앞포도막염 환자에서 Pranoprofen 점안제 사용 후 발생한 망막 결정 모양 침착물

Retinal Crystal-like Deposits after Topical Pranoprofen Administration in Anterior Uveitis Patient

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Purpose: To report the case of a patient with anterior uveitis who presented accumulation of multiple crystal-like deposits on the retinal surface without vitritis sign or visual disturbance following topical non-steroidal anti-inflammatory drug (NSAID) use.

Case summary: A 61-year-old man used pranoprofen, a topical NSAID, to treat recurrent anterior uveitis accompanied by suspicious steroid-induced glaucoma. After application of topical NSAID, intraocular pressure was controlled, and he did not experience visual disturbance. After one month of topical NSAID use, multiple yellow-green-colored glistening crystal-like deposits were identified on the macular area without signs of vitritis. Additionally, optical coherence tomography imaging revealed highly reflective deposits on the retinal surface. After three months of drug cessation, the number of deposits markedly decreased without additional retinal morbidity, and re-accumulation of crystal-like deposits was absent for two years.

Conclusions: Accumulation of multiple retinal deposits with crystal-like morphology on the macular area could be observed after application of topical NSAIDs without vitritis sign and visual disturbance symptom. The deposits resolved spontaneously following cessation of topical agent administration.

Keywords: Crystal deposits; Crystalline retinopathy; Pranoprofen; Retina; Topical non-steroid anti-inflammatory drugs

Introduction

Crystalline retinopathy is usually related to one of several metabolic diseases or drug intake [1,2]. Previously, crystalline retinopathy was associated with systemic or ocular dis-

orders such as oxalosis, cystinosis, hyperornithinemia, Bietti's corneoretinal crystalline dystrophy, and Sjögren-Larsson syndrome [1-3]. Embolic diseases, caused by calcium and cholesterol emboli, also could induce crystal-like deposits by affecting retinal arterioles [3]. Furthermore, accumula-

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Received: 2020. 7. 29.

Revised: 2020. 9. 6.

Accepted: 2020. 9. 7.

tions of crystal-like retinal deposits have been reported with toxic conditions of several drugs including methoxyflurane, canthazanthin, tamoxifen, talc, and nitrofurantoin [1-3]. We present a case of accumulation of crystal-like deposits on

the retinal surface following topical non-steroidal anti-inflammatory drug (NSAID) use to treat anterior uveitis with elevated intraocular pressure (IOP). This drug has not been reported to induce crystalline retinopathy.

Figure 1. Magnified fundus color photograph of the 61-year-old male patient reveals multiple crystal-like deposits on the macular area without vitritis in the left eye, which occurred after one month of topical pranoprofen use (A-C).

Figure 2. Consecutive changes of crystal-like deposits on the retina before and after discontinuation of topical pranoprofen. There were no specific findings on the fundus before pranoprofen administration (A). The number of crystal-like deposits increased on the macular area during six weeks of pranoprofen treatment (B, C). The deposits decreased over time after discontinuing the topical pranoprofen agent (D-G), and recurrence of the deposits has been absent on fundus examination for two years. The highly reflective materials (H, red arrows), observed on the surface of the internal limiting membrane layer on macular area in horizontal OCT scan, resolved after discontinuing pranoprofen treatment (I).

Case Report

A 61-year-old man was referred for uncontrolled IOP from a private clinic, despite maximum use of topical IOP-lowering agents. He had no documented history of systemic disease including hypertension, diabetes, or other rheumatologic disorder. Two months prior to the initial visit, he had been using topical prednisolone to treat anterior uveitis in both eyes. Initially, best-corrected visual acuity (BCVA) was 20/25. His IOP measured by Goldmann applanation tonometry was 36 mmHg in the right eye and 46 mmHg in the left. Fine keratic precipitates were identified under slit lamp biomicroscopy, but there was no inflammatory reaction in the anterior chamber. Furthermore, remarkable findings were not found on fundus examination.

IOP remained uncontrolled despite application of topical IOP lowering agents. Typical glaucomatous changes were found on an automated visual field test, and optical coherence tomography (OCT) revealed reduced retinal nerve fiber layer thickness in the inferior quadrant. IOP-lowering agents were continued, and an oral acetazolamide agent was added. After one week, his IOP was reduced to 21 mmHg in both eyes and stabilized under 14 mmHg after two weeks.

After one year, however, he experienced recurrent anterior uveitis with anterior chamber reaction and elevated IOP in the left eye. At that time, his BCVA was 20/25 and IOP was 30 mmHg in the left eye. Therefore, the topical NSAID pranoprofen (Pranopulin[®]; JW Shinyak, Seoul, Korea) was added due to a possible history of steroid-induced glaucoma. Although IOP was controlled below 18 mmHg in the affected eye, his BCVA maintained at 20/25 and the anterior chamber reaction was reduced after one month, multiple yellow-green-colored glistening crystal-like deposits were identified on the macular area without vitritis signs in the left eye (Fig. 1, 2B). Regular follow-up was performed because the patient did not complain of any specific symptoms. However, the number of crystal-like deposits on the macula was dramatically increased after two weeks (Fig. 2C). Multiple highly reflective deposits 10 to 30 μ m in diameter were identified on the internal limiting membrane surface on horizontal raster OCT scan (Fig. 2H). There was no definite disruptive lesion on the retinal surface, and no other abnormal findings were detected on other retinal layers. Topical pranoprofen instillation was discontinued immediately because of the retinal crystal-like deposits. Only IOP-lowering agents were continued.

After three months, crystal-like deposits on the retina decreased in the left eye (Fig. 2D); however, the signs of anterior uveitis were recurred. Therefore, based on the suspected relationship between retinal crystal-like deposits and topical pranoprofen, another topical NSAID, diclofenac sodium (Optanac[®]; Samil Co., Ltd., Seoul, Korea), was started. The retinal deposits resolved without an inflammatory reaction in the anterior chamber (Fig. 2D-G), and highly reflective retinal deposits were no longer observed on OCT scan (Fig. 2I). Thereafter, retinal surface remained clear on fundus examination and OCT imaging. After switching from topical pranoprofen to diclofenac, accumulation of retinal deposits was absent for up to two years (Fig. 2F, G).

Discussion

The present case showed accumulation of multiple retinal deposits with crystal-like morphology on the macular area on fundus examination and OCT imaging after topical NSAID use. After cessation of the drug, deposit accumulation resolved on the retinal surface. Moreover, the patient did not experience visual disturbance, and there was no evidence of inflammatory signs in the posterior vitreous body.

Accumulation of the deposits might be correlated with activation of uveitis, as it is associated with crystalline retinopathy [4]. However, we hypothesized that accumulation of crystal-like deposits on the retinal surface was related to topical NSAID treatment for several reasons. First, the deposits were found after initial administration of pranoprofen administration. There were no remarkable findings on the fundus examination before its use (Fig. 2A). Second, the deposits on the retina continued regardless of uveitis activity, and the number of deposits decreased after cessation of topical pranoprofen. Third, the distribution of deposits was limited to the retinal surface, and they did not induce vision-threatening intra-retinal lesions or other complications, despite accumulation. Fourth, hereditary etiology and other ocular disorders with crystalline retinopathy, such as Bietti's corneoretinal dystrophy and Sjögren-Larsson syndrome, were ruled out according to clinical features of the patient. Fifth, uveitis of the patient has recurred several times, even after the period of study. However, the retinal crystal deposits did not recur after replacement of topical NSAIDs. Based on these observations, we suggest that accumulation of crystal-like deposits

was associated with topical NSAID application, rather than organic reasons such as uveitis or other retinal morbidities. Unfortunately, vitrectomy with biopsy of the crystal-like deposits could not be performed, since the patient had no visual disturbance and the deposits disappeared spontaneously after several months of topical NSAID discontinuation. Scientific evidence for the relationship between topical NSAIDs and retinal crystals is insufficient. Considering the context before and after the topical agent use, topical NSAIDs might have affected the occurrence of retinal crystals in this uveitis patient.

In this report, we describe the clinical manifestations including fundus examination and OCT imaging findings concerning accumulation and resolution of multiple crystal-like deposits on the retinal surface, likely related to topical NSAID use in a patient with recurrent anterior uveitis. The composition of the crystal-like deposits and the pathogenic mechanism of deposition remain unknown. Future research should be conducted to identify the formation and structure of crystal-like deposits in patients without visual disturbance and vitritis sign following topical drug application.

Informed Consent

The need for informed consent was waived because of the retrospective single case report, and a waiver of consent was approved by the Institutional Review Board (IRB) (IRB No. 2020-07-044).

Acknowledgements

This report was supported by the national Research Foundation of Korea (NRF) grant funded by the Ministry of Science and Technology Information and Communication (No. 2020R1G1A1013752). The funders had no role in case selection, decision to publish, or preparation of the manuscript.

Conflicts of Interest

The authors have no conflicts to disclose.

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