

CORNEAL EDEMA AND DESCMET'S FOLDS CAUSED BY MISTAKEN INSTILLATION OF ROKUSHINGAN, A JAPANESE TRADITIONAL MEDICINE, CONTAINING TOAD VENOM.

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Four cases of ocular injuries induced by mistaken instillation of Rokushingan pills, a traditional Japanese medicine, to the conjunctiva and cornea were reported. Conjunctivitis, corneal edema, Descemet's folds and temporary decrease in vision were found. These findings disappeared without sequelae within 10 days. The ocular lesions were considered to be caused by Bufonis venenum, which is one of six crude biological extracts in the drug, and is known to contain an inhibitor of Na⁺,K⁺-adenosine triphosphatase. All the patients, aged between 53 and 78 years, were treated with either age-related cataract or glaucoma for 3 to 18 years. They confused the container of Rokushingan with that of their daily eyedrops because of the similar sizes and shapes of the bottles. Ophthalmologists should be aware of such cases and the measures to avoid such mistaken instillation should be seriously considered.

Key words: Corneal edema, Descemet's folds, Rokushingan, Toad venom

INTRODUCTION

Production and sale of traditional Japanese medicine is not only a historical activity but also a current activity especially in Toyama district. Taking such drugs remains a relatively common habit, especially among older family members. Rokushingan is one such drug that has been used for prophylaxis or

treatment of palpitations. The pill contains six crude materials including Panax ginseng, Fel ursi, Bufonis venenum, Bezoar bovis, Aquilariae lignum, and Moschus (Table). Among these components, Bufonis venenum, called Senso in Japanese, is a secretion of the submandibular gland of the toad (1) and is reported to induce severe conjunctivitis and corneal clouding(2). We present a series of 4 eyes of 4 patients with ocular injuries caused by mistaken instillation of Rokushingan pills and describe the management and outcome of these cases.

PATIENTS AND METHODS

We retrospectively reviewed the clinical data of 4 eyes in 4 patients with ocular injuries caused by mistaken instillation of Rokushingan pills treated at Toyama Medical and Pharmaceutical University Hospital between 1995 and 2002.

CASE REPORTS

Case 1.

A 78-year-old man with age-related cataract had been treated with topical instillation of pirenixine for 18 years. He mistakenly instilled a Rokushingan pill into his right eye, instead of pirenixine, on March 2, 1995. The pill was immediately removed. He complained of foreign body sensation and consulted our clinic 30 minutes later. On examination, his corrected visual acuity was 0.7 OD and 0.9 OS. The intraocular pressures were 16 mmHg OU. Conjunctival injection, superficial punctate keratopathy, corneal stromal edema, and Descemet's folds were seen in the right eye (Figure 1-A). The anterior chambers appeared clear bilaterally. Both fundi appeared normal. The

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Table. Crude Materials in Rokushingan

Crude materials (Japanese)	Weight per 75 pills (mg)
Panax ginseng (Otaneningin)	82.5
Bufo venenum (Senso)	75
Aquilariae lignum (Jinko)	75
Moschus (Jakoo)	11.25
Fel ursi (Yutan)	7.5
Bezoar bovis (Go-o)	7.5

Starch was added in the manufacturing of the pill

right conjunctival cul-de-sac was washed with 200 ml of 0.9% NaCl. The pH of the tear fluid was 7.4. The patient was treated with topical instillations of 0.3% ofloxacin and 0.1% fluorometholone four times per day. The next day, the corneal edema had resolved. Conjunctival injection and Descemet's folds persisted for one week. On March 9, the right corrected visual acuity was 1.2. There was no sequela noted.

Case 2.

A 74-year-old woman with primary open angle glaucoma had been treated with topical 0.5% timolol for nine years. Goldmann visual field testing showed a nasal step in both eyes. She mistakenly instilled a Rokushingan pill in the left eye on September 2, 1998. The pill was immediately removed. She complained of ocular pain in the left eye, and consulted our clinic one hour later. Her visual acuity was 0.8 OD and 0.6 OS. Conjunctival injection, superficial punctate keratopathy, and corneal edema were found (Figure 1-B). Large cupping of the optic discs was seen funduscopically. The left conjunctival cul-de-sac was washed with 200 ml of 0.9% NaCl. The pH of the tear fluid was 7.4. She was treated with 0.02% fluorometholone, four times daily. Two days later, the corneal edema resolved. Conjunctival injection decreased gradually and disappeared 8 days later. Left visual acuity improved to 0.8.

Case 3

A 68-year-old woman with age-related cataract had been treated with topical pirenexine for 8 years. She mistakenly instilled a Rokushingan pill into the right eye on January 15, 2000. The pill was immediately removed. On examination, her visual acuity was 0.5

OD and 1.0 OS. Corneal edema and Descemet's folds were seen in the right eye. The anterior chambers appeared clear bilaterally. The conjunctival sac was washed with 200 ml of 0.9% NaCl. The pH of the tear fluid was 7.4. The patient was treated with topical instillation of 0.3% ofloxacin and 0.1% fluorometholone, four times per day. On January 17, corneal edema had decreased. On January 24, the right visual acuity had improved to 1.0. There was no sequela noted.

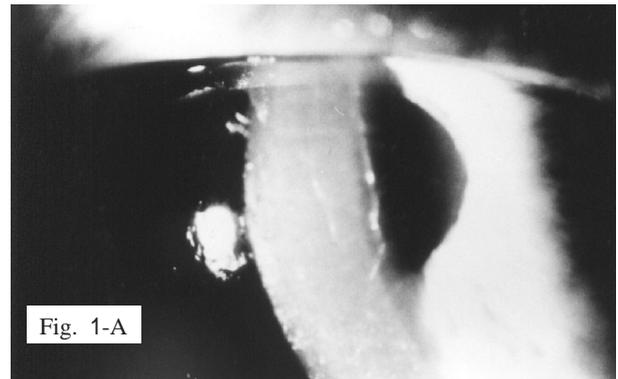


Fig. 1-A

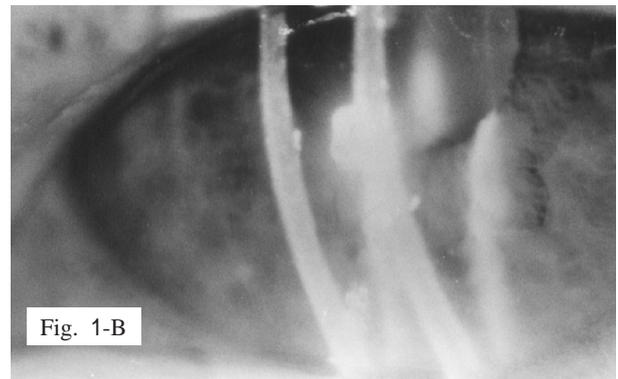


Fig. 1-B

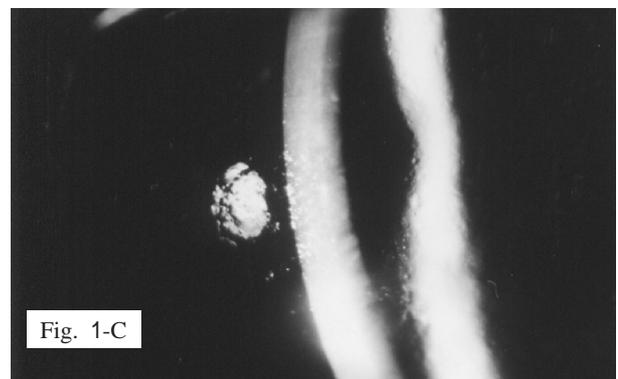


Fig. 1-C

Fig. 1-A. Case 1. Conjunctival injection, corneal edema, and Descemet's folds are seen in the right eye.

Fig. 1-B. Case 2. Conjunctival injection and corneal edema are visible in the left eye.

Fig. 1-C. Case 4. Erosion, stromal edema, and Descemet's folds are found in the right cornea.

Case 4

A 56-year-old man with age-related cataract had been treated with topical pirenoxine for 3 years. He mistakenly instilled a Rokushingan pill into the right eye on March 10, 2002. The pill was immediately removed. Four hours later, he consulted our clinic complaining of ocular pain. His visual acuity was 0.2 OD and 1.5 OS. Erosion, stromal edema, and Descemet's folds were seen in the right cornea (Figure 1-C). The anterior chambers appeared clear and deep in both eyes. Cortical cataract was seen bilaterally. The conjunctival sac was washed with 200 ml of 0.9% NaCl. The pH of the tear fluid was 7.4. The patient was treated with topical instillation of 0.3% ofloxacin and 0.1% fluorometholone, four times per day. The corneal lesions in the right eye gradually decreased. On March 20, there were no corneal lesions noted, and the right visual acuity had improved to 1.0. There was no sequela noted.

RESULTS

Four cases of mistaken instillation of Rokushingan were described. We encountered these cases between 1995 and 2002. These accidents occurred when the patients mistook a bottle of Rokushingan for a container of eye drops for cataract or glaucoma (Figure 2). The patients included 2 men and 2 women. The average age was 69 years (range, 56 to 78 years). Visual acuity ranged 0.2 to 0.7 in the involved eyes. The spectrum of ocular injury caused by Rokushin-



Fig. 2. This bottle of Rokushingan arrow is similar in size and shape to a bottle containing glaucoma or cataract eyedrops.

gan included conjunctival injection, superficial punctate keratopathy, corneal erosion, corneal stromal edema, and Descemet's folds. The ocular injuries were unilateral in all four cases. Corneal stromal edema was a characteristic ocular manifestation common to ocular injuries found in all four cases.

The conjunctival sac was washed with 200 ml of 0.9% NaCl in all four cases, and Cases 1, 3, and 4 were treated with topical instillation of 0.3% ofloxacin and 0.1% fluorometholon, case 2 was treated with topical instillation of 0.02% fluorometholon. The ocular injuries disappeared without sequelae within 10 days.

DISCUSSION

The patients we describe had corneal stromal swelling and Descemet's folds after instillation of Rokushingan. Rokushingan contains six crude materials. Of these materials, toad venom reportedly causes conjunctivitis and corneal clouding (2). To our knowledge, the other five materials do not induce any ocular injuries. Matsukawa et al. (3) identified 11- α -hydroxyhellebrigenin, which inhibits Na^+ , K^+ -adenosine triphosphatase, in toad venom. Riley et al. (4) reported that ouabain, which inhibits Na^+ , K^+ -adenosine triphosphatase, induced corneal stromal swelling in rabbits. Therefore, it is possible that Bufonis venenum in Rokushingan may have induced corneal swelling in our patients.

A bottle of Rokushingan appears similar to that containing cataract or glaucoma eyedrops. Ophthalmologists should be aware that Rokushingan pills have been mistakenly instilled in the eyes, resulting in corneal edema and Descemet's folds. Although there were no sequelae noted, the bottle of Rokushingan should be changed to avoid mistaken instillation.

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