LETTER

Focal limbal stem cell deficiency corresponding to an iris coloboma

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When the stem cells population is destroyed or their supporting stromal environment is dysfunctional, limbal stem cell deficiency (LSCD) manifests. Clinically, LSCD carries the hallmark of conjunctivalisation—that is, the corneal surface is covered by ingrowing conjunctival epithelium containing goblet cells. Conjunctivalisation is invariably associated with the destruction of the basement membrane, emergence of superficial neovascularisation, scarring, and diminished visual acuity.1–4

Corneal diseases associated with LSCD can be subdivided into two major categories.4 In the first category, limbal epithelial stem cells have been previously destroyed by a known or recognisable insult. The second category is characterised by a gradual loss of the stem cell population without a known or identifiable factor. In this second category, the limbal stromal environment, so called niche, is presumably affected progressively by different aetiologies including aniridia.5 Although iris coloboma has been noted to be associated with corneal surface abnormalities,6,7 no report appears to confirm if this developmental abnormality is also associated with LSCD. Here we report one such case, which manifested focal LSCD in the same area of iris coloboma.

Case report

In 1988, a 38 year old male patient was referred for evaluation of a peripheral vascularisation in his right eye and a persistent epithelial defect in the left eye after two previous failed penetrating keratoplasties. At that time, an inferonasal iris coloboma associated with regional peripheral superficial vascularisation and mild corneal haze was noted in the right eye, which also had a past history of amblyopia with a best corrected visual acuity of 20/200. Impression cytology performed then did not show any evidence of conjunctivalisation in the right eye. The left eye has received three additional penetrating keratoplasties (two for inadvertent blunt trauma leading to wound dehiscence) and with a contact lens he could see 20/30.

In 2002, he presented with a complaint of progressive foreign body sensation and redness in his right eye. Slit lamp examination revealed a central corneal epithelial defect and peripheral superficial corneal vascularisation located in the same quadrant where an iris coloboma was present (Fig 1A ). An irregular epithelium in a migratory pattern was noted in the affected corneal quadrant, where late fluorescein...
staining was also found (Fig 1B). Repeat impression cytology confirmed the presence of conjunctival epithelial cells and goblet cells on the peripheral cornea of this region, supporting the diagnosis of focal LSCD (Fig 1C).

Figure 1 (A) Slit lamp examination of the right eye of a 51 year old man showing a central corneal epithelial defect and peripheral superficial conical vascularisation located in the inferonasal quadrant. (B) An irregular epithelium in a migratory pattern noted in the affected corneal quadrant, and peripheral late fluorescein staining in the same area. (C) Impression cytology confirming the presence of conjunctival epithelial cells and goblet cells, shown by white arrows.

Comment
Previously, Soong and Raizman reported four patients with iris coloboma that were accompanied by corneal changes. Here, for the first time, we demonstrate that these corneal changes may represent or eventually evolve into a state of LSCD by the use of impression cytology disclosing the hallmark of conjunctivalisation. These abnormal epithelial changes were associated with corneal epithelial erosion adjacent to an irregular migratory epithelium with late fluorescein staining, and superficial peripheral corneal vascularisation. Other known aetiologies for partial limbal deficiencies were excluded in this patient. The strong anatomical correlation of focal LSCD in the region of iris coloboma resembles what has been reported in patients with aniridia in which total LSCD is found invariably in eyes lacking the development of the entire iris. In aniridia, these abnormal corneal changes develop as early as the first decade of age and progressed rapidly to total conjunctivalisation. Mutations in the PAX6 gene are associated with a wide range of ocular abnormalities including anophthalmos, aniridia, and various anterior segments anomalies with peripheral vascularisation. A reduction of PAX6 activity in heterozygotes for PAX6 mutation results in aniridia in humans and nanophthalmos in the knockout mice. We thus speculate that a less severe alteration of PAX6 might have a role in the ocular surface changes observed in coloboma. Such a similarity between iris coloboma and aniridia prompts us to speculate that these two diseases might share the same underlying pathogenesis. This interpretation strengthens our hypothesis that deficiency in the iris development is accompanied by the abnormality of the limbal stroma that is vital to the support of limbal epithelial stem cells. Future studies dissecting into this correlation will help unravel the secrecy concerning the regulation of limbal epithelial stem cells.

FOOTNOTES
Proprietary interest: None.

References
1. Dua HS, Forrester JV. The corneoscleral limbus in human corneal epithelial wound healing. Am J


