to be associated with HPV 16. Higher-weight cytokeratins are encountered in the epidermis as opposed to mucous membranes.\(^1,2\) The 2 major differential diagnoses were sebaceous and mucoepidermoid carcinomas.\(^3\) Sebaceous carcinoma was excluded by oil red O cytoplasmic negativity and immunohistochemical stains that demonstrated negativity for both adipophilin (except for faint focal positivity in necrotic zones) and androgen receptors.\(^5,6\) Sebaceous carcinomas are 100% positive for androgen receptors.\(^4\) Mucoepidermoid carcinoma was excluded by negative Alcian blue and mucicarmine stains.\(^5\) Cutaneous squamous cell carcinomas of epidermal origin are 100% androgen receptor negative, but conjunctival dysplasias may rarely be focally positive.\(^5\) Immunohistochemistry can therefore be helpful in distinguishing clear-cell squamous carcinoma from sebaceous cell carcinoma. Our findings should also help to resolve the controversy over whether sebaceous carcinoma can arise primarily in the conjunctival epithelium. Previous reports of this entity may in fact have been examples of clear-cell squamous carcinomas in situ. Accurate early diagnosis separating intraepithelial clear-cell squamous and sebaceous carcinomas should lead to improved clinical management of these disparate conditions.

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Effect of Topical Rebamipide on Human Conjunctival Goblet Cells

The conjunctival epithelium contains mucin-secreting goblet cells, which are essential for maintenance of a healthy ocular surface.\(^3\) It has been demonstrated that topical administration of rebamipide, an antiulcer agent, increases the mucin level of the tear film and improves the ocular surface in dry eye syndrome.\(^3\) Indeed, rebamipide increased the number of goblet cells in rabbit and murine conjunctivas in vivo.\(^3-4\) Rios et al demonstrated that rebamipide led to proliferation of cultured rat conjunctival goblet cells,\(^5\) subsequently stimulating secretion from the cells.\(^6\) However, there has been no evidence that rebamipide exerts a strong action on human goblet cell behavior. This is the first report, to our knowledge, showing markedly increased goblet cells after administration of topical rebamipide in a patient with conjunctival dysplasia.

Report of a Case | A man in his late 70s had conjunctival hyperemia in the left eye. He was referred to our hospital because a conjunctival tumor was initially observed at a clinic. His visual acuity was 20/25 OS and his intraocular pressure was normal. Slitlamp examination revealed a pinkish tumor located in the nasal bulbar conjunctiva (Figure 1A). Indocyanine green angiography of the anterior segment demonstrated a markedly stained lesion corresponding to the tumor (Figure 1B). Dilated vessels associated with the tumor extended to the cornea (Figure 1B). The right eye was healthy. Because carcinoma in situ was initially suspected, the conjunctival tumor and the...
associated corneal epithelial lesion were excised with a 3-mm surgical margin after obtaining written informed consent. The conjunctival defect was completely reconstructed using a rotation flap. Histologically, the conjunctival tumor showed mild dysplasia (Figure 2A). The lesion of the dysplasia was located at the site 2 mm nasal to the corneal limbus. The adjacent noncancerous conjunctiva contained a few goblet cells (2/high-power field) (Figure 2B). Surgical margins were free of dysplasia cells. The patient used topical rebamipide eyedrops 4 times a day for 3 months without other topical agents to support healing of the postoperative corneal erosion. Slitlamp examination demonstrated smooth bulbar conjunctiva of the left eye (Figure 1C) 3 months after starting treatment with rebamipide. Indocyanine green angiography showed no staining or dilated vessels in the conjunctiva (Figure 1D). After oral informed consent was obtained, a biopsy was performed at the bulbar conjunctiva 2 mm nasal to the corneal limbus to evaluate how the epithelial atypia changed. Histologically, the conjunctival epithelium contained an increased number of goblet cells (25/high-power field) without cellular atypia (Figure 2C). After 6 months’ follow-up, the patient is well without recurrence of the tumor.

Discussion | Rebamipide is considered to increase the number of goblet cells of the tissues in rabbit and mouse models.6,7 For the first time, to our knowledge, our study has demonstrated that use of rebamipide alone for 3 months resulted in a markedly increased number of goblet cells in the conjunctival epithelium of a human. The results also verify in vitro evidence that rebamipide led to an increased number of goblet cells of the rat conjunctiva.6,8

A limitation of this study is its short follow-up time. A previous article demonstrated that topical rebamipide could be safely used for 4 weeks in patients with dry eye syndrome and that its effectiveness would last for at least 2 weeks after the end of treatment.9 Careful observation is mandatory to ensure the safety of topical rebamipide. Also, the conjunctiva of the fellow eye was not available in this study. Further studies are needed to verify the goblet cells in the conjunctival tissues of human eyes that have not undergone surgery.