

Article

Ocular Findings in Canavan Disease

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ABSTRACT

Background

Canavan disease (spongiform leukodystrophy) is a rare neuro-degenerative disease with onset in infancy, most commonly found in Ashkenazi Jews. There is no known current treatment. There has been little discussion in the medical literature of the specific ocular abnormalities encountered in this unique population other than that these patients usually end up blind. The purpose of this paper is to document the ocular findings in this a group of patients with Canavan.

Case Report

This is a retrospective observational case series report of seven patients with Canavan disease. This group included all the Canavan patients in a facility of 200 residents. The examination included examination of the external and anterior segment structures, pupillary response, cycloplegic retinoscopy, direct ophthalmoscopy, cover test and visual tracking. Of the seven patients, four were male and three were female. The age range was 6-13 years with a mean of 9.6 years. The refractive status of all the Canavan patients was within normal range. Cover testing revealed that 43% had exotropia and 71% had abnormal pupillary responses. All had optic nerve pallor with three cases

of optic nerve hypoplasia. Tracking was subnormal in 3 and virtually absent in four of the patients.

Conclusions

Significant ocular abnormalities are encountered in Canavan disease. Although this disease has devastating neurologic involvement, maximal efforts should be made to provide appropriate intervention to improve the patient's quality of life.

Key Words

Canavan disease, neuro-degenerative disease, spongiform leukodystrophy, exotropia, pupillary defects, optic nerve hypoplasia, visual tracking deficits

INTRODUCTION

Canavan disease (OMIM #271900),* one of the spongiform leukodystrophies, is a rare fatal neuro-degenerative disease with onset in infancy. It is most frequently encountered in Ashkenazi Jews, but has been reported in many other populations as well. The carrier rate among Ashkenazi Jews is 1 in 37-58. Carrier detection as well as prenatal diagnosis can be accurately carried out using molecular analysis.¹ Although the course of the illness may show considerable clinical variation, the salient features of Canavan disease include atonia of neck muscles, hypotonia, hyperextension of the legs and flexion of arms, as well as deafness, paralysis, and blindness. Other features are severe mental retardation, megalcephaly, and eventual death that generally occurs by the end of the first decade of life. The neurologic findings are due to demyelination and leukodystrophy. Occasional late onset or long term survivors have been reported.² Canavan disease is an autosomal recessive anomaly with the gene being located on 17pter-p13.³ The disease is caused by mutations in the gene for aspartoacylase. Carriers can be diagnosed pre-natally.⁴ There is currently no cure, nor is there a standard course of treatment. The prognosis for Canavan

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Table 1: Ocular Abnormalities encountered in Canavan Disease patients

ID#	AGE	SEX	OPTIC NERVE APPEARANCE	CUP/DISC RATIO	PUPILS	STRABISMUS	TRACKING	OTHER
1	10	M	Mild/No pallor	Cup/Disc = 0.2	PERRLA	ALT XT = 25 PD	Some periph. awareness	
2	13	F	Severe pallor, hypoplasia	Cup/Disc = 0.4	Mod dilated, sluggish	LXT=45PD	Minimal tracking OU	
3	9	F	Severe pallor, hypoplasia	CRA/V displacement	RE None, LE sluggish	Ortho	Minimal response LE only	
4	8	M	Slight disc pallor	Cup/Disc = 0.1	Mid-dilated, sluggish OU	Ortho	Occasional slow tracking OU	Pendular nystagmus
5	10	F	Slight disc pallor	Cup/Disc = 0.2	PERRL	Ortho	Fixation, no tracking	Lagophthalmos, SPK OU
6	6	M	Slight disc pallor	Cup/Disc = 0.2	Mid-dilated, non-reactive	Ortho	Fixates light, no tracking	
7	11	M	Optic disc hypoplasia	Cup/Disc = 0.1	Optic disc hypoplasia	Cup/Disc = 0.1	Sluggish, but PERRLA	

Abbreviations: M=Male, F=Female; PERRLA=Pupils Equal round Reactive to Light and Accommodation; RE =Right Eye, LE=Left Eye, OU= Both eyes; ALT= Alternating, LXT= Left Exotropia, RXT = Right Exotropia, PD = Prism Diopter; SPK = Superficial Punctate Keratitis

disease is poor and management is based on symptoms and supportive therapy. However, early experimental treatments involving gene therapy have been shown to have beneficial effects clinically, as well as on the biochemical and radiologic level.⁵

Previously there has been no extensive discussion in the medical literature of the ocular abnormalities encountered in patients with Canavan Disease. The purpose of this paper is to document the findings a group of patients with this condition.

Case Reports

This is a retrospective observational clinical case report series of seven patients with Canavan disease who were examined with portable equipment in various residential group facilities. The examination and data collected included: demographic data (age and gender), medical history and medications used. Unfortunately the availability of much of this history was limited. Then an initial evaluation of the external structures and the anterior segment of the eye was performed using a transilluminator and an ophthalmoscope. The external exam findings were a combination of the result of the transilluminator evaluation without magnification and the ophthalmoscopic evaluation at 10 cm with a +10.00 lens in the ocular cell. While a measurement of visual acuity would have been advantageous this was not possible due to a combination of lack of appropriate equipment (such as Teller Acuity cards) and lack of patient cooperation. A further limitation was that all the patients were considered functionally non-verbal with limited gross motor capabilities. Pupil responses and initial media evaluation were also performed using the transilluminator. The evaluation continued with an examination of the lens, media, optic nerve head, macular area and posterior pole with direct ophthalmoscopy. Assessment of optic nerve head cupping and size were

determined. Evaluation of the cover test was performed to determine ocular alignment. Visual tracking ability was assessed initially utilizing a Wolf Wand (1.8 cm diameter shiny metal ball on a wand) and then a second attempt was made using a transilluminator. Retinoscopy was performed under cycloplegia (cyclopentolate 1%) and when deemed necessary ophthalmoscopy was performed a second time through dilated pupils.

RESULTS

The results of the ocular abnormalities encountered are summarized in Table 1. The age range was 6-13 years with a mean age of 9.6 years. Of the seven patients, four were male and three females. There did not appear to be an age or gender-based difference in findings.

Two of the seven (29%) patients had structural anomalies. Other than one patient who had lagophthalmos, no abnormalities of the anterior segment were encountered. The other patient had pendular nystagmus. Lens and media evaluation produced no findings of note.

Pupillary response testing demonstrated that 5/7 (71%) had abnormal magnitude and speed of pupil responses. Only two were round and reactive to light. These pupil reactions would be consistent with severely deficient visual acuity and cortical inattention. The evaluation of ocular alignment revealed that 3/7 (43%) had strabismus with all exotropias of significant degree (25-45 Prism diopters).

On examination of the posterior segment, all patients had at least mild optic nerve pallor. Three had significant or severe optic nerve pallor as well as hypoplastic optic nerves. The retinas were normal in 6/7 (86%) patients. One patient had extreme retinal vascular tortuosity.

Visual tracking behavior was significantly abnormal in all seven patients with no to minimal tracking. This was true notwithstanding the lack of refractive errors

Table 2: Refractive Error in Canavan Disease Patients

ID#	RE-SPHERE	RE-CYLINDER	RE-AXIS	LE-SPHERE	LE-CYLINDER	LE-AXIS
1	+0.50	-0.75	90	+0.5	0	0
2	0	0	0	0	0	0
3	-3.00	-2.50	170	-3.50	0	0
4	+1.50	0	0	+1.50	0	0
5	-1.00	0	0	-1.00	0	0
6	+2.00	0	0	+2.00	0	0
7	0	0	0	0	0	0

Abbreviations: RE = Right Eye, LE = Left Eye

significant enough to affect visual behavior at near. Although not part of the original testing protocol, these results lead to further attempts to assess visual tracking using a large hand held carousel with lights and bells. This did not change the results. Cycloplegic refractions revealed the refractive errors that are listed in Table 2. Two had no refractive error. Of the remaining five, one patient had mild mixed astigmatism, 1/7 (14%) had mild simple myopia and 2/7 (29%) had mild simple hyperopia. One had moderate myopia in one eye, with moderate compound myopic astigmatism in the other.

CONCLUSIONS

All of the patients evaluated in this study with Canavan disease have severely decreased visual behavior. The average age of the patients studied was older than the average lifespan quoted in the literature. In light of the fact that the major effect of the disease is neurologic damage it is reasonable to assume that the decreased visual behavior is cortical in origin. Notwithstanding the poor overall prognosis until severe cerebral changes render such assistance irrelevant it is worthwhile to treat all amendable conditions. The treatable entities encountered include refractive errors, astigmatism, myopia, and hyperopia, strabismus, and accompanying amblyopia. In addition, visual assessment of these individuals is critical in supplying caregivers with the necessary knowledge as to what stimuli are appropriate to use with these patients at each stage of the disease. Monitoring and treating relevant ocular conditions can enable the patients to maintain an optimal quality of life for as long as possible. Since it appears that early gene therapy attempts have been well tolerated and clinically useful, it is imperative to maintain the quality of life for these patients until further interventions become clinically available.

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* Online Inheritance in Man (Canavan Disease #271900)
<http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=271900>

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