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Review

Ocular surface inflammation impairs structure and function of meibomian gland☆

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ABSTRACT

Dysfunction of the meibomian glands alters secreted meibum quantitatively and qualitatively that can lead to damage to the ocular surface epithelium. In response to an unstable tear film cause by meibomian gland dysfunction, ocular surface epithelium is damaged and expresses inflammatory cytokines leading to secondary ocular inflammation. In turn, inflammatory disorders of the palpebral conjunctiva and lid margin may affect the structure and function of meibomian gland. The disorders include allergic conjunctivitis, long-term usage of contact lenses, dermatological diseases that affect conjunctival homeostasis, Stevens-Johnson's syndrome or chemical burning of the ocular surface and lid margin.

Contents

1. Introduction

Meibomian glands locate to the tarsal plates of the upper and lower eyelids and the orifice of the gland is opened at the lid margin. The glands play a critical role in ocular surface homeostasis. Lipid components secreted by the gland function as a barrier to prevent excess evaporation of the water component of the tear fluid. Therefore, dysfunction of the meibomian glands (MGD) leads

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to an impairment of ocular surface lubrication and wetness (dry eye syndrome) as well as induction of local inflammatory responses in the ocular surface. In turn, Suzuki et al. (2015) proposed a concept of one unit, i.e., the "meibomian gland and ocular surface" by encountering patients with meibomitis (an inflammatory form of MGD) of which successful management is essential to the treatment of inflammation in the ocular surface.

The etiology of MGD includes terminal duct obstruction and/or qualitative or quantitative changes in the glandular lipid secretion, impairing ocular surface homeostasis. In turn, we have noticed that primary ocular surface inflammation may also effect the function of the meibomian glands. In the present article we review the abnormalities of the meibomian glands in association with primary ocular surface inflammatory diseases.

2. Conjunctivitis and meibomian gland

It was reported that conjunctivitis affects the structure of meibomian glands as revealed by non-invasive meibography. Distortion of meibomian gland ducts were found to be significantly greater in patients with allergic conjunctivitis (Fig. 1, case 1) or atopic-keratoconjunctivitis (Ibrahim et al., 2012). Conjunctival inflammation could be associated with the meibomian gland abnormalities in eyelids of the patients with vernal keratoconjunctivitis (Wei et al., 2015). Continuous mechanical stress to the tarsal tissue by eye rubbing might be one of the causes (Arita et al., 2010; Ibrahim et al., 2012). Rynerson and Perry proposed a clinical entity named as DEBS (dry eye and blepharitis). Blepharitis caused by bacterial colonization in the lid margin could cause follicular inflammation, then MGD (Rynerson and Perry, 2016). Blepharokeratoconjunctivitis also causes loss of the gland as evaluated by non-invasive meibography (Yin and Gong, 2016). It was reported that treatment of posterior blepharitis and conjunctival inflammation due to MGD were treated with topical 1% azithromycin suppressed expression levels of IL-1β, IL-8, and MMP-9 mRNA. On the other hand, expression of TGFβ1 increased during treatment and does not decline after drug withdrawal, suggesting this growth factor contribution to the anti-inflammatory activity of azithromycin in MGD (Zhang et al., 2015). Because in other tissue TGFβ1 could be pro-inflammatory, it is to be further investigated if cytokines produced by inflammatory cells in the conjunctiva/subconjunctiva directly damage the acini via palpebral conjunctiva.

3. Contact lens wearing

Contact lens wearing impairs the function of meibomian gland. Mechanical stress and/or chronic, sub-clinical inflammation could be proposed as underlying mechanism, although it is to be further investigated detailed pathobiology of conjunctival inflammation associated with long-term contact lens wearing. One of the commonly observed characteristics in contact lens-related meibomian gland pathology was orifice pouting/plugging (Cox et al., 2016). Inflammation in the meibomian glands can be detected as punctate hyperreflective components by using in vivo laser scanning confocal microscopy (Fasanella et al., 2016). This technique of observation showed the presence of gland dropout, duct obstruction, and glandular inflammation in meibomian glands of contact lens wearers (Villani et al., 2011).

Soft contact lens could induce allergic reaction in the ocular surface epithelium or palpebral conjunctiva. This might also be the case in contact lens-related allergic conjunctivitis; the condition is associated with an increase in meibomian gland distortion (Fig. 1, case 2). The authors conclude that the allergic reaction, rather than contact lens wear, appears to be responsible for abnormal configuration of meibomian gland in patients with contact lens-related allergic conjunctivitis (Arita et al., 2012).

4. Medication-related meibomian gland diseases

Topical instillation of drugs might also cause ocular surface inflammation, leading secondarily to the damage of meibomian gland. For example, obstructive type of meibomian gland disorders were observed in patients treated with topical anti-glaucoma prostaglandin derivatives (Fig. 1, case 3) (Mocan et al., 2016). Although the exact mechanism underlying the condition is to be investigated, it is known that prostaglandin derivatives could damage the ocular surface epithelium resulting in the induction of local inflammation.

Currently, there is no evidence showing systemic medication induced MGD is due to inflammation. However, it was suggested that systemic medication also could damage the gland or impair its secretory function. We reported patients with loss of meibomian glands with superficial punctate epitheliopathy during treatment of cancer with an anticancer TS-1® combination capsules of tegafur, gimeracil, and oteracil potassium (Taiho Pharmaceutical Co. Ltd, Japan) (Mizoguchi et al., 2015) (Fig. 2). The possible mechanism underlie TS-1®-related MGD might be similar to the obstruction of

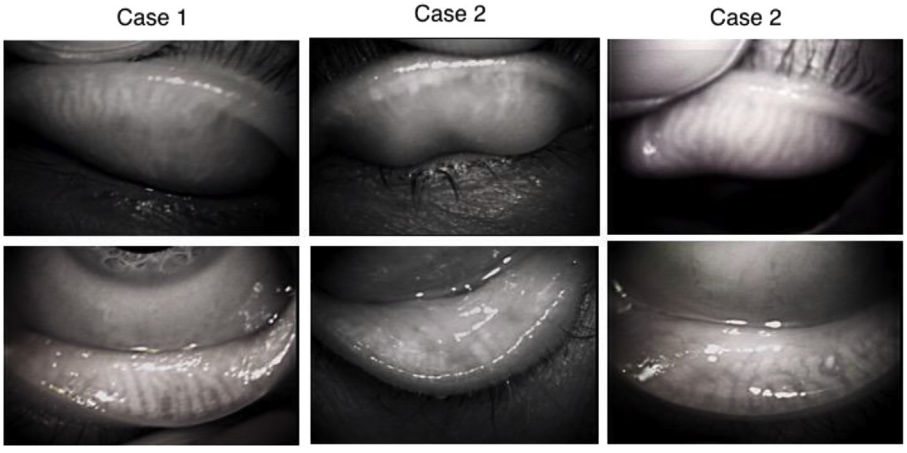

Fig. 1. Morphologically abnormal configuration of meibomian glands in a 35-year-old male patient with chronic allergic conjunctivitis (case 1), a long-term (approximately 20 years) female user (39-year-old) of a soft contact lens (case2) and a 74-year-old male patient with a long-term application of antiglaucoma medications (details unknown) (case 3).