



Case report

Corneal endothelial dysfunction caused by *Asclepias curassavica* in a young farmerYun Ji Lee^a, Sang Beom Han^{a,*}, Joon Young Hyon^b^a Department of Ophthalmology, Kangwon National University Hospital, Kangwon National University School of Medicine, Chuncheon, South Korea^b Department of Ophthalmology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea

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ABSTRACT

Purpose: To introduce a case of corneal endothelial toxicity caused by *Asclepias curassavica* (Milkweed) in Korea.**Observations:** A 37-year-old Asian man presented with decreased vision and redness in the right eye, which developed after contact with *Asclepias curassavica*. At presentation, best-corrected visual acuity (BCVA) was 20/60 in the right eye. Slit lamp examination demonstrated severe corneal stromal edema with Descemet's folds and conjunctival hyperemia. We prescribed topical prednisolone acetate 1% eye drops (8 times a day), cyclosporine 0.1% (once a day) and oral prednisolone (30 mg a day for 3 days). One day later, the BCVA improved to 20/40 and marked improvement in corneal edema was observed. At 5 days, BCVA was 20/22 and anterior segment examination showed minimal corneal edema with resolution of Descemet's folds. At 2 weeks, BCVA was 20/20 in the right eye and corneal edema completely resolved.**Conclusions and importance:** This case suggests that high index of suspicion for toxicity from *Asclepias* species is necessary when encountered with patients who present with corneal edema after exposure to these plants. Aggressive anti-inflammatory treatment might be helpful for early recovery, at least for young patients.

1. Introduction

Sodium–potassium adenosine triphosphatase (Na^+/K^+ -ATPase) pump at the corneal endothelial surface plays an essential role in the maintenance of corneal transparency,¹ and impairment of this pump can result in corneal edema.²

Plants of the genus *Asclepias* (milkweed) of the Asclepiadaceae family are wildflowers native to the tropical America,¹ and globally distributed as ornamental plants.^{1,3} Plants of the Asclepiadaceae family contain toxic cardenolides, also known as cardiac glycosides, in their stems, leaves, roots and latex for protection from their predators.¹ Clinically, the natural cardenolides inhibit the enzyme Na^+/K^+ -ATPase pump, and have cardiotonic effect similar to digitalis.¹ It can also bind to Na^+/K^+ -ATPase at the corneal endothelial cells and inhibit the activity of the pump, and can result in corneal endothelial toxicity.¹

To the best of our knowledge, only a few cases of corneal endothelial toxicity associated with *Asclepias* species have been reported.^{1–4} However, all the reported cases were among old patients of 60 years or older. We recently experienced a case of corneal endothelial dysfunction associated with contact with *Asclepias curassavica* in a

young patient that was successfully treated with aggressive anti-inflammatory treatment, so herein report the case.

1.1. Case report

A 37-year-old healthy Asian male farmer presented with decreased vision and redness in the right eye. He also complained of mild ocular pain and discomfort. His past medical history was unremarkable. He reported that the symptoms developed at the evening of the previous day, about 3 hours after he handled the leaves of *Asclepias curassavica*, also known as “milkweed”, and rubbed his right eye. On examination, his best-corrected visual acuity (BCVA) was 20/60 in the right eye and 20/12 in the left eye. Intraocular pressure (IOP) measured with pneumatic applanation tonometry was 18 mmHg in both eyes. Slit-lamp biomicroscopy showed conjunctival hyperemia and severe corneal stromal edema with Descemet's folds, which was confirmed with Anterior segment optical coherence tomography (AS-OCT; Carl Zeiss Meditec, Oberkochen, Germany (Fig. 1). There was no corneal epithelial defect or keratic precipitate. Anterior chamber was clear. Although detailed evaluation of the posterior segment was difficult due to the

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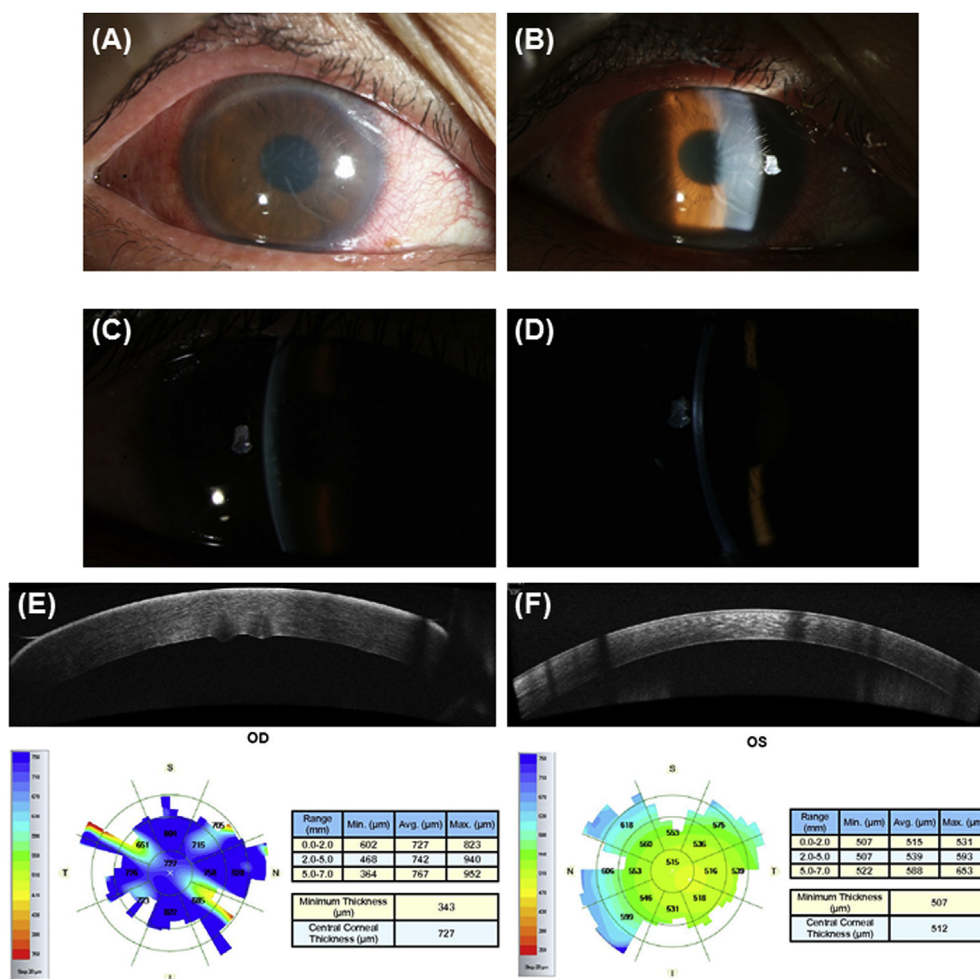


Fig. 1. (A, B and C) Anterior segment examination of the right eye shows severe corneal stromal edema with Descemet's folds and conjunctival hyperemia, (D) whereas no corneal edema was observed in the left eye. (E) Anterior segment optical coherence tomography (AS-OCT; Carl Zeiss Meditec, Oberkochen, Germany) demonstrates severe corneal edema and Descemet's folds with central corneal thickness (CCT) of 727 μm in the right eye, (F) while the AS-OCT shows normal cornea with CCT of 512 μm in the left eye.

corneal edema, no apparent abnormality in vitreous or retina was observed.

To remove the remaining toxin and prevent further penetration into corneal endothelium, the right eye was thoroughly flushed with normal saline. Topical prednisolone acetate 1% (8 times a day) and cyclosporine 0.1% (once a day) were prescribed. Oral prednisolone (30 mg a day for 3 days) was also added. The next day, the patients reported improvement in vision with BCVA of 20/40 in the right eye. Slit lamp examination revealed marked improvement in corneal edema. At 5 days after exposure, he reported considerable improvement in vision. BCVA was 20/22 and IOP was 16 mmHg in the right eye. Anterior segment examination showed minimal corneal edema with resolution of Descemet's folds. Endothelial cell density (ECD) was 2653/ mm^2 in the right eye and 2793/ mm^2 in the left eye. Topical Prednisolone acetate was tapered to 4 times a day. At 2 weeks after presentation, the patient showed complete improvement of the vision. Corneal edema completely resolved with a BCVA of 20/20 and IOP of 16 mmHg in the right eye. ECD was 2667/ mm^2 in the right eye and 2703/ mm^2 in the left eye (Fig. 2).

2. Discussion

We presented a case of corneal endothelial toxicity caused by the contact with *Asclepias curassavica* in a young male farmer that was resolved with aggressive anti-inflammatory treatment. To the best of

our knowledge, this is the first case of the corneal endothelial dysfunction associated with cardenolides from *Asclepias* species in Korea.

In this case, cardenolides from the leaf of the *Asclepias* plant induced corneal edema several hours after the contact to the eye, as in other case reports.^{1,3} Cardenolides can penetrate the intact cornea without damage to the epithelium,^{1,2} and cause corneal endothelial toxicity by inhibiting the endothelial Na^+/K^+ -ATPase pump function.¹ Topical application of digoxin, a purified cardiac glycoside, also led to similar corneal endothelial dysfunction by inhibiting endothelial Na^+/K^+ -ATPase, which was observed several hours after the application and completely resolved after withdrawal of the drug.⁵ Similar corneal edema was reported in a patient with systemic digoxin toxicity.⁶

The corneal endothelial toxicity caused by the cardenolides is suggested to be temporary, and the corneal edema can be self-limiting in a few days with the clearance of the cardenolides from the endothelial cells.¹ Anti-inflammatory treatment, i.e. steroid, may be helpful to alleviate ocular inflammatory symptoms, such as, conjunctival injection.¹ Treatment with topical steroid was often attempted because topical steroid might increase the activity of the remaining Na^+/K^+ -ATPase pump that was not blocked by cardenolides and facilitate the recovery process.^{1,3,7} An experimental study revealed that dexamethasone increased Na^+/K^+ -ATPase pump activity in cultured corneal endothelial cells.⁷

In the first case of corneal endothelial toxicity associated with *Asclepias curassavica* reported in 1995, the patient, a 60-year-old man,

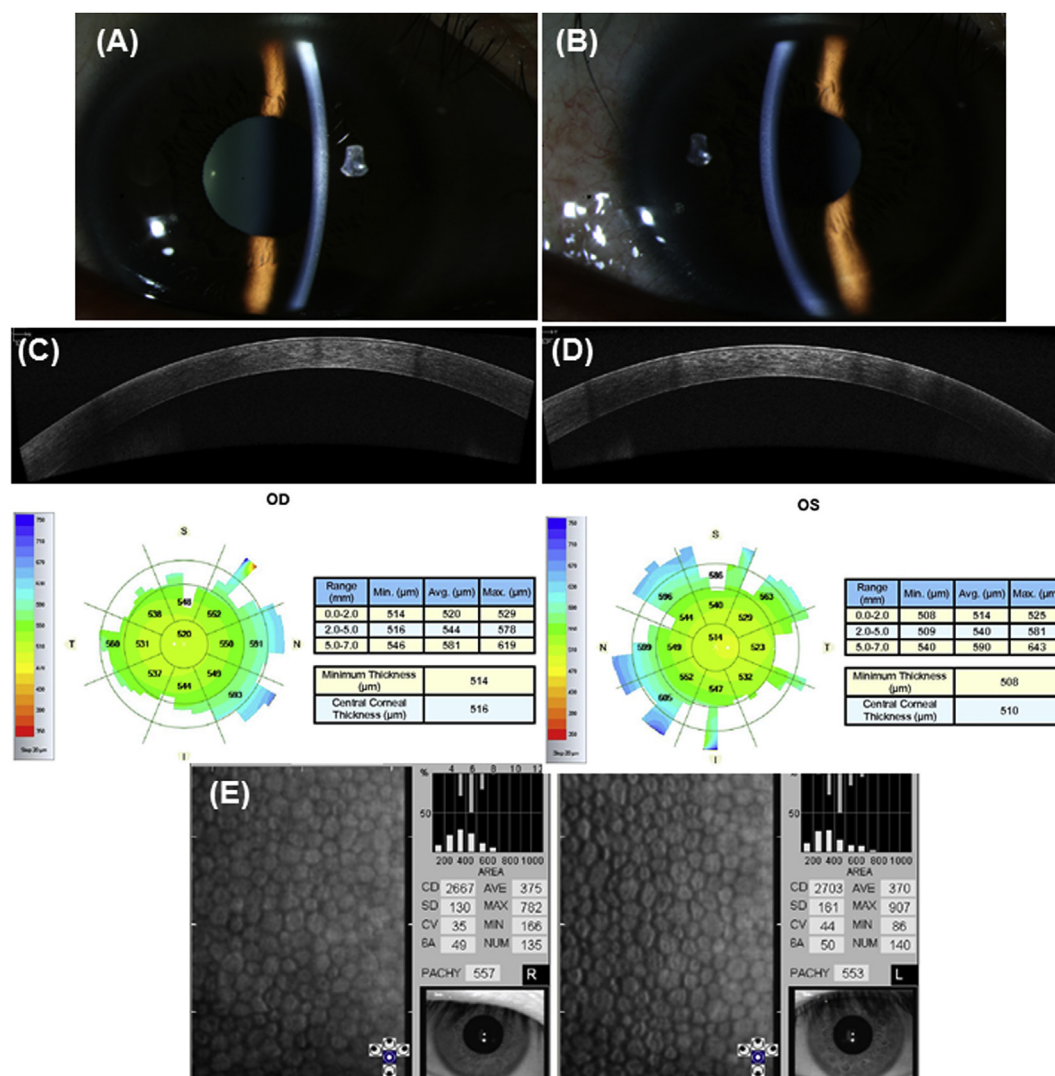


Fig. 2. (A) Slit lamp examination of the right eye shows complete resolution of corneal edema. (B) Normal cornea in the left eye. (C) AS-OCT shows no cornea edema with CCT of 516 μm in the right eye. (D) AS-OCT shows normal cornea with CCT of 510 μm in the left eye. (E) Endothelial cell counts density (ECD) was 2667/ mm^2 in the right eye and 2703/ mm^2 in the left eye.

attained rapid recovery in 48 hours with topical artificial tear only.² In a case of *Asclepias fruticosa* exposure in a 73-year-old male farmer, marked improvement was observed at day 3 after the use of 0.1% topical dexamethasone, and corneal edema completely resolved at 2 weeks.¹ Almost complete recovery was also obtained after using topical dexamethasone, ofloxacin and artificial tears in a case of *Asclepias physocarpa* exposure in a 76 year-old female patient,⁸ although there was a possibility of endothelial distress, such as, pleomorphism and polymegathism, as a sequelae at 6 months.⁸ Mikkelsen et al.⁴ used topical chloramphenicol 0.5%, dexamethasone 0.1% and scopolamine 0.2% in a 70-year-old male patient who was exposed to *Asclepias tuberosa*, and reported that the corneal edema resolved after 96 hours.⁴ However, it took 9 months for the BCVA to improve to 20/20 from 20/400 at initial presentation.⁴ In a case of bilateral *Asclepias physocarpa* exposure in a Japanese 74-year-old male patient, Matsuura et al.³ reported complete recovery of corneal edema in 6 days by rinsing with normal saline, topical levofloxacin 1.5% (6/day), bethamethasone 0.1% (6/day) and oral steroids (10 mg/ day).

Calotropis procera, a plant of the *Asclepiadaceae* family, also produces cardenolides, and can result in corneal endothelial toxicity.⁹ Although recovery of corneal edema and visual acuity was observed in most cases, permanent loss of the endothelial cells was remarkable,

suggesting that early aggressive anti-inflammatory treatment might sometimes be necessary in cases with corneal endothelial dysfunction associated with cardenolides.⁹

In our patient, we used aggressive anti-inflammatory treatment including topical prednisolone acetate 1% and cyclosporine 0.1% as well as oral prednisolone. Although previous reports suggest that the corneal endothelial toxicity associated with cardenolides can resolve spontaneously,^{1,2} and addition of topical steroid would be enough,^{1-4,8} all the patients in the cases were elderly of 60 year or older. The young age of our patient could be associated with an increased risk of more aggressive inflammation and tissue destruction, while the patient was healthy enough to tolerate vigorous topical and systemic anti-inflammatory treatment. Long-standing endothelial cell swelling could also lead to permanent cell death. Corneal endothelial cell toxicity associated with cardenolides toxin from another plant of the *Asclepiadaceae* family in patients at the ages of 32–40 years old resulted in permanent endothelial cell loss, supporting our assumption.⁹ Marked improvement in visual acuity and corneal edema was observed in a day, and almost complete recovery was attained in 5 days, suggesting that aggressive anti-inflammatory treatment could be useful, at least in young patients.

3. Conclusions

Although plants of *Asclepias* species are widely distributed, corneal endothelial toxicity associated with cardenolides from the plants is unfamiliar to ophthalmologists.³ Ignorance of the corneal toxicity of the plants can lead to misdiagnosis, such as, uveitis or endophthalmitis, and even unnecessary surgical interventions.³ Thus, knowledge of the corneal toxicity associated with *Asclepias* species and detailed history taking would be necessary for diagnosis and proper management of such cases.^{1,3}

We present a case of corneal endothelial toxicity caused by *Asclepias curassavica* in a young patient, in which aggressive anti-inflammatory treatment might be helpful.

3.1. Patient consent

Written informed consent to publish the report was obtained from the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for

Authorship.

Declaration of competing interest

None of the authors have financial disclosures.

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