

THE EXPANDING DIFFERENTIAL OF CORNEAL VERTICILLATA



Chai tea on the “rocks.”

BY JACOB LANG, OD, FAAO, DIPL ABO

Netarsudil ophthalmic solution 0.02% (Rhopressa, Aerie Pharmaceuticals), a rho kinase (ROCK) inhibitor, was approved by the FDA for the treatment of glaucoma in December 2017. This drug is a powerful IOP-lowering medication with no serious systemic side effects. However, it does have some interesting ocular effects, some of which may be viewed as detrimental or “adverse,” such as redness, and some of which may actually be beneficial to the eye (besides IOP lowering), such as corneal endothelial proliferation. These “off-label” effects have a lot of investigation pending, but the case reports and intercollegiate discussions are building.

ROCK INHIBITORS AND THE EYE

Every clinician should keep in mind the facts below when managing patients taking ROCK inhibitors.¹⁻⁴

- In clinical trials, mean IOP lowering was reported to be 3.5 mm Hg.
- ROCK inhibitors increased trabecular outflow by decreasing actomyosin-driven cellular contraction and reducing production of extracellular matrix proteins.
- ROCK inhibitors may decrease episcleral venous pressure.
- Netarsudil and latanoprost ophthalmic solution 0.02%/0.005% (Rocklatan, Aerie Pharmaceuticals) lowers IOP significantly more than monotherapy with either component, with IOP reductions of 30% or greater.
- Corneal verticillata was reported in 8.8% to 24.5% of study patients.

CORNEAL VERTICILLATA

There are a multitude of differentials with regard to the corneal finding known as *verticillate* or *whorl epitheliopathy* (Figure). The standard acronym is CHAI-T+F (Chloroquine, Hydroxychloroquine, Amiodarone, Indomethacin, Tamoxifen, Fabry disease).

There are many other reasons patients may present with corneal epithelial verticillate-like findings, including Lisch

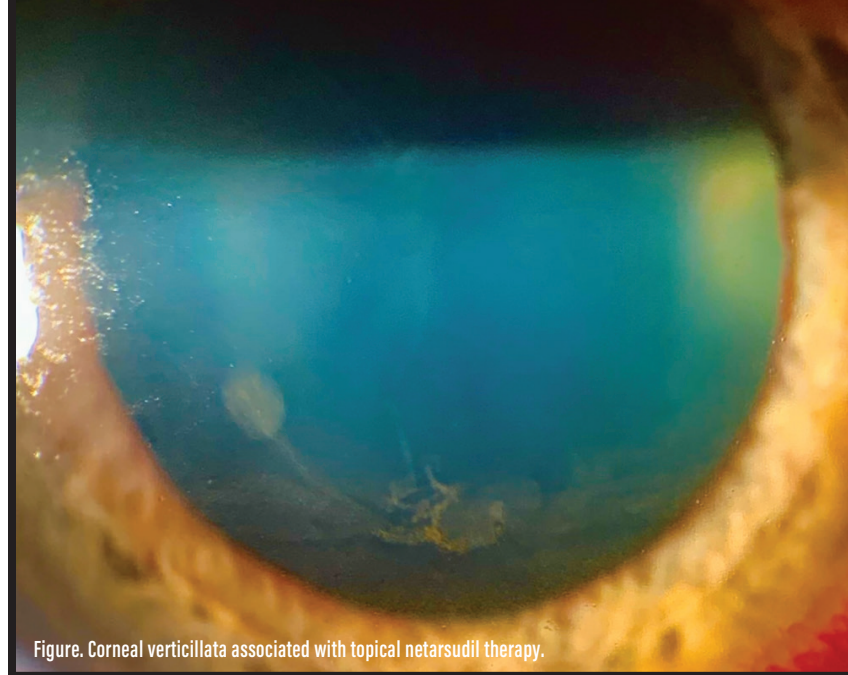


Figure. Corneal verticillata associated with topical netarsudil therapy.

corneal dystrophy or gold salts. I refer doctors to a major review in *Survey of Ophthalmology*, which discusses drug-induced corneal epithelial changes.⁵

ROCK inhibitors have a growing fan club for the clinical treatment of corneal endothelial diseases and conditions⁶ and may have some application in corneal epithelial diseases, such as corneal limbal stem cell deficiency.⁷

THINKING THROUGH THE POSSIBILITIES

Corneal verticillata can appear for a host of reasons, including signs of serious underlying metabolic disease, such as Fabry disease and cystinosis. It can also occur as a side effect of certain medications, amiodarone being the most common. However, it is pertinent for eye care providers to consider glaucoma medications, specifically ROCK inhibitors, when investigating the source of this clinical finding.

ROCK inhibitors might play an increasingly bigger role in eye care as we continue to harness their effect on the corneal endothelium and epithelium. Maybe our upcoming board preparatory classes should serve their CHAI-T (+F) on the “rocks”? ■

1. Serle JB, Katz LJ, McLaurin E, et al. Two phase 3 clinical trials comparing the safety and efficacy of netarsudil to timolol in patients with elevated intraocular pressure: rho kinase elevated IOP treatment trial 1 and 2 (ROCKET-1 and ROCKET-2). *Am J Ophthalmol*. 2018;186:116-127.

2. Khouri AS, Serle JB, Bacharach J, et al. Once-daily netarsudil versus twice-daily timolol in patients with elevated intraocular pressure: the randomized phase 3 ROCKET-4 study. *Am J Ophthalmol*. 2019;204:97-104.

3. Walters TR, Ahmed II, Lewis RA, et al. Once-daily netarsudil/latanoprost fixed-dose combination for elevated intraocular pressure in the randomized phase 3 mercury-2 study. *Ophthalmology Glaucoma*. 2019;2(5):280-289.

4. Peace JH, McKee HJ, Kopczynski CC. A Randomized, phase 2 study of 24-h efficacy and tolerability of netarsudil in ocular hypertension and open-angle glaucoma. *Ophthalmol Ther*. 2021;10(1):89-100.

5. Raizman MB, Hamrah P, Holland EJ, et al. Drug-induced corneal epithelial changes. *Surv Ophthalmol*. 2017;62(3):286-301.

6. Okumura N, Kinoshita S, Koizumi N. Application of rho kinase inhibitors for the treatment of corneal endothelial diseases. *J Ophthalmol*. 2017;2017:2646904.

7. Miyashita H, Yokoo S, Yoshida S, et al. Long-term maintenance of limbal epithelial progenitor cells using rho kinase inhibitor and keratinocyte growth factor. *Stem Cells Transl Med*. 2013;2(10):758-765.

JACOB LANG, OD, FAAO, DIPL ABO

- Optometrist, Associated Eye Care, Stillwater, Minnesota
- Member, *Modern Optometry* Editorial Advisory Board
- drjakelang@gmail.com; Instagram @seeoneteachone
- Financial disclosure: None