· Case report ·

Aberrant innervations in congenital cranial dysinnervation disorders: case reports

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Abstract

• We describe two cases of congenital cranial dysinnervation disorders (CCDD) who were seen at our centre. The first patient was a 7-year-old Chinese girl with no medical illness, who was noted by her parents to have a habit of tilting her head to one side and "lazy eyes" since she was a toddler. Best-corrected visual acuity (BCVA) in both eyes were 6/6 on Snellen chart and her head was tilted to the right. There was limitation of abduction in both eyes on horizontal gaze. Enophthalmos was seen associated with down shooting on attempted adduction. The second case was a 10-year-old Malay boy with no medical illness, who was noted by his parents to have "poor eye movements" since birth. BCVA in both eyes were 6/6 on Snellen chart with a left face turn and bilateral ptosis. Eye movements in all gazes were restricted and force duction test was positive. Both cases were diagnosed as congenital fibrosis of extraocular muscle (CFEOM) initially, but the diagnosis of the first case was later revised as bilateral Duane syndrome. Although both Duane syndrome and CFEOM are included under CCDD, both entities have distinct pathology. The presentation of CCDD is extremely variable. Nonetheless, the treatment is often limited and surgical outcome is often unpredictable. Hence, much research is still needed to be carried out for more in depth understanding of CCDD, so as to improve the management and outcome of the disease.

• KEYWORDS: congenital cranial dysinnervation disorders; aberrant innervation

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INTRODUCTION

Congenital cranial dysinnervation disorder (CCDD) is a term coined to address a group of non progressive neurodevelopmental disease involving the brainstem and the cranial nerves. Patients can have a myriad of presentation, with abnormalities involving the eyelid, facial and extraocular motility. The presentation and severity of CCDD varies from one individual to another and at times the diagnosis could be confusing to ophthalmologist. Here, we report two cases of CCDD that were encountered at our centre.

CASE REPORT

Case 1 A 7-year-old Chinese girl with no medical illness was noted by her parents to have "lazy eyes" and a habit of tilting head to one side since she was a toddler. Antenatal, intrapartum and postnatal history were unremarkable. There was no history of trauma. No one in the family has similar problem and the child has been doing very well academically in school. On examination, vision was 6/6 on Snellen chart in both eyes and her head was tilted to the right. There was limitation of abduction bilaterally during horizontal gaze. Enophthalmos was seen associated with down shoot on attempted adduction (Figure 1). Fundus examination was normal bilaterally.

Case 2 A 10-year-old Malay boy with no medical illness was noted by his parents to have "poor eye movement" since birth. Antenatal, intrapartum and postnatal history were unremarkable. There was no history of trauma. Family history was unremarkable with no one in the family having similar problems. On examination, vision was 6/6 in both eyes. There was a left face turn and bilateral ptosis (Figure 2). Eye movements in all gazes were restricted and force duction test was positive.

DISCUSSION

In CCDD, mutated genes are said to be responsible leading to the abnormal development of the brainstem and cranial nerves. So far, neurogenetics studies had identified the defective genes for the following diseases: Congenital fibrosis of extraocular muscle (CFEOM), isolated and syndromic form of Duane syndrome and horizontal gaze palsy with progressive scoliosis (HGPPS). Others which are also understood by clinical features and theoretic considerations as CCDD include Möbius syndrome, Marcus Gunn jaw winking phenomenon, some form of congenital ptosis and others[1,2].

Figure 1 Patient with right head tilt. Her eyes were almost straight in primary position (E), with retraction of globe on attempted adduction in both eyes (D,F), limitation of abduction (A,C,D,F), and downshoot on attempted adduction in both eyes(G, I). She has bilateral Duane syndrome (type 1).

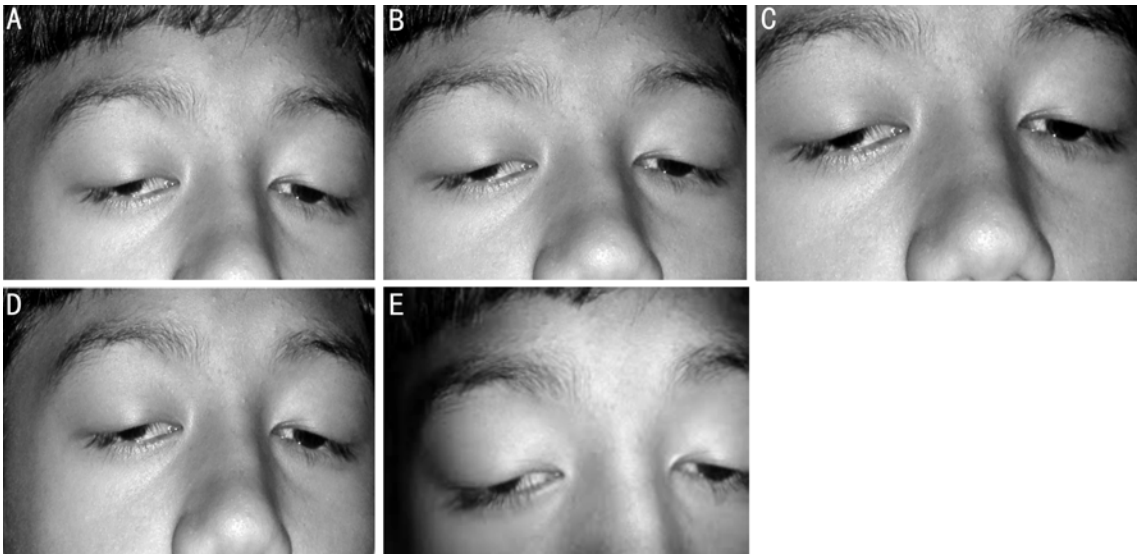

Figure 2 This patient has bilateral ptosis and at primary position, the eyes are fixed below horizontal by about 10 degree (A). Both eyes remained at the same position on all gazes due to restrictive ophthalmoplegia involving all the muscles (A-E). He has bilateral congenital fibrosis of extraocular muscle (CFEOM).

Both cases were diagnosed to have CFEOM initially. However, the diagnosis of case 1 was later revised as bilateral Duane syndrome after careful examination, and was further supported by negative force duction test. Both children did not have any positive family history and systemically have been well with no other medical illness. In case 1, on horizontal gaze, the child has retraction of globe on attempted adduction, and limitation of abduction in both eyes. Here, leash phenomenon could be observed clearly, whereby there was down shooting of the eyes on attempted adduction (Figure 1 G & I).

The basic understanding of Duane syndrome is that there is failure of innervations of the lateral rectus by the sixth nerve, with anomalous innervations of the lateral rectus by fibres from third nerve. Mutated genes reported to be associated with Duane syndrome are SALL4, HOXA1 and CHN1[1]. Some are associated with systemic defects including Goldenhar syndrome, Wildervanck syndrome, Okihiro syndrome and others, which was absent in our patient. Thalidomide exposure is also said to induce Duane syndrome[2,3]. Huber classification defines Duane syndrome into three groups: type 1 with poor adduction and exotropia; type 2 with poor

abduction, frequently with primary position esotropia; and type 3 with poor abduction and adduction, with or without primary position deviation. About 15% of patients will be affected bilaterally although frequently involvement of one eye may be very subtle[3]. Our patient has bilateral Duane syndrome (type 3). She has good vision and eyes are cosmetically acceptable in primary position, therefore management was conservative for her at this point in time.

The child in case 2 had bilateral ptosis with gross motility restriction and positive force duction test, which fits the description of CFEOM. In this condition, it is said that there is replacement of muscles by fibrous tissue[3,5]. They can present with a wide spectrum of presentation from isolated fibrosis of single muscle to bilateral involvement of all extra ocular muscle, as in this patient. Positive force duction test confirmed the muscles restriction. Mutations in the gene KIF21A and ARIX are found to be relevant, and it is said that the fibrous changes are secondary to the primary defective innervations in the muscles[1]. Three subgroups of CFEOM have been described according to clinical traits, they are CFEOM1, and CFEOM2 and CFEOM3[4]. Surgical treatment in this type of patient is typically difficult and requires release of the restricted muscles. The aim of surgery is to align the eyes in primary position, but the outcome is often unpredictable. Our patient has good vision in primary gaze, and his parents are keen for conservative management for now.

CONCLUSION

The presentation of CCDD is extremely variable, which could be confusing to ophthalmologist at times. As in above cases, Duane syndrome can sometimes mimic presentation of CFEOM, however in the former, the force duction test should be negative. Nonetheless, the treatment for CCDD is often limited and surgical outcome is often unpredictable. Hence, much research is still needed to be carried out for more in depth understanding of CCDD, so to improve the management and outcome of the disease.

REFERENCES

1 Antje N, Julia F. Congenital Cranial Dysinnervation Disorders: Facts and Perspectives to Understand Ocular Motility Disorders, in: Pediatric Ophthalmology, Neuro-Ophthalmology, Genetics. Springer Berlin Heidelberg 2010:77-94

2 Traboulsi EI. Congenital cranial dysinnervation disorders and more. *J AAPOS* 2007; 11(3):215-217

3 John WS, Aazy AA, Arlene VD. Special forms of strabismus. In: Pediatric Ophthalmology and Strabismus. American Academy of Ophthalmology 2007:152-153

4 Heidary G, Engle EC, Hunter DG. Congenital fibrosis of the extraocular muscles. *Semin Ophthalmol* 2008;23(1):3-8

5 Howard ME. Other vertical strabismus forms, in: Yanoff & Duker Ophthalmology. 3rd ed. Mosby Elsvier 2009:1360

先天性颅神经异常支配综合征 2 例

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摘要

我们报告两例在我们医疗中心治疗的先天性颅神经异常支配综合征(congenital cranial dysinnervation disorders, CCDD)。其中 1 例是 7 岁的中国女孩,无内科疾病,其父母注意到从婴孩时起患者习惯性向一侧倾斜头部,并伴有"眼懒惰"。双眼视力为斯内伦视力表 6/6,头向右倾斜。水平或垂直注视时双眼外展受限,试图内转向下看时伴眼球内陷。另 1 例是 10 岁的马来西亚男孩,无内科疾病,其父母注意到自出生该男孩就"眼球运动差"。双眼视力为 6/6,脸向左转并且双眼上睑下垂。在所有注视方位上眼球运动均受限,强制转向试验阳性。两个病例初步诊断均为先天性眼外肌纤维化(congenital fibrosis of extraocular muscle, CFEOM),后来第一个病例的诊断修订为双侧 Duane 综合征。虽然 Duane 综合征和 CFEOM 都包括在 CCDD 内,但两种疾病病理不同。CCDD 的表现非常多变,然而,治疗往往是有限的,且手术结果不可预测。因此,仍然需要进行大量研究以更深入了解 CCDD,改善其治疗和结局。

关键词:先天性颅神经异常支配综合征;异常神经支配