Congenital Ocular Fibrosis Syndrome Associated With the Prader-Willi Syndrome

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ABSTRACT

We report an 11-year-old boy with both the congenital ocular fibrosis and the Prader-Willi syndromes. Since birth he has had bilateral blepharoptosis and fixed ocular misalignment in downward gaze. Pathological examination of the extraocular muscles showed replacement by fibrous tissue. Additionally, the child had the typical clinical features of the Prader-Willi syndrome including mental retardation, hypotonia, short stature, hypogonadism, and obesity. The Prader-Willi syndrome has been consistently associated with interstitial deletions of the long arm of chromosome 15. Although our patient appeared to have normal chromosomes, he may indeed have an undetectable deletion which may be responsible for both syndromes. We believe that the gene(s) for the congenital ocular fibrosis syndrome may be located near the gene(s) for the Prader-Willi syndrome on the long arm of chromosome 15.

Introduction

The congenital ocular fibrosis syndrome, initially described by Baumgarten in 1840, is an isolated disorder evident at birth and characterized by blepharoptosis and fixed ocular misalignment, usually in downward gaze. Brown documented three cases in 1950 and coined the term “general fibrosis syndrome.” The disorder is inherited as an autosomal dominant trait and is usually devoid of other ocular or systemic abnormalities; less commonly, it is sporadic.

The Prader-Willi syndrome is characterized by neonatal feeding difficulties, hypotonia, compulsive eating tendencies, mental retardation, obesity, short stature, acromegaly, and hypogonadism. Since 1976, many deletions, duplications, and rearrangements of chromosome 15 have been reported with the syndrome. Recent studies with high resolution banding have shown interstitial deletions of the long arm of chromosome 15 in from 47% to 93% of patients with the Prader-Willi syndrome.

We have studied a patient with both the congenital ocular fibrosis and the Prader-Willi syndromes; our patient had a normal high resolution trypsin-Giemsa banding chromosome 15. Although the chromosomal location of the gene encoding for the congenital ocular fibrosis syndrome is not known, this case suggests that the gene for this ocular malformation may be in proximity to the gene for the Prader-Willi syndrome.

Case Report

The patient was the full-term product of a pregnancy characterized by poor fetal movements. He was delivered vaginally with forceps and was hypotonic and lethargic in the neonatal period.

The mother and father were 18 years of age at the time of birth and were not consanguineous. There was no family history of ocular disease or spontaneous abortions.

Although the parents report that the eyes were not normal at birth, the first ocular examination was at 10...
months of age. At that time, the patient had bilateral ptosis, an exotropia of over 100 prism diopters, and absent movement of both globes. Under general anesthesia, a forced duction test showed resistance to adduction bilaterally. The lateral rectus muscles were recessed 10 mm and the inferior oblique muscles were maximally recessed. The surgeon described the lateral rectus muscles as tight and fibrotic and the inferior oblique muscles as mildly fibrotic. Pathological examination of the lateral rectus muscles showed coiled remnants of collagenous tissue; no muscle fibers were identified.

Postoperatively, the exotropia was reduced but remained greater than 100 prism diopters. At 14 months of age, the lateral rectus muscles were disinserted. Postoperatively, the exotropia was reportedly 60 prism diopters.

When last examined, the child was 11 years of age and institutionalized in a state facility. His weight was 21.4 kg, his height was 109 cm, and his head circumference was 48.3 cm. He was profoundly mentally retarded with an estimated intelligence quotient of 17. He was hypotonic except for a spastic left upper extremity. Other physical findings included acromicria, decreased bifrontal cranial diameter, hypogonadism, cryptorchidism, micropenis, and chronic peripheral edema.

On ocular examination the patient had central, steady, and maintained fixation in each eye. Bilateral ptosis was evident, with less than 5 mm of levator palpebral function in each eye. A chin-up posture and a right head turn were assumed for fixation (Figure 1). The eyes were fixed in downward gaze with an exotropia of over 100 prism diopters as measured by the Krimsky light reflex (Figure 2); there was complete absence of extraocular movement. The pupils were 3 mm in diameter and there was no afferent pupillary defect. The anterior segment was normal bilaterally by slit-lamp biomicroscopy. Cycloplegic retinoscopy revealed a refractive error of +1.00 +1.50 ×105 in the right eye, and −1.50 +4.00 ×85 in the left eye. On ophthalmoscopy, the media were clear and the fundi were normal.

Chromosomal analysis with trypsin-Giemsa staining of cells in prophase showed the patient to have a normal 46XY karyotype; no deletion of the long arm of chromosome 15 was identified. The parents were unavailable for cytogenetic study.

Discussion

The congenital ocular fibrosis syndrome is characterized by fibrosis of the extraocular muscles with blepharoptosis and fixed ocular misalignment, usually in downward gaze. Heuck9 first reported its familial occurrence in 1879. The disorder exhibits variable expressivity and reduced penetrance10 and is usually bilateral.11 Surgical correction usually requires multiple step-wise procedures.12-14 Histological findings range from partial to complete replacement of muscle with fibrous tissue.12,15,16

Although multiple pedigrees with autosomal dominant transmission of the congenital ocular fibrosis syndrome have been reported10,13,14,17,18 isolated reports of the disorder are numerous19,20 and may represent new point mutations. Autosomal recessive19 and X-linked recessive20 inheritance have been described rarely. Chromosomal ana-

![FIGURE 1: Patient with blepharoptosis and right head turn.](image)

![FIGURE 2: Ocular alignment was fixed in exophthalmos.](image)

lyses on familial and isolated cases have been performed uncommonly and all have been reportedly normal.10,21,23

Most cases of the congenital ocular fibrosis syndrome occur in the absence of other ocular or systemic abnormalities; however, the occasional exceptions are listed in Tables 1 and 2.

In 1956, Prader and associates9 described a new syn-
SYSTEmIC ANOMALIES ASSOCIATED WITH THE CONGENITAL OCULAR FIBROSIS SYNDROME

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental retardation</td>
<td>27, 31</td>
</tr>
<tr>
<td>Facial palsy</td>
<td>16, 27</td>
</tr>
<tr>
<td>Craniofacial dysmorphisms</td>
<td>23, 27</td>
</tr>
<tr>
<td>Dental anomalies</td>
<td>21, 23, 27</td>
</tr>
<tr>
<td>Klippel-Feil deformity</td>
<td>32</td>
</tr>
<tr>
<td>Cardiac malformations</td>
<td>20, 33</td>
</tr>
<tr>
<td>Syringomyelia</td>
<td>34</td>
</tr>
<tr>
<td>Spina bifida</td>
<td>20, 32</td>
</tr>
<tr>
<td>Syndactyly</td>
<td>35</td>
</tr>
<tr>
<td>Bilateral inguinal hernias</td>
<td>12</td>
</tr>
<tr>
<td>Cryptorchidism</td>
<td>12</td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td>Present study</td>
</tr>
</tbody>
</table>

References


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