Catastrophic Visual Loss in a Patient With Friedreich Ataxia

Friedreich ataxia (FRDA) is an autosomal recessive neurodegenerative disorder usually characterized by progressive early-onset ataxia. The most common ophthalmic manifestation of FRDA is optic neuropathy, which is usually late in onset, is slowly progressive, and rarely causes severe visual loss. The genetic basis of FRDA in most patients is the homozygous expansion of a GAA trinucleotide repeat within the first intron of the FRDA gene, which encodes the mitochondrial protein frataxin. Mutations in frataxin cause progressive iron accumulation in mitochondria. Four percent of patients are compound heterozygotes for the GAA expansion on one allele and a point mutation on the other. We describe a patient with FRDA who was a compound heterozygote for the GAA expansion and a Gly130Val missense mutation, developed rapid-onset catastrophic visual loss, and was found to have clinical, electrophysiological, and radiological evidence of a severe optic neuropathy. In addition, she had pattern dystrophy. To our knowledge, this is the first description of a patient with FRDA with this phenotype.

Report of a Case. A 59-year-old woman with known FRDA and diabetes was referred for investigation of progressive loss of vision in the left eye. Two months previously, her visual acuities were 6/6 OU. On her first visit to the ophthalmology department, her visual acuities were 6/6 OD and 6/24 OS. Electrophysiology revealed normal rod, cone, and pattern electroretinographic results. The electro-oculographic results were normal, but the pattern reversal visual evoked potential showed increased latency in the right eye and no response in the left eye, consistent with optic nerve or optic tract disease. Clinical examination and autofluorescence imaging revealed multiple yellowish deposits at both posterior poles, consistent with pattern dystrophy (Figure). There were no signs of diabetic retinopathy. Twelve months later, her visual acuities were bilateral light perception.
only, with pale featureless optic discs. A computed tomographic scan of the brain and orbits excluded mass lesions or intraorbital abnormalities, and magnetic resonance imaging revealed severe atrophy of the optic nerves, optic chiasm, and optic tract.

Genetic analysis revealed compound heterozygosity, with a GAA expansion on one allele and a G to T base substitution in exon 4 (Gly130Val) on the other. The mitochondrial point mutations associated with MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes) or MIDD (maternally inherited diabetes and deafness), MERRF (myoclonic epilepsy with ragged-red fibers), NARP (neuropathy, ataxia, and retinitis pigmentosa), and Leber hereditary optic neuropathy were not identified.

Comment. This patient with FRDA had visual loss of a rapidity and severity not previously described in FRDA. She was also noted to have a pattern dystrophy but had normal electoretinographic results and pattern electoretinographic results, suggesting that it is the optic nerve or optic tract disease that is causing the visual loss rather than the pattern dystrophy. Macular abnormalities have been described in autosomal dominant spinocerebellar ataxia type 7 but not previously in FRDA; thus, this may be a coincidental finding in our patient.3 It is possible that the pattern dystrophy observed in this case could be associated with a mutation in peripherin/RDS gene,4 the ELOVL4 gene,5 or as-yet-unknown genes.

The cause of optic atrophy in FRDA is unknown, but it occurs more frequently in patients with larger GAA repeats and also more frequently in compound heterozygotes than homozygotes.2 Furthermore, optic neuropathy emerges late in the course of disease and may be more frequent in compound heterozygotes who tend to survive longer. Optic atrophy is a heterogeneous disorder often caused by inherited or acquired abnormalities of mitochondrial function. Further investigation of the molecular mechanisms causing FRDA in compound heterozygotes may provide important insights into the underlying pathogenesis that leads to optic atrophy.

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**Autofluorescence Findings in Acute Exudative Polymorphous Vitelliform Maculopathy**

Acute exudative polymorphous vitelliform maculopathy is a rare acute disorder characterized by multifocal, curvilinear or oval, yellow-white, posterior pole lesions with vision loss and preceding headaches.1 These retinal pigment epithelial (RPE) lesions are associated with bilateral serous detachments and evolve into deposits resembling those of Best disease. During subsequent weeks, patients experience gradual recovery of vision.1 Optical coherence tomography2,3 and indocyanine green angiography4 findings have been described. To date, 7 cases have been reported in the literature. The main aim of the current study was to ascertain the nature of the posterior pole lesions using autofluorescence imaging in 3 patients and to characterize macular, retinal, and RPE function using International Society for Clinical Electrophysiology of Vision–standard electrophysiology.5-7

Report of Cases. Case 1. A healthy 49-year-old man noticed a gradual decrease in both distance and near vision, worse in his left eye, preceded by a flu-like illness. There was no other relevant medical, ophthalmic, or family history. On first examination several months later, his best-corrected visual acuity (VA) was 20/30 OD and 20/60 OS. Anterior segments, optic discs, and the peripheral retina were within normal limits. Posterior segment examination showed bilateral yellow-white confluent macular deposits (Figure 1A and B). Autofluorescence imaging using a confocal scanning laser ophthalmoscope showed that the lesions were hyper-fluorescent (Figure 1C and D), consistent with lipofuscin deposits. Pattern and full-field electroretinogram5-6 (ERG) and electro-oculogram7 results were normal, the latter suggesting normal generalized RPE function that would not be in keeping with Best disease. Six months later, the patient’s VA improved to 20/30 OU. The macular deposits had diminished (Figure 1E and F), with a corresponding reduction in autofluorescence (Figure 1G and H).

Case 2. A previously well 33-year-old woman had sudden onset of bilateral ring scotomas and distortion in the right eye following a flu-like illness and headaches. On first examination elsewhere, bilateral RPE detachments were noted. These settled spontaneously over a month. When referred to our service 9 months later, she had photophobia and difficulty adapting to dark. Her VA was 20/16 OU. A pale white curvilinear lesion appeared at each macula, with multiple yellow circular lesions around the posterior pole that were brightly autofluorescent (Figure 2A and B). The pattern ERG results were normal, in keeping with normal macular function. The full-field ERG and electro-oculogram results were normal bilaterally. There was partial resolution of the lesions on color photographs and confocal scanning laser ophthalmoscopy over 2 years (Figure 2C and D).

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