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Limbal Stem Cell Deficiency Post Systemic Chemotherapy

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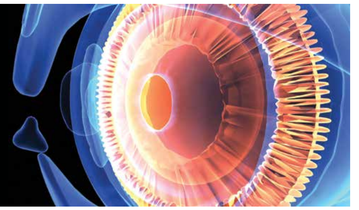

BACKGROUND

The corneal limbus is the location of where epithelial stem cells reside. These limbal stems cells act as the regenerative source for corneal epithelial cells and contribute largely to the maintenance of corneal integrity. Damage or disruption to the limbal area or cells can lead to limbal stem cell deficiency (LSCD). With LSCD, the cornea is subjected to conjunctivalization, persistent epithelial defects, scarring, chronic inflammation, neovascularization and fibrous growth.[1] Symptoms may include decreased vision, pain and photophobia.[2] A diagnosis is typically made from clinical features but impression cytology can confirm with the classic pathologic finding of goblet cell loss.[3]

There are two major causes of LSCD, the first is acquired through destruction of the limbal stem cells via chemical, thermal or mechanical trauma, severe microbial infection or iatrogenically from surgical procedures.[1] Chemotherapy induced LSCD is included in this category. The second cause is a flawed stromal environment caused by, but not limited to, aniridia, ectodermal dysfunction, chronic limbitis and peripheral ulcerative keratitis.[1]

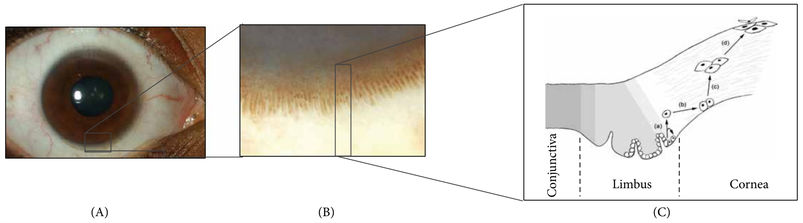

FIGURE 1: *(A) Overview of ocular surface (B) Limbal Palisades of Vogt between white conjunctiva and clear cornea (C) Cross section of conjunctival, limbal and corneal epithelium. Proliferation of stem cells, differentiation and migration into the cornea is shown.*
Source: Review Article Limbal Stem Cell Deficiency: Current Treatment Options and Emerging Therapies. Stem Cells Int 2016;2016:1–22. Figure 1.

TREATMENT

- Treatment is dependent on the amount of limbal epithelial stem cells, more healthy stem cells allow for more conservative treatment
- Mild to moderate cases: lubrication, autologous serum drops, therapeutic contact lenses, corneal scraping or amniotic membranes[2]
- Severe cases: limbal epithelial stem cell transplantation, autologous or allogeneic transplantation via ex vivo cultivated epithelial stem cells (CLET), or autologous transplantation via simple epithelial transplantation (SLET).[2]

CASE DESCRIPTION

- 69-year-old white female referred for: corneal ulcer with hypopyon, OS
- Entering uncorrected VAs
  - *OD: 20/70 PH: 20/25 and OS: CF@1ft PHNI*
- Pertinent findings: central 0.5x2.5mm epithelial defect with 1mm infiltrate, diffuse stromal haze and edema, 1+ fine KPs, 2+ cell with a 0.5mm hypopyon
- Bacterial cultures: MRSA positive
- Treatment: fortified vancomycin QID, OS
- Intact epithelium achieved in 4 weeks with the aid of an amniotic membrane and a 50% lateral tarsorrhaphy
- A penetrating keratoplasty (PKP) was indicated secondary to extensive scarring. An ulcer presented almost immediately following the PKP causing the graft failure and the patient to undergo a second PKP 6 weeks later
- 3 months s/p second PKP, complete re-epithelialization did not occur with aid from an amniotic membrane, autologous serum or a 50% lateral tarsorrhaphy
- 6 months s/p second PKP, intact epithelium was present with continual use of autologous serum and the presence of the 50% lateral tarsorrhaphy

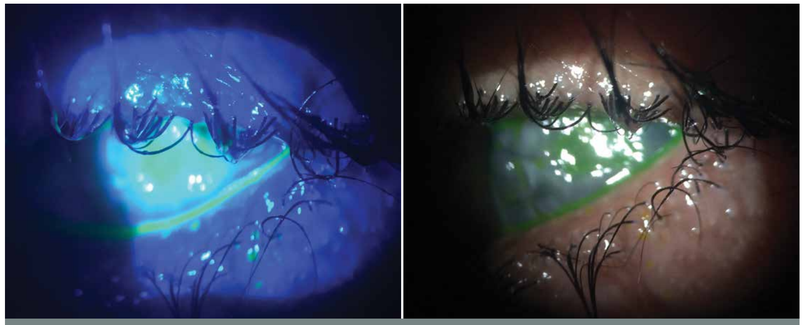

FIGURE 2: *Central corneal defect 3 months s/p PKP with a 50% lateral tarsorrhaphy*

DIAGNOSIS AND DISCUSSION

This case represents delayed corneal epithelial healing that is thought to be due to LSCD secondary to prior systemic chemotherapy. Cytotoxic agents are known to target rapidly dividing cells. As the cornea is avscular, the cytotoxic agents likely reached our patient's eye through a combination of routes including the tear film, aqueous humor and limbal vasculature. Similar cases of this nature are rare due to the low penetrance of systemic drugs to the eye.[1]
In previously reported cases of chemotherapy induced LSCD, cessation of the drug in early stages can lead to the successful resolution of complications.[3]

In this case, a lateral tarsorrhaphy was indicated prior to transplantation when other therapies failed. The procedure promotes natural protection and healing of the cornea by the body itself. Due to the success of the tarsorrhaphy and concerns of exposure and epithelial decompensation, the lateral tarsorrhaphy will remain permanent to protect the corneal graft.

CONCLUSION

- Although rare, there are similar case reports of patients with LSCD due to chemotherapy
- LSCD should be a differential in cases of non-healing or delayed re-epithelialization
- If medication toxicity is suspected, discontinuation or modification of the drug should be considered if possible.

BIBLIOGRAPHY

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2. Haagdorens M, Acker SI Van, Gerwen V Van, Dhubhghaill SN, Koppen C, Tassignon M, Zakaria N. Review Article Limbal Stem Cell Deficiency : Current Treatment Options and Emerging Therapies. *Stem Cells Int* 2016;2016:1–22.
3. Ding X, Bishop RJ, Herzlich AA, Patel M, Chan C-C. Limbal stem cell deficiency arising from systemic chemotherapy with hydroxycarbamide. *Cornea* 2009;28:221–3.