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Case Report

Ophthalmology Section

Bilateral Punctal Stenosis Following Netarsudil Therapy in Fuchs Endothelial Dystrophy: A Case Report

ROHAN JAGADISH[1], NILESH BALAJI GIRI[2], GAUTAMI RAMESH LATURKAR[3], KRITIKA AGGARWAL[4], SAUJAS SHAH[5]

ABSTRACT

Netarsudil, a Rho-Associated Protein Kinase (ROCK) inhibitor, is being increasingly used in the management of glaucoma and corneal endothelial disorders. Although conjunctival hyperaemia and corneal verticillata are well-recognised adverse effects, lacrimal drainage abnormalities have rarely been reported. The authors described a 52-year-old male with Fuchs endothelial dystrophy who developed progressive bilateral epiphora and punctal stenosis following initiation of topical Netarsudil 0.02% eye drops. The patient developed worsening watering and redness approximately four months after initiation of therapy. Slit-lamp examination revealed bilateral conjunctival congestion, corneal guttae with stromal oedema and cicatricial narrowing of both upper and lower puncta. Specular microscopy demonstrated reduced endothelial cell density bilaterally, while anterior segment optical coherence tomography showed increased central corneal thickness. Other causes of acquired punctal stenosis including trauma, autoimmune disease, cicatrising conjunctivitis, Stevens-Johnson syndrome and alternative medication-induced aetiologies were excluded clinically. Despite discontinuation of Netarsudil and initiation of preservative-free lubricants, punctal fibrosis persisted, necessitating bilateral punctoplasty with symptomatic improvement on follow-up. The temporal relationship with drug initiation, exclusion of alternate aetiologies and stabilisation after discontinuation supported a probable adverse drug reaction according to World Health Organisation – Uppsala Monitoring Centre (WHO-UMC) causality assessment criteria. The present case highlights a rare but clinically significant adverse effect associated with Netarsudil therapy and emphasises the importance of early recognition and punctal evaluation in patients receiving prolonged ROCK inhibitor therapy.

Keywords: Corneal oedema, Drug toxicity, Epiphora, Keratopathy, Lacrimal drainage obstruction

CASE REPORT

A 52-year-old male presented to the Ophthalmology Outpatient Department with progressive bilateral watering and redness for about 18 months associated with progressive diminution of vision over the preceding two years. He had been diagnosed with Fuchs endothelial dystrophy three years prior to presentation based on the presence of bilateral corneal guttae, stromal oedema and reduced endothelial cell density on specular microscopy.

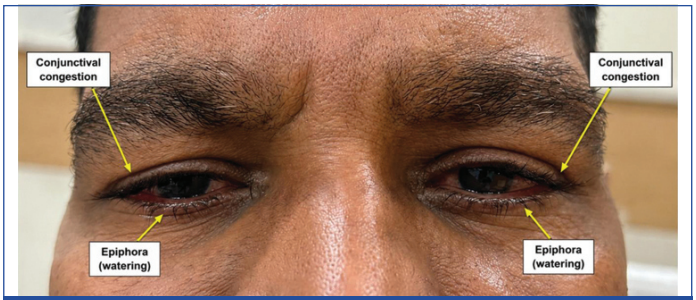
Topical Netarsudil ophthalmic solution 0.02% once daily had been initiated in both eyes approximately two years before presentation for management of endothelial dysfunction and associated ocular hypertension. Approximately, four months after initiation of therapy, the patient noted progressive worsening epiphora and ocular redness bilaterally which progressively increased during continued treatment.

There was no history of ocular trauma, chemical injury, radiation exposure, Stevens-Johnson syndrome, ocular cicatricial pemphigoid, chronic blepharitis, autoimmune disease, prior lacrimal surgery, or use of systemic medications known to cause punctal stenosis such as fluorouracil or docetaxel. These differential diagnoses were clinically excluded before arriving at the diagnosis of probable drug-induced punctal stenosis.

On examination, best-corrected visual acuity was 6/24 in the right eye and 6/36 in the left eye. External examination demonstrated bilateral epiphora with conjunctival congestion [Table/Fig-1].

Specular microscopy revealed reduced endothelial cell density in both eyes, measuring 2161 cells/mm^2 in the left eye [Table/Fig-2] and 1509 cells/mm^2 in the right eye [Table/Fig-3].

Anterior segment optical coherence tomography demonstrated increased central corneal thickness with stromal oedema in the right eye {Central Corneal Thickness (CCT)- 687 µm} [Table/Fig-4] and left eye (CCT- 662 µm) [Table/Fig-5].



[Table/Fig-1]: External photograph demonstrating bilateral epiphora and conjunctival congestion in both eyes. Yellow arrows indicate excessive tear overflow along the lower lid margin.

Slit-lamp examination showed bilateral corneal guttae consistent with Fuchs endothelial dystrophy [Table/Fig-6].

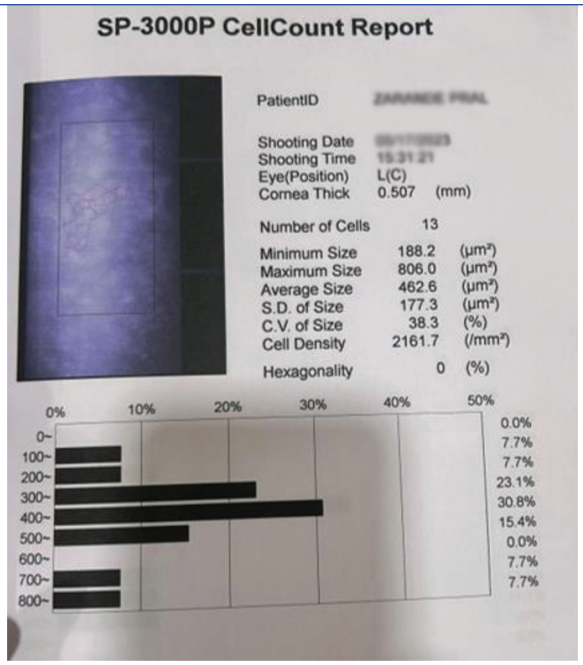
Detailed punctal examination demonstrated cicatricial narrowing of both upper and lower puncta bilaterally with surrounding fibrosis. The right lower punctum showed severe stenosis with near-complete narrowing [Table/Fig-7], while the left punctum demonstrated moderate stenosis [Table/Fig-8].

Lacrimal irrigation revealed partial passage with regurgitation through opposite puncta suggestive of proximal lacrimal outflow obstruction. However, no alternative medication-related cause was identified in the present case.

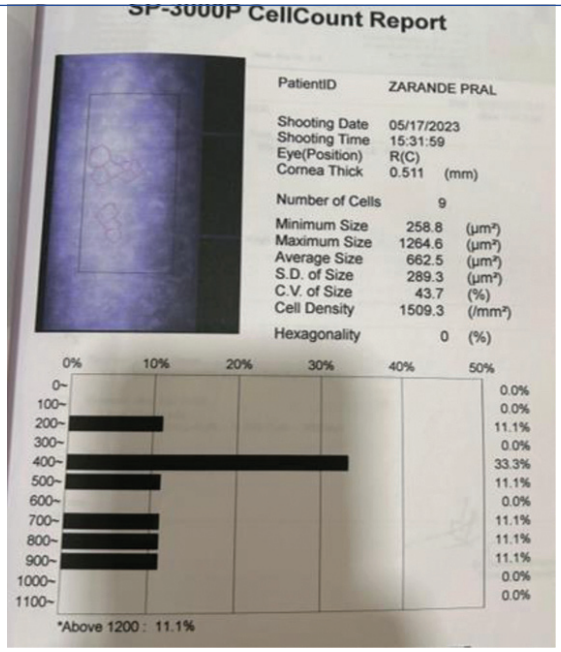
A clear temporal relationship was observed between initiation of Netarsudil therapy and progression of punctal narrowing.

The temporal relationship with drug initiation, exclusion of alternate aetiologies and stabilisation after discontinuation supported a probable adverse drug reaction according to WHO-UMC causality assessment criteria [1].

Netarsudil was discontinued and preservative-free carboxymethylcellulose 0.5% eye drops six times daily were initiated.



[Table/Fig-2]: Specular microscopy of the left eye showing reduced endothelial cell density, pleomorphism and polymegathism consistent with endothelial dysfunction.



[Table/Fig-3]: Specular microscopy of the right eye demonstrating decreased endothelial cell density with abnormal endothelial morphology.

However, due to persistent fibrosis and symptomatic epiphora, bilateral punctoplasty was performed.

At three-month postoperative follow-up, the patient reported significant symptomatic relief with improvement in watering and no recurrence of punctal narrowing.

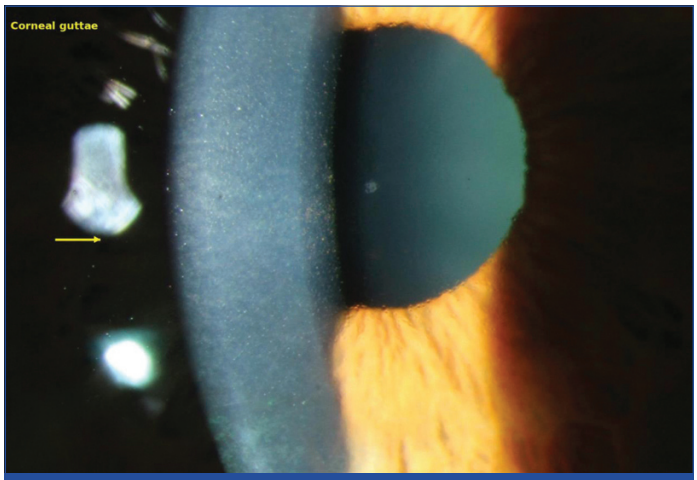
DISCUSSION

Fuchs endothelial dystrophy is a progressive corneal endothelial disorder characterised by corneal guttae, endothelial cell loss and stromal oedema [2]. Progressive endothelial dysfunction may lead to visual impairment secondary to corneal oedema and epithelial changes. ROCK inhibitors including Netarsudil have emerged as promising agents for reducing intraocular pressure and improving endothelial cell function through enhancement of trabecular outflow and modulation of cytoskeletal pathways [3-5].

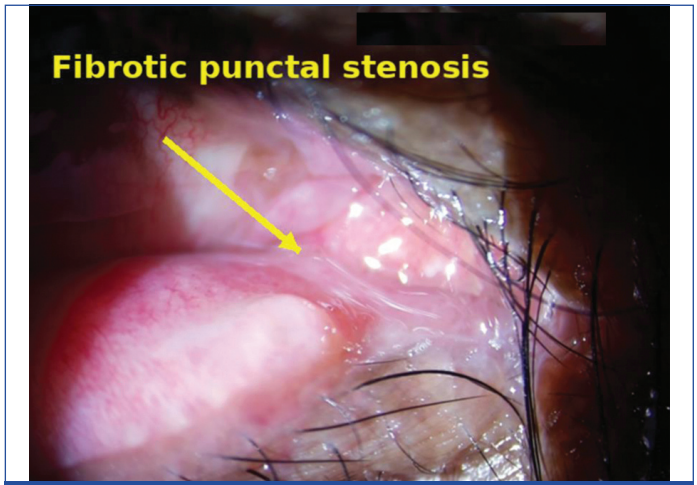
Acquired punctal stenosis is commonly associated with chronic inflammation, infection, trauma, autoimmune disorders and drug-induced cicatricial changes [6-8]. Persistent inflammation results in epithelial fibrosis and narrowing of the lacrimal punctum, eventually leading to symptomatic epiphora. Drug-induced punctal stenosis

[Table/Fig-4]: Anterior segment optical coherence tomography of the Right eye (OS) showing increased central corneal thickness (687 µm) and stromal oedema.

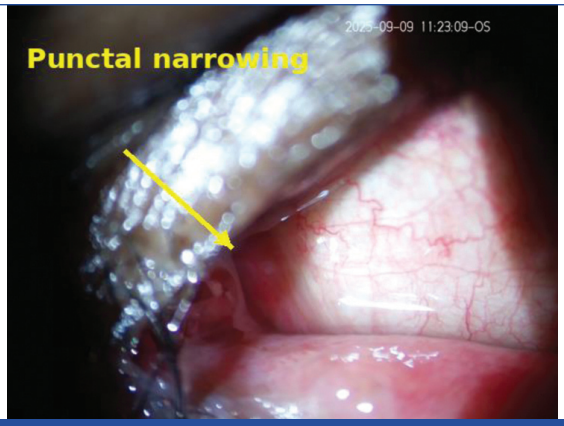
[Table/Fig-5]: Anterior segment optical coherence tomography of the Left eye (OS) showing increased central corneal thickness (662µm) and stromal oedema.



[Table/Fig-6]: Slit-lamp photograph demonstrating corneal guttae and stromal haze consistent with Fuchs endothelial dystrophy (Arrows depict corneal guttae).



[Table/Fig-7]: Slit-lamp photograph of the right eye showing severe punctal stenosis with fibrotic narrowing of the lower punctum (Yellow arrow).



[Table/Fig-8]: Slit-lamp photograph of the left eye showing moderate punctal stenosis with surrounding cicatricial changes (Yellow arrow).

has previously been described with systemic chemotherapeutic agents such as docetaxel and 5-fluorouracil, antiviral medications and topical antiglaucoma agents [6-9].

Netarsudil is a selective ROCK inhibitor that lowers intraocular pressure by increasing trabecular outflow facility, reducing episcleral venous pressure and decreasing aqueous production [4,5]. Commonly reported adverse effects include conjunctival hyperaemia, subconjunctival haemorrhage, corneal verticillata and ocular irritation [4,10,11]. ROCK pathway modulation influences extracellular matrix remodelling, fibroblast activity and inflammatory signalling pathways, thereby providing biological plausibility for fibrosis-related adverse effects involving the lacrimal drainage system [12].

In the present case, the patient developed progressive bilateral epiphora and punctal fibrosis several months after initiation of Netarsudil therapy. Alternative aetiologies including trauma, cicatrising conjunctivitis, autoimmune disease and systemic medication-related causes were excluded clinically [6,8].

The temporal association with initiation of therapy, progression during continued use and stabilisation following discontinuation supported a probable adverse drug reaction according to WHO-UMC causality assessment criteria [1].

Only limited literature is available regarding ROCK inhibitor-associated lacrimal drainage abnormalities. Similar reports of medication-induced punctal stenosis have emphasised the role of chronic ocular surface inflammation and epithelial fibrosis in the pathogenesis of lacrimal obstruction [8,9]. Eyes with pre-existing ocular surface compromise, including Fuchs endothelial dystrophy, may demonstrate increased susceptibility to inflammatory remodelling and fibrosis.

Early recognition of medication-related punctal stenosis is clinically important because persistent inflammation may result in irreversible fibrosis requiring surgical correction [7]. Clinicians prescribing Netarsudil and other ROCK inhibitors should remain vigilant for new-onset epiphora, punctal narrowing, or chronic ocular surface inflammation. Prompt discontinuation of the offending medication and early lacrimal evaluation may help prevent permanent obstruction and reduce the need for surgical intervention.

CONCLUSION(S)

Netarsudil-associated punctal stenosis is a rare but clinically significant adverse effect that may occur following prolonged ROCK inhibitor therapy. Patients presenting with new-onset epiphora during treatment should undergo careful punctal evaluation and lacrimal assessment. Early identification and discontinuation of the offending medication may prevent irreversible fibrosis and reduce the need for surgical management.

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PARTICULARS OF CONTRIBUTORS:
1. Resident, Department of Ophthalmology, Dr. D.Y. Patil University, Pune, Maharashtra, India.
2. Consultant (Vitreo Retinal Surgeon), Department of Ophthalmology, Dr. D.Y. Patil University, Pune, Maharashtra, India.
3. Resident, Department of Ophthalmology, Dr. D.Y. Patil University, Pune, Maharashtra, India.
4. Resident, Department of Ophthalmology, Dr. D.Y. Patil University, Pune, Maharashtra, India.
5. Resident, Department of Ophthalmology, Dr. D.Y. Patil University, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Gautami Ramesh Laturkar,
Resident, Department of Ophthalmology, Dr. D.Y. Patil University,
Pune-411018, Maharashtra, India.
E-mail: grlaturkar@gmail.com

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