized by a loose upper lid that can be readily everted on elevation of the lids, tarsal laxity, and diffuse papillary conjunctival changes involving the upper lid. This syndrome is an uncommon and frequently unrecognized cause of chronic unilateral or bilateral papillary conjunctivitis and superficial punctate keratitis. The purpose of this paper is to determine the nature of the corneal disorders associated with floppy eyelid syndrome.

CASE REPORTS

The medical records of the department of ophthalmology of Chung Ang University Hospital were reviewed to find all patients who were seen with the diagnosis of floppy eyelid syndrome from Jan. 1991 to Dec. 1993. A retrospective review of each of these 18 patients’ medical records and photographs was performed, and data were collected on the patients’ age, sex, corneal findings, and other ocular abnormalities.

Case 1

A 51-year-old man had a history of bilateral ocular discomfort for several years. The symptom was most noticeable upon awakening in the morning. He slept face down. The upper eyelids were floppy and easily everted. The palpebral & bulbar conjunctiva were injected and there were large papillae on the palpebral conjunctiva. There was also a fine punctate staining of the corneal...
epithelium (Fig. 1). The lesions were bilateral but more pronounced in the left eye. We advised the patient to have his eyelids taped shut during the night. Resolution of symptom and papillary conjunctivitis was noted.

Case 2

An 18-year-old woman had a history of conjunctival injection for several years (Fig. 2A). Her medical history was not significant. Visual acuity with correction was 20/50 bilateral. External ocular examination revealed marked laxity of both upper eyelids. These lids were easily everted by gently pulling the lid margin superiorly (Fig. 2B). The tarsal plates appeared soft, rubbery, and easily folded on themselves. His hand joint was hypermobile (Fig. 2C), and skin was hyperextensible. These findings were noted also in his mother. Slit lamp examination of both eyes revealed the tarsal conjunctiva to have a diffuse papillary reaction and mild injection. The bulbar conjunctivas were also mildly injected. The diffuse mild corneal opacity in anterior stroma was noted bilaterally. The

Fig. 1. Diffuse superficial punctate keratitis stained with fluorescein.

Fig. 2. A: Not obese woman with floppy eyelid syndrome. B: Tarsal plate is soft and rubbery and can be readily folded on itself. C: Wrist & hand joint hypermobility.
remainder of the results of the anterior segment examination were normal. Similarly, results of the examination of the pupils, motility, confrontation fields, and fundus were normal. Keratometric readings were approximately 45.5/45.0 (55°), OD and 44/43.5 (170°), OS. The corneal density was measured with a Scheimpflug camera (EAS-1000, Nidek, Japan). Both corneal densities were 255 CCT (Computer Compatible Tapes), in contrast to normal corneal density of 120-130. Videophotokeratoscopy of both cornea showed mixed astigmatism. She was advised to wear eyeshields at night on both eyes in combination with oral doxycycline treatment.

Case 3

A 21-year-old man presented a chief complaint of gradually decreasing vision in the right eye. Best corrected visual acuity was OD: -1.5 Dsp, 20/200 and OS: -1.5 Dsp, 20/200. External ocular examination revealed a marked redundancy and loss of elasticity of the skin of his face and lids. These lids were easily everted by simply pulling upward on the lateral aspects of the upper lid. His hand joint was hypermobile, and his skin was hyperextensible. Slit lamp examination of both eyes revealed palpebral conjunctival injection without any evidence of papillary conjunctivitis. The corneas were clear: However the right corneal finding was consistent with keratoconus. Apical corneal stromal thinning was found in the right eye. Keratometric readings were approximately 44/48 (150°), OD and 47/47.5 (90°), OS. The Corneal thickness was measured with a Scheimpflug camera (EAS-1000, Nidek, Japan). The right corneal thickness was 0.42 mm and the left corneal thickness was 0.53 mm. Videophotokeratoscopy of the right cornea demonstrated the typical clinical keratoconus pattern of inferior steepening: the left cornea showed slight inferior steepening (Fig. 3A, B). We recommended wearing an eye shield on the right eye while sleeping.

Case 4

A 22-year-old man presented a chief complaint of gradually decreasing vision in the right eye. Best corrected visual acuity was OD: -0.5 Dsp, 20/200 and OS: -4.0 Dsp; -1.0 Dcyl 180, 20/20. The superior lids were extremely flaccid. They everted easily in a rolling fashion with gentle upward pressure. There was a papillary conjunctival reaction of the upper and lower palpebral conjunctiva. The right corneal findings were consistent with early keratoconus. Apical corneal stromal thinning was found but Fleischer rings were not present. Keratometric readings were approximately 47.5/51 (180°), OD and 45.5/44.5 (180°), OS. Videophotokeratoscopy of the right cornea demonstrated the typical clinical keratoconus pattern of inferior steepening: the left cornea showed slight inferior steepening (Fig. 3A, B). We recommended wearing an eye shield on the right eye while sleeping.

Fig. 3. A: Videophotokeratoscopy of right cornea demonstrated typical keratoconus pattern of inferior steepening. B: Normal left cornea with slight inferior steepening.
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pattern of inferior steepening, the left cornea showed slight inferior steepening. We recommended wearing a hard contact lens on the right eye.

Case 5

A 30-year-old man had a history of red eyes bilaterally for 1 year. He complained of mucous discharge bilaterally, especially in the morning, with some redness and irritation. He had been treated with a variety of topical medications without relief. Both upper lids were floppy and everted easily. The conjunctiva had a papillary reaction with mucous threads noted over the surface of the cul-de-sac. The patient noted no preference in sleep position. Schirmer testing following topical anesthesia revealed wetting of 1mm bilaterally at five minutes. Tear break-up time was 3 seconds in each eye. The patient was treated with frequent application of preservative free artificial tears and lubricating ointment with taping at night. Three months later, the patient reported marked improvement in his symptoms of irritation and mucous discharge.

RESULTS

Of the 17 patients with floppy eyelid syndrome, 15 cases were men, and 2 cases were women. The patients ranged in age from 11 to 55 years (average 24 years). The most common abnormal corneal finding was punctate epithelial keratopathy (4 patients-24%) which was usually diffuse. Keratoconus was detectable in 3 patients (17%) overall. Keratoconus was bilateral in 1 case and unilateral in 2 cases. Two cases of clinical keratoconus and 1 case of subclinical were found. Other miscellaneous corneal findings were corneal astigmatism and corneal opacity. An extracorneal finding was dry eye syndrome in 4 patients (24%). These results are summarized in Table 1.

Table 1. Associated corneal abnormalities in 17 cases of floppy eyelid syndrome

<table>
<thead>
<tr>
<th>Corneal disease</th>
<th>No. of patients (%)</th>
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<tr>
<td>Superficial punctate keratitis</td>
<td>4 (24)</td>
</tr>
<tr>
<td>Keratoconus</td>
<td>3 (18)</td>
</tr>
<tr>
<td>clinical</td>
<td>2 (12)</td>
</tr>
<tr>
<td>subclinical</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Corneal astigmatism</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Corneal opacity</td>
<td>1 (6)</td>
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it upward, (2) a soft, rubberty tarsus that can be easily folded, and (3) chronic papillary conjunctival response.1,3

All the patients had symptoms of chronic ocular irritation or foreign body sensation. There was a eye reddening and mucous discharge, worse on awakening in the morning.1 The hallmark characteristic of floppy eyelid syndrome is its resistance to standard topical therapies. Floppy eyelid syndrome may be unilateral or bilateral and may affect both upper and lower eyelids.3 Conjunctival papillary hypertrophy, diffuse superficial punctate keratitis, rapid tear film break up time, and conjunctival injection are usually present.1 While patients with floppy eyelid syndrome usually have several of the classic signs and symptoms, the severity of complaints and clinical findings may vary considerably. Parunovic2 describes patients with unilateral floppy lids who had corneal and conjunctival lesions on both eyes, and he also reports cases of patients with floppy eyelids and no symptoms. Fleishman and Hoffman4 reported a case with loose upper eyelids and irritative symptoms with no accompanying papillary conjunctivitis. They state that floppy eyelid syndrome probably represents a clinical continuum ranging from the asymptomatic patient with rare nocturnal erosion to the patient with the complete syndrome. Differential diagnosis includes acne rosacea, vernal keratoconjunctivitis, conjunctival neoplasia, superior limbic keratoconjunctivitis, trachoma, molluscum contagiosum, and medicamentosa.5

Culbertson et al.6 reported that the most common corneal disorder in floppy eyelid syndrome is punctate epithelial keratitis, occurring in 45% of all patients. Keratitis was typically diffuse and was usually found only in the involved eye. We noted 5 cases (28%) of punctate epithelial keratitis in 18
cases of floppy eyelid syndrome. The cause of primary diffuse punctate keratitis in floppy eyelid syndrome is uncertain, but its diffuse distribution suggests that the papillary response on the upper tarsus plays a role.\textsuperscript{6} Clinically detectable keratoconus was present in 10\% of all patients. This confirms the earlier reports of keratoconus associated with floppy eyelid syndrome by Parunovic and Iliac\textsuperscript{7} and Donnenfield et al.\textsuperscript{8} Surprisingly, five (71\%) of seven randomly selected patients who had no clinical evidence of keratoconus were found to have a videokeratoscopic pattern consistent with keratoconus.\textsuperscript{9-15} We detected 3 cases (17\%) of keratoconus in 18 cases of floppy eyelid syndrome, 2 cases were bilateral. Also we found 1 case of corneal opacity associated with floppy eyelid syndrome, it was first report in floppy eyelid syndrome.

Tarsal conjunctival scraping of the upper lid revealed a predominant polymorphonuclear (PMN) leukocyte response. Cuhbertson and Ostler\textsuperscript{1} reported that biopsy specimens from the upper tarsus typically showed conjunctival keratinization, papillae and thickening of the epithelium. Eyelid cultures typically only grew Staphylococcus epidermidis.\textsuperscript{1,3,16}

The sequence of events and pathogenetic mechanisms that lead to floppy eyelid syndrome are uncertain. Most patients sleep face down with the affected eye pressed against the pillow or their hand. Obese patients who sleep face down often have low arterial oxygen tension due to poor ventilation often aggravated by sleep apnea. In addition, the face-down posture may cause local pressure-induced ischemia in the tarsus. When the patient moves and the pressure on the lid is temporarily relieved, reperfusion of the lid occurs that may lead to localized free-radical-induced damage to the tarsus.\textsuperscript{17,18} This damage may attract PMN leukocytes to the area, with resultant formation of papillae and gradual further damage to tarsal collagen and adjacent structure such as corneal stroma and endothelium. The histopathology of the upper tarsus revealed that tarsal elastin is decreased in floppy eyelid syndrome. Decreased amounts of tarsal elastin may play a role in the development of tarsal laxity.\textsuperscript{19}

Appropriate treatment should begin with the cessation of all topical medications except those used for associated conditions. Patients with significant tear film abnormalities should be placed on ocular lubricants such as Tears naturale\textsuperscript{®}, preferably unpreserved, and instructed to tape their lids shut at bed time. Hypoallergenic tapes, sterile eye patches, or eye shields have been recommended to prevent mechanical trauma to the upper tarsal conjunctiva and cornea.\textsuperscript{1,3} Horizontal surgical lid shortening is an alternative to shielding the eye. Surgical eyelid shortening is the definitive treatment of floppy eyelid syndrome. The surgical procedures performed generally include resection and/or excision of the lateral portion of the upper eyelid. Dutton\textsuperscript{20} describes the surgical treatment of four floppy eyelid patients who had experienced little improvement in signs or symptoms from eye shielding. Gernal et al.\textsuperscript{21} performed a tarsal strip procedure on 1 floppy eyelid syndrome patient who experienced complete relief from symptoms and involution of the papillae. Moore, et al.\textsuperscript{22} performed lid tightening surgery on 3 patients whose symptoms and inflammatory signs postoperatively improved dramatically.

We treated our patients with nocturnal eyelid shielding, taping, and local lubricants such as Tears naturale\textsuperscript{®}. We experienced symptom relief in almost all cases, but in intractable cases, oral doxycycline hyclate, known as a more potent inhibitor of collagenase by Stack et al.\textsuperscript{23} and tetracycline ointment, known as a scavenger of PMN-generated reactive oxygen compounds by Lauhio et al.\textsuperscript{24}, were used. The symptom was relieved in most patients. So we did not adopt the horizontal surgical lid shortening procedure.

Earlier reports of floppy eyelid syndrome indicated that it occurred almost entirely in obese men. But in our Oriental cases only 3 cases (17\%) overall were mildly obese, 2 cases occurred in women and most patients had no preference in sleep position. Also familial tendency of joint hypermobility and skin hyperextensibility was found in 2 patients. These are great differences compared with previous reports (Table 2). The possible pathogenesis is that reperfusion oxidation & local pressure induced lid ischemia have played a role in aggravating factors in patients who have
Table 2. Differences between our report and previous reports in floppy eyelid syndrome

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<tr>
<th>Characteristics</th>
<th>Previous reports(^{1-3})</th>
<th>Our report</th>
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<tr>
<td>General appearance</td>
<td>almost all obese</td>
<td>obesity 17%</td>
</tr>
<tr>
<td>Sleep pattern</td>
<td>face down sleep pattern</td>
<td>no preference</td>
</tr>
<tr>
<td>Joint hypermobility</td>
<td>absent</td>
<td>2/18 (11%) present</td>
</tr>
<tr>
<td>Skin hyperextensibility</td>
<td>absent</td>
<td>2/18 (11%) present</td>
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genetic collagen and/or elastin abnormality. Therefore the more important pathogenetic factors of floppy eyelid syndrome are not obesity and sleeping pattern, but genetic collagen and/or elastin abnormality. Further studies will be focused to determine the accuracy of this theory using molecular biological method.

REFERENCES