Epiretinal membrane:
A Reversible Cause for Visual Disability in Myotonic Dystrophy

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Abstract

Myotonic dystrophy type 1 is a multisystem disorder that affects skeletal and smooth muscle as well as the eye, heart, endocrine system, and central nervous system. In the eye it commonly causes ptosis and cataracts and has been associated with retinal pigmentary changes, low intra-ocular pressure and ciliary body detachment. Many of these changes may be due to a premature ageing process. Ocular Coherence Tomography (OCT) has demonstrated nerve fibre layer thinning in Parkinson's disease and multiple sclerosis. In a case control study of 30 patients not selected for eye symptoms and 28 age matched controls, we set out to find whether this was also the case in myotonic dystrophy by measuring thickness of the retro vitreous structures at the optic nerve head and macula. We also performed retinal photography and checked intra-ocular pressure and performed a thorough general eye examination.

We also assessed patients' CTG repeat size, age, 6 min walk and motor impairment rating scale (MIRS).

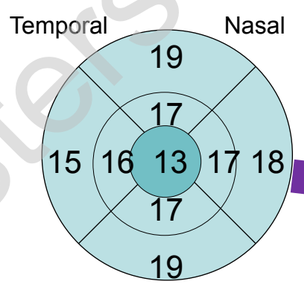
Results: We examined 59 eyes in 30 patients (1 patient had had recent eye surgery and was unable to be examined in that eye) and 56 eyes in 28 controls. In the myotonic dystrophy group16 eyes (27%) showed moderate and 11 eyes (19%) severe **epiretinal membranes** (ERM) compared with just 4 (7%) and 3 (5%) eyes in controls p=.0002, chi square. Taking the worst eye per patient, in the myotonic dystrophy group 9 (30%) had moderate and 8 (27%) had severe compared with just 4 (14%) and 2 (7%), respectively, in controls (p=.04) Most of the ERMs were asymptomatic at this time but three, amongst the myotonic patients, were impairing vision (visual acuity 6/15) and one patient was referred for retinal peel operation. About half the patients with ERM also had retinal pigmentary changes as well (compared with 4 controls).

In the myotonic group, but not controls, age was associated with ERM severity (p=.04) (average age 41, 40 and 55 in none/mild:mod:severe groups). There was also a suggestion of an association between the severity of ERM and disability as measured by MIRS but not the 6 minute walk test, nor CTG repeat length.

Conclusion: Epiretinal membrane is a common treatable cause of visual disability in myotonic dystrophy and should be specifically looked for in patients with impaired vision even when they don't have other signs of advanced disease.

Methods

- Design - Case Control study
- Study population - Myotonic dystrophy patients seen in neurogenetic clinic
- Numbers of patients/controls 30/28
- Comprehensive Eye Examination
  - Optical Coherence Tomography
    - Retinal nerve fibre layer at optic nerve head
    - Macula
  - Retinal Photography
  - Intra-ocular pressure
  - Visual Acuity
  - Colour Vision
  - Pupil Assessment
  - Visual Fields
  - Slit Lamp
  - Dilated Fundal Exam
- CTG Repeat
- Age/Sex
- Comorbity (diabetes)
- Motor Assessment
  - 6 minute walk test
  - Motor Impairment Rating Scale
- Assessment of Epiretinal Membrane
  - Independent rater
  - Blinded as to Case/Control
  - Based on OCT
- Statistics
  - ERM results: None and Mild were combined on a clinical basis prior to statistical analysis
  - Group comparisons were made using Student t and Chi square. Effects of age and MIRS/walk time by least squares regression.
  - Bonferroni correction to p value of .025 was made because of the two primary outcomes – OCT at macula and at optic nerve head



Grading of Epiretinal Membranes
None = no ERM
Mild = <1 mm long, <0.25 mm wide (continuous) for any hyper-reflective inner retinal patches
Moderate = >1mm > 0.25 mm continuous for hyperreflective inner retinal patches
Severe = premacular fibrosis (folding of ERM).

Results

- The cases and controls were well matched

	Controls (n=28)	Patients (n=30)	P Value
Age	44.5 (13.84) 28	44.6 (13.3)	0.99
Female Gender	15 (54%)	19 (63%)	0.6

- The previous finding of low intra-ocular pressure (IOP) was verified

	Controls (n=28)	Patients (n=30)	P Value
IOP (mm Hg)	13.9 (2.4)	9.1 (1.93)	<0.0001

- No evidence of an alteration in retinal nerve fibre layer thickness was found – rather than being thinner we found a suggestion that the patients had thicker RNFL

	Controls (n=28)	Patients (n=30)	P Value
Mean overall RNFL thickness (microns)	99.28 (8.9) 26	103.28 (8.8) 29	.1

- **Retinal thickness measurements at the macula** showed that the myotonic patients had thicker structures behind the vitreous . The extra thickness was greater further from the macula (see figure).
  This was demonstrated to be due to **Epiretinal Membranes.** Visual acuity was impaired in three patients whose ERMs involved the macula. The average extra thickness was 18.4 microns – a close correlation with thickness of ERMs in pathological specimens (1).

	Controls (n=28)	Patients (n=30)	P Value	Difference
Mean Mac thickness (microns)	307.95 (1.96)	326.31 (3.92)	0.0007	18.36

- We analysed patients eyes for the presence of ERM using OCT results. We established a grading scale on a clinical basis and then a blinded examiner classified the results. About half myotonic eyes and more than half of myotonic patients had a moderate or severe ERM.

	Myotonic Patients		Controls	
ERM Grading:	Worst Eye*	Total Eyes**	Worst Eye	Total Eyes
None/Mild	13	29	22	49
Moderate	9	16	4	4
Severe	8	11	2	3

*p=.04 ** p= .0002, for difference between cases and controls

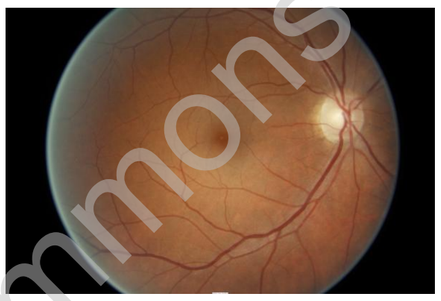
- The severity of ERM (worst eye) was
  - Possibly related to age in cases (p=.04) but not in controls (p=.6)
  - Possibly related to disease severity (MIRS p =.03 but not 6 min walk p=.4)

- Finally to look at the actual retinal Nerve fibre layer again we excluded all patients and controls who had any ERM at all. Still there was no evidence of thinning of retinal nerve fibre layer

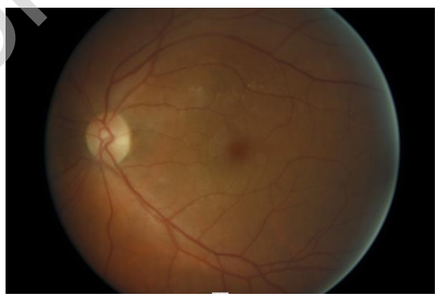
	Controls (n=28)	Patients (n=30)	P Value
Mean overall RNFL thickness (microns)	98.9 (8.9)	103.5 (10.1)	.1

Retinal photographs

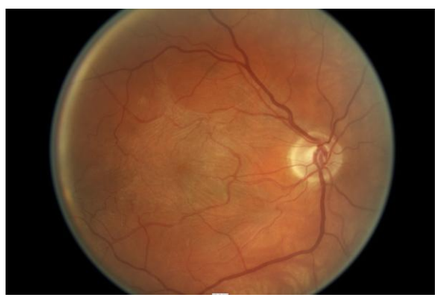
A. Normal



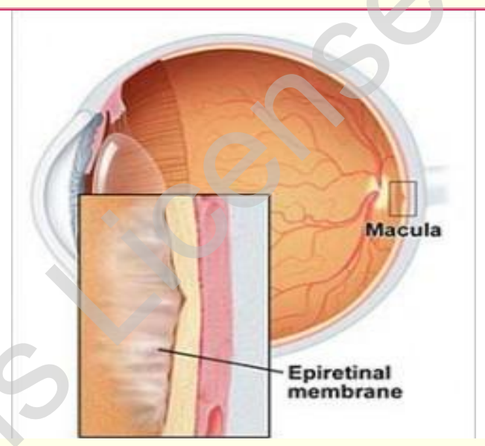
B. Cellophane Maculopathy



C. Pre macular fibrosis

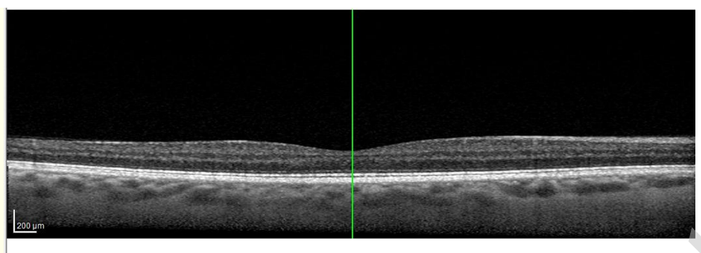


Epiretinal Membranes are thought to represent a pathological scarring process occuring during the normal process of shrinking of the vitreous away from the retina (posterior vitreous detachment) as part of ageing. Asymptomatic when mild, more severe ERM can present with decreased visual acuity and metamorphopsia.

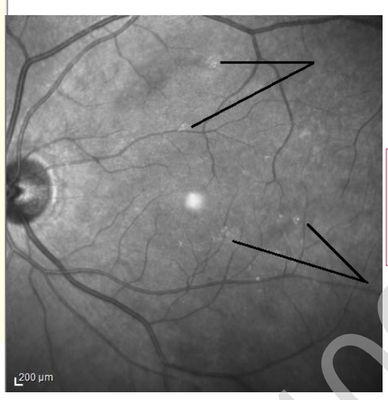


Ocular Coherence Tomography

A. Normal



B. "Moderate" Epirental Membrane

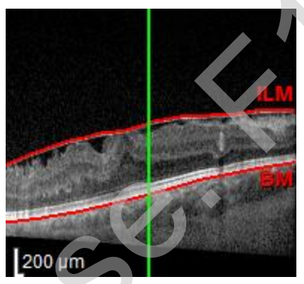


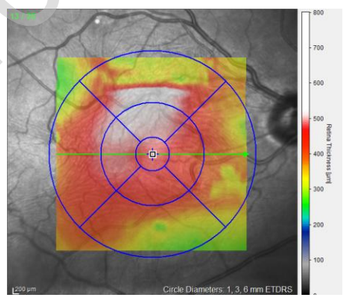
Lines indicate areas of "cellophane macular reflex"

C. Preretinal Macular Fibrosis

The Black and white images shows gross thickening of the retina and disruption of the normal retinal structure, with an overlying membrane.

In the colour map white is the thickest, followed by red/orange; green/blue show the areas of the retina that are thinnest. The circles used on the image have diameters of 1 mm, 3 mm and 6 mm. These circles correspond to the areas of the macular analysed in the table. The central 1 mm circle is the fovea





Discussion

Epiretinal membranes have only once before been described in myotonic dystrophy in a very small study of just 5 patients almost 30 years ago (1).

The mechanism is unclear but we propose that their occurrence is likely to be a premature ageing phenomenon similar to the early appearance of cataracts in this population and other signs of premature senescence in the condition (2). This would be consistent with the finding that age was associated with ERM score in cases but not controls.

The physical nature of these membranes also remains a subject of speculation as none of our patients have yet come to surgery. We speculate that they represent a form of glial proliferation.

Lower intra-ocular pressure in myotonic dystrophy patients has been previously noted (3). This is thought to be due to ciliary body detachment (CBD). It may be that the presence of ERM contributes to ciliary body detachment due to traction on the vitreous (4).

Conclusions

Epiretinal membranes occur at a much higher rate in myotonic dystrophy patients than in age matched controls

While common in a presymptomatic form (cellophane retinopathy), more severe forms (preretinal macular fibrosis) which cause visual disability are uncommon but because they represent an easily treatable (surgery) condition it is important that they be looked for. It is conceivable that patients might have mild cataracts removed in the belief that the cataracts are the cause of impaired vision whereas ERM may be the real cause

OCT is well tolerated and efficient. It has been shown reliably to predict the need for surgery in ERM patients (4)

Future Directions

Verification of this finding in a new sample of patients

Pathological inspection of ERM samples to determine their nature in this population

Following up our patients with presymptomatic ERM to follow its time course as membranes are likely to progress (5)

A parallel study in DM2 to see if ERM occurs in such patients as well

References

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