

Duane syndrome

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Abstract

Duane Syndrome is a congenital form of strabismus characterized by horizontal eye movement limitation, globe retraction with palpebral fissure narrowing in attempted adduction. This condition results from paradoxical innervation of rectus lateral muscle. The syndrome is classified in three types based on the presence of a defect in adduction, abduction or both. The incidence is approximately 1% of the total cases of strabismus. Duane syndrome can be isolated or associated with ocular anomalies (heterochromia, iris dysplasia, colobomas, Marcus-Gunn phenomenon...), and systemic anomalies (Goldenhar's syndrome, Klippel-Feil syndrome, sensory neural hearing loss..). Most cases are sporadic, however familial occurrence with dominant autosomal inheritance pattern has been reported. Duane syndrome has been linked to five loci and a first causative gene, SALL4, has been identified. The currently proposed etiologic mechanism is that Duane syndrome results from an innervational disturbance of brain stem origin in which the lateral rectus muscle is partially innervated by branches of the oculomotor nerve. When required, surgical procedures are used to improve the primary gaze alignment, face turn and postural position, but the results are limited.

Keywords

Strabismus, retraction syndrome, genetic.

Disease name and synonyms

- Duane syndrome
- Stilling-Turk-Duane
- Congenital retraction syndrome

The syndrome was first described in the last part of the 19th century by Hueck (1879), Stilling (1887) and Turk (1896). It was defined as a clinical entity by Duane in 1905 and Duane syndrome is the most commonly used name for the disorder.

Diagnosis criteria/Definition

Duane syndrome is a congenital disorder of ocular motility characterized by horizontal eye movement limitation, globe retraction with palpebral fissure narrowing in attempted adduction (1,2,3,4,5).

As suggested by Huber (6), Duane syndrome can be divided into three different types, depending on the distribution or development of aberrant innervation (2,7).

- Type I: Defective abduction, normal or minimal defective adduction.

- Type II: Defective adduction, normal abduction, there is exotropia of the affected eye.
 - Type III: Defective abduction and adduction.
 The distinction between type I and III can be difficult as it depends on the appreciation of the degree of adduction limitation.
 This classification is confirmed by electromyographic study.

Differential diagnosis

Duane syndrome must be differentiated from:

- VI nerve palsy
- Moebius syndrome
- Congenital oculomotor apraxia
- Congenital or familiar esotropia
- Acquired orbital post traumatic lesions (untrapment rectus medial)
- Atrophia rectus lateral after surgical extensive conjunctival scarring

Frequency

The incidence of Duane syndrome is approximately 1% of the total cases of strabismus (8). In a report of clinical features in 63 patients, Shauly *et al* (4) observed a female to male ratio of 3:2. An opposite trend of male preponderance was found in a small group of patients with Duane III since 5 out of 8 cases were male.

Clinical description

The clinical picture consists of limitation of horizontal eye movement, globe retraction with palpebral fissure narrowing on attempted adduction. The most common clinical presentation is Duane type I (70 to 90% of cases). The syndrome is bilateral in 10-20% of cases. Of the predominant bilateral cases, the left eye is more often affected.

Manifestations include also ocular elevation or depression (upshoot and downshoot) during adduction (1), and frequently enophthalmos. Patients present with a relatively small esotropia in the primary position, and sometimes a head turn towards the side of the affected eye to enable fusion in lateral gaze. Compensatory head turn to maintain single binocular vision is present in 66% of all cases and in 76% of unilateral cases. In patients affected with Duane type I, strabismus is evident in 77%, orthophoria in 45%, esophoria in 23%, and exophoria in 9% of cases.

The three types of Duane syndrome are frequently associated with other eye movement anomalies characterized by changes in the ocular axes causing either an A, V or X pattern of eye movements.

The other ocular anomalies include heterochromia, iris dysplasia, ptosis, cheratoconus, nystagmus, papillary anomalies, choroidal colobomas, dystichiasis,

microphthalmos, optic nerve hypoplasia, Morning Glory syndrome and Marcus-Gunn phenomenon (3,5).

Systemic associated anomalies include Goldenhar's syndrome, Klippel-Feil syndrome, vertebral column anomalies, facial anomalies, rib anomalies, sensory neural hearing loss, malformation of the external ear, Rubinstein-Taybi syndrome, Dandi-Walker syndrome, genitourinary anomalies and anomalies of the limbs, feet and hands (3,4,9).

Etiology

Pathophysiology

The etiology of DRS remains unclear, and several theories have been suggested (7). The most widely accepted is that Duane syndrome results from an innervational disturbance of brain stem origin where the lateral rectus muscle is partially innervated by branches of the oculomotor nerve. Different studies have reported innervational anomalies in patients with DRS. In 1957, Breinin (10) reported paradoxical electrical activity of the lateral rectus muscle by electromyography. Abnormal synergistic innervation between the medial and vertical rectus or oblique muscles are recorded by EMG. A constant finding in many autopsies has been the absence or hypoplasia of the abducent nucleus. There is also a possibility that the connections to this nucleus are abnormal. In this case, a central defect occurs concurrently with the suggested peripheral innervation anomalies.

In Duane Syndrome, even in presence of normal brain stem connection and adequately aligned muscle vectors, the third cranial nerve can replace the function of the sixth one.

However abnormal brain stem origin does not explain acquired cases where the etiology could be mechanical or supranuclear.

The Duane syndrome may be considered in most cases as an example of ocular miswiring. In fact the syndrome has been associated with oculocutaneous albinism. The retinostriate projections in albinism could be considered miswired.

Embryologic theories have suggested that a common teratogenic stimulus between the fourth and sixth week of gestation may cause both the ocular and systemic findings of Duane syndrome. In addition, an abnormal early intrauterine environment is suggested by an association of Duane syndrome with intracranial vascular malformations and Chiari I malformations. (11)

Genetics

Although Duane Syndrome is usually unilateral and sporadic, there could be up to 10% of familial cases, mostly with autosomal dominant

inheritance. Several autosomal dominant syndromes with dysmorphic features are associated with Duane syndrome (13). Duane syndrome was linked to chromosomal loci at 4q27, 8q13, 22pter-q11, 2q31 and 20q13 (14-18). A recent study refined the mapping in region 8q13 (DURS1; MIM 126800), reducing the critical region to about 40 kb (19).

Linkage to 2q31 (DURS2; MIM 604356) was confirmed and the genetic interval was reduced to an 8.8-cM region between markers D2S326 and D2S364 that includes the candidate homeobox D gene cluster (20).

A new member of the SAL family of proposed C2H2 zinc finger transcription factors, SALL4, is encoded by a gene situated within the region 20q13. Mutation analysis of SALL4 in three pedigrees revealed point mutations cosegregating with the Duane patients. SALL4 represents the first identified Duane syndrome gene and is likely to play an important role in abducens motoneuron development.

Treatment

All the patients with Duane syndrome should be first evaluated to assess the presence of refractive errors (3,7,12).

In patients with binocular vision in primary position without head turn a careful evaluation of visual acuity is necessary and refractive anomalies must be corrected before any other treatment is undertaken. The follow up of these children has to be very steady, because a decompensating strabismus might develop later. In Duane syndrome with esotropia, exotropia and head turn the first approach is the correction of amblyopia and head turn with lens, prism, occlusion. In any case, correction of visual defects must precede surgery.

The primary aim of surgery is to restore ocular alignment in primary position. In fact, patients with binocular vision in primary position without head turn do not need surgery.

Several types of surgical procedures have been proposed for the treatment.

Molarte and Rosenbaum (21) recommended transposition superior and inferior rectus muscles toward the lateral rectus to improve the abduction.

Saunders *et al.* (22) proposed surgery on the normal eye: recession or posterior fixation sutures on the basis of two theories: i) to improve the duction of the yoke muscle on the basis of the Hering's law; ii) to allow a wider field diplopia-free.

However Hering's law does not apply to Duane's syndrome: it's not correct to consider the abduction-limitation as the sixth nerve palsy.

The recession uni or bilateral medial or lateral muscle is the simple and advisable approach to correct the anomalous head position (23).

The amount of recession varies with the angle of deviation in forced primary position and intra-operative forced ductions.

The use of adjustable sutures is advantageous in some cases, especially in cooperative patients.

The up-shoot and down-shoot is believed to be caused by a tautness or leash effect from the lateral rectus muscle. The treatment used to reduce this motility disorder is the recession of the lateral muscle with Y-splitting proposed by Scott and Jampolsky: this procedure widens the muscular insertion and would have to avoid rectus lateral sliding stabilizing the same muscle (24).

Conclusions

The Duane's syndrome is a complex disorder of ocular motility with variable features that needs expert ophthalmologist on strabismus to have a right diagnosis and a consequent surgical indication for the better result.

In our experience the best surgical result is obtained in Duane type 1.

However, surgery rarely allows complete clinical recovery, and limited expectations are appropriate.

References

1. Duane A (1905). Congenital deficiency of abduction, associated with impairment of adduction, retraction movements, contractions of the palpebral fissure and oblique movements of the eye. *Arch Ophthal* 34:133-159
2. Isenberg S, Urist MJ (1977). Clinical observations in 101 consecutive patients with Duane's retraction syndrome. *Am J Ophthalmol* 84:419-425
3. Gutowski NJ (2000). Duane's syndrome. Review. *European J. of Neurol* 7:145-149
4. Shauly Y, Weissman A, Meyer E (1993). Ocular and systemic characteristics of Duane syndrome. *J Pediatric Ophthalmol Strabismus* 30:178-183
5. Raab EL (1986) Clinical features of Duane's syndrome. *J. Pediatric Ophthalmol Strabismus* 23:64-68
6. Huber, A (1974). Electrophysiology of the retraction syndrome. *British Journal of Ophthalmology* 58:293-300
7. Alexandraxis G, Saunders RA (2001). Duane retraction syndrome. *Ophthalmol Clin.of North America*. 14:407-17
8. Gurwoods AS, Terrigno CA (2000) Duane's retraction syndrome: literature review. *Optometry* 71:722-6

- 9.** Okihiro MM, Tasaki T, Nakano KK, Bennett BK (1977). Duane syndrome and congenital upper limb anomalies: a familial occurrence. *Arch Neurol* 34:174-179
- 10.** Breinin GM (1957). Electromyography –a tool in ocular and neurologic diagnosis. II. Muscle palsies. *Arch Ophthalmol* 58: 293-300
- 11.** Prats JM, Garaizar C (1994). Duane retraction syndrome associated with Chiari I malformation. *Pediatric Neurol.*10:340
- 12.** De Respinis PA, Caputo AR, Wagner RS, Guo S (1993). Duane's retraction syndrome. *Surv Ophthalmol* 38:257-288
- 13.** Marshman WE, Schalit G, Jones RB, Lee JP, Matthews TD, McCabe S (2000). Congenital anomalies in patients with Duane retraction syndrome and their relatives. *J AAPOS* 4:106-9
- 14.** Chew CK, Foster P, Hurst JA, Salmon JF (1995). Duane's retraction syndrome associated with chromosome 4q27-31 segment deletion. *Am J Ophthalmol* 119:807-9
- 15.** Calabrese G, Stuppia L, Morizio E, Guanciali Franchi P, Pompetti F, Mingarelli R, Marsilio T, Rocchi M, Gallenga PE, Palka G, Dallapiccola B (1998). Detection of an insertion deletion of region 8q13-q21.2 in a patient with Duane syndrome: implications for mapping and cloning a Duane gene. *Eur J Hum Genet* 6:187-93
- 16.** Cullen P, Rodgers CS, Callen DF, Connolly VM, Eyre H, Fells P, Gordon H, Winter RM, Thakker RV (1993). Association of familial Duane anomaly and urogenital abnormalities with a bisatellited marker derived from chromosome 22. *Am J Med Genet* 47:925-30
- 17.** Appukuttan B, Gillanders E, Juo SH, Freas-Lutz D, Ott S, Sood R, Van Auken A, Bailey-Wilson J, Wang X, Patel RJ, Robbins CM, Chung M, Annett G, Weinberg K, Borchert MS, Trent JM (1999). Localization of a gene for Duane retraction syndrome to chromosome 2q31. *Am J Hum Genet* 65:1639-46
- 18.** Al-Baradie R, Yamada K, St Hilaire C, Chan WM, Andrews C, McIntosh N, Nakano M, Martonyi EJ, Raymond WR, Okumura S, Okihiro MM, Engle EC (2002). Duane radial ray syndrome (Okihiro Syndrome) maps to 20q13 and results from mutations in SALL4, a new member of the SAL Family. *Am J Hum Genet* 71:1195-9
- 19.** Calabrese G, Telvi L, Capodiferro F, Morizio E, Pizzuti A, Stuppia L, Bordoni R, Ion A, Fantasia D, Mingarelli R, Palka G (2000). Narrowing the Duane syndrome critical region at chromosome 8q13 down to 40 kb. *Eur J Hum Genet* 8:319-24
- 20.** Evans JC, Frayling TM, Ellard S, Gutowski NJ (2000). Confirmation of linkage of Duane's syndrome and refinement of the disease locus to an 8.8-cM interval on chromosome 2q31. *Hum Genet* 106:636-8
- 21.** Molarte AB, Rosenbaum AL (1990). Vertical rectus muscle transposition surgery for Duane's syndrome. *J Pediatr Strabismus* 171-7.
- 22.** Saunders RA, Wilson ME, Bluestein EC, et al (1994). Surgery on the normal eye in Duane retraction syndrome. *J Pediatr Ophthalmol Strabismus* 31: 162-9
- 23.** Barbe ME, Scott WE, Kutschke PJ (2004). A simplified approach to the treatment of Duane's syndrome. *Br J Ophthalmol* 2004 88: 131-8
- 24.** Jampolsky A. Discussion of Eisenbaum AM, Parks MM. A study of various surgical approach to the leash effect in Duane's syndrome. Presented at the joint session of the American Association for pediatric ophthalmology and strabismus and the American Academy of Ophthalmology, Chicago, IL, November 5, 1980.