Euphorbia sap keratopathy: four cases and a possible pathogenic mechanism

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Abstract

Aims—To report four cases of *Euphorbia* sap causing anterior segment toxicity.

Methods—Medical records of four patients who presented with *Euphorbia* sap keratoconjunctivitis were reviewed. Clinical findings were compared with previously published reports.

Results—All of these patients experienced a similar clinical course. Initial contact with *Euphorbia* sap caused punctate epitheliopathy; patients noted immediate burning and photophobia, but no visual loss. In all cases, patients experienced epithelial slough with delayed healing, requiring approximately 9 days to heal the epithelial defect. Patients were treated with topical antibiotics, pressure patching, or a bandage contact lens, and final visual acuities were excellent in all cases. A review of the literature revealed that *Euphorbia* sap contains a diterpenoid diester which exhibits antineoplastic activity in rodents.

Conclusions—Individuals who work with *Euphorbia* plants should be cautioned to wear eye protection. Patients with *Euphorbia* sap anterior segment toxicity should be informed that their condition may worsen initially, but that visual outcome is generally excellent. The progressive corneal epithelial sloughing and delayed corneal epithelial healing may be secondary to the antineoplastic effects of *Euphorbia* sap.

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Species of the plant genus *Euphorbia* are commonly employed as ornamental plants. These plants characteristically produce a milky sap which has been used to treat cancers, tumours, and warts from at least the time of Hippocrates.¹ Keratoconjunctivitis has been reported to occur secondary to exposure to the sap of several *Euphorbia* species, including *tirucalli*,^{2,3} *helioscopia*,^{4,5} *peplus*,^{4,7} *cyprisias*,^{4,7} *royleana*,^{8,9} *lathyrus*,¹⁰⁻¹² and *lactea*.³ The pathogenesis of *Euphorbia* sap keratoconjunctivitis, however, is unknown.

We report four cases of *Euphorbia* sap keratoconjunctivitis, including the first reported case of keratoconjunctivitis secondary to the sap of *Euphorbia trigona*, and compare our clinical findings with previously published reports.

Methods

The medical records of all known patients who presented to the Bascom Palmer Eye Institute

Figure 1 *Euphorbia lactea* sap dripping from the plant belonging to the patient described in case 1.

or the W K Kellogg Eye Center with keratoconjunctivitis secondary to plant sap between 1 January 1985 and 31 December 1994 were reviewed. One patient presented to the W K Kellogg Eye Center in Ann Arbor, Michigan, and three presented to the Bascom Palmer Eye Institute in Miami, Florida. Clinical findings were compared with previously published reports of plant sap keratoconjunctivitis. The genus and species of each plant were determined by a horticulturist.

Results

CASE 1

A 38-year-old man was moving his plant (*Euphorbia lactea*), when he felt 'plant juice' splash into his right eye (Fig 1). The patient experienced immediate burning and photophobia in his right eye. He noted no vision changes. His symptoms persisted despite irrigating his eye with water.

Examination revealed a visual acuity of 6/6 in each eye. Slit-lamp examination revealed mild conjunctival injection, diffuse corneal punctate epitheliopathy, and marked anterior chamber flare in the right eye. The remainder of the examination of both eyes, including the fundus examination, was unremarkable. The patient was treated with cyclopentolate

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Figure 2 Case 1. A 38-year-old man with corneal epithelial defect (arrows) and underlying stromal oedema secondary to *Euphorbia lactea* sap toxicity.

1%, bacitracin ophthalmic ointment, and a pressure patch. Examination of the right eye on the following day revealed a visual acuity of 6/18, moderate conjunctival injection and chemosis, a 3.0×5.5 mm area of corneal epithelial sloughing, and mild corneal oedema (Fig 2). The patient was treated with cyclopentolate 1% and bacitracin ophthalmic ointment. On day 3, the patient's visual acuity in the right eye was 6/60. The remainder of the examination was unchanged. Treatment was continued and the patient was followed daily. His corneal epithelial defect required 9 days to heal and the patient's examination returned to normal, including a visual acuity of 6/6.

CASE 2

A 59-year-old man was repotting his plant (*Euphorbia trigona*), when he felt sap from the plant splash into his eyes. He experienced the acute onset of burning, photophobia, and itching in both eyes (Fig 3). He reported no change in his vision. His symptoms persisted despite irrigating his eyes with water.

Examination 1 day after injury revealed a visual acuity of 6/15 in the right eye and 6/12 in the left eye. Slit-lamp examination revealed moderate conjunctival injection and diffuse corneal punctate epitheliopathy bilaterally. The remainder of the biomicroscopic examination and the funduscopy examination of both eyes were unremarkable. The patient was treated with artificial tears. Examination the following day revealed a visual acuity of 6/21 in the right eye and 6/12 in the left eye. A 2.5×3.5 mm corneal epithelial defect was present in the right eye (Fig 4); the punctate epitheliopathy in the left eye had improved. The remainder of the examination was unchanged. The patient was treated with a bandage contact lens and polymyxin B sulphate-trimethoprim ophthalmic drops in the right eye and followed daily. The patient wore a bandage contact lens for 2 days and his corneal epithelial defect required 9 days to heal. His visual acuity returned to 6/6 in each eye.

CASE 3

A 59-year-old woman was trimming her pencil tree (*Euphorbia tirucalli*) (Fig 5) when she felt sap from the plant splash into her right eye. She noted immediate photophobia and foreign body sensation in her right eye, but no vision changes.

Figure 3 *Euphorbia trigona* belonging to the patient described in case 2.

Figure 4 Case 2. A 59-year-old man with corneal epithelial defect (arrows) and necrotic epithelium (under left arrow) secondary to *Euphorbia trigona* sap toxicity.

Figure 5 *Euphorbia tirucalli* belonging to the patient described in case 3.

Examination revealed a visual acuity of 6/12 in each eye. Slit-lamp examination revealed marked conjunctival chemosis and mild diffuse corneal punctate epitheliopathy in each eye. The remainder of the examination of both eyes, including the funduscopy examination, was unremarkable. Examination of the right eye on the following day revealed a best corrected visual acuity of 3/60, marked conjunctival injection and chemosis, moderate corneal oedema, and a 5.0×7.0 mm area of corneal epithelial sloughing (Fig 6). The patient was treated with a pressure patch for 3 days, and prednisolone acetate 1% and hyoscine (scopolamine) hydrobromide 0.25% for 10 days. The corneal epithelial defect and corneal oedema required 10 days to resolve. Her best corrected visual acuity returned to 6/6 in each eye.

CASE 4

A 44-year-old man was trimming his pencil tree (*Euphorbia tirucalli*) when he felt sap from the tree 'spray' into his eyes. He noted the

Figure 6 Case 3. A 59-year-old woman with corneal epithelial defect (arrows) secondary to *Euphorbia tirucalli* sap toxicity.

Figure 7 Case 4. A 44-year-old man with corneal epithelial defect in the left eye secondary to *Euphorbia tirucalli* sap toxicity. There is heaped up epithelium at the margins of the defect.

acute onset of burning and foreign body sensation in both eyes, but experienced no change in his vision. His symptoms persisted despite irrigating his eyes with water.

The patient presented to his local ophthalmologist, who further irrigated the patient's eyes and applied antibiotic drops and pressure patches bilaterally. Because the patient noted decreased visual acuity the following day, he presented to the Bascom Palmer Eye Institute. Examination revealed a best corrected visual acuity of 2/60 in the right eye and 6/60 in the left eye. Slit-lamp examination revealed moderate conjunctival injection and chemosis, diffuse corneal erosions, moderate corneal oedema, and mild anterior chamber cells and flare in each eye. There was a 5.0×4.0 mm central corneal epithelial defect in the right eye and a 3.5×2.8 mm paracentral corneal epithelial defect in the left eye (Fig 7). The remainder of the examination was unremarkable. The patient was treated with pressure patches bilaterally and was followed up by his local ophthalmologist.

Discussion

The *Euphorbiaceae* plant family includes approximately 1500 species¹³ and is named after Euphorbus, the physician to King Juba II of Mauritania in AD 18.¹⁴ Euphorbus discovered the therapeutic properties of *Euphorbiaceae* plants growing in the Atlas mountains.¹⁴ In his 1655 translation of the first century AD Greek herbal of Dioscorides, John Goodyear wrote that *Euphorbia* sap 'takes away...hanging warts ...[and] is good also for...pterygia and carbuncles...gangrenes, fistulas'.¹⁵ In the early 19th century in England, it was reported that *Euphorbia* sap 'removeth all blemishes of the skin'.¹⁶ *Euphorbia* sap is used in India and Africa to treat warts^{17,18} and in China to treat skin diseases.¹⁹ Geran reported that *Euphorbia* sap extract showed significant antineoplastic activity when tested in rodents against the sarcoma 180, Walker 256 carcinosarcoma, Lewis lung carcinoma, and P-388 lymphocytic leukaemia.²⁰ Kupchan *et al* isolated a diterpenoid diester, ingenol 3,20-dibenzoate, as the major antileukaemic component of sap from *Euphorbia esula* extract.²¹

Although few cases of *Euphorbia* sap anterior segment toxicity have been reported, the literature available does demonstrate similarities in the mode of presentation and clinical course.

Euphorbia sap can lead to a spectrum of anterior segment changes, including conjunctivitis, keratitis, and uveitis. In our patients, and nearly all reported cases, symptoms began immediately and worsened several hours to days after exposure.^{2,3,7-10,12} Further, in cases where an examination was performed on the day of injury and on the subsequent day, worsening vision and/or progressive epithelial sloughing were evident.^{2,3,7} This emphasises the importance of frequent follow up for patients with recent *Euphorbia* sap injuries. Patients should be warned that their symptoms may worsen before improving. Cases treated promptly were left without visually significant residua,^{2-7,10} while patients with delayed treatment developed complications such as corneal ulcers and corneal perforation, and were left with corneal scarring and decreased visual acuity.^{8,9}

All of our cases experienced a similar clinical course. Initial contact with *Euphorbia* sap caused a corneal punctate epitheliopathy which progressed to larger corneal epithelial defects requiring 9 or more days to heal despite prompt treatment with pressure patching or a bandage contact lens. This may be explained by the antineoplastic effects of *Euphorbia* sap, which may hinder corneal epithelial replication.

Patients who work with *Euphorbia* plants should be cautioned to wear eye protection. Patients with *Euphorbia* sap anterior segment toxicity should be informed that their condition may worsen for several hours to days, but that visual outcome is generally excellent. Ophthalmologists need to be aware of the importance of following such patients closely, especially during the first several days, when a mild corneal punctate epitheliopathy may progress to corneal slough.

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