

CASE REPORT

Diclofenac-Induced Unilateral Vortex Keratopathy

JESSPREET KAUR HARBAN SINGH, TECK CHEE CHENG*, SAFINAZ MOHD KHALDIN

*Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia***Correspondence: eddiecheng88@gmail.com: Tel: +603 91456513**Received: 03 April 2025 / Accepted: 12 October 2025*

ABSTRAK

Laporan ini menunjukkan satu kes keratopati vorteks pada sebelah mata dalam seorang pesakit yang menggunakan emulgel Diclofenac. Ini ialah kes pemendapan di kornea yang jarang berlaku akibat penggunaan ubat anti-radang bukan steroid (NSAID) topikal. Laporan ini membincangkan kes seorang lelaki berusia 77 tahun dengan pelbagai komorbiditi sistemik yang menjalani pemeriksaan susulan secara berkala di klinik oftalmologi bagi glaukoma pseudoeksfoliatif pada kedua-dua matanya dan penyakit vaskulopati koroid polypoid pada mata kiri. Semasa salah satu lawatan susulan, didapati terdapat pemendapan berwarna kelabu pada epithelium kornea mata kirinya, yang menimbulkan kecurigaan terhadap keratopati vorteks. Pesakit tidak mengalami simptom penurunan penglihatan. Penglihatan terbaik mata kirinya adalah 6/36, yang dikaitkan dengan parut fovea dan 'pigment epithelium detachment' akibat komplikasi penyakit vaskulopati koroid polypoid. Penglihatan terbaik untuk mata kanan pula adalah 6/12 tanpa tanda-tanda keratopati vorteks. Pesakit dilaporkan menggunakan emulgel Diclofenac setiap hari untuk kedua-dua lututnya yang mengalami osteoarthritis, seperti yang telah dipreskripsikan oleh doktor ortopedik selama dua tahun yang lalu. Tiada ubat sistemik lain yang didapati berpotensi menyebabkan perubahan pada mata ini. Selepas pemberhentian penggunaan emulgel Diclofenac selama enam bulan, pemendapan pada kornea hilang sepenuhnya. Laporan kes ini menekankan bahawa keratopati vorteks pada sebelah mata adalah sangat jarang berlaku, terutamanya dalam kalangan pesakit yang menggunakan ubat topikal, sekali gus menekankan keperluan untuk kajian lanjut bagi memahami mekanismenya dengan lebih tepat. Selain itu, para pengamal perubatan perlu mempertimbangkan dengan teliti risiko dan manfaat NSAID sebelum diberikan kepada pesakit. Pemantauan berkala dan pendidikan kepada pesakit adalah penting bagi pengesanan awal serta rawatan kesan sampingan okular.

Kata kunci: Emulgel Diclofenac; keratopati vorteks pada sebelah mata; ubat anti-radang bukan steroid

ABSTRACT

This report highlights a case of unilateral vortex keratopathy in a patient utilising diclofenac emulgel, highlighting the rare occurrence of corneal deposits secondary to topical nonsteroidal anti-inflammatory drugs (NSAIDs). This article presented a 77-year-old male with multiple systemic comorbidities who was on regular follow-ups in the ophthalmology clinic for bilateral pseudoexfoliative glaucoma and left eye polypoidal choroidal vasculopathy. He was noted to have grayish deposits on his left eye cornea epithelium during one of the visits, prompting suspicion of unilateral vortex keratopathy. He did not have any visual symptoms during the presentation. His best-corrected visual acuity of the left eye was 6/36 which was attributed to the foveal scarring and pigment epithelial detachment as complications of polypoidal choroidal vasculopathy. The best-corrected the visual acuity of the right eye was 6/12 with no sign of vortex keratopathy. For the past two years, he has been using diclofenac emulgel on

both knees daily, as prescribed by his orthopedic doctor for bilateral knee osteoarthritis. There were no other systemic medications prescribed that could potentially induce these ocular findings. Following the discontinuation of diclofenac emulgel for six months, the cornea deposits disappeared completely. This case report emphasises that unilateral vortex keratopathy is uncommon especially in patients with topical medications, highlighting the need for additional research to elucidate its precise mechanism. Additionally, healthcare providers should carefully consider the risk-benefit profile of NSAIDs before prescribing them. Regular monitoring and patient education are essential for the early detection and management of ocular side effects.

Keywords: Diclofenac emulgel; nonsteroidal anti-inflammatory drug; unilateral vortex keratopathy

INTRODUCTION

Vortex keratopathy, also known as cornea verticillata manifests as a distinctive whorl-like pattern characterised by greyish or golden-brown deposits within the corneal epithelium. Most of the time, corneal deposition occurs symmetrically and bilaterally, following a characteristic progression influenced by both the dosage and duration of drug exposure (Moshirfar et al. 2022; Raizman et al. 2017; Sahyoun et al. 2022). Besides systemic medications such as amiodarone, hydroxychloroquine, chloroquine and phenothiazines, vortex keratopathy can be associated with several non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin, ibuprofen and naproxen. However, there is no reported case on diclofenac, particularly in topical application for skin (Raizman et al. 2017; Shoughy et al. 2022).

CASE REPORT

A 77 year-old man with underlying diabetes mellitus, hypertension, dyslipidemia, ischemic heart disease and bilateral knee osteoarthritis was under ophthalmology clinic follow-up for bilateral pseudoexfoliative glaucoma and left eye polypoidal choroidal vasculopathy (PCV). He had bilateral cataract surgeries and multiple glaucoma procedures over his right eye, including trabeculectomy and iStent Trabecular Micro-bypass Shunt implantation. He required topical anti-glaucoma eye drop medications for both eyes and intravitreal injections of anti-vascular endothelial growth for his left eye PCV.

During one of the recent visits, he was noted with greyish corneal epithelial deposits over his left eye, which appeared in a whorl-like pattern that merged into a horizontal line at the inferior one-third of the cornea (Figure 1). Fluorescein staining was negative. There were no similar features observed in the fellow eye. The patient did not have any visual symptoms. His best-corrected visual acuity was 6/12 for the right eye and 6/36 for the left eye. There was a flat conjunctival bleb at the superotemporal region of the right eye, indicating a failed trabeculectomy. Fundus examination revealed bilateral glaucomatous optic discs with a foveal scar and pigment epithelium detachments in his left eye, which explained the poorer vision.

A comprehensive medication review was done and there were no other offending medications besides his daily diclofenac emulgel which was prescribed by the orthopaedic team for his bilateral knee osteoarthritis two years ago. Following the discontinuation of the emulgel for six months with ketoprofen plaster and methyl salicylate ointment as substitutes, his left vortex keratopathy completely resolved without any residual signs (Figure 2). However, his visual acuity remained unchanged. His knee osteoarthritis pain remained well controlled with the substitute topical medications.

DISCUSSION

Corneal epithelial deposits can result from drug accumulation or disturbances in epithelial metabolism caused by drugs. The exact

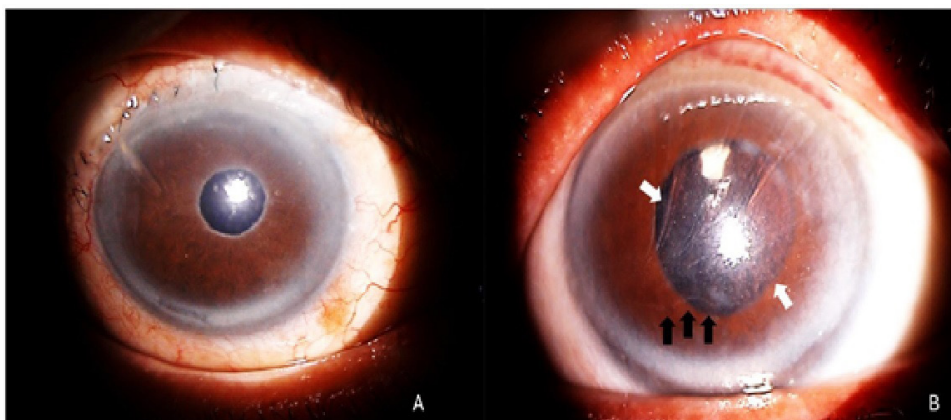


FIGURE 1: Anterior segment photos showing (A) right eye clear cornea, presence of pseudoexfoliative materials over the pupillary margin, a surgical peripheral iridectomy and a flat conjunctival bleb indicating a failed trabeculectomy, with no sign of vortex keratopathy as compared to (B) whorl-like opacities (white arrows) merging into a horizontal line (black arrows) in the left eye which was very characteristic of vortex keratopathy

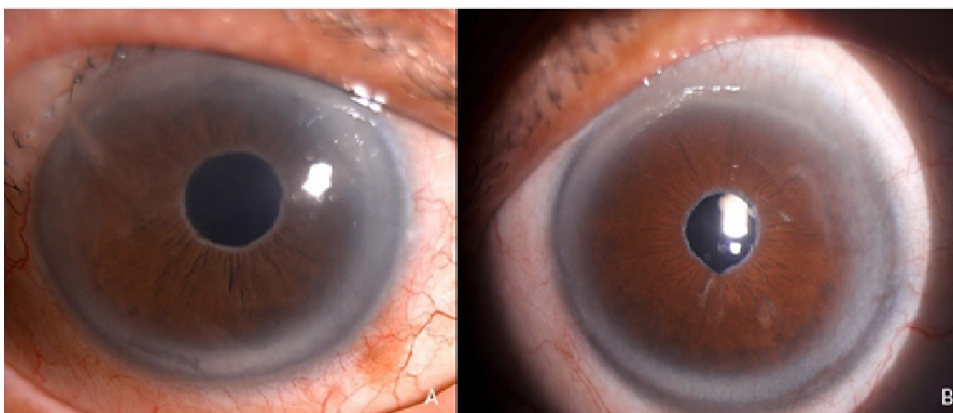


FIGURE 2: Anterior segment photos showing (A) right eye cornea remained the same and (B) a complete resolution of left eye vortex keratopathy after discontinuation of diclofenac emulgel for six months

pathophysiology of vortex keratopathy is not fully understood. Lipid accumulation in the cornea was proposed to be due to lysosomal dysfunction either from endogenous factors like Fabry disease or exogenous factors (drug-induced). Fabry disease which is a rare X-linked recessive disease contributes to 90% of vortex keratopathy cases. The glycosphingolipids are accumulated in the corneal lysosomes due to alpha-galactosidase A deficiency in Fabry disease (Eng et al. 2006).

For exogenous factors, cationic amphiphilic drugs were believed to cause inhibition of lysosomal enzymes and the aggregation of drug-lipid complexes promotes corneal deposits (Raizman et al. 2017; Shoughy et al. 2022). For examples, amiodarone causes phospholipase A2 inhibition in lysosomes resulting in susceptibility to proteases degradation in the cell inner membrane, while suramin results in glycosaminoglycans accumulation by inhibiting iduronate sulfatase (Sahyoun et al. 2022).

NSAIDs were hypothesised to promote corneal deposits due to their amphiphilic and cationic properties, featuring a hydrophobic ring and hydrophilic cationic amine side chain that enable membrane permeability (Hollander & Aldave 2004). This process culminates in the intracellular deposition of phospholipids within the cornea, manifesting as vortex keratopathy (Md et al. 2020). Diclofenac have a relative high lipophilicity compared to ketoprofen, which may increase the membrane permeability contributing to the drug-lipid complex accumulation, hence causing the corneal deposits (Benjamine et al. 2019; Czyrski 2019). We suspected that chronic use of diclofenac emulgel on both knees is the culprit of left vortex keratopathy in our patient. This is because we could not find any other offending systemic medications and the condition has resolved after discontinuation of diclofenac emulgel. Recurrence of vortex keratopathy was not seen after switching to ketoprofen plaster and methyl salicylate ointment.

Emulgel, a combination of emulsion and gel, is effective in transporting hydrophobic drugs. This could inadvertently increase the systemic absorption of the drug leading to phospholipid accumulation in the cornea epithelium. However, vortex keratopathy is almost always presented in bilateral eyes (Raizman et al. 2017). We postulate that the unilateral presentation in this patient could be attributed to multiple glaucoma surgeries in the fellow eye which has caused corneal epithelium dysfunction and subsequently hinder the drug lipid complex from passing through lysosomes for degradation, thus preventing deposit formation in that eye (Hollander & Aldave 2004; Moshirfar et al. 2022; Sahyoun et al. 2022).

Other potential contributors to asymmetry such as tear film dynamics, vascular supply or nerve function was considered but no abnormalities were identified, further supporting our proposed mechanism. Confocal microscopy is a valuable tool in diagnosing and monitoring vortex keratopathy as different causative agents produce distinct epithelial and stromal patterns (Ikegawa et al. 2018). Unfortunately, this was not

performed in our patient as the facility was not available at our centre.

Only one reported case of unilateral vortex keratopathy has been documented. It was a case of unilateral partial limbal stem cell deficiency likely due to prolonged contact lens overwear, evidenced by delayed corneal healing, corneal pannus with limbal tissue changes extending around the entire limbus and vortex keratopathy (Moshirfar et al. 2022). The unilateral presentation has highlighted the need for further research into drug-induced corneal epithelial changes to enhance our understanding of drug-induced vortex keratopathy.

CONCLUSION

Healthcare providers should be vigilant in monitoring patients for ocular adverse effects associated with systemic or topical NSAIDs and consider alternative treatment options when appropriate. Additionally, further research is warranted to better understand the pathophysiology and management of vortex keratopathy.

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