Dendriform corneal epithelial lesion due to floppy eyelid syndrome

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Introduction

Floppy Eyelid Syndrome (FES) is an entity characterized by upper eyelid hyperlaxity, allowing the eyelid to evert easily. Epidemiologically, it is common in obese men and is associated with obstructive sleep apnea syndrome (OSAS). This excess in eyelid laxity may be asymptomatic or predispose to certain alterations in the eye. At the level of the cornea and ocular surface, FES is associated with a variety of symptoms including tearing, ocular redness, foreign body sensation, mucous secretions, dryness and superficial punctate keratitis. It often occurs during the first hours of the day and is usually more pronounced if the patient has the habit of sleeping in lateral prone position. In most severe cases, it can lead to keratoconus, corneal ulcers and loss of visual acuity (1-3).

The examination of the eyelids and tarsus should not be overlooked where papillary tarsal reaction and chronic inflammation can be found as well as blepharitis, ectropion, entropion, blepharochalasis and ptosis, among others (1-3).

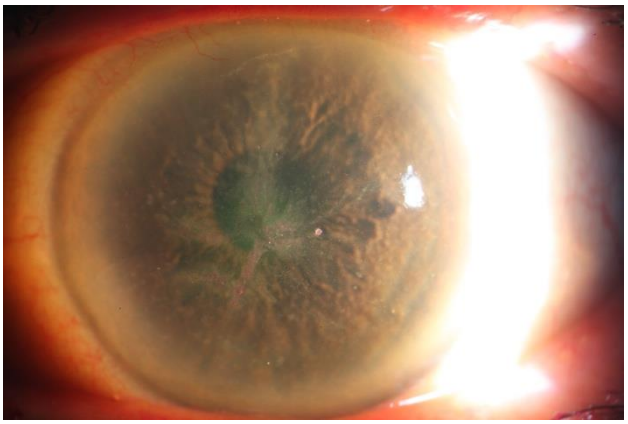
Meanwhile, the appearance of a dendriform lesion at the corneal epithelium should lead to a suspicion of epithelial herpetic keratitis caused by HSV1 (4). However, other possible differential diagnoses where pseudo dendriform lesions are present should be borne in mind such as HZV keratitis (5), tyrosinemia (6), toxic keratoconjunctivitis (7) or in the early onset of Acanthamoeba keratitis, especially in contact lens wearers (8).

Case presentation

We present a case of a 64-year-old male patient who came in with loss of vision in the left eye for 3 years. He had been visited by different ophthalmologists with the diagnosis of herpetic epithelial keratitis. He has had several episodes of recurrence, the last one being a month ago. He has currently been treated with acyclovir 200 mg orally per day and artificial tears on demand.

On examination, best corrected visual acuity (BCVA) was 1.0 in the right eye and 0.15 in the left eye. Biomicroscopy revealed seborrheic blepharitis in both eyes while in the left eye, irregular corneal epithelium was observed in the middle one-third of the cornea that stained with fluorescein as well as Rose Bengal in a dendriform pattern (Figure 1 and 2). Mild central superficial corneal opacity was also detected. On this first visit, the patient was diagnosed with recurrent herpetic keratitis and eyelid hygiene,

artificial tears every hour and tears gel at bedtime were prescribed as well as continuing with oral acyclovir 800 mg per day.



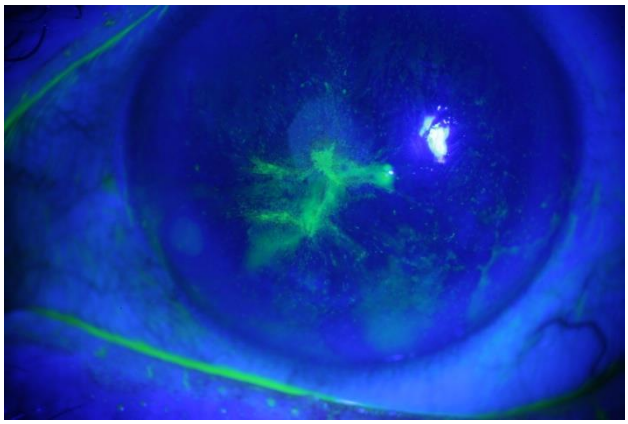
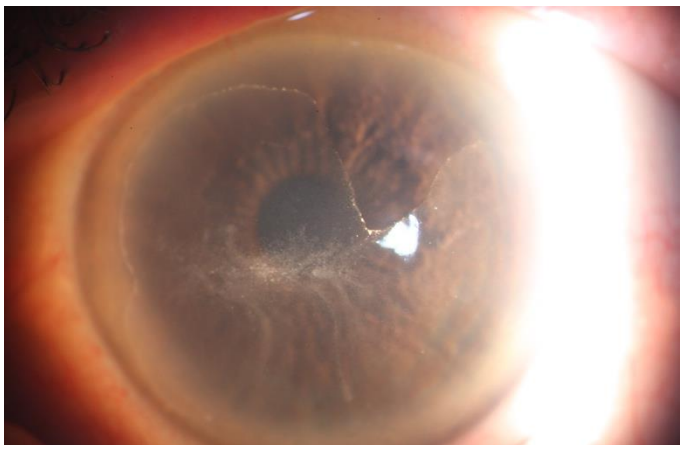


Figure 1 and 2. Left eye - Irregular corneal epithelium especially in middle one-third of the cornea. Fluorescein staining shows a positive staining in a dendriform pattern.

On subsequent visits, the patient reported no symptomatic improvement. On examination, he continued to have the same corneal dendriform epitheliopathy and central superficial corneal haziness. Based on this clinical evolution, toxic corneal epitheliopathy due to chronic use of topical antiherpetic ointment was considered and 50% autologous serum was added hourly for a few months with no improvement. On one visit, the patient mentioned that he had been using soft contact lens to correct his myopia for many years until his eye problem started 3 years ago and that between episodes of "herpetic keratitis", he had never completely regained vision. Taking this into consideration, acanthamoeba keratitis was suspicious and whole corneal epithelium was removed and taken for HSV and acanthamoeba PCR test. While awaiting the results, topical Chlorhexidine and Diamidine every two hours were started. Two weeks later, hazy corneal epithelium grew over almost the entire cornea with a demarcation line separating normal from abnormal epithelium at the superior part of the cornea. Central irregular epithelium was observed in a vortex-like pattern (Figures 3 and 4). Epithelial mapping topography depicted abnormal thickening of entire corneal epithelium except for the peripheral superotemporal and inferonasal areas corresponding to clinically normal epithelium observed by biomicroscopy (Figures 5 and 6). On the other hand, PCR for both microorganisms were negative.



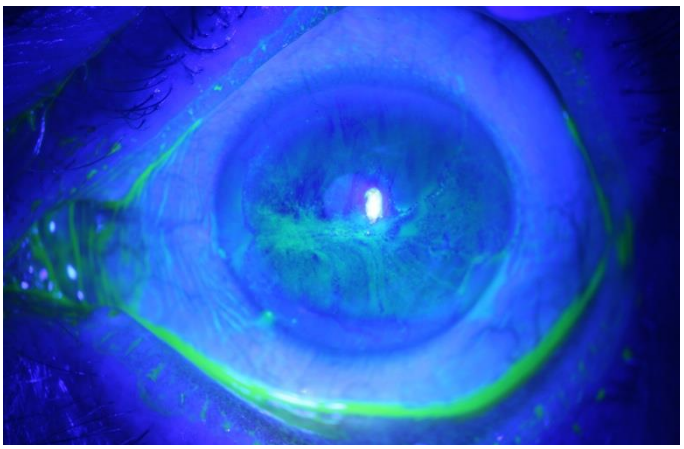
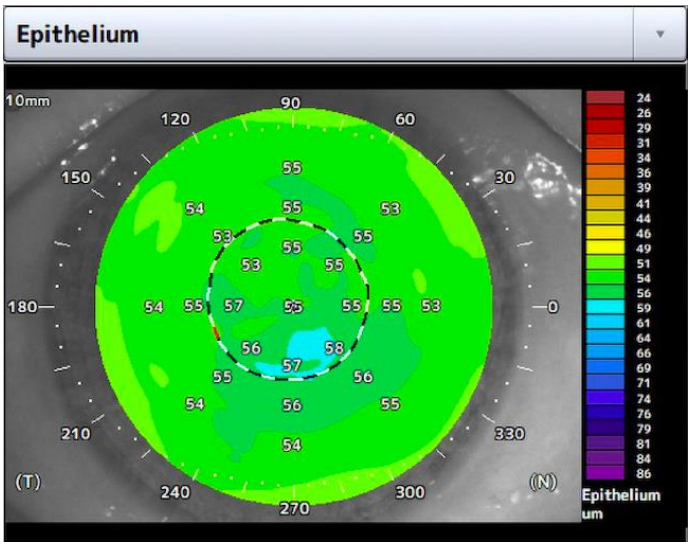


Figure 3 and 4. Left eye – Demarcation line in the superior part of the cornea with an irregular epithelium in the central part. Fluorescein staining shows a positive staining in a vortex-like pattern.



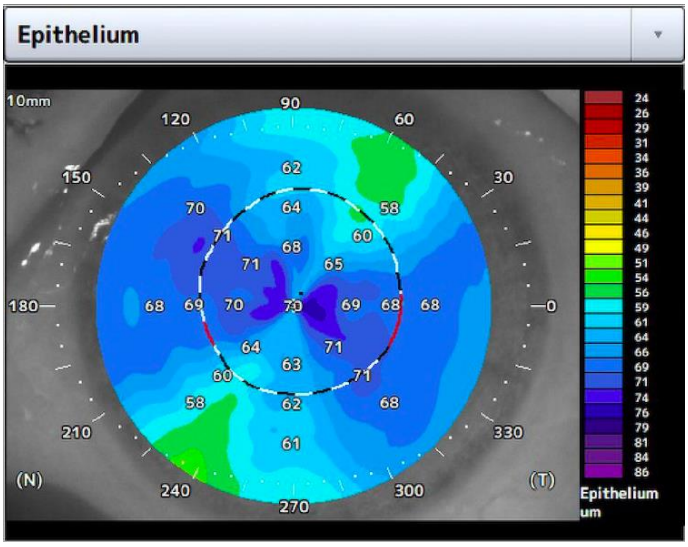


Figure 5 and 6. Right and left eye epithelial topography – Comparison of both eyes shows an augmented thickness in the epithelium of the central part of the left eye cornea, coinciding with the hazy corneal epithelium observed in Figure 3

Since both HSV and acanthamoeba keratitis were ruled out and taking into account the unilateral chronic growth of an abnormal corneal epithelium, total epithelium curettage was carried out again for biopsy to rule out corneal intraepithelial neoplasia (CIN). Meanwhile, upper eyelid hyperlaxity was detected on examination, especially left upper eyelid. Patient's habits were asked thoroughly when it was revealed that he used to snore and has been sleeping in left lateral decubitus position with face down on the pillow all his life (Figure 7). Therapeutic contact lens was placed over the cornea and an eye shield was given to protect his left eye at bedtime. Topical tobramycin 3 times a day, 50% autologous serum every hour and dexamethasone eye drop 3 times a day with tapering off regimen were prescribed. The result of the biopsy revealed stratified flat epithelium with no cellular atypia nor mitosis, thus ruling out CIN.

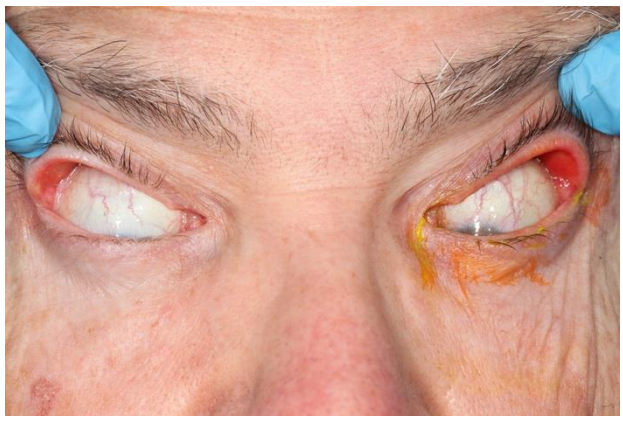
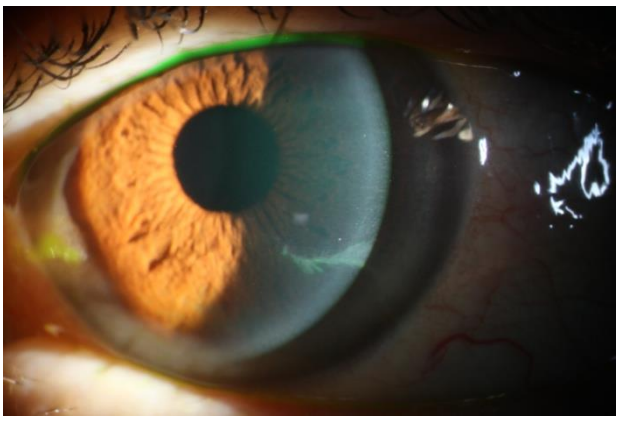


Figure 7. Both eyes - Examination shows an increased laxity of upper eyelids, especially in the left eye.

On one month follow-up, the patient refers improvement in his vision and has no eye discomfort. On examination, BVCA in his left eye was 1.2 and the corneal epithelium was entirely normal except for a mild advancing waved-like epitheliopathy at inferotemporal periphery with negative fluorescein staining (Figures 8 and 9).



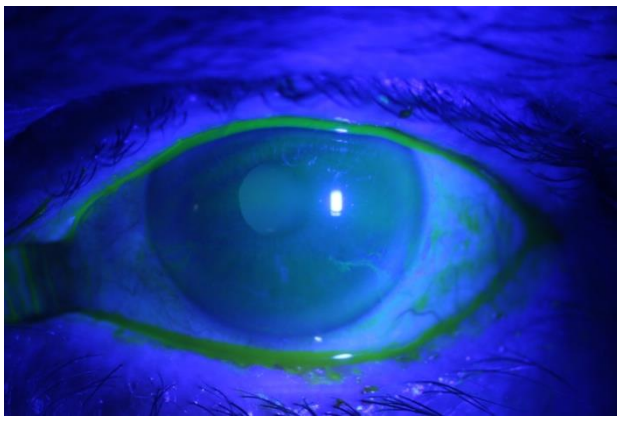


Figure 8 and 9. Left eye – Normal corneal epithelium can be observed with no epithelium haziness nor demarcation line. Mild infero-temporal waved-like epitheliopathy shows negative fluorescein staining.

Discussion

The term FES has been the subject of discussion in the literature over the years, as there is no consensus on what it implies. Early published cases, such as the one presented by Culberston WW et al. (9) described FES as a set of corneal surface irritation symptoms associated with an increased laxity of the upper eyelids in obese men. Subsequently, other authors such as Van den Bosch et al. (10) or Fowler et al. (11) introduced the term Lax eyelid syndrome (LES) as an entity that groups together all types of patients with chronic papillary conjunctivitis and ocular surface irritation related to upper eyelid hyperlaxity, regardless of the origin of this hyperlaxity, the sex or the BMI of the patient, entering FES as a subtype of LES. However, there is no clear consensus on when to use each term, since the pathogenesis of the eyelid laxity caused by FES is not fully described (1), so we have decided to use the term "Floppy Eyelid Syndrome" in this article even though the patient in our case did not have high BMI.

Furthermore, the association between FES and OSAS was described by authors such as Woog J. (12) and subsequently corroborated in studies such as those carried out by Ezra RG (13) or Mojon et al. (14). In the latter, palpebral laxity and ocular surface scans were performed on patients who were candidates for polysomnography due to suspicion of OSAS, finally confirming this correlation. However, according to the study carried out by Fox TP et al. (15) also comparing the relationship between FES and OSAS

with polysomnography and measuring eyelid laxity, the results are contrary to those described above, demonstrating that there is no association between the two entities. In the case of our patient, he does not have OSAS diagnosed by polysomnography, but presents symptoms suggestive of this pathology.

The corneal involvement in FES is variable. Regardless of irritation symptoms, the relationship with keratoconus is the most common, either clinically or subclinically (1, 13, 16). However, no cases with dendriform epitheliopathy have been published in the literature. In our case, taking this finding into consideration, we must first rule out the most likely causes that could lead to this clinical manifestation such as herpes simplex epithelial keratitis and acantamoeba keratitis which were ruled out later on with the lack of response to the treatment and with PCR test.

On the other hand, CIN is a slow-growing type of epithelial neoplasm without involvement beyond the corneal epithelium presenting with a thickened and translucent appearance. It often involves the adjacent conjunctiva but this is not a requirement. Histologically, it is a dysplasia of the epithelial cells, which does not affect the basement membrane (17). The gold standard for diagnosis is biopsy (18) however, we can be guided by corneal epithelial topography to assess the possible diagnosis and the extent of the lesion. In our case, the diagnostic suspicion of CIN is also supported by the performance of this complementary test, where we can see a thickening of the epithelial layer at the central level, compared to that of the contralateral eye (Figures 10 and 11). Subsequently, following the biopsy, CIN was ruled out.

The chronic progressive unilateral corneal epitheliopathy in our patient was most likely caused by mechanical rubbing during sleep due to upper eyelid hyperlaxity. This led to ocular surface inflammation and limbal stem cells alterations causing abnormal epithelial growth almost over the entire cornea. Therapeutic contact lens, eye shield protection during sleep and topical autologous serum were the clues to restore normal corneal epithelial growth and to prevent its alteration.

Conclusion

The role of the eyelids in maintaining the homeostasis of the ocular surface is of utmost importance. For this reason, we should not overlook their examination when there is an alteration of the corneal epithelium, especially in cases of palpebral malposition, incomplete palpebral closure, or marked hyperlaxity, as in our case.

Thorough anamnesis such as sleep habits and eye lid exploration are essential to reach the right diagnosis and the cause of ocular surface pathology.

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