Review Article

Vortex Keratopathy

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Abstract

Cornea verticillata, also known as vortex keratopathy, is characterised by a distinctive whorl-like pattern of epithelial deposits in the cornea. It is commonly associated with systemic medications such as amiodarone, hydroxychloroquine, and chloroquine, among others. These deposits are usually asymptomatic and reversible upon discontinuation of the causative drug. The pathogenesis involves lysosomal dysfunction triggered by cationic, amphiphilic drugs, leading to phospholipid accumulation in corneal epithelial cells. Although most cases are benign and do not affect visual acuity, rare instances of optic neuropathy and retinopathy have been reported, especially with prolonged amiodarone use. Management typically involves observation, with drug discontinuation reserved for symptomatic or vision-threatening cases. Emerging therapies such as topical heparin have shown promise in limited reports.

Keywords: Cornea verticillata, Vortex keratopathy, Drug-induced corneal deposits.

Introduction

Cornea verticillata, also known as vortex keratopathy, whorl keratopathy, or Fleischer vortex, refers to a whorl-like pattern of golden-brown or gray opacities in the corneal epithelium. Several oral medications, including amiodarone, hydroxychloroquine, chloroquine, indomethacin, and phenothiazines, can cause this condition.[1] Topical Rho-kinase inhibitors have also been linked to cornea verticilliata.[2] Other, less commonly associated agents include gentamicin, tamoxifen, meperidine, chlorpromazine, atovaquone, suramin, tilorone, perhexiline maleate, and the tyrosine kinase inhibitors vandetanib and osimertinib.[1,3,4] Recently, netarsudil-induced cornea verticillata was reported in a patient who experienced glare and hazy vision, symptoms that resolved after discontinuing the medication.[5]

Many medications are known to produce ophthalmologic side effects, often impacting specific anatomical structures of the eye. Some drugs can even result in deposits within the cornea. These iatrogenic drug-induced deposits are typically asymptomatic but cause visible opacities, often affecting particular layers or regions of the cornea. Although medications can reach the cornea via tears, aqueous humor, or perilimbic vasculature, the underlying pathophysiology and mechanisms responsible for layer-specific deposits remain poorly understood.

Pathogenesis

Under normal epithelial turnover, the movement of epithelial cells from the periphery to the center of the cornea is not visible. However, in various clinical conditions, these cells become visible due to the intracellular deposition of substances such as pigment, iron, drug metabolites, glycogen, and sphingolipids. In these cases, a vortex or whorl pattern appears on the corneal surface, a condition known as vortex keratopathy or cornea verticillata.[6-8]

Many corneal epithelial keratopathies are associated with lysosomal dysfunction, which both exogenous and endogenous factors can trigger. Exogenous causes typically involve certain medications that induce lysosomal dysfunction, leading to the accumulation of excess phospholipids across all corneal layers and surrounding structures.[9] The drugs responsible for cornea verticillata share cationic, amphiphilic properties, which enable them to penetrate lysosomes in the basal epithelial

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Table 1: Shows the grading of amiodarone-associated of cornea verticillata

Grade I	Golden-brown microdeposits just anterior to the Bowman layer
	Appear as dusting at the inferior pupillary margin in the midperiphery
	No fluorescein staining
	Asymptomatic
	Transient stage
	All patients with >1 year consumption pass to grade II
Grade II	Deposits become aligned in a linear pattern.
	Appearance of 'cat's whisker'
	Clear zone between the margin of the deposits and limbus
	Do not necessarily pass to grade III
Grade III	Increase in number of the filament-like deposits seen in grade II
	Extend as branches from the inferior pupillary area into the visual axis
	Whorled pattern is seen in the pupillary axis
	Amiodarone >1 year
Grade IV	Additional 'clumps' of gold-brown deposits
	Whorled branching patterns

layer of the cornea, where they bind to cellular lipids. These drug-lipid complexes resist enzymatic degradation, leading to their accumulation as deposits in the cornea. Specifically, amiodarone inhibits lysosomal phospholipase A2, making the inner cell membrane more vulnerable to degradation by proteases. Suramin, on the other hand, inhibits iduronate sulfatase, causing the buildup of glycosaminoglycans.[10] Other causes include multiple myeloma, multiple sulfatase deficiency, Generalized gangliosidosis, Neurotrophic keratitis, Lisch corneal dystrophy, epidemic keratoconjunctivitis, iron deposition (i.e., after radial keratotomy), stromal deposition (gold, silver, antacid, retinoid depositions)

Medications Associated

Amiodarone is the most commonly used antiarrhythmic drug and belongs to class III antiarrhythmic medications. Almost all patients on this drug (98%) develop corneal epithelial changes at doses starting from 200 to 300 mg/day.[11] While visual acuity is typically unaffected, patients may experience photophobia, halos, and irritation. Corneal changes typically begin within 2 weeks to 1 to 4 months of treatment. The characteristic clinical finding is bilateral vortex keratopathy with brown to golden deposits. The cornea typically clears 3 to 20 months after discontinuing the medication. The configuration of these deposits evolves based on the duration of amiodarone therapy, as demonstrated by the grading system proposed by Orlando *et al*.[12] (Table 1).

Clinical Features

Keratopathy typically starts at the inferior pupillary margin, forming collections that gradually become linear over time, eventually progressing to the well-known swirl of vortex-like patterns (Figure 1). There is no epithelial fluorescein staining or corneal neovascularization. Although the deposits are primarily located in the epithelium just anterior to the Bowman layer on confocal microscopy, the keratopathy affects all layers of the cornea. The condition is usually bilateral and symmetric, though it may begin in one eye before the other. In most cases, there is no loss of visual acuity or significant ocular symptoms; however, a potential link between amiodarone and optic neuropathy has been reported.[13] This optic neuropathy can present with unilateral or bilateral optic disc edema, decreased visual acuity, and sometimes acute vision loss. Amiodarone-induced retinopathy has also been documented in a case report.[14] In such cases, routine monitoring, including automated visual field testing and optical coherence tomography (OCT), should be performed to assess the optic nerve and retinal structure and function. To prevent visually significant adverse events, dose reduction or switching to an alternative medication should be considered in patients presenting with new visual symptoms. In patients taking rifabutin, particular attention should be given to investigating ethambutol-related optic neuropathy, as these drugs are often used together.

Other Associations

Cornea verticillata is seen in 90% of patients with Fabry disease, a rare X-linked recessive lysosomal storage disorder, which is also linked to progressive nephropathy and peripheral neuropathy. Female carriers may only present with corneal findings. Unlike drug-induced cornea verticillata, the condition in Fabry disease is caused by a deficiency of alpha-galactosidase A, a lysosomal enzyme. This leads to the accumulation of glycosphingolipids in lysosomes throughout body tissues, including the cornea. The cornea verticillata in Fabry disease presents as fine golden-brown or gray opacities in the basal epithelium, which branch out from a central whorl,

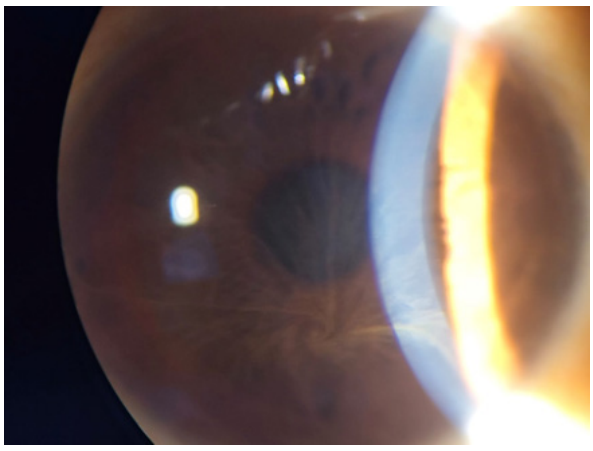

Figure 1: Cornea verticillata in a patient on amiodarone treatment

typically in the inferior cornea. These deposits do not stain and are almost always bilateral.

Patients with cornea verticillata from Fabry disease typically do not experience visual complaints or eye discomfort. Rarely, patients may report seeing blue-green rings or halos around lights. Occasionally, subtle differences may be observed on slit-lamp microscopy between drug-related opacities and those seen in Fabry disease. Drug-induced opacities may appear as horizontal lines with fine branching at the edges, while Fabry disease-related opacities typically form curving lines that create whorls before becoming almost straight at the periphery of the cornea.

Treatment

Due to the limited number of cases in the literature, there is no clear recommended treatment. Corneal deposits associated with amiodarone are reversible within 3-20 months after discontinuation of the drug. Since these deposits are rarely symptomatic, treatment is usually not stopped for this reason. However, if optic neuropathy is present, discontinuing the medication may be necessary. In such cases, it is important to consult with a cardiologist before making any changes to the medication regimen.

While the management of corneal drug-induced deposits is typically limited to observation and conservative care, some treatments have been suggested in the literature. For instance, topical heparin eye drops, prepared with a sterile phosphate-free solution of 0.1% sodium hyaluronate, have been reported as a potential treatment for amiodarone-induced vortex keratopathy.[15,16] Other local therapies, such as topical lubricants or corticosteroids, may help improve symptoms.

References

1. Raizman MB, Hamrah P, Holland EJ, Kim T, Mah FS, et al. Drug-induced corneal epithelial changes. Surv Ophthalmol. 2017;62(3):286-301.
2. Wu JH, Chang SN, Nishida T, Kuo BI, Lin JW. Intraocular pressure-lowering efficacy and ocular safety of Rho-kinase inhibitor in glaucoma: a meta-analysis and systemic review of prospective randomized trials. Graefes Arch Clin Exp Ophthalmol. 2021 Sep 7.
3. Shah GK, Cantrill HL, Holland EJ. Vortex keratopathy associated with atovaquone. Am J Ophthalmol. 1995;120(5):669-71.
4. D'Amico DJ, Kenyon KR. Drug-induced lipidoses of the cornea and conjunctiva. Int Ophthalmol. 1981;4(1-2):67-76.
5. Rivera SS, Radunzel N, Boese EA. Symptomatic netarsudil-induced verticillata. JAMA Ophthalmol. 2023;141(5): e232949.
6. Bron AJ. Vortex patterns of the corneal epithelium. Trans Ophthalmol Soc U K. 1973;93:455-72.
7. Lemp MA, Mathers WD. Corneal epithelial cell movement in humans. Eye (Lond). 1989;3(Pt 4):438-45.
8. Bloch FJ. Vortex-shaped dystrophy of the cornea. Arch Ophthalmol. 1940;23:825-8.
9. D'Amico DJ, Kenyon KR. Drug-induced lipidoses of the cornea and conjunctiva. Int Ophthalmol. 1981;4:67-76.
10. Shayman JA, Abe A. Drug induced phospholipidosis: an acquired lysosomal storage disorder. Biochim Biophys Acta. 2013;1831(3):602-11.
11. Ingram DV, Jaggarao -S, Chamberlain DA. Ocular changes resulting from therapy with amiodarone. Br J Ophthalmol. 1982;66(10):676-9.
12. Orlando RG, Dangel ME, Schaal SF. Clinical experience and grading of amiodarone keratopathy. Ophthalmology. 1984;91(10):1184-7.
13. Passman RS, Bennett CL, Purpura JM, et al. Amiodarone-associated optic neuropathy: a critical review. Am J Med. 2012;125(5):447-53.
14. Joshi KM, Gill MK. Amiodarone: a potential risk factor for retinal phototoxicity. Am J Ophthalmol Case Rep. 2017;5:119-23.
15. EyeWiki. Drug-induced maculopathy [Internet]. Available from: https://eyewiki.aao.org/Drug_Induced_Maculopathy
16. Frings A, Schargus M. Recovery from amiodarone-induced cornea verticillata by application of topical heparin. Cornea. 2017;36(11):1419-22.