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journal homepage: www.theocularsurface.comOcular surface alkali injury damages meibomian glands in mice[☆]

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ABSTRACT

Purpose: To examine effects of alkali injury of the ocular surface on meibomian gland pathology in mice. **Methods:** Three μL of 1 N NaOH were applied under general anesthesia to the right eye of 10-week-old BALB/c ($n = 54$) mice to produce a total ocular surface alkali burn. The meibomian gland morphology was examined at days 1, 2, 5, 10, and 20 by stereomicroscopy and non-contact infrared meibography. Mice were then sacrificed and eyelids processed for histology with hematoxylin-eosin and immunohistochemistry for ELOVL4, PPAR γ , myeloperoxidase (a neutrophil marker) and F4/80 macrophage antigen, as well as TUNEL staining. Another set of specimens was processed for cryosectioning and Oil red O staining.

Results: Alkali injury to the ocular surface produced cellular apoptosis, infiltration of neutrophils and macrophages, degeneration of the meibomian gland, and ductal dilation. Inflammation in and destruction of acinar stricture seemed more prominent in the lower eyelid, while duct dilation was more frequently observed in the upper eyelid during healing. Surviving acinar cells were labeled for ELOVL4 and PPAR γ . Oil red O staining showed that the substance in the dilated duct contained predominantly neutral lipid.

Conclusions: Alkali injury to the ocular surface results in damage and destruction of the eyelid meibomian glands. The pattern of the tissue damage differs between glands of the upper and lower eyelids.

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1. Introduction

While alkali injury to the cornea and ocular surface is known to cause severe damage to the cornea, limbal epithelial stem cells, and conjunctiva [1,2], little is known about the effects of alkali injury to the meibomian glands. Recently, we reported that inflammation associated with severe allergic conjunctivitis is associated with

abnormal morphology of meibomian glands [3]. We also reported that conjunctival inflammation caused by systemic TS-1 anticancer therapy may cause obstruction of the gland orifice, leading to damage of the gland [4]. Because ocular surface alkali injury causes damage to both the conjunctiva and lid margin, leading to severe inflammation, it would seem likely that alkali injury may effect meibomian gland function either through direct damage to the meibomian gland, leading to scarring and plugging of the gland orifice or mediated through palpebral inflammation. To our knowledge, the effects of alkali injury to the meibomian gland has not been investigated in detail.

To determine whether meibomian glands are damaged following alkali injury, we recently conducted a preliminary simple histological examination of the meibomian gland in C57BL/6 mice and showed abnormal ductal dilation of the meibomian glands [5]. However, melanin pigments in tissue disturbed detailed

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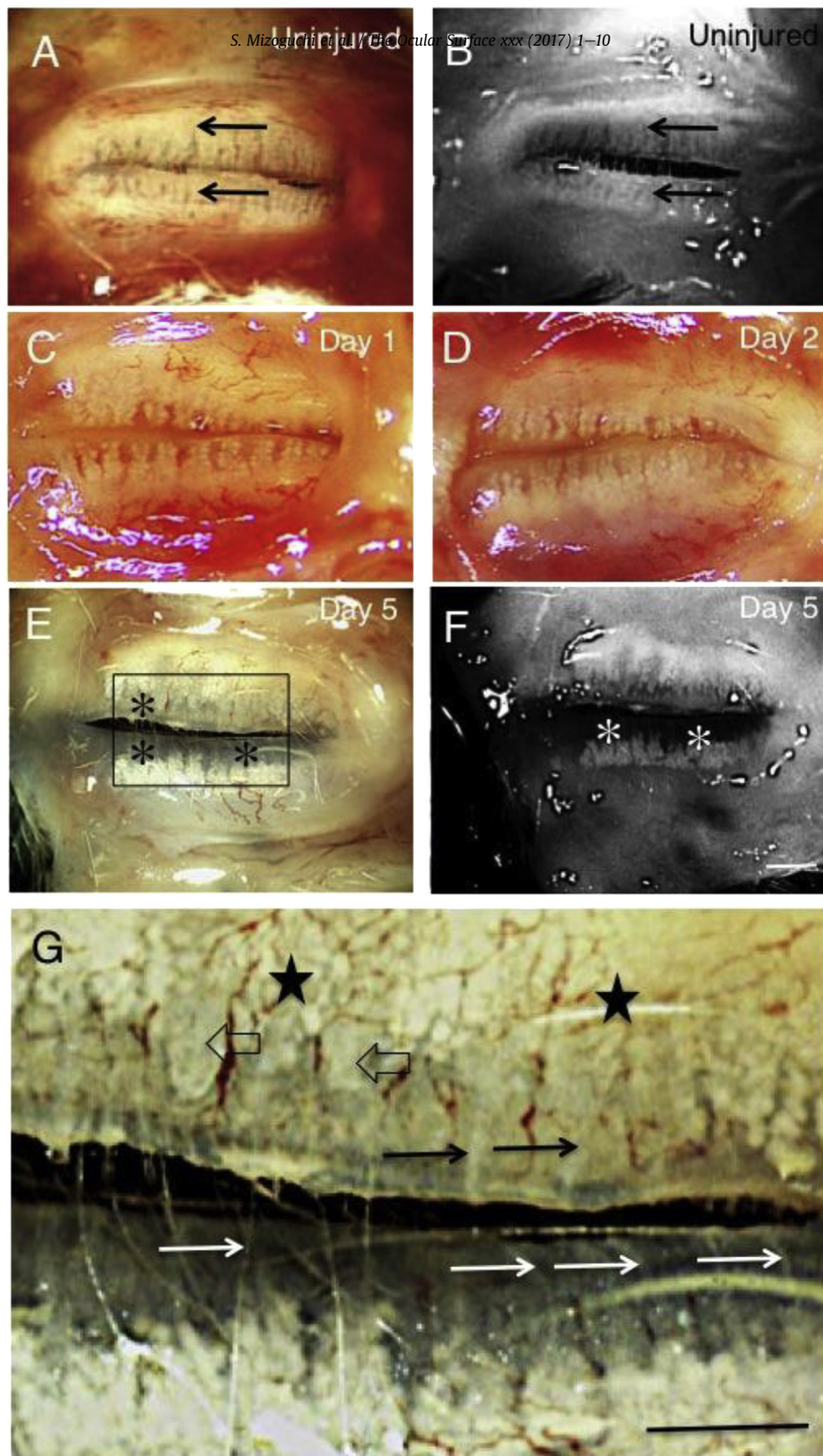


Fig. 1. Binocular microscopy and meibography findings in mouse meibomian glands following alkali injury. **A and B.** In an uninjured mouse, in both the upper and lower eyelids meibomian glands contain large numbers of small acini arranged perpendicularly to the eyelid margins (arrows). **C and D.** At days 1 and 2, no significant abnormalities in the meibomian glands of the upper and lower eyelids are shown by binocular microscopy. **E and F.** At day 5 post-alkali treatment, deletion of acini is seen in the area close to the meibomian gland orifice in the lower eyelid (asterisks). Moderate dilation is seen in the duct of the glands in the upper eyelid. **G.** Higher magnification picture of the boxed area of day 5 specimen in frame E. Acini are not seen adjacent to the lid margin, but are clearly seen in the area relatively far from the margin (stars) in the upper meibomian glands. Naked ducts were also seen. Some ducts appear dilated (open arrows), while other are not (arrows). The loss of the acini was more marked with remaining ducts (white arrows) in the lower glands. **H and I.** At day 10, many ducts in the upper eyelid show marked dilation with reduction in the number of acini (arrowheads). Dilation was less severe in the lower eyelid, but the deletion of acini appears more marked in the lower eyelid (asterisks). **J and K.** Findings at day 20 after alkali injury are similar to those at day 10: duct dilation (arrowheads) and reduction of the number of the acini were more marked in the upper eyelid. Most of the lower eyelid showed loss of both ducts and acini (asterisks). **L.** Higher magnification picture of day 20 specimen in frame J. Acini were severely lost, and remaining ducts were markedly dilated (black arrows) in the upper meibomian glands. Acini and ducts are not seen in the lower eyelid. A, C, D, E, G, H, J, L: binocular microscopy; B, F, I, K: Meibography. Bar, 1 mm.

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