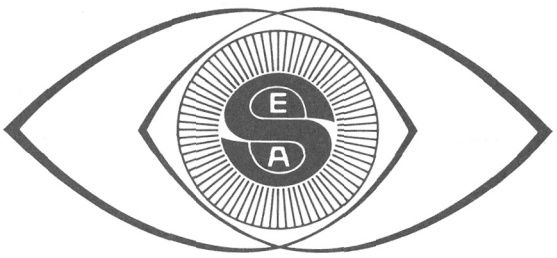


# TRANSACTIONS

# 20th MEETING

# EUROPEAN STRABISMOLOGICAL ASSOCIATION

Brussels, May 1992

Editor: Herbert Kaufmann

# Bilateral Congenital Vertical Gaze Disorders: Congenital Muscle Fibrosis or a Congenital Central Nervous Abnormality?

**Ahmed A. Assaf, MD**
**Department of Ophthalmology**
**College of Medicine, King Saud University**
**Riyadh, Saudi Arabia**

## ABSTRACT

Bilateral congenital disorders of the vertical gaze are rather uncommon. The etiology and classification in many instances are not clear. Different terms and etiologies were described, among these congenital fibrosis syndrome is the most common.

Eight patients with bilateral vertical ocular motility disorders were described. Features, findings and etiologies were presented and discussed. All these patients were congenital and their ocular motility defects were present since birth. Four patients had family history of similar pathology associated with consanguineous marriages.

The majority of these patients fitted in the classical condition described as congenital fibrosis syndrome. It was suggested that the primary pathology in all these cases is central nervous than peripheral muscular in origin.

## KEY WORDS

Congenital ocular muscle fibrosis syndrome, Congenital vertical gaze disorders, congenital ocular muscular neurogenic abnormalities

## INTRODUCTION

Vertical ocular motility disorders are uncommon. They can involve upgaze, downgaze or a combination of both. Among these, isolated downgaze is the least frequent.

Vertical ocular motility disorders can occur alone or in association with defects in the horizontal eye movements. The involvement of the horizontal ductions can vary from a partial loss of a duction movement in one eye, to total bilateral loss of eye movements in all directions of horizontal gaze.

The most frequent cause of bilateral congenital involvement of gaze is congenital fibrosis syndrome. Other causes include myopathy and third cranial nerve palsy. Unilateral cases are mostly cause by third cranial nerve palsy of various etiologies.

Khodadoust & von Noorden[1] described vertical retraction syndrome in two members of a family. The authors suggested that the clinical features of the vertical retraction syndrome are similar to Duane's syndrome although they affect different muscles. The result of the forced duction test indicated structural rather than neurogenic anomalies as the probable cause in their patients.

Congenital generalized fibrosis syndrome of extra-ocular muscles is characterized by ptosis and marked restrictions of eye movements. It is almost always bilateral. These patients frequently have positive family history with some cases being inherited as autosomal dominant, the majority being

sporadic. Divergent strabismus and abnormal head position, especially chin elevation, are common findings.[2-4]

In this article 8 cases with congenital bilateral disorder of vertical gaze were described. The majority of these fitted in the classical picture of generalized fibrosis syndrome. Discussion followed with emphasis on etiology.

## MATERIAL AND METHODS

The eight cases with congenital bilateral vertical eye movement disorders described, have attended King Khaled Specialist Eye Hospital (KKESH), Riyadh over a period of six years. The patients presented at various ages and were included under various diagnoses of Parinaud syndrome, third nerve palsy, and Duane's syndrome. Three, had an attempted surgical correction of their defect of eye movements and forced duction test and muscle specimens were obtained during surgery.

## RESULTS

As indicated in tables 1, 2 , and three.

Table 1. Patients Analysis

| No. | Sex | Age | Family History |
|---|---|---|---|
| 1. | M | 1 year | Parents are second cousins |
| 2. | M | 1 year & 4/12 | Parents are second cousins.<br>Brother has a similar condition (case 3) |
| 3. | F | 7 years | Sister case 2 |
| 4. | M | 4 years | negative |
| 5. | F | 5 years | Parents are first cousins.<br>Maternal grandmother had ptosis |
| 6. | F | 6 years | negative |
| 7. | F | 9 years | Parents are first cousins<br>Brother patient 8 |
| 8. | M | 10 moths | Sister patient 7 |

### Surgical Findings

Case 3: A seven years female with congenital etiology. She had an intraoperative forced duction test (FDT) which indicated limited elevation of both eyes right more than left. The inferior recti were tight in both eyes. The superior and horizontal recti were normal. The patient had recession of both inferior recti.

Case 6: A six years old female with congenital etiology. She had left recession and resection of the horizontal recti with bilateral inferior rectus recession. Intraoperative FDT showed limitation of elevation in both eyes (-2 to -3 OD and -3 OS). Depression was less involved with -0.5 OD and -1 OS. Horizontally only the left eye showed -4 limitation of adduction, otherwise within normal. The left lateral rectus and inferior recti in both eyes were very tight and fibrotic.

Case 7: A nine years old female with congenital etiology. Intraoperative FDT showed the right eye had -2 limitation of elevation and -0.5 limitation of depression with normal horizontal ductions.

The left eye had -4 limitation of elevation, -3 limitation of depression and -4 limitation of adduction. Abduction was normal.

**Systemic Findings**

Seven patients were normal with no associated systemic abnormalities. All had CT-scan and one had NMI all of which were normal. In one case CT-scan indicated agenesis of superior rectus in both eyes that was not confirmed by the NMI.

In the remaining case (case 1) the patient had mental retardation with delayed milestones of development. Additionally there was low set ears and blepharophimosis. The NMI indicated possible cerebellar hypoplasia.

Table 2. Eye movements analysis.

| No. | UG | DG | ADD | ABD | Other eye movement disorders |
|---|---|---|---|---|---|
| 1. | -4 | -2 | - | -1 (OD) | Bilateral convergence on attempted upgaze |
| 2. | -4 | - | - | - | Esotropia OS on attempted elevation |
| 3. | -4 | -2(T) | - | - | Bilateral convergence on attempted upgaze +2 Overaction of the superior obliques OU |
| 4. | -4 | - | -1.5 (OU) | -2 (OU) | Bilateral Convergence on attempted upgaze |
| 5. | -3 | -4 | -2 (OD) | -3 (OD) | Narrowing of the palpebral fissure (PF) on adduction OU with retraction of the globe OD. Widening of the PF on abduction OS |
| 6. | -4 | -2/3(T) - 1/2(N) | -2 (OS) | - | Bilateral convergence on attempted elevation |
| 7. | -4 | -4 | -4 (OU) | -2 (OS) | Bilateral retraction on horizontal and vertical gaze |
| 8. | -4 | -4 | -4 (OU) | -4 (OD) -1 (OS) | Globe retraction OD on attempted movement |

UG = Upgaze; DG = Downgaze; ADD = Adduction; ABD = Abduction
-1 to -4 = Limitations of eye movements out of scale of 4
-2/3 = -2 to -3; -1/2 = -1 to -2
T= Temporally; N= Nasally

## DISCUSSION

The present accepted view of the congenital fibrosis syndrome is that ocular motility defects result from primary replacement of extraocular muscle fibers with fibrous tissue.[4] This is associated with abnormal insertions of the extraocular muscles (EOM). These are the main arguments for a primary muscular pathology for this disease. Histopathologically this condition is characterized by total replacement of muscle fibers with fibrosis with marked generative changes of the muscles.[3]

The relationship between normal muscle innervation and normal muscle fiber anatomy is well accepted. Drachman etal[5] studied changes in the EOM after third cranial nerve sectioning. They observed secondary histological changes in the EOM similar to many features seen in myopathy. It was clear to the authors that experimental denervation of the EOM produced a histological picture characteristic of primary myopathy. Accordingly, they concluded that histological examination of the extraocular muscles may be unreliable means to distinguish neurogenic from myopathic ocular motor weakness. Beside these findings in the EOM, degenerative changes were documented to

occur in the centers controlling vertical eye movements in the midbrain in patients with progressive external ophthalmoplegia.[5,6] From the above, it is not unreasonable to expect that congenital abnormal development of innervation can result in poor development of the muscle fibers, which in turn results in abnormally muscle with abnormal insertions. The severity of these changes will depend on the severity and the stage of development at which the defect in innervation had occurred.

Table 3. Strabismus, ocular findings and abnormal head position

| No. | Strabismus | Ocular Findings | Head Position |
|---|---|---|---|
| 1. | ET OD(0-30)<br>XT at times | Nystagmus,<br>ptosis<br>blepharophimosis<br>myopia<br>blurred disc margins OU | Chin elevation<br>Left face turn |
| 2. | None | - | Chin elevation |
| 3. | None | Ptosis<br>amblyopia | Chin elevation/<br>Right face turn |
| 4. | None | Ptosis<br>nystagmus<br>amblyopia OU | Chin elevation/<br>Right head tilt |
| 5. | ET/XT OD<br>40 ET -<br>20 XT | Amblyopia OD>OS<br>Eccentric fixation OD<br>Partial ptosis OD<br>Pupils normal | None |
| 6. | XT 0-60 OS | Amblyopia<br>No ptosis<br>Prefer OD, holds with difficulty | Chin elevation/<br>right face turn |
| 7. | XT 90 OD | Myopia and anisometropia<br>Amblyopia OS>OD<br>Ptosis OU<br>No Bells | Right face turn/<br>chin depression |
| 8. | XT 60-90<br>OD HT 15 | Ptosis OU<br>Pupils dilated OD<br>miosed OS<br>Alternate fixation<br>No Bells | Shifting head position<br>R/L turn |

The central cause of Duane's retraction syndrome is well accepted now. This condition is also characterized by fibrotic and tight muscles. Additionally, recently a case of congenital ocular fibrosis has been associated with neuronal misdirection.[7]

The majority of cases described in this article fitted in the traditionally documented cases of congenital fibrosis syndrome as described by various authors. On the other hand they have shown many clinical indicators supporting neurogenic rather than pure muscular etiology.

First, many of patients described showed evidence of co-contraction of EOM. Three had retraction of the globe, one on adduction and two on all direction of gaze. One patient had narrowing the palpebral fissure on adduction, which was associated with retraction as mentioned in the three above patients. In the absence of abnormalities of vertical gaze, these patients would have been easily diagnosed as type third Duane's retraction syndrome especially patient number five. The convergence on attempted upgaze observed in some patients is analogous to the up and down shoots seen in Duane's retraction syndrome and indicative of tight antagonist muscle.

Second, the presence of variable angle horizontal strabismus, is common to many of these patients which is against muscle fibrosis. One patient had a variable exotropia between 0-60 prism diopter in the primary position (case 6) and two had variable XT-ET suggestive of abnormal patterns of innervation.

Third, exotropia is a common finding in cases with generalized muscle fibrosis. Of the patients described, 3 had exotropia, 2 had variable ET-XT, and three had no horizontal strabismus; no patient had pure ET. If the primary etiology is generalized fibrosis of EOM, then one would expect a more or less equal incidence of esotropia and exotropia in such patients. The presence of exotropia, in almost all of these cases with strabismus, points towards involvement of the third cranial nerve. Also, the presence of variable angle exotropia esotropia cases and retraction on adduction in some cases points towards paradoxical innervation between the third and sixth cranial nerves. The opposite of the innervation pattern in cases of Duane's retraction syndrome where the third nerve is documented to innervate the lateral rectus in the absence of normal VI cranial nerve supply.

Fourth, 5 patients had convergence on upgaze, 4 bilateral and one unilateral. As mentioned earlier this is suggestive of tight inferior rectus muscles. No patient had convergence on downgaze. If the primary cause is myopathy then superior and inferior recti should be involved more or less equally. On the other hand, it is well accepted that supranuclear lesions involving upgaze are much commoner than those involving downgaze. Bilateral intact, or less involved, downgaze associated with congenitally absent upgaze will result in long-standing ocular depression and chin elevation, with secondary changes in the inferior recti.

Fifth, in some patients there was less limitation of depression on adduction suggesting sparing of the superior obliques. In one patient there was an obvious overaction of the superior obliques in both eyes (patient 3). This is again pointing against muscle fibrosis of theory, but towards third cranial third nerve involvement.

Sixth, the degree of clinical limitation of ocular movements did not always correlate with the degree of the tightness of the agonist or antagonist muscle as indicated by the intraoperative FDT. This is again suggestive of an innervational problem as a contributing factor to the motility defect rather than pure fibrotic tight muscle situation.

The anatomical proximity of the riMLF to the third nerve nucleus could result in a variable combined involvement of the riMLF, it's efferent pathway and/or the third cranial nerve nucleus. Cases with pure congenital symmetrical vertical gaze involvement represent a congenital pathology involving the supranuclear gaze center or it's efferent pathways to the oculomotor nuclei. The most common type of vertical gaze involved is elevation, as reported by various authors.[8,9] On the other hand, associated variable horizontal eye movements abnormalities point towards a third cranial nerve nuclear lesion of variable severity combined with involvement of the supranuclear vertical gaze centers. This third cranial nerve nuclear involvement is the source of ptosis seen frequently in these patients. True ptosis should be differentiated from pseudoptosis associated with pure loss of elevation with intact downgaze. Thus, the condition could be seen as a spectrum of pathology involving vertical gaze with or without a variable degree of horizontal gaze involvement and ptosis. Aberrant innervation and variable degree of muscle function could explain many of the features described above. This picture is compounded by secondary abnormal muscle development and muscle fibrosis resulting from loss of innervation at an early stage of intrauterine development.

Abnormal head position occurred in all patients except one. Chin elevation occurred in patients with fairly less affected downgaze. Cases with most marked limitation of downgaze did not have chin elevation (cases 5, 7 and 8). The prolonged chin elevation, associated with loss of elevation and less affected downgaze, will result in the contracture of the inferior recti; a common finding in such cases.

One would expect to see few of these patients, if any, having Bell's phenomenon because of the associated contracture of the inferior recti. In one patient there was evidence of exposure keratitis during sleep with corneal staining inferiorly (table 2).

Congenital fibrosis syndrome is known to be inherited in a dominant or a sporadic fashion. Two families among the described patients, with two members involved in each, were associated with consanguineous marriages. The father of one family was married to another wife with 10 normal siblings. From the first wife he had two involved, a male and female, in addition two other normal sisters. This is suggestive of recessive inheritance pattern in the patients described. This mode of inheritance was also documented to occur by Waardenburg[4] but less commonly.

In summary, patients were described with bilateral loss of upgaze, with or without involvement of downgaze. This was associated with a variable degree of horizontal involvement. These patients could easily fit in the well documented disorder of generalized fibrosis syndrome. On the other hand there are many clinical indicators pointing towards neurogenic causes representing a spectrum of pathology. Among these patients two families were described with recessive inheritance.

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**Correspondence to:**

Ahmed A. Assaf, MD
Department of Ophthalmology
P.O. Box 7085
Riyadh, 11472, KSA