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Case Report

# Corneal Ulcer Following Prolonged Topical Chloroquine Phosphate

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**Abstract**

*Chloroquine and hydroxychloroquine are well known weapons in a rheumatologist's armamentarium. Chloroquine, (N'-(7-chloroquinolin-4-yl)-N,N-diethyl-pentane-1,4-diamine) is an antimalarial drug which has been in use since the early 1950s, in the treatment of Discoid and Systemic Lupus Erythematoses, Rheumatoid Arthritis and dermal light sensitivity eruptions. Hobbs in 1959 recognised a retinopathy which was produced by the long-term administration of this drug. Since the proposal of its anti-inflammatory effect, chloroquine phosphate has been used for the treatment of dry eyes. Among the many side-effects following systemic use of chloroquine; pruritus, urticaria, alopecia, lymphedema of forearm, headache, nausea etc are noteworthy. Ophthalmological complications like bull's eye maculopathy, keratopathy, corneal deposits have also been observed, although infrequently. Majority of the complications arise from the long-term use of the drug which leads to its accumulation in specific sites. Here, we present a rare case report of sterile corneal ulcer following prolonged use of preservative free topical chloroquine phosphate (0.03%w/v) in the form of unims.*

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***Keywords:*** *Chloroquine toxicity, corneal ulcer, chloroquine eye drops, chloroquine phosphate*

## Introduction

An elderly female patient, aged about 60 years presented to our outpatient's department (OPD) with complaints of pain and diminution of vision in her right eye since the past few days. Visual acuity at presentation was 6/18 on Snellen's chart. She was on topical chloroquine phosphate eye drops (0.03% w/v) prescribed to her three months earlier for dry eye. On slit lamp evaluation a large ulcer measuring about 5mm* 3.5mm was seen in the inferior half of the cornea. The margins were clearly defined and floor was clean. It was associated with minimal congestion of the surrounding conjunctiva, with the symptoms remarkably less for the size of the ulcer. It was not associated with any other pathology like foreign body, trichiasis or lagophthalmos. She had been using chloroquine eye drops for the past three months with multiple instillations every day from a single unim's pack despite being advised for a three weeks course. Anterior segment OCT was done and a clear epithelial defect with stromal edema was seen (Figure 1). She was advised to stop the medication immediately. A bandage contact lens was placed after scraping of margins and floor of the ulcer with a sterile BP (Bard-Parker) blade no.15. The small amount of material was sent for microscopic evaluation and culture. Both were eventually found to be normal. She was started on topical moxifloxacin eye drop (0.5%), instilled every 2 hourly. The patient was followed up after a week. On slit lamp evaluation, the cornea was clear, with no epithelial staining pattern on fluorescent sodium strip (1%) staining. Anterior segment OCT was repeated. The ulcer had healed without scarring (Figure 2). The patient was followed up again after 10 days without any further complains. Thus, though the corneal ulcer was due to the long-term abuse of the drug, it was reversible on cessation of the drug, in contrast to chloroquine retinopathy which is mostly irreversible in nature.

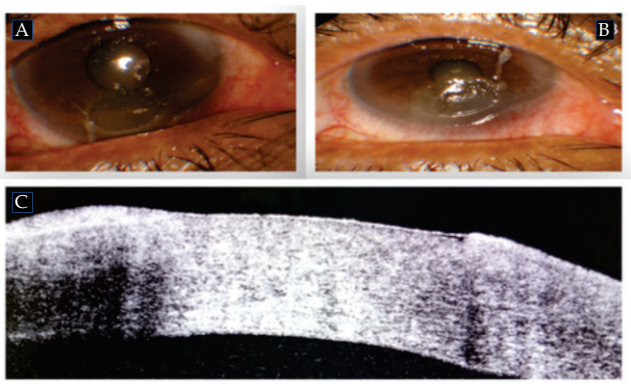


**Figure 1:** ***a)*** *Corneal ulcer of 5mm*3.5mm in the inferior half of the cornea. Note the clear margins and base of the ulcer without any mucopurulent discharge.* ***b)*** *Corneal ulcer after scraping with a Bard Parker's blade no 15.* ***c)*** *Anterior segment OCT image of the corneal ulcer demonstrating the loss of epithelium.*

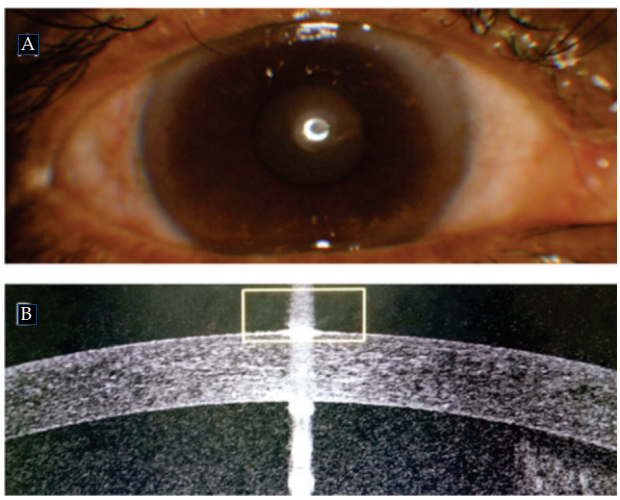


**Figure 2:** ***a)*** *Follow up after a week showing complete healing of the ulcer without any scarring*
***b)*** *Anterior segment OCT confirming the complete healing*

## Discussion

Chloroquine has long been in use for diseases like Rheumatoid Arthritis, Systemic Lupus Erythematosus, Dermatomyositis, Sjögren's Syndrome, Sarcoidosis and Chronic Juvenile Arthritis.[1] Chloroquine binds to deoxyribonucleic acid and gets concentrated in the pigmented tissues in the eye. It interferes with the metabolism in the ellipsoids of the rods and cones by inhibiting the enzyme diphosphopyridine nucleotide diaphorase. In bull's eye maculopathy, there is destruction of rods and cones and dispersal of the retinal pigment. This stage is irreversible and it is therefore necessary to diagnose toxicity before it is reached.

Long term chloroquine use has been well documented to cause corneal deposits. The pattern of the deposits was found to vary. It is seen to pass from a stage of diffuse punctate deposits, which later on aggregate into curved lines beneath the centre of the cornea to a final stage in which a denser, less regular, and greenish-yellow pigmented line appears.[2] Chloroquine phosphate eye drops in dry eye has been in use due to its anti-inflammatory action, as dry eye is thought to be associated with an excessive inflammatory reaction. Chloroquine has a lysosomotropic effect and works by inhibiting the lymphocyte proliferation, phospholipase A2, antigen presentation in dendritic cells, release of enzymes from lysosomes, release of reactive oxygen species from macrophages, and production of interleukin-1 (IL-1). It also has an action on pro inflammatory cytokines, Interferon gamma, Tumor necrosis factor (TNF) alpha, IL-6 levels in peripheral blood mononuclear cells[3] and causes an augmented lipopolysaccharide induced expression of TNF alpha, IL-1 alpha, IL-1 beta and IL-6 in monocytic and microglial cells.[4] A non lysosomotropic anti inflammatory activity has been proposed.[5] A disruption of gene transcription and m-RNA synthesis has also been reported.[5-6]

## Conclusion

A study on topical chloroquine phosphate use for more than three weeks duration has not been reported till date. As this is a single isolated case report, we cannot comment on the long-term side effects of the topical use of chloroquine phosphate in general. However, this case report aims to warn clinicians about the possible chronic side effects of the drug. There is a need for further research on this with a larger pool of data to look into the long-term complications of chloroquine phosphate eye drops (0.03% w/v).

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