### Abstract

**Background/aims**—Congenital fibrosis of the extraocular muscles (CFEOM) is an autosomal dominant, non-progressive disorder characterised by congenital ptosis and external ophthalmoplegia. CFEOM has previously been divided into several clinical entities; general fibrosis syndrome, strabisimus fixus, vertical retraction syndrome, and congenital fibrosis of the inferior rectus. The purpose of this study was to identify families with CFEOM in this geographical region in order to perform a study of the clinical presentation of this disorder and to estimate its minimum prevalence in the population.

**Methods**—Four families were identified with CFEOM in the Wessex region from whom a full history with a pedigree was obtained. All individuals underwent ophthalmological examination.

**Results/Conclusion**—This study shows that several of the CFEOM entities can be present within one family suggesting that these are variants of the same condition. It is suggested that subclassification is, therefore, not appropriate. The minimum prevalence of this disorder was found to be 1/230,000. (Br J Ophthalmol 1998; 82:676–679)

Congenital fibrosis of the extraocular muscles (CFEOM) is an inherited, non-progressive disorder characterised by congenital ptosis and external ophthalmoplegia. The syndrome was first described by Heuk in 1879\(^1\) who showed on postmortem examination that the extraocular muscles were fibrotic and abnormally inserted. The condition was described in detail by Brown in 1950.\(^2\) Laughlin reported the condition in at least four generations in 1956.\(^3\) Since then regular additional reports have occurred in the literature\(^4–14\) describing approximately 100 cases.

The pattern of inheritance is autosomal dominant with descriptions of male to male transmission. Sporadic cases have been described. Recently, possible linkage of CFEOM to markers in the pericentromeric region of chromosome 12 has been shown.\(^15\)\(^16\)

The purpose of this study was to identify families with CFEOM in this geographical region in order to perform a clinical study and estimate the minimum prevalence of this disorder in the population.

### Methods

All ophthalmologists in the region were contacted and asked for details of any patients who might have CFEOM. All patients contacted were willing to participate in the study and were visited at home by a clinical geneticist (EH) and an ophthalmologist (ACR). A full history was obtained and a pedigree constructed (Fig 1). Both affected and unaffected individuals underwent ophthalmological examination (Tables 1 and 2).

#### FAMILY 1

**Case 1.1**

A healthy 54 year old woman was referred for evaluation of her bilateral ptosis which was causing marked chin elevation. She had undergone ptosis and squint surgery when age 11 years.

#### FAMILY 2

**Case 2.1** (Fig 2)

A 13 year old boy was referred for ptosis surgery. He was generally fit and well. At the age of 2 he had undergone bilateral anterior levator resections. Preoperative forced duction tests confirmed tight inferior recti. Both inferior recti and the superior obliques were

### Table 1  Ophthalmological details of affected individuals

<table>
<thead>
<tr>
<th>Case</th>
<th>Corrected visual acuity</th>
<th>Pupillary aperture (mm)</th>
<th>Levator function (mm)</th>
<th>Aberrant movements</th>
<th>Chin elevation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family 1 case 1.1</td>
<td>R: 6/12</td>
<td>6</td>
<td>0</td>
<td>Convergence on upgaze, adduction of the left eye.</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>L: 6/12</td>
<td>6</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family 2 case 2.1</td>
<td>R: 6/6</td>
<td>8</td>
<td>1</td>
<td>Convergence on up and down gaze</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>L: 6/6</td>
<td>8</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family 3 case 3.1</td>
<td>R: 6/18</td>
<td>5</td>
<td>1</td>
<td>Bilateral convergence on upgaze</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>L: 6/18</td>
<td>3</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family 4 case 4.1</td>
<td>R: 6/12</td>
<td>6</td>
<td>11</td>
<td>Nystagmoid movements in any attempted direction of gaze</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>L: 6/12</td>
<td>6</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family 1 case 1.1</td>
<td>R: 6/12</td>
<td>5</td>
<td>0</td>
<td>Abduction of right eye on left gaze</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>L: 6/60</td>
<td>5</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family 2 case 2.1</td>
<td>R: 6/9</td>
<td>5</td>
<td>0</td>
<td>None</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>L: 6/6</td>
<td>4</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family 4 case 4.1</td>
<td>R: 6/6</td>
<td>5</td>
<td>1</td>
<td>Synergistic divergence on attempted lateral gaze</td>
<td>no</td>
</tr>
<tr>
<td></td>
<td>L: 6/9</td>
<td>5</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
recessed. Subsequently he underwent bilateral brow suspension with autogenous fascia lata. Postoperatively his abnormal head posture was improved.

**Case 2.2 (Fig 3)**

A 44 year old woman was fit and well apart from mild arthritis. She had undergone a left brow suspension aged 9 months.

**Case 2.3 (Fig 4)**

A 63 year old woman was fit and well. She had undergone previous surgery which was unknown. Family 2 shows that several of the CFEOM entities may be present within one pedigree. Cases 2.1 and 2.2 are typical examples of congenital fibrosis of the inferior recti while case 2.3 would be classified as the general fibrosis syndrome.

**Family 3**

Case 3.1

A 5 year old boy was referred. Apart from problems with speech and language development he was otherwise fit and well.

Case 3.2

A 30 year old woman was fit and well. She had undergone unspecified surgery to both upper lids as a child.

Both affected members of family 3 are phenotypically very similar and would be classified as having the generalised fibrosis syndrome.

**Family 4**

Case 4.1

A 30 year old woman with good general health had been seen as a child by an ophthalmologist, but had never had any treatment.
Case 4.2
A 12 year old boy was attending a school for children with emotional behavioural problems, but was otherwise fit and well. At 18 months he had undergone bilateral ptosis and squint surgery. At age 12 he had undergone bilateral brow suspension and inferior rectus tenectomies.

Case 4.3
A healthy 8 year old boy, had undergone bilateral brow suspension with donor fascia lata at age 2. Postoperatively, he developed an abscess on the left side causing drooping of the left lid, and the right lid gradually dropped over the following year. At age 4 he had a repeat bilateral brow suspension with donor fascia lata and 5 mm recessions of the inferior recti. Postoperatively the left upper lid was still low and a further brow suspension with donor fascia lata was performed on the left side 18 months later resulting in a good lid position.

Case 4.4
A 5 year old boy had tracheomalacia but was otherwise fit and well. At age 1 he had had bilateral brow suspension with donor fascia lata and bilateral inferior rectus recessions. Postoperatively his abnormal head posture was improved. At age 3 he had a repeat bilateral brow suspensions with donor fascia lata and bilateral inferior rectus tenectomies to treat his remaining chin up head posture.

Family 4 all show markedly reduced vertical movements, with variable involvement of the horizontal muscles and levator muscle.

Results/discussion
We have found the minimum prevalence of CFEOM in the Wessex region (population 2.3 million) to be 1/230 000.

CFEOM has been subclassified into several similar syndromes—general fibrosis syndrome, strabismus fixus, vertical retraction syndrome, and congenital fibrosis of the inferior recti with or without ptosis. These are all static disorders and probably represent a developmental defect of the extraocular muscles. Histopathological examinations show a combination of fibrous tissue replacing muscle, adhesions between muscle and Tenon’s capsule, absent muscles in some cases and anomalous muscle insertions. Occasionally the muscles look normal even on microscopic examination.1 11

Recently computed tomography has been used to investigate this condition. Gillies et al11 described a family with five affected members. Computed tomography showed reduction in the size of the extraocular muscles particularly the superior recti as well as abnormal globe shape (two patients) and cranial ventricular asymmetry (three patients). Hupp et al9 likewise found atrophy of involved muscles on computed tomography.

General fibrosis syndrome2 has been characterised as extensive involvement of all the ocular muscles with marked ptosis present in all patients. The eyes are fixed in a downward position and the patients adopt a chin up head position to compensate. Often aberrant movements occur on attempts to move the eyes into the restricted field of vision. Strabismus fixus is
Phenotypic heterogeneity may occur in congenital fibrosis of the extraocular muscles

Characterised by involvement of the inferior recti, congenital fibrosis of the inferior recti is characterised by fixed exotropia or vertical retraction syndrome. Ptosis is almost invariably present.

In summary, we believe that CFEOM should be used to describe a condition with variable involvement of the extraocular muscles, and that attempts at further subclassification of this condition on purely clinical criteria may not be justified. Future classification may be aided by improved knowledge of the molecular basis of this condition, but it is possible that the genotype/phenotype correlation will not always be strong, as demonstrated in our second family.

Phenotypic heterogeneity may occur in congenital fibrosis of the extraocular muscles

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