Type IV Duane Syndrome

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ABSTRACT:

Purpose: To identify cases of synergistic divergence and suggest that this entity is a form of Duane syndrome, with additional features that would characterize this entity as a separate type.

Methods: The records of all patients with a Duane syndrome diagnosis, including standardized eye position photographs, from the E-Consultation program of Cybersight, Orbis International were analyzed.

Results: 350 Duane syndrome cases were identified. 19 (5%) of these cases had features consistent with Type IV Duane syndrome or synergistic divergence. There was a male predilection as 16 (84%) were male. 15 (79%) had palpebral fissure narrowing. 19 (100%) patients had anomalous head posture. 18 (95%) patients were exotropic. Only 9 (47%) patients with Type IV were reported to have undergone surgery.

Conclusions: Synergistic divergence is a rare entity with features similar to those of Duane syndrome. We suggest that this entity be classified as Type IV Duane syndrome as it has unique findings and an innervation pattern different from the other three types.

INTRODUCTION

Duane syndrome encompasses a spectrum of strabismus entities that have as common features: mis-innervation and co-contraction of extraocular muscles in addition to enophthalmos with palpebral fissure narrowing.[1-3] Other findings often include an abnormal compensatory head posture and vertical upshoots or downshoots. Historically, Duane syndrome has been classified into three types. Type I includes patients with poor eye abduction and esotropia. Type II includes patients with poor eye adduction and exotropia. Type III includes patients with both poor eye adduction and abduction. Duane syndrome has been considered a continuum of diseases with variability in mis-innervation and resultant clinical features.[1] Initially described in the 1800's by multiple authors, Duane was the first to obtain a relatively large case series of patients and described abnormal motility, head position, globe retraction, and pseudoptosis.[4] With electrophysiology testing, Huber demonstrated paradoxical mis-innervation of rectus muscles and further classified Duane syndrome into the three subtypes classically observed.[5]

Simultaneous abduction or synergistic divergence has previously been reported in the literature.[1-3,6,7] These case reports demonstrate typical findings of a Duane syndrome variant as well as an extreme form of mis-innervation. Patients typically have exotropia in primary gaze with synergistic divergence of the affected eye despite expected adduction (Figure 1).

Due to advancements in technology and communication our ability to understand diseases is growing. The Internet allows physicians from all over the world to communicate and consult on challenging cases while still maintaining patient confidentiality. Cybersight® is a telehealth and education program of Orbis International. Through Cybersight physicians are able to consult expert eye care professionals for help regarding challenging cases. This collaboration helps provide education and care to patients all over the world.

METHODS

Utilizing the Cybersight database, 350 cases of Duane syndrome were presented between the years of 2003-2012 for electronic consultation. A retrospective review of patient demographics including age and gender, ophthalmologic history, medical history, patient/family description of eye problem was obtained from the database. Exam results including visual acuity, head position, refraction, description of ductions and versions and laterality of abnormality were also noted.

The cybersight website has an extensive template for entering and uploading patient information. This standardization simplifies the consultation process. Cybersight receives cases from all over the world. Lastly, an assigned mentor via the Cybersight consultation service analyzed patient photographs of eye alignment of

the 9 diagnostic positions of gaze including right and left head tilt. Multiple mentors volunteer as consultants and were involved in these electronic consultations.

This study and all of the data collection performed conform to all local laws and were compliant with the principles of the Declaration of Helsinki. Indiana University School of Medicine ethics committee approved this study.

RESULTS

350 cases of Duane syndrome were identified. 179 (51.1%) patients with Type I Duane syndrome were identified. 81 (23.1%) patients with Type II Duane syndrome were identified. 71 (20.3%) patients with Type III Duane syndrome were identified. Patients with features of synergistic divergence were observed in 19 (5%) of patients with Duane syndrome. 13 out of 19 of these cases were initially labeled as type II Duane syndrome or Duane variant. However, upon careful review of images, the telemedicine consultant identified synergistic divergence.

More males (16) than females (3) were identified with synergistic divergence. Laterality was equal. This entity was observed early in life, with parents reporting an average onset of 0.5 (0-4) years (AE-1 comm.). The average age of presentation for evaluation was 11.5 (1-26) years. Most patients were exotropic and showed palpebral fissure narrowing on attempted adduction of the involved eye (AE02 comm.). An anomalous head posture was identified in all patients with synergistic

divergence (Table 1). Infraduction deficit was observed in 6 patients. One patient had a supraduction deficit. Dramatic upshoots were only observed in two patients.

Neuroimaging had been performed on 4 of the 19 patients, and only one of these patients had an abnormality picked up by the radiologist. The abnormality was described as “an asymmetry of the right half of the midbrain”. One patient with Goldenhar syndrome and one patient with cerebral palsy also had synergistic divergence. Nystagmus was observed in one patient. Anisometropia was observed in three patients (Table 2).

Eye muscle surgery was performed on nine patients. On forced duction testing, patients were reported to have a tight lateral rectus (AE-4 comm.), Bilateral lateral rectus recession was performed on three patients. A single lateral rectus recession was performed on five patients. One patient underwent vertical muscle transposition with single lateral rectus recession (Table 3). Post-surgical data was only available for 7 patients. Of these 7 patients, 6 had good alignment in primary position with decreased face turn after one surgery. The one patient who had a significant amount of residual exotropia and face turn had undergone ipsilateral lateral rectus recession(AE-3 comm.). All patients had persisting synergistic divergence after surgery.

DISCUSSION

Type IV Duane syndrome has been called simultaneous abduction, synergistic divergence, the “splits”, and perversion of the extraocular muscles.[1,3,6,7] Type IV Duane syndrome has previously been described in the literature, but only case reports have been reported.

We characterize Type IV Duane syndrome as exotropia in primary gaze, face turn opposite the involved eye, essentially full abduction of the involved eye, absent adduction of involved eye with simultaneous abduction in gaze opposite the involved eye and narrowing of the palpebral fissure. Figure 2 shows the potential innervation differences to the medial and lateral rectus that can result in the pathology seen with Duane syndrome.[3] Wilcox et al performed electromyographical testing on a single patient with synergistic divergence. His results showed evidence of anomalous innervation that was on the continuum of Duane syndrome.[3] Similar findings have been reported in over corrected patients who have undergone ipsilateral medial rectus recession for Type I Duane syndrome.[8] None of our patients had a history of previous medial rectus surgery.

In the case of simultaneous abduction the oculomotor nerve sends nerve fibers to the lateral rectus and the signal causes the eye to abduct and co-contract when it should simply adduct. Several questions remain unanswered including: 1) Does the oculomotor “dividing” weaken the medial rectus? 2) Does this contribute to the wide range of expressions? 3) Does the relative amount of abducens innervation from none to robust influence the tendency toward XT (resistance to adduction)?

The surgical technique most suggested for this condition was weakening of the ipsilateral lateral rectus muscle. In our case series multiple patients underwent bilateral lateral rectus recession. One might argue that weakening the contralateral lateral rectus muscle could worsen the simultaneous abduction due to Hering's law. However, none of our patients, for whom we had postoperative data, had worse synergistic divergence following surgery. All had improved alignment and face turn despite persisting synergistic divergence. This is likely because patients had a large recession of the lateral rectus of the involved eye, which would cripple the muscle's action.

Some have suggested transposition procedures for these patients. Many of the patients were found to have a tight lateral rectus and weak medial rectus, so transposition of vertical recti to the medial rectus would not likely help against a restricted or tight lateral rectus. Weakening or crippling the tight lateral rectus is key in these patients.

Review of electronic or e-consultation cases provides a unique method to evaluate a strabismus population. E-consultation provides the advantage of collecting a large number of patients to retrospectively assess cases provided by expert consultants. Cybersight allows for collaboration between a mentor ophthalmologist and a partner ophthalmologist from around the world. This helps ophthalmologists in underserved areas of the world to gain the confidence they need to provide expert

care to patients. This collaboration leads to gained knowledge for both the requesting ophthalmologist and the mentor.

Our understanding of the pathophysiology of Duane retraction syndrome comes much from the electromyographical studies of the last century. Huber classified Duane retraction syndrome into different types as they corresponded to different innervation patterns seen on electromyography.[5] Many clinicians have moved away from Huber's classification and have simplified Duane syndrome patients to either esotropic or exotropic Duane syndrome. We would argue, that although this simplified approach to Duane syndrome might seem appealing; it does not help us better understand the pathophysiology of this complex disease. Understanding that each Duane syndrome type has unique innervation anomalies aids in the management of each patient.

Multiple studies have looked at the epidemiology of Duane retraction syndrome. The typical incidence of Type I reported among these papers is 73 to 92%. Type II and Type III have similar incidences and range from 4 to 13% of cases of Duane retraction syndrome.[9-12] Our study population had less type I and more type II and type III patients. This is likely a selection bias. Because our patient database was composed of patients needing expert consultation, we were more likely to see less routine Duane syndrome patients. Although bilateral synergistic divergence has been reported in the literature, only unilateral synergistic divergence was observed in our patients.[13]

There are other limitations to our study. Although our collection of patients with synergistic divergence is the largest to date, an even larger collection of patients would be useful to study. Additional information including forced duction results and electromyography would be useful in further studying and characterizing this entity. Although a few patients had imaging, more imaging data would be useful to characterize the extraocular muscles. Post-operative data was available for some of the patients; however, more post-operative information would have been useful. Genetic testing for Duane syndrome has been performed and genetic mutations have included Duane syndrome into the classification of Congential cranial dysinnervation disorder (CCDD). CCDD also includes congenital fibrosis of the extraocular muscles, congenital ptosis, and Möbius syndrome.[14] Further work on the genetics of Duane syndrome and its individual types may help us understand the complexity of this condition.

While many questions remain, there should be better recognition of this fourth class of Duane syndrome that has been noted for more than 50 years. Using Cybersight we were able to collect the largest case series of patients with synergistic divergence to date. We show that these patients have features consistent with a Duane type syndrome. However, these patients also demonstrate findings that would indicate a unique innervation pattern. We characterize these patients as Type IV Duane syndrome.

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Table Legends

Table 1 – Characteristics of Type IV Duane syndrome patients.

Table 2 – Associated neurologic, systemic, or other ocular findings observed in patients with Type IV Duane syndrome.

Table 3 – Surgical interventions performed on patients with Type IV Duane syndrome.

Figure Legends

Figure 1 – External photograph of patient with type IV Duane syndrome

Figure 2 – Right eye illustration of potential innervation patterns in different types of Duane syndrome. VI indicates fibers of the sixth cranial nerve. III indicates fibers of the third cranial nerve. Dashed lines indicate hypoplastic or absent nerve fibers. Thin lines indicate relative decreased innervation.