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Amantadine induced interface fluid formation after LASIK. A case report

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ABSTRACT

Purpose: To describe a case of bilateral interface fluid formation 2 years after laser-assisted in situ keratomileusis (LASIK) surgery caused by the side effect of amantadine.

Observations: A 47-year-old male patient with a history of Parkinson's disease treated with amantadine who had uneventful LASIK surgery in both eyes 2 years ago, presented with a decline in vision over the past 6 weeks. Results: Best corrected vision was 20/200 and 20/400 in the right and left eye respectively. Intraocular pressures were measured within the normal range. Biomicroscopic exam showed bilateral corneal edema. Anterior segment optical coherence tomography (AS-OCT) revealed fluid accumulation within the LASIK flap interface in both corneas. The patient's corneal edema and fluid in the interface began to gradually resolve, and vision improved 2 weeks after discontinuing amantadine.

Conclusions and Importance: Although there is no previous report, it is possible that amantadine may cause interface fluid formation in patients with LASIK surgery.

1. Introduction

Corneal edema is a reported adverse effect of amantadine and is understood to be dose dependent and a result of cumulative toxicity.[1] The incidence of this is unknown with reports of corneal edema occurring up to 6 years after starting amantadine.[1] Prompt diagnosis of this is important as failing to discontinue amantadine can lead to permanent vision loss.

Laser-assisted in situ keratomileusis (LASIK) is the most widely used laser refractive surgery to correct various types of refractive error and has corneal edema and interface fluid formation as an, albeit uncommon, postoperative complication.[2] The differential diagnoses in these cases include diffuse lamellar keratitis (DLK), post-LASIK interface fluid syndrome (IFS), and pressure-induced interlamellar keratitis (PISK).[3] These conditions are often misdiagnosed, and different terms have been proposed to name some of these pathologies.[3] While conditions such as IFS and PISK are more likely causes of corneal edema than amantadine, it is still important to include amantadine as a potential cause of bilateral corneal edema. We describe a case of corneal edema and interface fluid formation occurring six weeks after initiating amantadine in a patient post-LASIK surgery, and subsequent resolution following drug discontinuation.

2. Case report

A 47-year-old male with a history of Parkinson's disease, who has been recently started on amantadine 100 mg twice daily for gradually worsening tremors six weeks prior to presentation, and had LASIK surgery in both eyes two years ago, presented to an outpatient Ophthalmology clinic complaining of gradual deterioration of vision in both eyes and photophobia, symptoms that began six weeks prior. According to the patient's history, the LASIK surgery on both eyes was successful, resulting in 20/20 vision in both eyes. The patient denied any eye pain, double vision, flashes, floaters, headaches, recent trauma, or systemic symptoms. The patient was seen two weeks prior to this visit by an outside Ophthalmologist who diagnosed the patient with bilateral corneal edema and started the patient on 5% hypertonic sodium chloride and prednisolone acetate 1% eye drops four times a day in both eyes. Due to the lack of improvement, the patient was referred to a cornea specialist for further evaluation and management. Best corrected vision was 20/200 and 20/400 in the right and left eye respectively. Using applanation tonometry, the intraocular pressures (IOP) were measured as 17 mmHg in the right eye and 18 mmHg in the left eye, although these values might not be reliable due to presence of corneal edema and interface fluid. Due to the unavailability of dynamic contour tonometry and pneumotonometer, a portable electronic applanation tonometer (Tono-Pen) was used to measure the intraocular pressure

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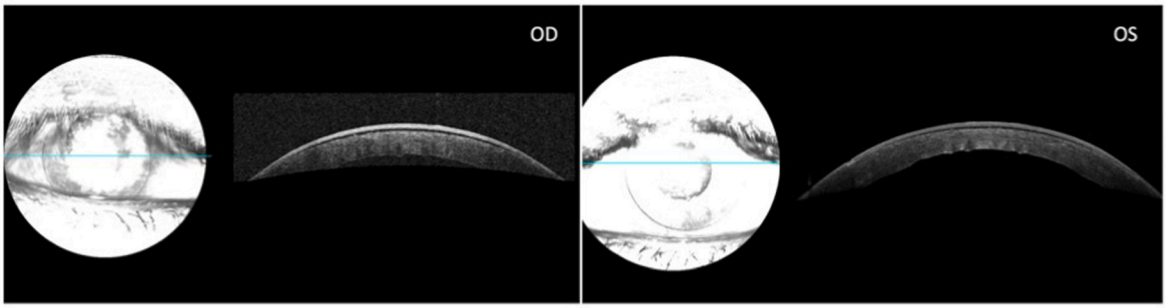

Fig. 1. Representative anterior segment optical coherence tomography (AS-OCT) images at presentation show interface fluid formation within the LASIK flap interface in both corneas. Also, corneal stromal edema and Descemet's membrane folds are evident.

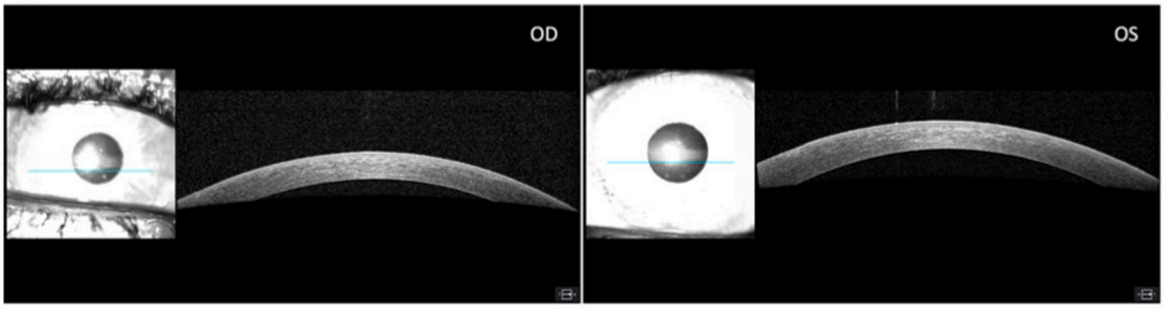

Fig. 2. Representative anterior segment optical coherence tomography (AS-OCT) images at 2 weeks after discontinuation of amantadine show interface fluid resolved in both corneas. However, the corneas still have mild edema and LASIK flap interfaces are not clearly delineated.

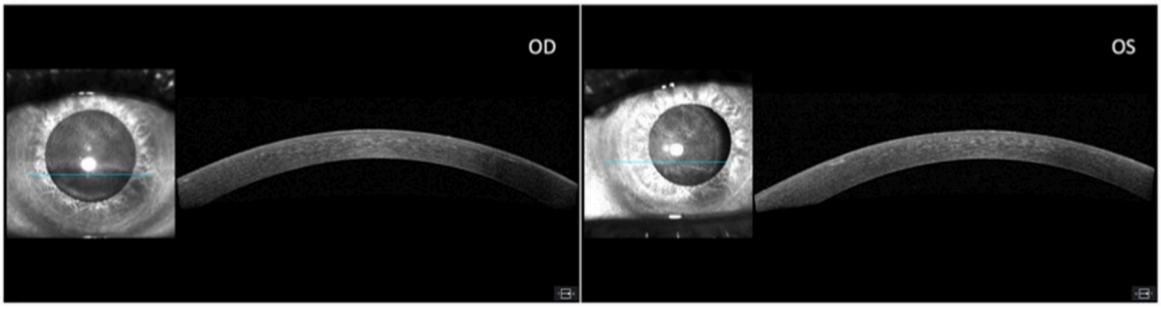

Fig. 3. Representative anterior segment optical coherence tomography (AS-OCT) images at 2 months after discontinuation of amantadine show clear corneas with no interface fluid or edema in both eyes. LASIK flap interfaces are clearly visible.

near the limbus, which showed no elevated pressure. Digital estimation of the IOP was also unremarkable. Biomicroscopic examination showed white and noninflamed conjunctivas. There were smooth, superiorly hinged flaps in both corneas with significant diffuse corneal edema extending past the LASIK flaps. Corneal edema/haze was slightly more noticeable in the flaps stroma than in the beds in both eyes. Both corneas displayed visible folds in Descemet's membrane. No signs of deep stromal vessels, keratic precipitates (KPs), or endothelial guttae were observed. The anterior chambers (AC) were deep and quiet, and the iris and lens were normal. Dilated fundus examinations were normal. Pentacam imaging demonstrated significant diffuse corneal thickening with a central corneal thickness of 682 μm. Anterior segment optical coherence tomography (AS-OCT) revealed fluid accumulation within the LASIK flap interface in both corneas (Fig. 1). The corneal edema was suspected to be an adverse effect of amantadine, which was discontinued. Ruling out PISK was challenging as the measurement of pressures using applanation may have been affected by the corneal edema; therefore, topical steroid was discontinued and brimonidine 0.2% was started out of precaution. Other reported causes of IFS secondary to keratouveitis or endothelial decompensation were ruled out by lack of KPs, AC inflammation, deep stromal vessels, or endothelial guttae. After stopping amantadine for 2 weeks, the corneal edema started to resolve, and the patient's vision began to improve gradually. Even though some haze and edema was still visible during a biomicroscopic examination, the AS-OCT imaging revealed that the gap between the flap and residual stromal bed had disappeared in both eyes (Fig. 2). Repeat pachymetry showed a corneal thickness of 565 μm. Two months after discontinuation of amantadine, the corneal edema had fully resolved as shown in AS-OCT (Fig. 3), the patient's vision returned to normal, and the patient worked with his neurologist to find an alternative medication to amantadine.

3. Discussion

Bilateral corneal edema has been previously described as a rare side effect of amantadine toxicity in several case reports.[4] We present a case of a 47-year-old man with gradual worsening of bilateral post-LASIK corneal edema and interface fluid formation as a potential side effect

of amantadine. The relatively close temporal relationship between the initiating treatment with amantadine and the diagnosis of corneal edema/interface fluid formation, as well as the rapid resolution of the condition once the drug was discontinued, strongly suggest a causal link.

According to a post marketing surveillance study of amantadine,[5] 36 out of 13,137 patients (0.27%) were diagnosed with corneal edema or Fuchs dystrophy. This makes the relative risk of developing corneal edema while taking amantadine 1.7 compared to the general population.[5] The primary action of amantadine is through an indirect increase in extracellular dopamine by non-competitive inhibition of N-methyl--D-aspartate (NMDA) receptors.[6] The exact mechanism in which amantadine leads to corneal edema is poorly understood; however, is thought to be related to the presence of dopamine receptors on the corneal endothelial cells, since other dopaminergic agonists have also been shown to cause corneal edema.[7,8] Histopathologic findings by Jeng and coauthors[4] showed that amantadine can cause permanent damage to corneal endothelial cells. In most reported instances, corneal edema caused by amantadine subsided within a few weeks after stopping the drug. However, early detection is crucial as prolonged corneal edema resulting from toxicity can become irreversible.[4]

In the case described here who had pervious LASIK surgery, it is crucial to eliminate other possible causes of corneal edema and interface fluid formation.[3] It is well-known that the LASIK flap does not fully heal and leaves a potential space for fluid formation, which can potentially lead to the occurrence of the rare complication of IFS. The reasons of IFS are described as high IOP, endothelial cell dysfunction, and uveitis. In 1999, Lyle and Jin[9] and then in 2000 Najman-Vainer et al.[10] reported the first cases of IFS as a side effect of increased IOP in steroid responder patients. In 2002, Belin et al.[11] reported 4 cases of IFS with significantly elevated IOP, and they named this condition pressure-induced interlamellar stromal keratitis (PISK). Dawson et al.[12] conducted a well-designed experimental study on the underlying causes of IFS, and discovered that it could be a result of various conditions that lead to corneal edema, including, but not limited to, increased IOP and endothelial failure. Cases of IFS have been reported without the presence of high IOP in patients with other etiologies including endothelial cell dysfunction, and uveitis.[13–18]

Our case report illustrates the occurrence of corneal edema and interface fluid formation in a patient who had LASIK surgery 2 years prior, and developed this syndrome 6 weeks after starting amantadine treatment. No signs of high IOP, intraocular inflammation, or abnormalities in the corneal endothelial cells were observed. The condition fully resolved upon discontinuing treatment with amantadine. While this has not been reported previously, it is possible that amantadine may lead to interface fluid syndrome in patients who have undergone LASIK surgery by impairing the function or harming the corneal endothelial cells.

Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

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Authorship

All authors attest that they meet the ICMJE criteria for Authorship.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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