Monocular Nystagmus in a Case of Septo-Optic Dysplasia

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ABSTRACT

A case of septo-optic dysplasia in a 2-year old boy is presented. The variable symptoms and characteristics of the disorder are described in relation to its aetiology, with particular emphasis on the unusual occurrence of monocular nystagmus.

Keywords: septo-optic dysplasia, monocular nystagmus, de Morsier syndrome

INTRODUCTION

Septo-optic dysplasia (SOD), also known as de Morsier syndrome, is a rare congenital disorder loosely characterised by a triad of optic nerve hypoplasia (ONH), midline abnormalities of the brain (including agenesis of the septum pellucidum, hypoplasia of the chiasm, infundibulum or corpus callosum) and hypothalamic-pituitary dysfunction.[1-6] A diagnosis of SOD features two or more of these characteristics. The incidence of SOD appears to be in the order of less then 10 per 100,000 of the population of which around one-third present with a complete manifestation of the triad.[7,8]

Symptomatically SOD is highly variable and may encompass a large array of manifestations.[6] There can be varying degrees of endocrinological defects such as pituitary dwarfism or growth hormone deficiency, hypothyroidism, panhypothyroidism, diabetes insipidus or hyperprolactinaemia. This may be in isolation or in addition to neurological defects that can result in developmental delays and intellectual disabilities.[1,3,5] Visual disturbances are more commonly found in SOD cases and are often the primary reason for clinical presentation.[9] Some of these disturbances may include depression in visual acuity, bilateral or unilateral nystagmus, strabismus or afferent pupillary defects.[10]

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CASE REPORT

Master J was referred to the ophthalmologist after his doctor discovered an abnormal light reflex at two months of age. On his initial appointment a right exotropia was suspected but when reviewed five months later, examination under cycloplegia revealed an intermittent right pendular horizontal nystagmus. The amplitude and frequency of the nystagmus were not noted. The unusual presentation of congenital monocular nystagmus led to spasmus nutans suspected as a possible diagnosis, however to rule out any underlying intracranial pathology, magnetic resonance imaging (MRI) and an examination under anaesthesia (EUA) were performed. The EUA showed healthy and normal discs and retinae and no venous pulsation, however, the MRI revealed an absent septum pellucidum, hypoplasia of the optic nerves and optic chiasm, thinning of cerebral white matter and box-like formation of the lateral ventricles. It is proposed that the optic nerve hypoplasia (ONH) was likely to have been missed during the EUA due to the symmetrical and bilateral nature of the condition. Given both the presenting monocular nystagmus and MRI findings, the patient was diagnosed with septo-optic dysplasia.

Despite a delay in Master J's visual development, whereby fixing and following was not achieved until 4 months of age, regular appointments with a paediatrician showed that he was reaching developmental milestones and had a normal linear growth. By 14 months of age, Master J was demonstrating a persistent left-sided head tilt that appeared to a greater extent since he had started walking independently. The head tilt was noted to place his eyes in a null position that reduced or settled his nystagmus. At 19 months he also began to show an intermittent right esotropia as well as

the right intermittent pendular nystagmus. On examination by retinoscopy no significant refractive error was found. At two years of age his nystagmus was only occasional and an accurate visual acuity was unattainable. Because of the potential for amblyopia to develop, particularly in the right eye, management involved regular appointments for vision assessments and occlusion of the left eye with close monitoring. Although the use of dilation as a means of occlusion can reduce the impact of nystagmus,[11] patching 4 hours a day was the preferred management in this case. Subsequent visits have shown vision of 3/60 in the right eye and 3/9 in the left. Unfortunately many appointments were missed and a more accurate vision has been unattainable. In addition adherence to the occlusion program has been difficult and the level of amblyopia, particularly in the right eye, and the effect of treatment remains relatively unknown.

Despite the initial possible diagnosis of spasmus nutans, a comprehensive investigation has shown that Master J appears to have septo-optic dysplasia associated with right intermittent monocular nystagmus, a left compensatory head tilt, right intermittent esotropia and amblyopia.

DISCUSSION

The malformation of the optic disc, nerve and chiasm, absence of the septum pellucidum and regular hypothalamic and pituitary disturbances cause an array of symptoms.[12] Where some patients may have impaired visual acuity or legal blindness, often causing developmental delays, additional to intellectual disabilities and linear growth disturbances, milder cases, like Master J, may only have mild to moderate vision impairment and lack any functional defects of the central nervous system or endocrine system.[5,10]

As a result of defects to the midline structures, clinical manifestations of SOD are quite variable among individuals.[6,13] Damage to the endocrine system can have an extensive impact on linear growth and pubertal development due to the reduction in secretion of growth hormone (GH), thyroid-stimulating hormone or adrenocorticotropic hormone. It is suggested that the extent of the abnormalities to the septum pellucidum and hypothalamo-pituitary axis on an MRI may help predict the severity of endocrinal damage.[6] Effects on GH secretion are somewhat manageable via hormone replacement therapy if the condition is diagnosed early.[14] However, some cases with GH deficiencies do not show signs of delayed growth until after the age of 1 to 3 years.[4,15] In Master J's case, while an early diagnosis was important and showed good long-term prospects with his vision being his only ongoing concern, regular monitoring will be equally important in observing visual capacity and any growth changes.

Neurological deficits can range from global disabilities to focal defects, such as epilepsy or hemiparesis.[6] Interestingly, the septum pellucidum, a key structure in the diagnosis of SOD, is quite mysterious in relation to its function. It is a thin sheet of membrane that separates the lateral ventricles in the centre of the brain and runs from the corpus callosum down to the fornix.[16] In SOD the septum pellucidum is absent and thus there is no connection between the fornix and corpus callosum.[15] Because of its numerous connections with subcortical areas it is unclear what function the septum pellucidum serves in the brain and researchers are unsure whether the neurodevelopmental defects in SOD are a consequence of its absence or merely damaged tissue.[3]

Optic nerve hypoplasia is exhibited in 75 - 80% of SOD cases and can cause a range of ophthalmic presentations.[6] Clinically ONH shows a characteristic 'double ring sign' caused by the retina and pigment epithelium abnormally extending over the outer portion of the lamina cribrosa.[5] Decreased visual acuity seems to be the greatest risk, however manifestations such as bilateral or monocular nystagmus and esotropia can be attributed to midline damage or may be secondary to sensory disturbances.[6]

Master J's case was unusual in that his only presenting symptom was infantile monocular nystagmus. His nystagmus though not assessed in detail or with eye movement recordings, was noted as horizontal, intermittent and pendular. Literature and case studies showing nystagmus associated with SOD describe quite varied presentations.[5,17-20] Monocular nystagmus associated with SOD is thought to be quite rare, however, one other case has been reported.[1] This case, presented by Anderson,[1] discusses a 4-year old girl with monocular nystagmus and sectoral ONH associated with SOD. The child's nystagmus was characteristic of monocular nystagmus, which typically presents with a pendular waveform and has a high frequency and low amplitude.[1] It is possible that, if assessed further, Master J's nystagmus may be similar. Other cases of nystagmus, also associated with SOD, have presented pendular,[5,17] jerk[18,19] and see-saw[20] waveforms. These cases seem to follow the more varied characteristics of infantile nystagmus, which often present with pendular or jerk waveforms or a mixture of both.[21-23]

Monocular nystagmus presenting on its own, is very rare.[24] It can be associated with spasmus nutans, a benign condition that presents with asymmetric or occasionally unilateral nystagmus.[24] Occurring in the first year of life, it classically presents with a triad of nystagmus which is usually intermittent and pendular with a small amplitude and high frequency, head nodding and torticollis and typically resolves by 3 to 6 years of age.[25,26] Monocular nystagmus may also be associated with more serious intracranial pathologies such as gliomas or craniopharyngiomas of

the chiasm. For this reason, neuroimaging of patients with monocular nystagmus is very important in ruling out more sinister intracranial pathologies.[1,25,26] For Master J, neuroimaging was essential in exposing the presence of SOD.

The aetiology of SOD is largely unknown and what is understood is rudimentary in nature.[14] Several suggestions have been developed to account for its sporadic occurrence including viral infections, environmental teratogens or vascular or degenerative damage.[10] It is reported to be common in children of mothers with gestational diabetes or younger mothers and has been shown to cluster in areas of large population where teenage pregnancy rates are higher.[8]

Singh et al[2] discussed two main theories, namely, the developmental and destructive theories. The developmental theory describes a disruption in the gestational development causing a differentiation of the septum pellucidum, hypothalamus and the retinal ganglion cells. The second and more widely accepted theory suggests that there is an insult during pregnancy before the visual system is fully developed.[2] The mechanism of injury can differ between cases,[5] but the insult is thought to damage the already established hypothalamus, septum pellucidum and retinal ganglion cells.[2] On the other hand Lubinsky[27] argues that the combination of affected organs and variable times of development is not conducive to SOD being described as a developmental anomaly or dysplasia. He proposes that a vascular disruption sequence of the anterior cerebral artery makes more sense because of its proximity to the optic tract and chiasm and its particular supply to both the optic nerves and chiasm and the anterior hypothalamus and septum pellucidum.[27]

More recent research has indicated genetic involvement. Identification of mutations in key developmental genes has helped implicate a possible genetic defect underlying developmental mechanisms and may explain the cause of some cases of SOD.[6] The HESX1 gene was identified as playing a role in the pathogenesis of rare familial forms and the more common mild sporadic forms of SOD.[28] However, studies showed that mutations of the HESX1 gene turned out to be quite rare. Familial cases of SOD found in a study by McNay et al,[8] did not even involve HESX1, further suggesting that there must be other factors causing this condition. It is suggested by Campbell[10] that the aetiology of SOD is likely to be multi-factorial in nature where there is a combination of both genetic and environmental factors playing a role.

For Master J, the cause of his SOD is not known. His mother is thought to have been quite young during her pregnancy. This could potentially be related to the aetiology, however her exact age at the time of pregnancy remains unknown to the authors.

CONCLUSION

SOD is a rare condition that can cause numerous problems in endocrinological, neurological and visual development. Its aetiology is largely unknown and barely understood. Early diagnosis is very important in SOD for best treatment results and prognosis. The presentation of monocular nystagmus in isolation, as in the case of Master J, is unusual in SOD and a detailed assessment of all the possible causes was essential for his final diagnosis and ongoing treatment.

REFERENCES

1. Anderson ML. Monocular nystagmus with sectorial optic nerve hypoplasia in a patient with septo-optic dysplasia. Clin Exp Optom 2009;92(1):38-41.
2. Singh H, Singh D, Sobti MK, Singh G. Septo-optic dysplasia. Indian Pediatr 1996;33(18):698-700.
3. Williams J, Brodsky MC, Griebel M, et al. Septo-optic dysplasia: the clinical insignificance of an absent septum pellucidum. Dev Med Child Neurol 1993;35(6):490-501.
4. Manelfe C, Rochiccioli P. CT of septo-optic dysplasia. Am J Roentgen 1979;133(6):1157-1160.
5. Leloup E, Delbeke P. Septo-optic dysplasia (de Morsier syndrome). Bull Soc Belge Ophtalmol 2007;305:45-48.
6. Kelberman D, Dattani MT. Septo-optic dysplasia - novel insights into the aetiology. Horm Res 2008;69(5):257-265.
7. Patel L, McNally RJ, Harrison E, et al. Geographical distribution of optic nerve hypoplasia and septo-optic dysplasia in northwest England. J Pediatr 2006;148(1):85-88.
8. McNay DE, Turton JP, Kelberman D, et al. HESX1 Mutations are an uncommon cause of septo-optic dysplasia and hypopituitarism. J Clin Endocrinol Metab 2007;92(2):691-697.
9. Miller SP, Shevell MI, Patenaude Y, et al. Septo-optic dysplasia plus: a spectrum of malformations of cortical development. Neurology 2000;54(8):1701-1703.
10. Campbell CL. Septo-optic dysplasia: a literature review. Optometry 2003;74(7):417-426 [Abstract].
11. Calcutt C, Crook W. The treatment of amblyopia in patients with latent nystagmus. Br Orthopt J 1972;29:70-72.
12. National Institute of Neurological Disorders and Stroke. NINDS Septo-optic dysplasia information page; 2008 [updated 2008; cited 2009 7th Nov]; Available from: http://www.ninds.nih.gov/disorders/septo_optic_dysplasia/septo_optic_dysplasia.htm.
13. Amatyakul P, Panthasri T, Vutyavanich T. Septo-optic dysplasia associated with abnormal pubertal development. J Med Assoc Thai 2007;90(6):1239-1243.
14. Robinson J. Septo-optic dysplasia/de Morsier syndrome. See/Hear Archives; 2002 [updated 2002, cited 2009 7th Nov] Available from: http://www.tsbvi.edu/Outreach/seehear/fall97/septo.htm.
15. Brook CG, Sanders MD, Hoare RD. Septo-optic dysplasia. Br Med J 1972;3(5830):811-813.
16. Marieb EN, Hoehn K. Human Anatomy & Physiology. 7th Ed. San Francisco: Pearson Benjamin Cummings; 2007.
17. Pierre Filho P, Bovo LB, Marcondes AM. Septo-optic dysplasia: case report. Arq Bras Oftalmol 2004;67(4):653-655.
18. Kwak JG, Jung S, Kwon SB, et al. A patient with septo-optic dysplasia plus. J Neurol Sci 2008;264(1-2):166-167.
19. Nayak V, Bhat KR. Septo-optic dysplasia (case report). Indian J Ophthalmol 1991;39(4):186-187.

20. Davis GV, Shock JP. Septo-optic dysplasia associated with see-saw nystagmus. Arch Ophthalmol 1975;93(12):137-139.
21. Abadi RV. Mechanisms underlying nystagmus. J R Soc Med 2002;95(5):231-234.
22. Casteels I, Harris CM, Shawkat F, Taylor D. Nystagmus in infancy. Br J Ophthalmol 1992;76(7):434-437.
23. Maybodi M. Infantile-onset nystagmus. Curr Opin Ophthalmol 2003;14(5):276-285.
24. Shawkat FS, Kriss A, Thompson D, et al. Vertical or asymmetric nystagmus need not imply neurological disease. Br J Ophthalmol 2000;84(2):175-180.
25. Shawkat FS, Kriss A, Russell-Eggitt I, et al. Diagnosing children presenting with asymmetric pendular nystagmus. Dev Med Child Neurol 2001;43(9):622-627.
26. Kiblinger GD, Wallace BS, Hines M, Siatkowski RM. Spasmus nutans-like nystagmus is often associated with underlying ocular, intracranial, or systemic abnormalities. J Neuroophthalmol 2007;27(2):118-122.
27. Lubinsky MS, Hypothesis: septo-optic dysplasia is a vascular disruption sequence. Am J Med Genet 1997;69(3):235-236.
28. Thomas PQ, Dattani MT, Brickman JM, et al. Heterozygous HESX1 mutations associated with isolated congenital pituitary hypoplasia and septo-optic dysplasia. Hum Mol Genet 2001;10(1):39-45.