

The Horticulturist With Blurry Vision

Carmen Hill,* a 48-year-old architect, went to sleep on a Saturday night in her normal state of health and woke up the next morning with blurred vision and irritation of the right eye. Alarmed by this sudden development, she went to her local emergency room.

In the Emergency Room

We examined Ms. Hill in the ER, where she reported no trauma, redness, discharge, flashes, floaters, or visual field loss. She related her medical history, notable for acne rosacea, for which she used MetroGel (metronidazole 0.75% topical gel) once weekly on Saturday nights. She also had a history of oral herpesvirus without ocular involvement. Ms. Hill used reading glasses, and she had no history of contact lens use or ocular surgeries. A brief slit-lamp exam revealed corneal edema.

We Get a Look

Shortly afterward, we did a more thorough exam in the clinic. Ms. Hill's pupils were equal, round, and reactive to light and accommodation. Ocular movements were intact, and confrontation visual fields were full bilaterally. Intraocular pressure (IOP) by applanation tonometry was 19 mm Hg in the right eye and 18 mm Hg in the left. Her best-corrected visual acuity was hand motions in the affected right eye and 20/25 in the left. Measurement of the

tear film pH was normal.

On slit-lamp microscopy, her eyelids were normal, and the conjunctiva and sclera of both eyes were white and quiet. The corneal epithelium was normal bilaterally, showing no fluorescein staining. Diffuse corneal edema with Descemet membrane folds were present in the right eye. The anterior chambers were deep and quiet, and we observed a 1+ nuclear cataract in both eyes. The posterior exam was unremarkable in each eye, although the view in the right eye was limited by corneal edema.

History Revisited

Having gathered the notable exam finding of unilateral, acute-onset corneal edema in a phakic, noninflamed eye, we questioned Ms. Hill further. She was fairly certain that she did not get MetroGel in her right eye. Family history was negative for corneal disease including Fuchs endothelial dystrophy.

Review of systems was negative. She denied substance use and was not a smoker. However, she told us she had an unusual hobby—she kept pet caterpillars that she raised into monarch butterflies.

Differential Diagnosis

Given Ms. Hill's sudden presentation on a Sunday morning following her use

of metronidazole gel the night before, the differential diagnosis included irritation from ocular exposure to the medication. MetroGel is a known eye irritant, and the formulation she used

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contains 28 mEq of sodium per gram of metronidazole. However, the patient was certain that she had not applied the medication anywhere near her eyes and said that she always washed her hands after application.

Other possible diagnoses included corneal edema secondary to fluctuations in IOP, but no signs pointed to such a condition. Infectious causes such as herpetic keratitis were unlikely given the apparent lack of ocular inflammation.

Our Diagnosis

With infectious and primary ocular disease processes ruled out, we focused on exposures. A quick Google search of her caterpillar hobby led to the milkweed plant. Upon questioning, she said that she had worked on such plants without gloves the day before her vision loss. The diagnosis was most likely corneal edema secondary to endothelial toxicity from milkweed sap exposure.

We prescribed treatment with preservative-free tears every two hours and Muro 128 (sodium chloride hypertonicity ophthalmic ointment,

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5%) twice daily. She was seen in the clinic for follow-up two days after starting treatment. She reported significant improvement but was not yet back to normal. Visual acuity had improved to 20/30 in the affected eye, and the corneal edema was reduced significantly.

Ms. Hill returned six days later, at which point the corneal edema was completely resolved, and her vision had normalized. Throughout follow-up examinations at six months and annually for two years thereafter, her cornea has remained normal.

“Milkweed Endotheliopathy”

The genus *Asclepias* includes more than 140 species of plants known as “milkweeds,” so named for their milky sap, which contains an alkaloid latex and cardenolides. Otherwise known as cardiac glycosides, these cardenolides are compounds that the plants have evolved as natural chemical defense mechanisms to repel herbivores.¹ Specifically, their mechanism of action includes binding with and inhibiting Na⁺/K⁺ ATPase (also known as the sodium-potassium pump), which is the driving force of the electrochemical gradient in most membranes, including that of the corneal endothelium.

Researchers in the 1960s discovered a further effect of these compounds: Monarch butterflies that feed on these plants sequester the cardenolides in their bodies, making them toxic and bitter tasting. This was not only a strategy that the butterflies evolved to avoid predation but is also one that butterfly gardeners use when raising the insects.²

Contact with the cornea. A normally functioning cornea requires active ATPases to maintain the transparency of the tissue. Cardenolides can penetrate the epithelium without damaging it and reach the basolateral membrane of the corneal endothelium. There, the toxin interferes with the function of the ATPase pump, causing edema and blurring of vision.³

Ms. Hill presented the morning after exposure. The milky substance from the plant contaminated her hands as she fed her pet caterpillars. A similar time from exposure to onset of symptoms has been reported in published

cases of *Asclepias* toxicity—induced corneal edema.^{4,5} This time course also matches that seen in digitalis keratopathy following topical administration of digoxin drops.⁶

Treatment options. Therapeutic regimens mentioned in the literature range from supportive treatment with artificial tears alone to use of topical steroids, which are thought to increase the activity of the Na⁺/K⁺ pumps and thus expedite recovery.⁷ However, recovery times were similar at approximately 24 to 48 hours after symptom onset, corresponding with the effect time of cardiac glycosides.

Take-Home Points

Toxic exposures to the cornea are common, and the clinician should keep them in mind when forming a differential diagnosis for a patient presenting with corneal edema. Further, as demonstrated by this case, the value of a thorough history cannot be overstated. Supportive therapy appears to be sufficient to manage *Asclepias* corneal toxicity; although steroid therapy may theoretically facilitate recovery, no demonstrable change has been reported in recovery time or long-term consequences. Education about this ocular toxin and preventive measures (e.g., gloves, eye protection, hand washing) may reduce the incidence in those handling these plants and insects.

*Patient name is fictitious.

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