

Case Study

Topical steroids, HIV status, CD4 cells and corneal health

Author details: E. O. Megbelayin^{1*}, S.M. Ekpenyong and C.K. Ojide

¹Department of Ophthalmology, University of Uyo Teaching Hospital, Uyo, Akwa-Ibom State, Nigeria

²Department of Microbiology, Federal Medical Centre, Abakaliki, Ebonyi State, Nigeria
favouredolu@yahoo.com

Running title: Enabling milieu like depleted CD4 cells makes cornea more susceptible to steroid effects.

favouredolu@yahoo.com

ABSTRACT

A 36 year old patient presented with a history of pain and progressive loss of vision in the right eye which had lasted for 2 months. He was on topical steroids for about one year before presentation with a CD4 cell of 200cells/ μ L. Examination reviewed a perforated cornea with a huge uveal prolapse. Topical steroids were immediately discontinued and patient placed on topical and systemic antibiotics. Following resolution of the clinical signs, Gunderson's flap was raised to cover the prolapsed uvea. By 6th week post-op, a vascularised pseudocornea had covered the exposed uvea resulting in cessation of pain in the eye. Conclusion: Gunderson's flap is viable option for a prolapsed uvea in an immuno-incompetent patient.

Key words: Steroids, CD4 cells, HIV, Cornea

27 **INTRODUCTION**

28 Topical steroids are often used to manage many ocular surface conditions.
29 Unfortunately these drugs are also associated with serious ocular abnormalities,
30 especially when used injudiciously [1, 2]. A lot has been documented on the propensity
31 of topical steroids to cause corneal ulceration or perforation but little has been reported
32 on the results of immune deficiency on corneal health. It appears reduction in number of
33 CD4 cells makes cornea more susceptible to steroid effects. It also appears immune
34 deficiency makes cornea succumb to steroid toxicity after shorter period of steroid
35 treatment than it would in healthy state. The finding in this report might have been
36 coincidental but its plausibility deserves further scientific scrutiny.

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39 **PRESENTATION OF CASE**

40

41 A 36 year old HIV positive driver presented with a history of pain in the right eye that
42 had lasted for 2 months and a progressive loss of vision. Prior to presentation to our
43 centre in December 2012, he had presented at another clinic in the previous year where
44 he was placed on guttae maxidex (dexamethasone), mydriacyl (tropicamide), spersadex
45 (dexamethasone), ivedexone (dexamethasone), tears naturale, cipromed
46 (ciprofloxacin), zovirax (acyclovir) eye ointment, hypotears gel, chloramphenicol eye
47 ointment at various times during the course of the eye problem.

48

49 With deteriorating eye condition he presented to us with 3 empty bottles of
50 dexamethasone, a bottle of atropine and a bottle of tears naturale. He has been on
51 topical steroids for about a year. Details of the initial ocular condition could not be
52 ascertained but he remembered that it was a red painful right eye that took him to the
53 first primary level eye clinic.

54

55 There was no antecedent trauma, previous eye surgery or use of refractive spectacles.
56 He is not a known diabetic, asthmatic, hypertensive or sickle-cell patient. He was
57 diagnosed with HIV infection 10 months before presentation to our facility and has been
58 on lamivudine, zidovudine and efavirenz. He neither smokes nor takes alcohol. He is
59 single and attained secondary school education

60

61 On examination, vision was light perception (PL) with inaccurate projection on the right
62 eye. The left eye was essentially normal with a visual acuity of 6/5.

63

64 Further reports on examination are those of the right eye. There was a full range of
65 ocular movements with a diffuse conjunctival hyperemia and muco-purulent discharge.
66 Cornea was perforated centrally with inferotemporal extension. A huge prolapsing uvea

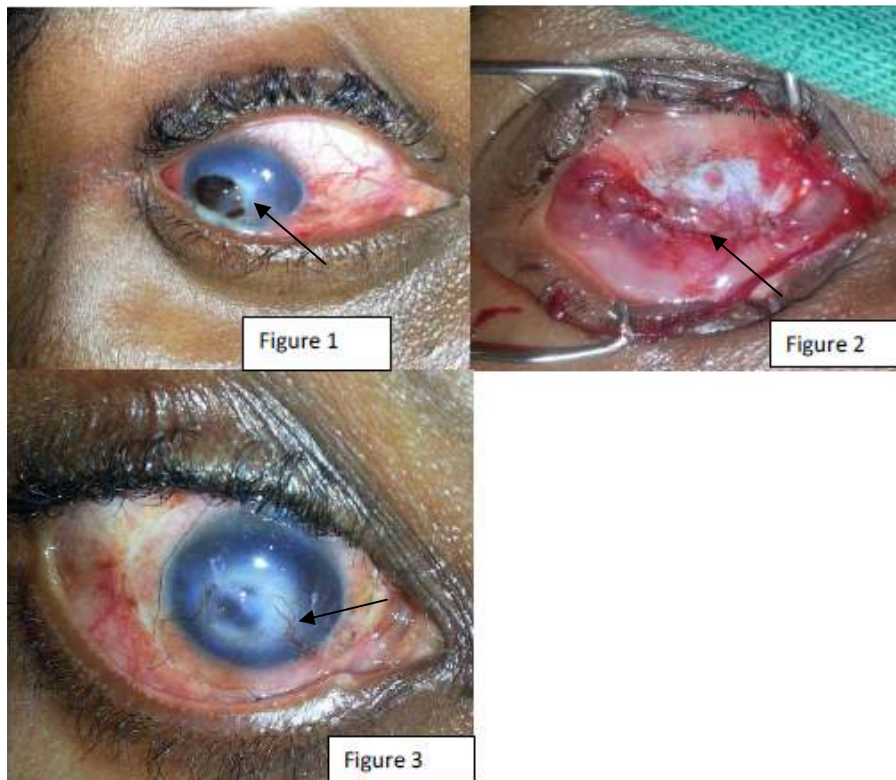
67 tissue from the perforation and descemetocoele precluded further view and a reliable
68 corneal sensitivity test (figure 1).

69
70 Corneal swab was taken for culture on blood agar, chocolate agar, thioglycolate broth
71 and sabouraud dextrose agar. Culture results were negative. However CD4 cell count,
72 carried out at a government facility designated for free HIV treatment, was 200 cells/ μ l.

73
74 Topical steroids were discontinued and patient placed on guttae atropine, ciprofloxacin
75 topically and systemically for 1 week. He then had Gunderson's flap raised to cover the
76 exposed uvea (figure 2). He was seen first day and two weeks postoperatively. He
77 defaulted till sixth week post-operative period.

78 Examination on the sixth post-operative week showed a vascularised pseudo-cornea
79 over the prolapsed uvea. (Figure 3)

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83 **Figures** 1, 2 and 3 respectively show perforated cornea at presentation. The arrow in
84 figure 1 shows a huge iris prolapse with associated muco-purulent discharge. The arrow
85 in figure 2 shows Gunderson's flap raised to cover exposed uvea. The arrow in figure 3
86 shows a vascularised pseudo-cornea 6 weeks post-operatively.

87

DISCUSSION

The deleterious effects of topical steroids on the cornea are well known [1, 2]. However, there is paucity of report on the combined effects of HIV, levels of CD4 cells and topical steroids on corneal health. It can be rationally hypothesized that HIV and topical steroids combine immunosuppressive activities to unleash lethal effects on the cornea. But at what stage in the spectrum of HIV-immunosuppression-AIDS is cornea most susceptible? Certain ocular conditions have been associated with declining CD4 cells. The most common ocular complication of HIV infection is a retinal microvasculopathy called HIV retinopathy. It occurs in 50-70% of patients with CD4 cell counts below 100 cells/ μ L [3, 4]. Cytomegalovirus retinitis develops in 7.5% to 30% of AIDS patients at CD4 counts less than 50 cells/ μ L and Kaposi's sarcoma at less than 200 cells/ μ L [5]. It is likely that these ocular complications occur earlier in HIV patients if there are comorbidities.

An unusual and possibly new keratopathy was reported among HIV patients by Chu et al [6]. This indicates that the cornea may have yet to be identified unique predisposition to pathologic changes in HIV patients. This susceptibility may become pronounced with declining CD4 cells. Until such a time antigen-specific tests of T-lymphocyte function become widely available, CD4 cells remain the predicting parameter for the occurrence of specific ocular infection in patients who are HIV positive [7-9].

The pathogenesis of corneal perforation in our patient is most likely multifactorial. That the left cornea which had no topical steroid instillations was normal at presentation is instructive. Could the continued topical steroid instillations on the right eye have provided the environment for corneal melting at CD4 count of 200 cells/ μ L? Or at what CD4 cut-off is cornea most likely to get compromised? Our patient was on anti-retroviral, could patients not on treatment at same CD4 cell counts have a different corneal susceptibility? Further studies are necessary to address some of these questions.

Patient being placed on Acyclovir ointment at the previous eye center suggested that he may have had herpes simplex keratitis which we could not confirm. In our setting, diagnosis of HSV keratitis is on clinical ground, often based on a typical dendritic corneal ulceration and loss of corneal sensation. Some patients present with geographic corneal ulcers following use of harmful traditional eye medications (HTEMs) and injudicious topical steroid use. CD4 cells are a key component of the adaptive immune system. They act as helper cells that induce cytotoxic CD8-positive T cell clones and recruit macrophages responsible for apoptosis of infected cells [10-12]. Where CD4 cells are depleted as seen in HIV infections, HSV virulence is likely to increase.

129 The response of our patient to discontinuation of frequent topical steroid drops,
130 Gunderson's flap, topical and systemic antibiotic was remarkable. Only twice daily
131 steroid ointment, 2-hourly topical and twice daily tablets 500mg ciprofloxacin were
132 required to control postoperative inflammation and curtail infection. Since the entire
133 cornea with the exposed uvea was covered with conjunctiva further corneal melting was
134 unlikely despite post-operative corneal steroid ointment. Topical steroid was
135 discontinued 2 weeks when post-operative inflammation had subsided significantly.

136
137 We therefore advocate a detailed study to find the association between topical steroids
138 and immunosuppression on corneal health and conclude that evisceration seems no
139 immediate option for a huge iris prolapse following corneal perforation in a retro-viral
140 positive patient with depleted CD4 cells.

141

142 **CONSENT**

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144 All authors declare that written informed consent was obtained from the patient.

145

146 **ETHICAL APPROVAL**

147

148 All authors hereby declare that this study has been performed in accordance with the ethical
149 standards laid down in the 1964 Declaration of Helsinki.

150

151 **ACKNOWLEDGEMENTS**

152 This was a non-funded study.

153 **COMPETING INTEREST**

154 Authors have declared that no competing interests exist.

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