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Case report

Amantadine-related corneal edema and endothelial cell loss: Four case reports

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ABSTRACT

Amantadine is widely used in treating influenza A, hepatitis, Parkinson's disease, and fatigue in multiple sclerosis. In the past, only a few case reports have demonstrated that amantadine is associated with corneal edema, endothelial dysfunction, and other corneal comorbidity. We herein present four cases with reversible corneal edema and endothelial loss after taking amantadine, including two cases with delayed presentation of corneal edema after use of amantadine for 18 months and 12 months.

1. Introduction

Amantadine was originally utilized as an antiviral medication for influenza A or hepatitis.[1] It was later introduced in the treatment of Parkinson's disease, associated drug-induced dyskinesia, and even fatigue of multiple sclerosis patients.[1,2] Corneal edema associated with amantadine therapy has been noticed during the past 4 decades, with few cases having been reported in the literature.[3–11] Here, we report four cases of corneal edema and endothelial cell loss caused by oral intake of amantadine.

2. Case reports

2.1. Case 1

An 80-year-old female with a history of dementia and bipolar disease consulted our clinic due to bilateral blurred vision. She had undergone bilateral cataract surgery 6 months previously uneventfully. At the first presentation in our clinic, her best-corrected visual acuities (BCVAs) of the right and left eyes were 0.3 and 0.05, respectively. Slit-lamp examination revealed bilateral corneal stromal edema (Fig. 1). The anterior chamber was silent, both the intraocular lenses were in good positions, and the intraocular pressure was normal. Optical coherence tomography (OCT) showed the corneal thickness of the right and left eyes to be 650 μm and 731 μm, respectively. In the absence of infectious or inflammatory signs, pseudophakic bullous keratopathy or virus infection-related corneal edema was suspected. Topical 3% NaCl and Alphagan were given for relieving corneal edema. Two weeks later, corneal edema in both eyes decreased slightly, to 625 μm and 730 μm, respectively.

Her medication was then carefully reviewed, which was as follows: triazolam 0.25 mg/day, amantadine 200 mg/day, quetiapine 200 mg/day, and bupropion 150 mg/day. Among these drugs, amantadine was prescribed 3 weeks prior to the initiation of ocular symptoms. Considering the possible side effect of amantadine to induce the corneal edema, we suggested discontinuation of amantadine use. However, this suggestion was disapproved by her psychiatrist due to the clinical demand for her psychological symptoms. Two months later, the patient's corneal edema and Descemet's membrane wrinkling deteriorated. To rule out virus infection, polymerase chain reaction of aqueous humor was performed for the detection of cytomegalovirus and herpes simplex virus, and the results were negative for both viruses. After further discussion with the psychiatrist, amantadine was eventually discontinued. The corneal edema subsided gradually. Four weeks after the cessation of amantadine, BCVAs of both eyes improved to 0.6. Corneal thickness of the right and left eyes decreased to 484 μm

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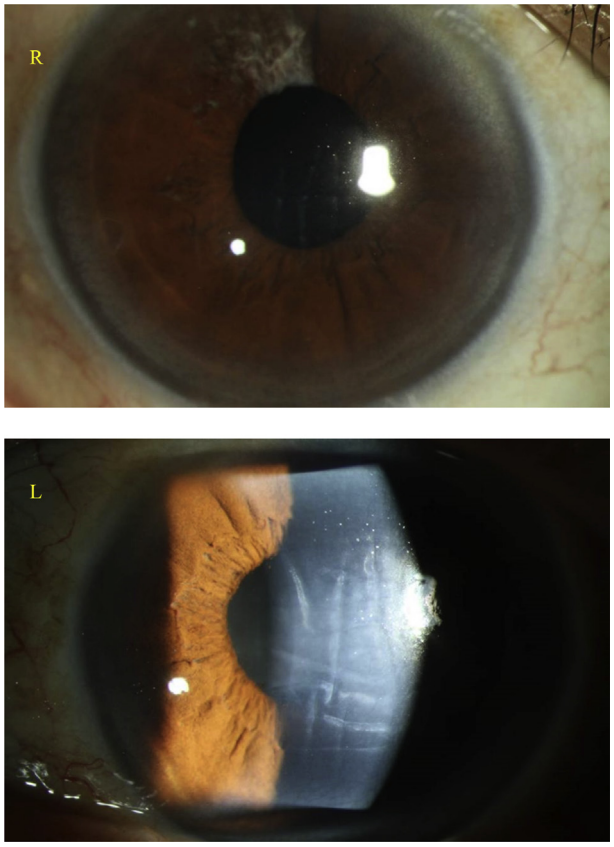

Fig. 1. Bilateral corneal edema with a corneal thickness of 650 μm in the right eye and 731 μm in the left eye (Case 1).

and 504 μm, respectively. Specular microscopy showed that corneal endothelium counts were 1828 cell/mm^2 and 1927 cell/mm^2, respectively. Hexagonicity of endothelial cells decreased in the left eye, with a large amount of cells having irregular shapes (Fig. 2). The last follow-up was 3 months after cessation of amantadine, and the BCVA remained at 0.6 in both eyes.

2.2. Case 2

A 53-year-old female with Parkinson's disease and major depression suffered from painless blurred vision, with visual hallucination for 3 weeks. She had undergone bilateral cataract surgery 2 years previously. When she visited our clinic, the BCVA was 0.1 in both eyes. Slit-lamp examination showed bilateral corneal stromal edema in the central one-third (Fig. 3). In the absence of an anterior chamber reaction or vitreous opacity, 1% prednisolone and 3% NaCl were prescribed for treating the corneal edema. However, no subjective visual improvement was noticed after 2 weeks of treatment.

We reviewed her medication and found that she was taking levodopa, pramipexole, and amantadine for Parkinson's disease from 6 weeks prior to the onset of ocular symptoms; additionally, she took quetiapine for depression. Without an obvious cause of corneal edema, amantadine-related corneal edema was suspected. Amantadine was thus discontinued with approval from her neurologist. Two weeks later, her BCVA of the right eye remained at 0.1, but that of the left eye improved to 0.4. OCT showed the corneal thickness of the right and left eyes to be 739 μm and 697 μm, respectively. One percent prednisolone was then tapered gradually. Four weeks later, her BCVA improved to 0.7 in both eyes, and the corneal thickness decreased to 560 μm and 565 μm, respectively.

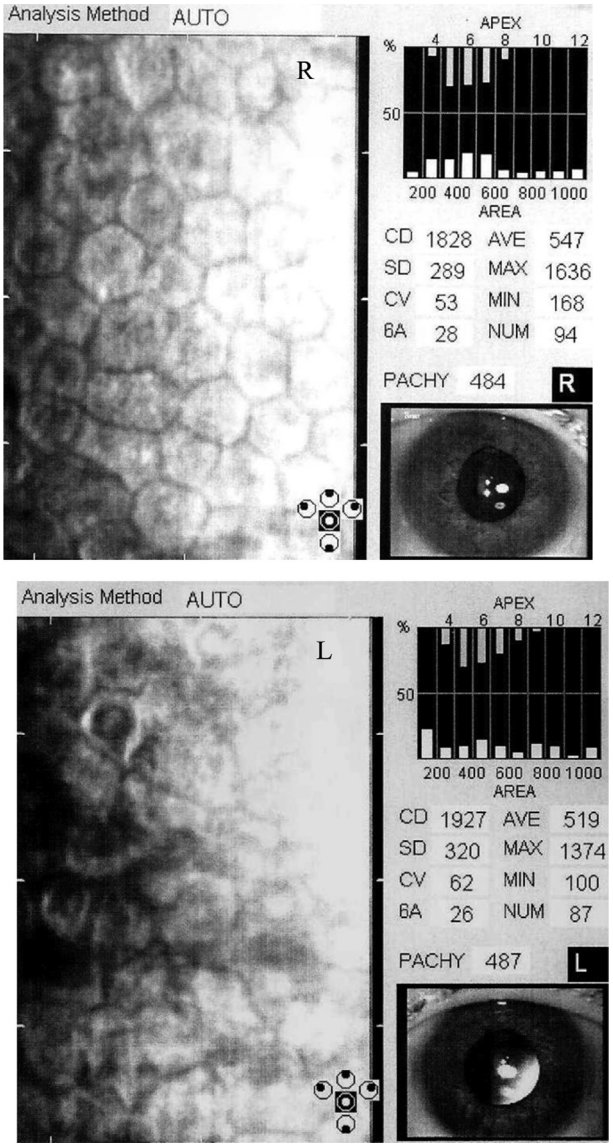

Fig. 2. Decreased endothelial cell count with increased polymorphism and polymegathism (Case 1).

2.3. Case 3

A 72-year-old female with Parkinson's disease complained of gradual bilateral blurring of vision for 1 month. She denied ocular trauma or surgery history. No other ocular symptoms such as tearing, pain, and foreign body sensation were observed. On the first ophthalmologic visit, the BCVAs of the right and left eyes were 0.04 and 0.06, respectively. The autorefractor failed to show the refraction data. During slit-lamp examination, bilateral symmetric corneal edema in the central two-thirds and Descemet's membrane folding were found. No guttata was observed, and the anterior chamber was quiet. Grade 2 cataracts were noted in both eyes. There was no conjunctival congestion or chemosis. Fundus was veiled due to corneal edema even after mydriasis, but there was normal retinal red reflex and the optic discs were not pale. Pachymetry and specular microscopic endothelial count failed due to marked corneal edema. Intraocular pressure and light reflex were normal. Sonography showed no vitreous opacity or retinal detachment. After reviewing her medication history, it was found