Cornea 16(5): 534–536, 1997.

Keratoconus and Turner's Syndrome

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Purpose. To report the association of keratoconus and Turner's syndrome in three patients and to review the ophthalmic manifestations of Turner's syndrome. **Methods.** Three patients with keratoconus and Turner's syndrome were identified and reported in a retrospective review. **Results.** These three cases represent the first series of patients with keratoconus and Turner's syndrome. All three patients underwent penetrating keratoplasty with good visual rehabilitation. None of the patients had other ocular features associated with Turner's syndrome. **Conclusion.** Turner's syndrome is commonly associated with ocular problems. In this series we identify an association of keratoconus with Turner's syndrome. Clearly, a careful ocular examination in this condition with attention to ocular features of Turner's syndrome is important.
Key Words: Cornea—Turner's syndrome—Keratoconus.

Turner's syndrome, which was first described in 1938, is a chromosomal anomaly in which the absence of the second X chromosome results in phenotypic females who have a missing or abnormal X chromosome (45,XO) (1).

This syndrome occurs in 1 of 3,000 live female births (2). Ovarian dysgenesis, primary amenorrhea, undeveloped breasts, infantile genitalia, scanty pubic hair, short stature, web neck, shield chest, and cubitus valgus are cardinal features of the syndrome. Coarctation of the aorta and other cardiovascular anomalies, multiple pigmented nevi, hypertension, urinary tract anomalies, and congenital lymphedema occur often (Table 1) (3). There are a number of reports in the ophthalmic literature on the ocular findings in Turner's syndrome that include a wide spectrum of abnormalities (Table 2) (4–11).

Nucci et al. (12) first reported the association of keratoconus and Turner's syndrome in 1991. We now present two additional cases with follow-up on the original case of keratoconus and Turner's syndrome.

CASE 1

A 13-year-old (in 1985) white girl with Turner's syndrome showing complete absence of one chromosome (45,XO) initially presented with complaints of blurred vision at distance and near (12). She had no history of atopic diseases, eye rubbing, mitral valve prolapse, osteogenesis imperfecta, or other connective tissue diseases. Her IQ was within normal limits. She had no history of contact lens wear. Her best corrected visual acuity with contact lenses was 20/30 OU. Keratometric readings revealed distorted mires. Slit-lamp examination revealed bilateral noninflammatory thinning of the corneas with protrusion of the central thinned areas. Initial examination also revealed bilateral radial cortical lens opacities. No Vogt's striae or Fleischer rings were seen. She was followed for a few years with progressive thinning and ectasia of both corneas. She subsequently underwent penetrating keratoplasty in the left eye at age 19 (1991); after surgery her vision was corrected to 20/60 with contact lenses. The most recent examination of her right eye revealed a best-corrected visual acuity with a contact lens of 20/100, and she was scheduled for penetrating keratoplasty.

CASE 2

A 27-year-old woman (in 1978) initially presented with blurred vision and inability to function with her prescription glasses. She had previously been diagnosed with Turner's syndrome (45,XO) and was maintained on Premarin 0.625 mg daily (3 weeks on, 1 week off) and Provera 2 mg daily (1 week a month).

Her medical history was significant for a diagnosis of Rendu-Osler-Weber syndrome (hereditary hemorrhagic telangiectasia) in childhood after she underwent an exploratory laparotomy for an acute abdomen. At age 13

Submitted March 12, 1997. Revision received April 30, 1997. Accepted May 2, 1997.

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These cases were collected after an inquiry on the kera-net list server through the internet.

TABLE 1. *Systemic features of Turner's syndrome*

Short height
Short webbed neck (pterygium coli)
Low nuchal hairline
Broad shield-like chest with widely separated nipples
Multiple pigmented nevi
Hypoplastic nails
Lymphedema of extremities at birth
Cardiac anomalies
Urinary tract anomalies
Coarctation of the aorta
Mental retardation
Sexual infantilism, amenorrhea, sterility
Increased carrying angle of the elbow (cubitus valgus)
Low set ears
Undeveloped breasts
Scant pubic hair
Ovarian dysgenesis
Diabetes
Myxedema

she underwent partial small bowel resection for uncontrollable bleeding.

Keratoconus was diagnosed due to the presence of bilateral irregular central corneal mires with central corneal thinning and protrusion in the absence of corneal inflammation. She had no significant history of atopy, contact lens wear, osteogenesis imperfecta, mitral valve prolapse, or eye rubbing and was of normal intelligence. After initial hard contact lens fit, she noted significant improvement in vision.

Because of progressive intolerance to contact lenses, she underwent corneal transplantation in the right eye in 1980 and in the left in 1981. After both transplants, the patient showed a marked steroid response that necessitated bilateral argon laser trabeculoplasty for advancing cup-to-disc ratios and bilateral nasal steps on visual field testing. In 1988 the intraocular pressure increased to 40 mm Hg in the right eye and 36 mm Hg in the left eye on maximal medical therapy; trabeculectomies were performed in April 1988 in the right eye and June 1988 in the left eye. Intraocular pressure stabilized to 16 mm Hg in both eyes without medications. However, 6 weeks after the left trabeculectomy, a graft rejection developed and was controlled with topical steroids. Best-corrected visual acuity was maintained at 20/25 with contact lenses in both eyes, and the patient remained on no medications in the right eye and Timolol 0.5% in the left eye twice a day. In 1990, posterior subcapsular cataracts were noted in the right eye, and the patient underwent phacoemulsification with intraocular lens implantation after her best-corrected visual acuity dropped to 20/80. Her vision recovered to 20/25 postoperatively. At present, the patient maintains corrected visual acuity of 20/25 OD and 20/30 OS with gas permeable contact lenses. Her intraocular pressures are stable at 14 mm Hg OD and 19 mm Hg OS with topical Timolol 0.5% OS twice a day. Visual fields and optic discs remain stable.

CASE 3

A 22-year-old woman presented with bilateral decreased vision. She is a fraternal twin who at presentation was not diagnosed with Turner's syndrome. She presented with short stature, a short webbed neck with a low nuchal hair line, hypoplastic nails, and a history of amenorrhea. She had no history of eye rubbing, atopy, or connective tissue disease. She was of average intelligence and had successfully completed high school. At presentation her best-corrected spectacle visual acuity was 20/200 in each eye. A contact lens was successfully fit in the right eye to improve her visual acuity to 20/40. However, no contact lens could be fit to improve the vision in the left eye. External examination was significant for coarse eyebrows. Extraocular motility was full. There was no relative afferent pupillary defect. Slit-lamp examination revealed bilateral central corneal thinning with ectasia and no evidence of corneal inflammation. Vogt's striae were found in both corneas. The anterior chambers were quiet. Lenses were clear. Intraocular pressure was 15 mm Hg OU. Dilated fundus examination revealed no gross abnormalities. She underwent penetrating keratoplasty in the left eye in May 1994 and recovered 20/30 vision in the eye with spectacle correction. The cone in the right eye advanced over the next year, and she underwent penetrating keratoplasty in the right eye in May 1995, with no postoperative complications. When last seen in July 1996, the patient had a spectacle visual acuity of 20/40 OD and 20/30 OS. The corneal grafts were clear and compact. The anterior chambers were quiet with normal intraocular pressures of 16 mm Hg OD and 14 mm Hg OS. She was referred for an ob/gyn evaluation. Examination confirmed a 45,XO karyotype consistent with Turner's syndrome. She was noted to have sexual infantilism, amenorrhea, scant pubic hair, undeveloped breasts, and ovarian dysgenesis. A diagnosis of Turner's syndrome was made. Her twin was also examined and found to have a normal karyotype with normal reproductive function and no slit-lamp or topographic evidence of keratoconus.

TABLE 2. *Ocular features associated with Turner's syndrome*

Bilateral epicanthus	Anti-mongoloid slant
Amblyopia	Choroidal coloboma
Hypermetropia	Persistent pupillary membrane
Strabismus	Microcornea
Congenital cataract	Microphthalmos
Ptosis	Absence of the caruncle
Myopia	Eccentric pupils
Nystagmus	Diminished retinal pigmentation
Color blindness	Lid hemangioma
Hypertelorism	Abducens palsy
Blue sclerae	Retinitis pigmentosa
Iris coloboma	Hypoplasia of the lacrimal gland
Congenital glaucoma	Oval cornea
Corneal nebulae	Duane's syndrome
Congenital lymphangiectasia	Keratoconus
Brushfield spots	

DISCUSSION

These three cases represent the first series of patients with keratoconus and Turner's syndrome. In each case, the patient presented with a noninflammatory bilateral thinning disorder of the cornea leading to progressive distortion and steepening of the central corneal curvature and subsequent visual impairment. All three patients underwent penetrating keratoplasty with good visual rehabilitation.

Keratoconus has been reported to occur frequently in patients with Down syndrome, atopy, mitral valve prolapse, and osteogenesis imperfecta and in patients who rub their eyes or wear hard contact lenses (12–16).

In many of these disorders, eye-rubbing has been hypothesized to cause corneal thinning due to chronic mechanical trauma. In Turner's syndrome, no pathognomonic eye findings have been reported. There is a marked increase in the incidence of amblyopia, strabismus, ptosis, and epicanthus. However, numerous ocular anomalies have been reported (Table 2). Nucci et al. (12) hypothesized that corneal thinning in Turner's syndrome is an expression of a mesodermal defect because mesodermal structures are sometimes affected in Turner's syndrome. In our series all three patients presented with bilateral keratoconus and Turner's syndrome. One patient had bilateral radial lens opacities, but none of the patients had other ocular features associated with Turner's syndrome. Interestingly, in case 3, the twin had a normal karyotype and no topographic or slit-lamp evidence of keratoconus, which has been previously identified to occur in twins. Advocates of a genetic etiology for keratoconus point to the association with Down syndrome as well as the reports of keratoconus in twins. Perhaps the absence of genetic material in Turner's syndrome predisposes these patients to keratoconus. Theoretically, a second chromosome abnormality may play a role in the etiology of keratoconus in these patients. Clearly, this series provides further evidence that Turner's syndrome is commonly associated with ocular problems, enforcing the importance of careful ocular examination in this condition.

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