Ultrastructure of cataract in myotonic dystrophy. JOSEPH ESHACHIAN,* WAYNE F. MARCH,* WILLIAM GOOSSENS,** and NANCY S. RAFFERTY.**

Four cataractous lenses from patients with myotonic dystrophy were studied by transmission electron microscopy. All lenses showed whorls of what appeared to be plasma membranes.

Myotonic dystrophy is a multiorgan disease characterized by cataract, frontal alopecia, infertility, muscular atrophy, a grip which is slow in its release phase, a specific electromyographic pattern, and autosomal dominant inheritance.1

Lens opacities associated with myotonic dystrophy appear to have a complete hereditary penetrance, i.e., are present in close to 100% of dystrophic patients.1 The severity of the cataract is not related to the severity of the general disease.1 Myotonic cataract has two major features. The first lesion has been described as “iridescent dust”2 or “fine points mixed with colored crystals”1 localized in a thin band of anterior and posterior cortex beneath the capsule. Burian and Burns3 found these colored crystals to be present in 40 eyes of 20 patients studied in a group of 25 patients with myotonic dystrophy. The second characteristic lesion, seen in 24 eyes of 12 patients in this same group of 25 patients, is a stellate grouping of opacities at the posterior pole along the posterior suture lines.4 The stellate configuration of opacities is considered by Vos1 to be a later stage than that of the colored “crystals,” due to condensation of the point-like opacities along the sutures.

The nature of the iridescent “crystals” and punctate opacities is unresolved. It has been speculated that they are “crystals” of cholesterol or droplets of lipids from degenerating lens fibers.2 Electron microscopy of myotonic cataract could provide clues to the nature and formation of these cytoplasmic lesions. We studied the fine structure of four cataracts associated with myotonic dystrophy.

Materials and methods

Case reports

CASE 1. R. M. is a 32-year-old man who noted progressive weakness of his hands and arms since the age of 19. His brother, father, grandfather, uncle, and two cousins had myotonic dystrophy. R. M. presented classic symptoms of myotonic dystrophy, ptosis, wasting of temporalis muscles, diffuse muscle weakness, and areflexia. Myotonic grip release and percussion myotonia of the thenar eminence were present. Myotonic discharges were seen on electromyography. Muscle biopsy showed changes consistent with myotonic dystrophy (i.e., variability in fiber size, many fibers with central nuclei, type I fiber atrophy, and sarcoplasmic pad formation). Both lenses showed star-shaped cortical cataracts close to the posterior capsule (Fig. 1). With the slit lamp, the anterior cortex of each lens showed iridescent dustlike opacities.

CASE 2. D. S. is a 54 year old woman whose symptoms began at age 42 when she became unable to run or climb stairs. Symptoms of muscle weakness worsened in the cold. Her father had developed leg weakness and cataracts in his fifties. She displayed signs of diffuse cerebral dysfunction. She had a receding hairline, ptosis, and facial and peripheral muscle weakness. There was percussion myotonia of the tongue and thenar eminence, myotonic grip release, and areflexia. Myotonic discharges were obtained on electromyography. Electrocardiogram showed first-degree atrioventricular block. Both lenses had posterior cortical cataracts with vacuoles and polychromatic iridescent granules.

Electron microscopy. The four lenses from the two patients with myotonic dystrophy were ex-
Fig. 2. Electron micrograph of anterior central epithelial cells, capsule, and cortical fibers of lens of Patient D. S. with myotonic dystrophy. Swollen intercellular spaces and degenerated mitochondria are shown. Note varying density of cytoplasm in adjacent lens fibers. (×23,350.)

Results. The lenses of both patients showed similar morphological features. The anterior central and peripheral epithelial cells (Fig. 2) contained nuclei with clumped chromatin, degenerating mitochondria, and enlarged intercellular clefts or cisternae. Plasma membranes were poorly delineated. Clumps of filamentous material, similar to clumps found in the capsule, were present in some of the cisternae. Generally, then, the morphological picture of the anterior structure of the lens was not normal, compared with that of normal adult human lens⁴,⁵, the picture resembled that of the cataractous or aging lens.⁶,⁷

The most severe pathology was seen deeper in the posterior pole, at about 10 fibers or more deep. Small, round globular profiles appeared in prolific numbers (Fig. 3). Projections of plasma membrane appeared to constrict off corrugated fiber membranes, enclosing lens fiber cytoplasm. Accumulations of these profiles were associated with swirling membrane configurations resembling myelin figures (Fig. 4). These observations suggest that the plasma membranes wind around themselves to form myelin-like bodies. Small amounts of cytoplasm were layered between the
Fig. 3. Electron micrograph of lens fibers at posterior pole of lens of Patient D. S. with myotonic dystrophy, showing development of a myelin body from groups of membranous globular processes which appear to wind about themselves. (×30,100.)
Fig. 4. Electron micrograph of lens fibers at posterior pole of lens of Patient D. S. with myotonic dystrophy, showing a later stage in development of myelin figure than Fig. 3. (×25,000.)
whorls (Fig. 3). The largest myelin-like figure measured 3.6 by 7.1 μm, whereas the average single globule was between 0.14 and 0.20 μm in diameter. The myelin-like bodies could account for the colored dust observed with the slit lamp, and their accumulation along the posterior suture could account for the stellate opacity observed in Fig. 1.

Discussion. The four cataractous lenses showed some ultrastructural changes also found in cataracts of other etiologies, e.g., senile and traumatic cataracts.7 These changes, however, do not appear to be an artifact from cryoprobe damage; that is, cryoprobe freezing causes damage other than that seen in our myotonic cataracts.7 Development of enlarged intercellular spaces, loss or masking of plasma membranes, modification in appearance of cell organelles, and compression and variation in cytoplasmic density of adjacent lens fibers represent the response of lens cells to a variety of insults, including aging.7 In the cases reported here, the characteristic lesion of myotonic cataract is superimposed on other morphological changes. The characteristic slit-lamp appearance of colored flecks or “crystals” may correspond to these large myelin-like figures. They are not crystals at all, but derivatives of plasma membrane which refract light to give the appearance of colored crystals.

There is some question whether the membranous myelin-like figures are specific for myotonic cataract. Somewhat similar membrane inclusions, “multilamellar bodies,” have been described in cataract associated with retinitis pigmentosa.6 Dilley et al.8 also found figure-eight structures consisting of the regular alignment of globular interdigitating processes measuring 0.1 to 0.17 μm in diameter. Similar-sized globular processes were found in myotonic cataract but did not display a figure-eight configuration. In both cataract types, however, the globular processes appear to be formed from lens fiber plasma membranes.

In conclusion, the “iridescent crystals” seen in myotonic cataract seem to result from whorls of plasma membrane; they are not crystals. These findings suggest that the plasma membranes of lens fibers in myotonic dystrophy may be defective.

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References


Effect of timolol therapy on outflow facility.

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A 14-week course of timolol therapy in 38 eyes with open-angle glaucoma produced a statistically significant drop (6 mm Hg) in their mean intraocular pressure but had no effect on the mean coefficient of aqueous outflow. These data are compatible with those of Zimmerman et al. obtained after a single drop of treatment and suggest that timolol reduces intraocular pressure by inhibiting aqueous production.

Timolol is a beta adrenergic blocking agent that has been shown to be effective in reducing intraocular pressure.1,2 Zimmerman et al.3 have reported that a single drop of timolol reduces the intraocular pressure without significantly altering the outflow facility. The purpose of this paper is to report tonographic data obtained from primary