Duane Retraction Syndrome: Clinical Presentation and Management Strategy

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Abstract

Duane retraction syndrome (DRS) is a special strabismus with variable presentation. It has been best classified by Huber based on electromyography in 1974 into three types. Huber type I is the most common form of DRS with an earlier presentation and also has satisfactory surgical outcomes. Huber type II is the least common presentation. Ahluwalia et al. in 1988 have further divided it into subgroups A, B, and C based on the alignment in primary position, indicating esotropia, exotropia, and orthophoria. Type I has esotropia, type II has exotropia, and type III has esotropia and exotropia equally common. DRS can be associated with other ocular abnormalities and systemic issues when present in syndromes. Hence, these patients need a more detailed evaluation. Management strategy aims at alignment in primary position, correcting anomalous head posture, improving palpebral fissure size, and alleviating upshoots and downshoots. It is challenging to address these patients and they need to be counseled before surgery regarding the outcome that is expected of the surgery.

Keywords: Congenital cranial dysinnervation disorder, Duane retraction syndrome, esotropic Duane retraction syndrome, exotropic Duane retraction syndrome, Huber classification, globe retraction, overshoots

Introduction

Duane retraction syndrome (DRS) was described as early as 1879 by Heuck and it was illustrated by Stilling et al. and Turk. Therefore, in European literature, it is often referred as Stilling–Turk–Duane syndrome. Now, a broader terminology has been used to bring under one umbrella all disorders with associated loss of innervation to motor muscles. This includes DRS, congenital fibrosis of extraocular muscles, monocular elevation defect, and Mobius syndrome. They are all labeled as congenital innervation dysgenesis syndrome/congenital cranial dysinnervation disorders (CCDDs). DRS is an ocular motility disorder characterized by defective horizontal eye movements with palpebral fissure narrowing on adduction and widening on abduction. It is mostly a unilateral disorder and sporadic in occurrence.

Genetics in Duane syndrome

The majority of cases of DRS are sporadic in origin. Genes do play a role in the development of DRS. Familial reporting has been documented in literature from 10% to as high as 23%. Genetic studies of autosomal dominant DRS has led to the identification of CHN1 as a DRS gene. Mutations in the CHN1 gene alters the development of abducens and to some extent the oculomotor axons. In some families, DRS skips a generation due to reduced penetrance. Recessive forms of inheritance have also been documented. The majority of cases of DRS are sporadic in origin.

Syndromic DRS is always associated with gene mutations. Duane radial ray syndrome (DRRS) where there is unilateral or bilateral Duane syndrome associated with a skeletal change of radial dysplasia ranging from thumb hypoplasia to phocomelic limb. Truncating mutations of SALL4 gene deletions have been found in DRRS families. The HOXA1 gene homozygous mutations have been found in autosomal recessive disorder where DRS along with deafness, facial weakness, vascular malformations, and learning difficulties has been noted.

A study of chromosomes of individuals with Duane syndrome has shown that deletions of chromosomal material on...
chromosomes 1, 4, 5, 8 and the presence of an extra marker chromosome derived from chromosome 22.

Epidemiology
It is one of the most common among special strabismus. Female preponderance and unilateral presentation with left eye preference are the common occurrences. A minority of patients have bilateral disease. Patients with bilateral disease may be asymmetrically affected.

Classification
Huber proposed, in 1970, a classification based on electromyography (EMG) studies. This is popular because it utilizes clinical description.

Type I (70%-80%)
Abduction is more limited than adduction (lateral rectus [LR] receives little/no innervation from the sixth nerve and paradoxical innervation from the third nerve. Medial rectus [MR] was found to have normal electric behavior). Globe retraction and palpebral fissure narrowing on adduction and widening on abduction are noted.

Type II (7%)
Marked limitation of abduction with primary position exotropia of the affected eye, abduction normal or slightly limited with globe retraction and palpebral fissure narrowing on attempted adduction is the presentation. On EMG, LR showed peak impulses on abduction and a second paradoxical impulse on attempted adduction while the electrical activity of MR was normal.

Type III (15%)
Limitation or complete absence of abduction and adduction with globe retraction and palpebral fissure narrowing in attempted adduction is observed. EMG showed simultaneous innervation of LR and MR muscles in primary gaze, adduction, and abduction.

Alphabet patterns of DRS have been also noted in DRS due to synergistic innervation of the vertical rectus.

Ahuwalia et al. modified Huber’s classification to include subgroups. Depending on the alignment in primary gaze, each Huber type was divided into A, B, and C, including esotropia, exotropia, and orthotropia, thus making it relevant clinically and surgically.

Clinical Features
A child with DRS presents with anomalous head posture, affected eye appearing smaller due to globe retraction and pseudoptosis in adduction. The other eye is often mistaken to be esotropic when the child looks in the direction of the eye with DRS associated with abduction deficit. This is due to over adduction of the uninvolved eye as per the Hering’s law. Refractive error and amblyopia can be associated with DRS; hence, cycloplegic refraction is mandatory for all cases of DRS. Anisometropic and ametropic amblyopia have been reported to be common causes of amblyopia in DRS although O’Malley et al. found strabismic amblyopia to be a common cause. Type I (Huber) DRS is the most common form of presentation while type II is the least common type of DRS. Type I DRS is associated with esotropia [Figure 1] more frequently than exotropia. Type II DRS has exotropia and type III has esotropia, exotropia, and orthotropia occurring equally among them. The most notable feature in DRS is abduction limitation, but the primary position squint is small as opposed to the abduction deficit; this helps it to distinguish from sixth cranial nerve palsy. The esotropia is lesser though there is an abduction deficit because of the presence of varying amounts of associated adduction deficits. This can be demonstrated by a remote near point of convergence. While measuring the deviation, the head has to be held in primary position, and then, the cover test has to be performed to elicit the correct deviation. The deviation should also be measured in lateral and vertical gazes due to varying amounts of esotropia and exotropia in the lateral gazes. The deviations should also be measured in up- and down-gaze to look for pattern strabismus. V pattern strabismus is more common than A pattern. Whenever there is an A pattern, bilateral DRS has to be suspected. Sometimes, an X pattern may be present due to both upshoot and downshoot in the patient. Upshoots [Figure 2] and downshoots are movements that occur due to mechanical or innervational anomalies. Kekunnaya et al. have reported an incidence of 43% of overshoots of which type I and type III DRS were more commonly seen to be associated unlike Mohan et al. who found it greater in type III DRS. Globe retraction is also an other noted feature in DRS. Kekunnaya et al. have published a novel clinical grading system for globe retraction and overshoots.

Grading for globe retraction
with the involved eye in maximum adduction, a scale is used at the center of the palpebral fissure to measure the height and compare it with the fellow eye in abduction.

- Grade 0: No narrowing
- Grade 1: <25%
- Grade 2: 25%–<50%
- Grade 3: 50%–<75%
- Grade 4: ≥75%.

Grading for overshoots
with the involved eye in adduction, a straight line parallel to the intermedial canthal line is drawn from the pupillary center of the fellow eye.

- Grade 0: Line bisects the pupil of the involved eye
- Grade 1: Line lies between the pupillary center and the pupillary margin
- Grade 2: Line lies between the pupillary margin and the limbus
- Grade 3: Line lies at the limbus or over the sclera
- Grade 4: Cornea disappears below the lid (pumpkin seed sign).
Head posture is seen in unilateral cases of DRS in both the esotropic and exotropic types; this can be measured with a goniometer. Patient adopts this to maintain binocular single vision and to make up for the duction deficit. Kekunnaya et al. were the first to report lower incidence of head turn in type II DRS as compared to type I and type III.\[17\]

Bilateral DRS (Figure 3) is less frequent as compared to unilateral forms. Zanin et al. have classified it into three types based on the functional prognosis.\[20\]
- Bilateral DRS with fusion-type I bilateral DRS with small angle of deviation or orthotropia and minimal head posture
- Bilateral DRS without fusion-prominent eso or exo deviation
- Bilateral DRS with an alphabet pattern.

Bilateral DRS is associated with lower visual acuity due to ametropia, anisometropia, and vertical strabismus.\[21\]

**Sensory status**

Many cases of DRS have found to have good stereopsis due to fusion with appropriate head turn.\[22\] These patients rarely complain of diplopia as they ignore the second image rather than suppressing it.

**Variants of Duane retraction syndrome**

1. Vertical retraction syndrome: This has been reported in Chinese literature. There is limitation of elevation or depression (variable) associated with globe retraction and palpebral fissure narrowing. The affected eye may be ortho-, hypo-, or hyper-tropic in primary position along with horizontal retraction. This may be due to fibrosis of vertical rectus muscle or innervational abnormality or tethering effect of horizontal rectus\[23\]
2. Congenital adduction deficit with synergistic divergence: This is another variant of DRS presenting unilaterally with adduction deficit and simultaneous abduction of the affected eye on attempted adduction.\[24\] Patient presents with a large exotropia and head turn to the uninvolved side. This is sometimes considered to be a variant of Huber type II DRS.
3. DRS can be associated with congenital anomalies both ocular and nonocular in syndromes such as Goldenhar syndrome (ptosis/epibulbar dermoid/coloboma/preauricular tags/deafness), Klippel–Feil syndrome (microcornea/optic nerve hypoplasia/Marcus-Gunn Jaw wink), Holt-Oram syndrome (Horner’s syndrome/keratoconus/morning glory disc/cardiac anomalies), Wildervanck syndrome (nystagmus/coloboma/myelinated nerve fibers/limb deformities), oculocutaneous albinism (Brown syndrome, renal dysplasia, vesicoureteral reflux), and fetal alcohol syndrome (microcephaly, persistent fetal vasculature).
4. Acquired retraction syndrome: Duane et al.\[25\] have described this entity and it is called as a pseudo-Duane syndrome. There is limitation of abduction along with globe retraction in abduction. This occurs with trauma, systemic illness, orbital tumors, and presence of diplopia and differentiates it from true DRS.

**Management of Duane retraction syndrome**

Surgical plan is based on factors such as:
1. Primary position deviation
2. Degree of abnormal head posture
3. Severity of globe retraction and overshoot
4. Degree of limitation of duction
5. Forced duction test (FDT).

DRS classification based on the primary position deviation eso-, exo-, or ortho-tropia is very useful and relevant before planning surgery.

**Esotropic Duane retraction syndrome**

Co-existing accommodative component should be first ruled out before considering surgery to avoid consecutive exotropia. Glasses should be prescribed wherever necessary. A tight MR muscle will elicit a positive FDT. Intraoperatively, one needs to look for anomalous muscle bands if there is very tight FDT. Unilateral MR recession can be performed and this corrects up to 20 prism Diopters (PD) of esotropia.\[26,27\] MR recession >5 mm should be avoided as it can induce exotropia in the contralateral gaze along with adduction deficit. MR recession corrects the primary position esotropia as well as improvement in abduction if there was some lateral movement beyond midline before surgery. Bilateral MR recessions may be required in some situations. However, surgeons should be cautious while operating the contralateral MR in patients with severe co-contraction as this may lead to co-contraction of...
the anomalous LR muscle during attempted rotation toward the affected gaze. However, bilateral MR surgery may be required if esotropia >20 PD; single MR recession of <6 mm is insufficient. If there is severe globe retraction is present, MR along with LR recession is done which may worsen the esotropia, and therefore, recessing the contralateral MR may help correcting the total esotropia. Bilateral MR recession may also prevent contracture of the MR in the affected eye by creating fixation duress. After surgery, the MR of the fixing eye receives increased innervation to fixate and this reduces the innervation to the antagonist LR of the same eye and therefore reduces the innervational tone of the contralateral MR in the affected eye, lowering the risk of contracture. MR recession followed by vertical rectus transposition as a second stage procedure is performed in the same eye if necessary. This is known to improve the abduction by 15°–45°;[28] there is also no marked vertical deviation after Superior rectus transposition (SRT) with or without augmentation sutures to the LR. MR recession combined with SRT can be done as a primary procedure in the same sitting. Combining both surgeries has shown it to be more effective than unilateral or bilateral MR recession in terms of improving abduction. Figure 4 shows preoperative and postoperative pictures of a patient with DRS type I esotropia right eye that has undergone MR recession with SRT to LR. Figure 5 shows recessed MR muscle on an adjustable noose and superior rectus transposed to LR. A combined procedure also allows to perform a smaller MR recession for the improvement of deviation in primary position and compensatory head posture.[29] In certain cases of esotropia >25 PD with minimal limitation of abduction, MR recession can be combined with LR resection when there is no severe globe retraction or up/down-shoots. In patients with residual esotropia after MR recession and SRT, another alternative is to add inferior rectus transposition to LR muscle. However, there is a risk of anterior segment ischemia with this procedure.

**Exotropic Duane retraction syndrome**

Figure 6 shows patient with DRS Type III exotropia with upshoot preoperative picture and postoperative picture LR recession with Y split.

Patients with exotropic DRS usually will have type III or type II DRS. Cases with unilateral exotropic DRS can be managed with unilateral LR recession if the deviation within 20 PD increasing the surgical dosage as compared to standard
surgical dose. If larger deviation is present, bilateral LR recession with larger recession is done on the contralateral eye as this may prevent worsening of abduction limitation in the DRS eye. Patients with type II exotropic DRS may have significant globe retraction. Supramaximal LR recession and LR periosteal fixation can also be done with or without vertical rectus transposition. The paradoxical innervation of the LR during adduction will be improved by recession or periosteal fixation while the abduction can be improved by the vertical rectus transposition. Sharma et al. in their series have concluded good results with this procedure as it corrects the exo deviation and anomalous head posture. In bilateral exotropic Duanes, asymmetrical bilateral LR recession with or without Y splitting is found to be effective. Synergistic divergence which is an extreme form of exotropic Duanes has no satisfactory surgical procedure.

**Globe retraction**

For significant globe retraction, both the co-contracting muscles need to be addressed. MR recession ranging from 5 to 6.5 mm and LR recession from 7 to 9 mm will be needed. If there is a primary position esotropia, MR should be recessed more than the LR. If not, the LR can be recessed 1 mm more than the MR muscle. Adults need larger recession because of long-standing globe retraction causing orbital tissue changes.

**Overshoots**

Y splitting of the LR along with the recession is used to treat the overshoots caused by the mechanical leash effect. In Y split, one half of the muscle balances the other. When the eye elevates in adduction, the lower arm contracts and prevents the globe from slipping up. The converse happens in depression. Inferior oblique weakening is done if overaction is documented.

**Conclusion**

DRS is a challenge to an ophthalmologist, it can have a complex set of ocular presentations along with systemic abnormalities. When it is a syndrome DRS, complete systemic evaluation should be done such as audiometry to rule out unilateral or bilateral sensorineural hearing loss; X-ray spine for skeletal abnormalities and renal function tests are mandatory. Since CCDD is associated with genetic mutations, a genetic analysis would also be useful. A neuroimaging such as magnetic resonance imaging is also valuable though we expect to see abnormal LR muscle most commonly; superior oblique hypoplasia can also be noted. All these tests will help in understanding the clinical entity as well as provide better care to the patients and counseling to the family.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Heuck G. About innate inherited motility defects in the eyes. Klin Monatsbl Augenheilk Bl 1879;17:1233.
2. Stilling J, Bergmann JF, editors. Investigations about the emergence of myopia. Germany; Wiesbaden; 1887. p. 13.
3. Turk S. Comments to a case of retraction of the eye. Cbl Prax Augenheilk Bl 1899;23:12.
4. Miyake N, Chilton J, Paatha M, Cheng L, Andrews C, et al. Human CHN1 mutations hyperactivate alpha2-chimaerin and cause Duane’s retraction syndrome. Science 2008;321:839-43.
5. Al-Baradie R, Yamada K, St. Hilaire C, Chan WM, Andrews C, McIntosh N, et al. 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 2002;71:1195-9.
6. Kohlhase J, Heinrich M, Schubert L, Liebers M, Kispert A, Laccone F, et al. Okihiro syndrome is caused by SALL4 mutations. Hum Mol Genet 2002;11:2979-87.
7. Tischfield MA, Bosley TM, Salih MA, Alorainy IA, Sener EC, Nester MJ, et al. Homozygous HOXA1 mutations disrupt human brainstem, inner ear, cardiovascular and cognitive development. Nat Genet 2005;37:1035-7.
8. Huber A. Electrophysiology of the retraction syndromes. Br J Ophthalmol 1974;58:293-300.
9. Ahluwalia BK, Gupta NC, Goel SR, Khurana AK. Study of Duane’s retraction syndrome. Acta Ophthalmol (Copenh) 1988;66:728-30.
10. Hering E. The doctrine of binocular seeing. Leipzig, Germany; WilhelmEnglemann; 1868.
11. Kirkham TH. Anisometropia and amblyopia in Duane’s syndrome. Am J Ophthalmol 1970;69:774-7.
12. O’Malley ER, Helveston EM, Ellis FD. Duane’s retraction syndrome – Plus. J Pediatr Ophthalmol Strabismus 1982;19:161-5.
13. Hugonnier R, Clayette-Hugonnier S. Strabismus, heterophoria, ocular motor paralysis. In: Veronnean-Troutman S, editor. Clinical Ocular Muscle Imbalance. St. Louis, MO: C.V. Mosby; 1969. p. 322-7.
14. Isenberg S, Urist MJ. Clinical observations in 101 consecutive patients with Duane’s retraction syndrome. Am J Ophthalmol 1977;84:419-25.
15. Ro A, Gummesson B, Orton RB, Cadera W. Duane’s retraction syndrome: Southwestern Ontario experience. Can J Ophthalmol 1989;24:200-3.
16. Chung M, Stout JT, Borchert MS. Clinical diversity of hereditary Duane’s retraction syndrome. Ophthalmology 2000;107:500-3.
17. Kekunnaya R, Gupta A, Sachdeva V, Krishnaiah S, Venkateshwar Rao B, Vashist U, et al. Duane retraction syndrome: Series of 441 cases. J Pediatr Ophthalmol Strabismus 2012;49:164-9.
18. Mohan K, Sharma A, Pandav SS. Differences in epidemiological and clinical characteristics between various types of Duane retraction syndrome in 331 patients. J AAPOS 2008;12:576-80.
19. Kekunnaya R, Moharana R, Tibrewal S, Chhablani PP, Sachdeva V. A simple and novel grading method for retraction and overshoot in Duane retraction syndrome. Br J Ophthalmol 2016;100:1451-4.
20. Zanin E, Gambarelli N, Denis D. Distinctive clinical features of bilateral Duane retraction syndrome. J AAPOS 2010;14:293-7.
21. Jampolsky A. Duane syndrome. In: Rosenbaum AC, Santiago AP, editors. CSM, Principles and Surgical Techniques. Philadelphia, PA: W.B. Saunders; 1999. p. 325-46.
22. DeRespinis P, Caputo A, Wagner R, Guo S. Duane’s retraction syndrome. Surv Ophthalmol 1993;38:257-88.
23. Wildervanck LS. A case of Klippel – Feil disease combined with abducens paralysis, retraction bulb and deafness. Ned T Geneesk 1952;96:2752-5.
24. Wilcox LM Jr, Gittinger JW Jr., Breinin GM. Congenital adduction palsy and synergistic divergence. Am J Ophthalmol 1981;91:1-7.
25. Duane TD, Schatz NJ, Caputo AR. Pseudo-Duane’s retraction syndrome. Trans Am Ophthalmol Soc 1976;74:122-32.
26. Kraft SP. Surgery for Duane’s syndrome. Am Orthop J 1993;43:18-26.
27. Kaban TJ, Smith K, Day C. Single medial rectus recession in unilateral Duane syndrome type I. Am Orthop J 1995;45:108-14.
28. Johnston SC, Crouch ER Jr., Crouch ER. An innovative approach to transposition surgery is effective in treatment of Duane’s syndrome with esotropia. Invest Ophthalmol Vis Sci 2006;47:2475.
29. Yang S, MacKinnon S, Dagi LR, Hunter DG. Superior rectus transposition vs. medial rectus recession for treatment of esotropic Duane syndrome. JAMA Ophthalmol 2014;132:669-75.
30. Holmes JM, Hatt SR, Leske DA. Intraoperative monitoring of torsion to prevent vertical deviations during augmented vertical rectus transposition surgery. J AAPOS 2012;16:136-40.
31. Velez FG, Thacker N, Britt MT, Alcorn D, Foster RS, Rosenbaum AL, et al. Rectus muscle orbital wall fixation: A reversible profound weakening procedure. J AAPOS 2004;8:473-80.
32. Sharma P, Tomer R, Menon V, Saxena R, Sharma A. Evaluation of periostial fixation of lateral rectus and partial VRT for cases of exotropic Duane retraction syndrome. Indian J Ophthalmol 2014;62:204-8.
33. Kekunnaya R, Negalur M. Duane retraction syndrome: Causes, effects and management strategies. Clin Ophthalmol 2017;11:1917-30.
34. Shauly Y, Weissman A, Meyer E. Ocular and systemic characteristics of Duane syndrome. J Pediatr Ophthalmol Strabismus 1993;30:178-83.
35. Rogers GL, Bremer DL. Surgical treatment of the upshoot and downhill in Duane’s retraction syndrome. Ophthalmology 1984;91:1380-3.
36. Awadein A. Inferior oblique myectomy for upshoots mimicking inferior oblique overaction in Duane retraction syndrome. J AAPOS 2013;17:253-8.
37. Kirkham TH. Duane’s syndrome and familial perceptive deafness. Br J Ophthalmol 1969;53:335-9.
38. Graeber CP, Hunter DG, Engle EC. The genetic basis of incomitant strabismus: Consolidation of the current knowledge of the genetic foundations of disease. Semin Ophthalmol 2013;28:427-37.