Chronic lymphangiectasis in Turner's syndrome

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SUMMARY A 3½-year-old female presented with Turner's syndrome and Nonne-Milroy-Meige disease. Ocular findings included strabismus and bilateral chemosis which was unchanging and persisted throughout the four years the patient was followed up. Histopathological findings included diffuse lymphangiectasia and dense connective tissue surrounding the dilated lymph channels. Although the association between congenital lymphoedema and Turner's syndrome is common, the lymphoedema usually disappears by the first year of life. The persistence of the lymphoedema beyond this age is rare, as is the presence of the persistent chemosis. This report represents the first histopathological documentation of congenital lymphangiectasis in association with Turner's syndrome.

In 1938 Turner described a chromosomal anomaly in which there are 45 chromosomes due to the absence of the second sex chromosome.¹ Females with Turner's syndrome have numerous features such as short stature, webbed neck, shield shaped chest, cubitus valgus, amenorrhoea, and infantile sexual development. Recently we have encountered a patient with Turner's syndrome and Nonne-Milroy-Meige disease. This is the first time the association between Turner's syndrome and congenital lymphoedema has been reported with ocular findings and histopathological confirmation.^{2,3}

Case report

A 3½-year-old white female with Turner's syndrome (karyotype XO) was referred for ophthalmic examination. She was referred because of a vision defect, and the family pediatrician noted that she was holding things very close. According to her history the patient did not open her eyes until 7 weeks of age owing to swelling and ophthalmia neonatorum. She had developmental delay and was attending a special school for handicapped children. Anomalies included bilateral inguina hernias, bladder hypotony, congenital hip dysplasia, and congenital lymphoedema.

Ocular examination in May 1980 showed the vision to be 20/200 OD and 20/200+1 OS. External exam-

ination showed a very apprehensive, short 3½-year-old white female with a prominent webbed neck. (Fig. 1). Cycloplegic refraction OD +3.50-5.50 axis 90°, OS +2.25-5.50 axis 90° improved the vision to

Fig. 1 Full face external photograph showing nasal conjunctival cysts, oedema of the right eye, and prominent webbed neck.

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Fig. 2 Slit-lamp photograph of the right eye showing diffuse conjunctival oedema of the nasal conjunctiva.

20/60 OU. There was a constant A pattern exotropia of 35 prism dioptres and a bilateral ptosis, OS greater than OD. Slit-lamp examination of the anterior segments revealed diffuse conjunctival oedema with bullae present nasally OD and temporally OS (Fig. 2). The rest of the ocular examination, including examination of the fundus under dilatation, was unremarkable. Further external examination revealed left hand and right pedal lymphoedema (Fig. 3 and 4).

A diagnosis of Nonne-Milroy-Meige disease was made from the association between the conjunctival

Fig. 3 External photograph of both hands showing marked oedema of the right 2, 3, 4 fingers and of the entire left hand and wrist.

chemosis and lymphoedema in the left hand and right foot. In August 1980 the patient underwent a bilateral 7 mm recession of the lateral rectus muscles with half tendon infrapacements. A conjunctival biopsy was taken at the time of surgery from the right eye and fixed in 10% buffered formalin. The patient did well postoperatively except for a small dellen located temporally on the left cornea, which cleared up by the second postoperative week. After four years of follow-up the patient has a monofixational microexotropia with best corrected visual acuities of 20/30— in each eye.

The conjunctival specimen measured 1×3 mm and was pale white. The specimen was embedded in paraffin and sections were stained in Haematoxylin and eosin, periodic acid Schiff, Masson trichrome, Verhoeff-van-Gieson, and von Kossa stains. Haematoxylin and eosin showed the conjunctival epithelium to be unremarkable. Pertinent findings were limited to the substantia propria, where there were multifocal areas of dilated vascular channels with delicate septa lined on both sides by non-contiguous, flattened endothelial cells. Most of the spaces contained acellular fibrinous debris with only occasional red blood cells noted. The surrounding stromal collagen fibres were thickened and proved to be the most striking differentiating feature from normal conjunctiva. This thickened stroma resembled that seen in conjunctival dermoids. (Fig. 5 and 6). The supplementary stains added nothing.

Discussion

The ophthalmic disorders in Turner's syndrome include hyperopia, myopia, ptosis, cataracts, strabismus epicanthus, hypertelorism, blue sclera,

Fig. 4 External photograph of lower extremities showing severe oedema of both feet and ankles.

Fig. 5 Relatively normal bulbar conjunctiva lying over a thickened substantia propria with a prominence of dense connective tissue. (Haematoxylin and eosin, $\times 30$).

anti-Mongolian slant, red-green colour blindness, exophthalmos, choroidal coloboma, persistent pupillary membrane, microcornea, microphthalmos, nystagmus, absence of the caruncle, diminished

Fig. 6 Several dilated lymph channels are noted in the dense connective tissue of the conjunctiva. (Haematoxylin and eosin, $\times 37$).

retinal pigmentation, lid haemangioma, abducens palsy, retinitis pigmentosa, hypoplasia of the lacrimal gland, oval cornea, and Duane's syndrome.⁴ Here we report the occurrence of chemosis and an ophthalmic finding not previously recorded. The chemosis was chronic and unchanging in amount and degree in the four years the patient was followed up.

The association between Turner's syndrome and congenital lymphoedema is not uncommon. Hereditary lymphoedema with an onset at or near birth has been termed Milroy's disease, while that of later onset is referred to as Meige's disease.⁵ In Izakovic's study of 26 children with congenital lymphoedema 18 out of 22 girls had the 45 X karyotype.⁶ Henriksen reported two cases of Turner's syndrome associated with congenital lymphoedema in newborn babies.⁷ In their study of lymph vessel defects in patients with ovarian dysgenesis Vittay and co-workers⁸ mention the occurrence of the lymphatic defects in patients with Turner's syndrome. They argue that the defects are no more common in Turner's syndrome than in other cases of ovarian dysgenesis. The persistence of lymphoedema beyond the first year of life is unusual according to Gordon *et al.*⁹ The occurrence of conjunctival lymphoedema is rare, as is the occurrence at a young age.¹⁰ Klein and Doret reported a case of congenital lymphoedema with the development of chemosis at age 50.¹¹ Tabbara and Baghdassarian reported on a 7-year-old girl with congenital lymphoedema of the conjunctiva and of the extremities.² This girl also had moderate amblyopia of the right eye and esotropia. However, they described the patient as otherwise normal. A requested biopsy was refused by the patient's family. Our patient thus presented an unusual opportunity to evaluate the conjunctival changes of Nonne-Milroy-Meige disease in association with Turner's syndrome. The occurrence of lymphoedema at a young age should suggest Turner's syndrome.^{3, 12}

Histopathologically our findings of dilated lymph channels with thin endothelium lined walls is similar to previous reports of Milroy's disease in the lower extremities. In addition these reports also stressed prominent fibrosis, which in our case appeared very much like the thickened collagen fibres characteristic of a conjunctival dermoid. Over all, the histopathological features were distinctive, and the presence of the thickened collagen fibres allowed the condition to be differentiated from a lymphangioma.

References

- 1 Turner HH. A syndrome of infantilism, congenital webbed neck and cubitus valgus. *Endocrinology* 1938; 23: 566-74.
- 2 Tabbara KF, Baghdassarian SA. Chronic hereditary lymphoedema of the legs with congenital conjunctival lymphoedema. *Am J Ophthalmol* 1972; 73: 531-2.

- 3 Chrousos GA, Ross JL, Chrousos G, *et al*. Ocular findings in Turner's syndrome: a prospective study. *Ophthalmology (Rochester)* 1984; **91**: 926–8.
- 4 Lessel S, Forbes AP. Eye signs in Turner's syndrome. *Arch Ophthalmol* 1966; **76**: 211–3.
- 5 Wheeler ES, Chan V, Wassman R, Ramon DL, Lesuaoy A. Familial lymphedema praecox: Meige's disease. *Plast Reconstr Surg* 1981; **67**: 362–4.
- 6 Izakovic V. Congenital lymphedema and monosomy X. *Bratisl Lek Listy* 1979; **72**: 530–4.
- 7 Henriksen HM. Turner's syndrome associated with lymphedema, diagnosed in the newborns. *Z Geburtshilfe Perinatol* 1980; **184**: 313–5.
- 8 Vittay P, Bosze P, Gaael M, Laszlo J. Lymph vessel defects in patients with ovarian dysgenesis. *Clin Genet* 1980; **18**: 387–91.
- 9 Gordon R, Eileen R, O'Neill M. Turner's infantile phenotype. *Br Med J* 1969; **i**: 483–5.
- 10 Duke-Elder S. *System of ophthalmology*. London: Kimpton, 1963; **3**: 909.
- 11 Klein D, Doret M. Chronic hereditary lymphedema. In: Babel J, Streiff, EB, eds. *Mod Probl Ophthalmol* 1957: 576.
- 12 Nelson WE, ed. *Textbook of pediatrics*. Philadelphia: Saunders, 1979: 461.

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