Rod-Cone Dystrophy in Spinocerebellar Ataxia Type 1

Matthew J. Thurtell, Emory University
Valerie Biousse, Emory University
Nancy Newman, Emory University

Journal Title: Archives of Ophthalmology -New Series-
Volume: Volume 129, Number 7
Publisher: American Medical Association (AMA) | 2011-07-01, Pages 956-958
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1001/archophthalmol.2011.172
Permanent URL: https://pid.emory.edu/ark:/25593/trs9z

Final published version: http://dx.doi.org/10.1001/archophthalmol.2011.172

Copyright information:
© 2011, American Medical Association

Accessed September 27, 2019 4:54 PM EDT
a toxic or dominant negative effect of the truncated protein is possible. It is difficult to propose that the complete unilateral nature of the disease in this patient is due to differences in environmental or genetic exposures between the two eyes. One possibility might be a somatic mutation in a progenitor cell during the development of the unaffected retinal tissue that ameliorates the effect of the mutation.

To conclude, this represents the first report to our knowledge of unilateral disease occurring in a patient with a germline mutation for a known RP-associated variant. The phenotype, even when investigated carefully, is entirely normal in the unaffected eye. A somatic, embryonic mutation causing mosaicism at this locus is proposed.

Rajarshi Mukhopadhyay, MRCOphth, MS
Graham E. Holder, PhD, MRCOphth
Anthony T. Moore, FRCS, FRCOphth
Andrew R. Webster, FRCOphth


Correspondence: Dr Mukhopadhyay, University College London Institute of Ophthalmology, 11-43 Bath St, London EC1V 9EL, England (docrajarshi@doctors.org.uk).

Financial Disclosure: None reported.

Funding/Support: This work was supported by grants from the British Retinitis Pigmentosa Society, Foundation Fighting Blindness USA, Fight for Sight, and the National Institute for Health Research UK to the Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital and University College London Institute of Ophthalmology.


Rod-Cone Dystrophy in Spinocerebellar Ataxia Type 1

Spinocerebellar ataxia type 1 (SCA1) is a rare autosomal dominant neurodegenerative disease caused by a CAG triplet repeat expansion in the SCA1 gene on chromosome 6, encoding for a protein called ataxin-1.1 Spinocerebellar ataxia type 1 typically produces a progressive cerebellar syndrome, with prominent ataxia, dysarthria, and bulbar palsy.2 Early ophthalmologic manifestations include saccadic hypermetria, gaze-evoked nystagmus, and rebound nystagmus, with saccadic slowing and ophthalmoplegia developing in the later stages of the disease.3,4 Decreased visual acuity, dyschromatopsia, and optic atrophy are less commonly reported, with attenuation of oscillatory potentials on full-field electroretinography (ERG) also reported in 6 patients.3 We describe a patient with genetically confirmed SCA1 who developed progressive painless binocular vision loss and had evidence of rod and cone photoreceptor dysfunction on full-field ERG.

Report of a Case. A 56-year-old woman had an 8-year history of progressive painless binocular vision loss, blepharospasm, and cerebellar ataxia. There was a strong history of cerebellar ataxia with associated vision loss on the paternal side of her family.

On examination, best-corrected visual acuity was 20/70 OU. She identified only the control Ishihara color plate bilaterally. Confrontation visual fields revealed bilateral central scotomas. External examination revealed blepharospasm and occasional facial grimacing. Anterior segment examination findings were unremarkable. The pupils were normal. Ocular motor examination revealed slow saccades and impaired smooth pursuit, without nystagmus. General neurologic examination revealed dysarthria, head titubation, and appendicular, truncal, and gait ataxia. Funduscopic examination revealed absent foveal light reflexes, drusen and subtle pigmentary changes in the posterior poles, and retinal arteriolar attenuation (Figure 1). The optic discs were normal and no pigmentary changes were noted in the retinal peripheries (Figure 1).

Goldmann visual fields showed central depression and constriction of all isopters. Brain magnetic resonance imaging showed brainstem, cerebellar, and cervical spinal cord atrophy. Full-field ERG showed attenuated responses to all stimuli in both eyes, with prolonged implicit times for dim white flashes and maximal white b-waves (Figure 2 and eTable, http://www.archophthalmol.com). Genetic testing revealed an increased CAG repeat number of 46 (normal <34) in 1 SCA1 allele, confirming the diagnosis of SCA1. Genetic testing results for SCA7 were negative. Other laboratory studies were unrevealing.

Comment. Prior to the era of molecular diagnosis, it was known that vision loss in the SCAs could result from primary optic neuropathies or, less commonly, retinal degeneration.5 Detailed studies of vision in the different SCA genotypes have not yet been performed, although it is well established that SCA7 is the only genotype in which retinal degeneration commonly occurs.5 In a prior series of patients with genetically confirmed SCA1, decreased visual acuity, dyschromatopsia, and optic atrophy were reported, but no other fundusoscopic abnormalities were noted.6 All 6 patients in that series had attenuated oscillatory potentials and some had decreased b-waves,4 possibly indicating inner retinal dysfunction. Another report described a patient with genetically confirmed SCA1 who had progressive vision loss and a pigmentary macular dystrophy,7 similar to that described in SCA7.8 Full-field ERG revealed photoreceptor dysfunction and genetic testing had negative results for SCA7, suggesting that a pigmentary macular dystrophy can occur in SCA1.9 Our patient with genetically confirmed SCA1 had progressive binocular central vision loss and subtle fundusoscopic changes suggestive of retinal de-
generation, without optic atrophy. Full-field ERG revealed rod and cone dysfunction. The presence of vision loss in other family members with cerebellar ataxia and presumably SCA1 suggests that the vision loss was a manifestation of SCA1 and not due to a second pathology. Our findings therefore suggest that vision loss in
SCA1 can be due to rod-cone dystrophy and should prompt evaluation by ERG, even in the absence of obvious retinal changes.

Matthew J. Thurtell, MBBS, FRACP
Valérie Biousse, MD
Nancy J. Newman, MD

Author Affiliations: Departments of Ophthalmology (Drs Thurtell, Biousse, and Newman), Neurology (Drs Biousse and Newman), and Neurological Surgery (Dr Newman), Emory University School of Medicine, Atlanta, Georgia. Dr Thurtell is now with the Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa City. Correspondence: Dr Newman, Department of Ophthalmology, Emory Eye Center, 1365-B Clifton Rd NE, Atlanta, GA 30322 (ophthnjn@emory.edu).

Financial Disclosure: None reported.

Funding/Support: This study was supported in part by a departmental grant to the Department of Ophthalmology from Research to Prevent Blindness, Inc, New York, New York, and by core grant UL1-RR025008 to the Department of Ophthalmology from the National Institutes of Health, Bethesda, Maryland. Dr Newman is a recipient of a Research to Prevent Blindness Lew R. Wasserman Merit Award.

Online-Only Material: The eTable is available at http://www.archophthalmol.com.


Sudden Growth of a Choroidal Melanoma and Multiplex Ligation-Dependent Probe Amplification Findings Suggesting Late Transformation to Monosomy 3 Type

Current wisdom is that uveal melanomas develop monosomy 3 very early.1 It is hypothesized that metastatic spread commences years before presentation,2 and therefore ocular treatment may not influence survival.3 We describe a melanoma with apparently delayed transformation from disomy 3 to monosomy 3.

Report of a Case. In 2001, a 65-year-old woman was referred with an inferonasal, pigmented, choroidal tumor in her left eye. The lesion was 10.1 mm wide and 1.6 mm thick (Figure 1A and B). Scattered drusen were noted. Orange pigment and subretinal fluid were not seen. The differential diagnosis included nevus and melanoma. The patient was monitored every 6 months. She underwent photocoagulation for diabetic retinopathy in 2005 and epiretinal membrane peel in 2006. The tumor appeared unchanged in serial evaluations, but by December 2007 its thickness had increased to 2.3 mm (Figure 1C and D).

In 2009, the patient had an acutely painful left eye with visual acuity of light perception and an intraocular pressure of 40 mm Hg. Ophthalmoscopy and ultrasonography showed the tumor to have a collar-stud shape, measuring 14.0 mm basally and 10.5 mm in thickness (Figure 1E and F). The eye was enucleated.

Microscopy showed a choroidal melanoma with extensive necrosis but with viable epithelioid cells at its apex and spindle cells at its base (Figure 2A-C). The mitotic rate was 4 per 40 high-power fields. Closed connective tissue loops were not present and lymphocytic infiltrate was minimal. Melanoma cells were also present on the surface of the iris extending into the chamber angle. The ciliary body was infiltrated by a melanoma satellite. Following microdissection, molecular genetic evaluation using multiplex ligation-dependent probe amplification revealed monosomy 3 and chromosome 6p gains in the melanoma cells at the tumor apex and disomy 3 at the base (Figure 2D). The patient was well 6 months postoperatively with no evidence of metastasis.

Comment. We report the case of a melanoma that, after 8 years of apparent quiescence, suddenly enlarged. It developed a collar-stud shape, became necrotic, and made...