Ophthalmic features and visual prognosis in the Treacher-Collins syndrome

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Abstract
The ocular findings and visual prognosis were reviewed in 24 patients with the Treacher-Collins syndrome who were evaluated in the craniofacial clinic in the Division of Pediatric Ophthalmology at Children's Hospital of Philadelphia between 1980 and 1991. All patients had some abnormality. Vision loss was present in 37% of patients. Amblyopia was present in 33%, significant refractive errors were present in 58%, and anisometropia was documented in 17%. Strabismus was present in 37% and significant lid and adnexal abnormalities were seen in 96%. The prognosis for normal vision in at least one eye is good but vision loss secondary to amblyopia is more resistant to treatment owing to other medical problems and social concerns.

(Br J Ophthalmol 1993; 77: 642–645)

The Treacher-Collins syndrome (TCS) is an autosomal dominant facial malformation with variable penetrance and is also known as zygoma-mandibular dysplasia or mandibulofacial dysostosis (MFD). This bilateral anomaly represents a cluster of malformations resulting in zygomatic, temporooral, and mandibular dysplasia. It was first reported by Berry in 1889 in a mother and daughter. Rogers,1 and Franceschetti and Klein1 further clarified the clinical findings in their case reports. Most patients with TCS are of normal intelligence, but may be socially affected owing to their appearance or appear retarded secondary to hearing loss.

TCS is characterised by hypoplasia and retraction of the malar region, obliteration of the frontonasal angle, and a receding chin. Protrusion of the nose and maxilla may produce an enophthalmic appearance. The inferior lateral angle of the orbit is defective and the superolateral part of the orbit is displaced caudally giving the orbit an egg shaped appearance. The orbital contents appear displaced into the deficiency created by the malar hypoplasia—

(Fig 1).

Ocular abnormalities include pseudo-colobomas (hypoplastic subcutaneous tissue, and muscle) and true colobomas (full thickness absence of tissue) of the lids, especially inferolaterally, canthal dystopia, orbital lipodermoids, limbal dermoids, and occasional microphthalmos and anophthalmos.1,4 Cataracts, lacrimal duct atresia, pupillary ectopia, dystichiasis, and uveal colobomas have all been reported.4,6 Strabismus has been reported in several forms including esotropia, exotropia, Duane’s syndrome, and cranial nerve palsies.6–9

A large variety of ear abnormalities can be present. Respiration can be affected by sinus and

choanal atresia, and lingual obstruction because of mandibular retraction.5–8 Cleft lip and palate, enlarged sphenoid bone fissures, and skeletal and cranial synostoses are other reported abnormalities.12–15 This report summarises our experience managing 24 patients as part of the craniofacial clinic in the division of ophthalmology at the Children’s Hospital of Philadelphia.

Methods
The craniofacial clinic is a monthly multispecialty clinic at the Children’s Hospital of Philadelphia. Patients have an ophthalmic examination as part of a day long process which includes evaluation by many paediatric subspecialties including: plastic and reconstructive surgery, neurosurgery, oral and maxillofacial surgery, dentistry, genetics, ophthalmology, otolaryngology, psychiatry/psychology, social work, and speech and hearing. This group meets at the end of the clinic day to discuss patient evaluations and proposed treatments.

The clinical records of 329 patients seen for a complete ocular examination from 1980 to 1991 have been entered into a computerised database in the Division of Pediatric Ophthalmology. Data include name, ages at first and most recent examinations, craniofacial diagnosis, best and worst visual acuities, amblyopia, pupillary abnormalities, motility disturbances, results of fusion testing, intraocular, disc or retinal abnormalities, lid and adnexal abnormalities, cycloplegic refraction (40 minutes after 1% cyclopentolate (Cyclogyl) in children older than 1
Table 1  Clinical characteristics of 24 patients with Treacher-Collins syndrome

<table>
<thead>
<tr>
<th>PT</th>
<th>VA</th>
<th>Refraction</th>
<th>Strabismus</th>
<th>HX amblyopia</th>
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<tbody>
<tr>
<td>1</td>
<td>20/30 OD</td>
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</tr>
<tr>
<td></td>
<td>20/20 OS</td>
<td>+1.75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>20/20 OD</td>
<td>-1.00 +0.75x90</td>
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<td>No</td>
<td>Posis, pseudocoloboma, telecanthus, epicanthus OU</td>
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</tr>
<tr>
<td>4</td>
<td>F&amp;P OD</td>
<td>Plano</td>
<td>XT</td>
<td>No</td>
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</tr>
<tr>
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<tr>
<td>5</td>
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<td>OALSO</td>
<td>OS</td>
<td>Posis OU</td>
</tr>
<tr>
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<tr>
<td>7</td>
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<td>9</td>
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<td>CN VI palsy,</td>
<td>OD</td>
<td>Pseudocoloboma OU, canthal dystopia OU</td>
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<tr>
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<td>LHT</td>
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<tr>
<td></td>
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<td>11</td>
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<td>ET</td>
<td>OS</td>
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<tr>
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</tr>
<tr>
<td></td>
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<td></td>
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<td>OD</td>
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<tr>
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<td>OD</td>
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<tr>
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<tr>
<td>22</td>
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<td>V-XT</td>
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<tr>
<td>23</td>
<td>20/40 OD</td>
<td>+1.00 +0.75x60</td>
<td>OAIO OU</td>
<td>OD</td>
<td>Posis OU, canthal dystopia OU</td>
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<tr>
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<td>Ortho</td>
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<td>Canthal dystopia</td>
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<tr>
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<td>+1.25 +3.00x165</td>
<td>ET</td>
<td>OS</td>
<td>Canthal dystopia pseudocoloboma OU</td>
</tr>
</tbody>
</table>

VA = visual acuity; OD = right eye; OS = left eye; OU = both eyes; CSM = central, steady, and maintained gaze; Ortho = orthophoria; XT = exotropia; OAIO = overaction of left superior oblique; CN VI = cranial nerve VI; LHT = left hypertropia; RHT = right hypertropia; ET = exotropia; F&P = fixation and follow; V-XT = V-pattern exotropia; OAIO = overaction of the inferior oblique.

year of age and 0·5% under 1 year of age), and type of strabismus procedures and results.

Fifty one per cent of these patients had craniofacial stenoses, 25% had clefting syndromes, 17% had other varied and often singular craniofacial deformities, 7% had orbital tumours or trauma and were evaluated by the entire team.

The data included in this report are from all patients who were examined in the craniofacial clinic between 1980 and 1991 with the diagnosis of TCS. Patients who had other first and second branchial arch syndromes (for example, Goldenhar's, facial microsomia) or clefting syndromes (for example, Stickler's syndrome, typical orofacial ocular clefts) were excluded from analysis. All data used for this analysis were accumulated from one or multiple examinations of each patient. Twenty patients were examined on more than one occasion and four were examined once. If an oculat abnormality was present at any examination the date of onset and follow up treatments and results were recorded. The follow up on the 20 patients with repeat examinations ranged from 1 to 12 years with an average of 4·5 years. All abnormalities reported were diagnosed during either their initial or subsequent evaluations in the Division of Pediatric Ophthalmology.

Ametropic refractive errors were defined as hyperopia greater than +2·00 sphere, myopia greater than −0·75 sphere, or astigmatism greater than 0·75 dioptres at any examination. Anisometropia was defined as greater than 1·50 dioptres difference between the eyes in any meridian at any examination.

Results

Twenty four of 329 (7%) patients or 17% of patients excluding craniofacial stenoses, tumours, and trauma were diagnosed with TCS. Patient age at first examination ranged from 2·5 months to 20 years (median 2·7 years). Fourteen patients were male.

All patients examined in this study had some ocular and adnexal abnormality (Table 1). Refractive errors were present in 14 (58%) patients. Five patients had anisometropia, 13 had mixed astigmatism, and one had simple myopia.

Ten eyes (21%) in nine (37%) patients had or have abnormal vision. Eight eyes in eight patients (33%) had amblyopia at some time during their evaluation and follow up as part of the craniofacial clinic. One patient having 20/200 visual acuity bilaterally by Teller acuity card testing had central visual impairment (post-chiasmal dysfunction of unknown aetiology) and was also
mentally retarded (patient 29). The visual acuities listed in the table are those at the last examination. All patients with amblyopia have had or are currently receiving treatment. This consisted of refractive correction when indicated combined with occlusion therapy. At the time of this report total treatment periods ranged from 3 months to 4 years, with a median of 21 months. Six of the eight patients did not have equal visual acuities at their most recent examination. All these patients had poor compliance with the instructed occlusion regimen.

Strabismus was diagnosed in nine (37%) patients. There were two patients with esotropia, five with exotropia, one with a cranial nerve six palsy, and one with overaction of the left superior oblique muscle. One patient had a V pattern and associated inferior oblique muscle overaction in addition to the exotropia (Table 1).

Except for one patient with bilateral pseudo-papilloedema secondary to buried drusen, no intraocular abnormalities were observed.

Lid and adnexal eye disorders were present in 24 patients (100%) (Table 1). Canthal dystopia was present in 24 patients, dacryostenosis in three patients, blepharoptosis in six patients, lateral lower lid true coloboma in six patients, and pseudocolobomas in 13 patients. Entropion and trichiasis were each present in one patient.

Discussion

The TCS belongs to a group of craniofacial anomalies having in common maldevelopment of the first and second branchial arches. Characteristic clinical, familial, and chromosomal findings justify separation of this syndrome from other abnormalities in development of the first and second branchial arches. The others include facial clefting syndromes, Goldenhar's syndrome, facial microsomias, Miller's syndrome (digit and limb abnormalities, and acrofacial dysostosis), and Nager's syndrome (radial limb deficiencies). Franceschetti and Klein suggested a classification system consisting of five clinical forms: (1) the complete form, having all known features, (2) the incomplete form, presenting variably with less severe ear, eye, zygoma, and mandibular abnormalities, (3) the abortive form, in which only the lower lid pseudocoloboma and zygoma hypoplasia are present, (4) the unilateral form, with the anomalies limited to one side of the face regardless of severity, and (5) the atypical form or incomplete form combined with other abnormalities not usually part of the typical syndrome.

They reported that the most common forms were the typical and atypical (1 and 5) varieties. The existence of the unilateral form has been challenged and may actually represent a type of facial microsomia which is often unilateral and shares many common features with TCS. This classification system represents a spectrum of variability in the clinical presentation of this malformation. This system is presented for historical purposes as the functional and cosmetic consequences and treatment options do not depend on one or another form.

The aetiology of the facial defects in TCS are unknown. Recent evidence suggests that the genetic defect responsible for TCS maps to the long arm of chromosome 5. Postulated consequences of this genetic defect may cause a complete absence of embryonic malar bone centres or their outgrowth, or hypoplasia of bones or parts of bones after development. There is experimental and embryological evidence which suggests that abnormal neural crest migration as early as 4 months' gestation may be related to the defects of TCS. The genetic defect in TCS may be responsible for creating this deformity by disrupting migration of these neural crest cells. It is believed that these defects occur before the 17 mm crown to rump length (17–20 weeks). In other work with animal embryos abnormal stapedial artery blood supply during the sixth week of embryogenesis can produce ear and facial abnormalities similar to TCS. In this model the associated overlying soft tissue and muscular defects are the results of underlying aberrant bony maldevelopment.

Abnormal lid and adnexal morphology and function, ocular motility problems, refractive errors, and amblyopia are the abnormalities which most frequently require treatment. Specific treatment of associated ophthalmic abnormalities in patients with craniofacial anomalies follow similar principles utilised in patients without the anomalies.

Lid malpositions, colobomas, and pseudo-colobomas are usually treated surgically. Inadequate underlying bone in the lateral canthal area presents a unique challenge. Lateral canthal dystopia can be repaired at the time of maxillary reconstruction but the maxillary hypoplasia may need several staged procedures. It is sometimes advantageous to postpone definitive lateral canthal reconstruction until these procedures have been completed.

Motility problems are treated after amblyopia therapy and correction of refractive errors. Surgical treatment of strabismus proceeds according to the strabismus diagnosis and not necessarily delayed until other craniofacial surgery is performed. We prefer to use the fornix incision in approaching the muscle because it is easier to examine all the muscle insertions. Anomalous insertions are seen with increased frequency in patients with other craniofacial malformations and in some instances may contribute to the type of strabismus. Discovering anomalous muscle position or number during surgery may influence the surgical plan.

The percentage of patients with vision loss (37%) and strabismus (37%) in this series is higher than in the general paediatric population. Other series do not report the vision in their patients making comparison between series difficult. The overall visual prognosis in these patients is favourable although there is a much higher incidence of unilateral visual loss. The most common reason for this is amblyopia. A mixed surgical treatment is used in patients with other craniofacial syndromes this is due to a combination of factors which are independently amblyogenic. Refractive errors, anisometropia, strabismus, and ptosis combined to various degrees were responsible for this amblyopia. This often increases the duration of treatment and often results in a poor visual outcome.
for the amblyopia in our patients. No patients had structural problems of the globe which contributed to their vision loss. Patient 20 had post-chaismatic visual dysfunction (central visual impairment) which, by history, was the result of a perinatal anoxic insult. Of the eight patients with amblyopia, equal vision was only obtainable in two at the last examination. This emphasises compliance difficulties in these patients. Oral and auricular function may also be affected and cosmetic deformities in these patients can be severe. Because of this the patient and family may be more concerned with the correction of these defects. This contributes to the poor prognosis of amblyopia therapy.

Ocular abnormalities are frequent associations of major craniofacial malformations. In general the eye, orbit, and adnexa are more likely to be involved in deformities affecting the cranium and upper face. Abnormalities of the lower face, jaw, maxilla, and oral structures are more often observed without associated ocular involvement. Previous reports of the ocular abnormalities associated with the TCS have concentrated on the deformities of the skin and soft tissue structures affected by the underlying bony deformity. This report summarises the ocular and visual consequences of a malformation related to but not directly affecting the eye. This emphasises the intimate developmental relationship of all cranial and facial structures during embryogenesis. Visual acuity, amblyopia and its response to treatment, refractive errors, strabismus, and to the adnexal abnormalities frequently described with this syndrome thus characterising the full spectrum of ocular involvement.

Early ophthalmic examination to diagnose and treat refractive errors and strabismus will aid in detection of preventable causes of vision loss. This loss is most likely the result of amblyopia. Vision can improve with treatment but normal acuity was not obtained in most of the affected eyes. The need for aggressive amblyopia treatment, persistent encouragement and support of this treatment, and return visits to monitor compliance are essential to restore or prevent visual loss.


4 Treacher Collins E. Case with symmetrical congenital notches in the outer part of each lower lid and defective development of the malar bone. Trans Ophthalmol Soc UK 1900; 20: 190.


12 Feingold M, Gellis SS. Ocular abnormalities associated with first and second arch syndromes. Surv Ophthalmol 1968; 14: 30-42.


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