Ocular Features and Clinical Approach to Cataract and Corneal Refractive Surgery in Patients with Myotonic Dystrophy

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Abstract: Myotonic dystrophy is the most common inherited muscular dystrophy in adults and presents as two forms, type 1, and type 2. Ocular manifestations such as premature cataract formation, may be the first diagnostic sign or symptom of the disease, offering ophthalmologists a unique diagnostic role. Fuchs’ endothelial corneal dystrophy, ptosis and ocular melanoma are other possible findings. Systemic features can help providers better understand the disease and any accommodations to be made in clinical or surgical settings. Some patients with this disease may request evaluation of certain cataract or corneal refractive procedures. This article focuses on pertinent information for clinicians to utilize when evaluating and treating patients with myotonic dystrophy and specific surgical perspectives to consider prior to any ocular interventions. Hydrophobic intraocular lenses are still recommended in these patients with careful observation of capsular phimosis and posterior capsular opacities.

Keywords: corneal endothelium, intraocular lens, IOL, laser assisted in situ keratomileusis, LASIK, small incision lenticule extraction, SMILE, yttrium aluminum garnet, YAG, capsulotomy

Introduction

Myotonic Dystrophy (Dystrophy Myotonica, DM) is an autosomal dominant disease that primarily affects individuals of European descent. There are two forms of the disease, type 1 and type 2. DM1 is commonly known as Steinert’s Myotonic Dystrophy, named after the German neurologist Dr. Hans Gustav Wilhelm Steinert, who first described the disease in 1909. The genetic mutation that causes DM1 was not identified until 1992. Shortly after, the genetic sequence from DM1 patients was compared to a population of individuals believed to have the disease, and it was discovered that this other group of patients had a different genetic mutation. In Europe, this alternate disease was termed “proximal myotonic myopathy”, whereas in the US the term “myotonic dystrophy with no CTG expansion” or “myotonic dystrophy type 2” was adopted. It is estimated that the prevalence of DM type 1 ranges from 1 in 8300 to 1 in 10,700, making DM1 the most common muscle disease in adults. Although the prevalence of DM2 is much less known, some believe that it may be just as common as DM1. Patients with these diseases may be present seeking refractive surgery. Understanding the ocular features, risks and surgical adjustments that should be made will undoubtedly aid a refractive surgeon in providing favorable outcomes in this specific subset of patients.

Pathophysiology

DM1 is the expansion of the cytosine-thymine-guanine (CTG) trinucleotide on the dystrophia myotonica protein kinase (DMPK) gene of chromosome 19. The repeats cause a decreased expression of protein from the DMPK gene found primarily in skeletal muscle, cardiac muscle, and endocrine glands, and lead to abnormal DNA repair throughout life. The extraocular muscles, ciliary body and retina can be affected as the DMPK gene is present in all three. In normal adults, DMPK is not
expressed in the crystalline lens, making its involvement in cataract formation unlikely. However, in the promoter region, a segment known as six5, which is present in the lens, has been hypothesized to have a role in cataract formation for DM1 patients. The expansion of CTG trinucleotides in the DMPK gene has been shown to contribute to Fuchs Endothelial Dystrophy (FECD). One study showed the incidence of FECD in families with DM1 ranging from 36% to 46% compared to the public population at only 4%. FECD has a similar genetic pattern to an associated trinucleotide mutation in the TCF4 gene. However, DM1 patients do not have this TCF4 mutation. It is believed that excess RNA from the mutated DMPK gene leads to a FECD phenotype. This puts patients with DM1 at higher risk for FECD. No literature describing similar correlations in DM2 was found. The number of repeats does correlate to the severity and onset of DM. Repeats of 5–37 trinucleotides are present in normal individuals, 50–150 in mild cases, and from 100 to greater than 1000 are found in classic adult cases of DM. Congenital DM (a subtype of DM1) contains greater than 2000 repeats.

DM2 is caused by an expansion of a tetranucleotide, CCTG repeat, of CNBP (CCHC-type zinc finger nucleic acid-binding protein) gene of chromosome 3. Ophthalmological features are reportedly identical between the two and therefore a similar clinical approach should be taken.

**Systemic Features**
DM1 and DM2 share several features with the main distinction being prominent distal weakness and atrophy in DM1 versus primarily proximal in DM2. Distal weakness manifests as trouble opening jars, turnings keys, gait instability or foot drop. Proximal weakness involves the arms and legs, making lifting objects overhead, rising from a seated position or climbing stairs difficult. Approximately 75% of patients with DM1 are diagnosed between the second and fourth decades of life (classic DM1), another 15% present at birth (congenital DM1) and the remainder occur before the age of 10 years old (childhood DM1). DM2 presents on average later than DM1, between the second and sixth decades. One review of 204 DM1 patients found that 86% were ambulatory, 11% required walking aids, and 3% needed wheelchair assistance. DM2 patients tend to require less assistance with maneuverability. Reasonable adjustments may be necessary for different examination positions such as the slit lamp or other testing devices. Patients have myotonia exacerbated by excitement, extreme temperatures, and fatigue. This often presents as grip myotonia, where they have difficulty releasing their grip during a handshake or other task. Cardiac conduction abnormalities, insulin resistance, and premature balding are other presenting signs and symptoms. Malignancies are also associated with this disease in both type 1 and type 2 ranging from choroidal melanoma, non-Hodgkin lymphoma, and neoplasms of the brain, thyroid, colon and reproductive organs of both males and females. These cancers make up 10% of deaths associated with DM compared to the 40% from respiratory and cardiac complications. Respiratory failure is the leading cause of death with cardiac conduction abnormalities the second leading cause. Only about 18% of DM1 patients live to the age of 65 compared to those with DM2 who tend to have a normal life expectancy.

**Ocular Features**
Ocular findings may be the first clinical sign of DM. Patients most likely present with decreased visual acuity secondary to cataract formation or visually significant ptosis. It is common to find lower than average intraocular pressures (IOP) in this disease. In addition, there are corneal, retinal and potential neoplastic findings associated with DM (Table 1).

The most common ocular finding in DM is cataract formation, specifically the classic Christmas tree cataract (CTC) featuring punctate iridescent opacities in the lens. CTC is usually not visually significant but can cause vision impairment as they progress. Nearly 100% of patients with DM1 or DM2 have bilateral iridescent cataracts, however not all patients with DM will display this unique cataract. Reiter and Gramar found only approximately 16% of patients with Christmas tree cataracts were diagnosed with DM. At present, myotonic dystrophy remains the only known associated disease with CTCs. A patient with cataracts prior to age 55 or a positive family history of premature cataract development in conjunction with muscle symptoms could suggest the diagnosis of DM, and workup for the disease should be warranted. The diagnosis is made with genetic testing searching for mutations of the DMPK or CNBP genes. However, if younger patients present with bilateral CTCs as the only presenting sign in the absence of other systemic or ocular symptoms, requesting genetic testing should be offered as an option for exploration.
Ophthalmologists have the unique ability and timely opportunity to diagnose DM prior to when systemic symptoms may arise. This will often involve identifying early cataract formation but can also be other features mentioned in Table 1. Workup for DM patients should include extraocular muscle testing, pupil response, a thorough slit lamp exam looking for corneal guttata, iris melanomas, and cataracts. A dilated fundus exam should rule out reticular or other pattern maculopathies and subtle nevi that may suggest ocular melanoma. Spectral microscopy should be performed if FECD is suspected, and different retinal imaging technologies can be utilized for possible retinal pathologies (OCT, fundus

<table>
<thead>
<tr>
<th>Ocular Finding</th>
<th>Description</th>
<th>DM1 or DM2</th>
<th>Clinical Application</th>
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<tbody>
<tr>
<td>Ptosis</td>
<td>Often bilateral and symmetrical. May have absent bells phenomenon as well.</td>
<td>Both</td>
<td>Caution with frontalis sling technique as patients may have muscle weakness/atrophy. Consider levator resection and advancement.</td>
</tr>
<tr>
<td>Ophthalmoplegia</td>
<td>Extraocular muscle involvement is rare, usually only found in advanced disease.</td>
<td>Both</td>
<td>It is possible to be presenting sign of DM in patients with history/family history of premature cataracts.</td>
</tr>
<tr>
<td>Pupillary light-near dissociation</td>
<td>Pupils do not react to light but react to accommodation. May also display sluggish response to mydriatics.</td>
<td>Both</td>
<td>Usually benign. If only presenting sign must rule out more severe causes (dorsal midbrain syndrome, Argyll-Robertson pupil, pineal tumor, Wernicke’s encephalopathy)</td>
</tr>
<tr>
<td>Low Intraocular Pressure</td>
<td>Mechanism not fully understood. Possibly due to ciliary body detachment.</td>
<td>Both</td>
<td>Perform intraocular assessment to identify patients with low IOP. A study with 102 eyes had mean IOP 10.9±3.1 mmHg</td>
</tr>
<tr>
<td>Fuchs Endothelial Corneal Dystrophy (FECD)</td>
<td>FECD has incidence in 36–46% of DM1 patients versus 4% in the general population. It is believed that excessive RNA from mutated genes in DM leads to FECD phenotype.</td>
<td>DM1 (unknown if it occurs in DM2)</td>
<td>Check for guttata and perform spectral microscopy to evaluate endothelial integrity, guttata, and polymegathism.</td>
</tr>
<tr>
<td>Christmas Tree Cataract (CTC)</td>
<td>Most common ocular feature of DM. Occur in 100% of DM patients. Iridescent punctate opacities. Usually not visually significant but can advance to cause visual impairment. Due to elevated calcium in the crystalline lens leading to protein breakdown.</td>
<td>Both</td>
<td>Often the first clinical sign of DM. Patients with CTC and muscle weakness suspect DM and refer for genetic testing.</td>
</tr>
<tr>
<td>Posterior subcapsular cataract (PSC)</td>
<td>More common in DM2 than DM1.</td>
<td>Both</td>
<td>Cataract extraction is visually significant</td>
</tr>
<tr>
<td>Ciliary body detachment (CBD)</td>
<td>Rosa et al found fluid behind at least one quadrant of the ciliary body in all patients with DM, and none in control group. Associated with low IOP.</td>
<td>Both</td>
<td>Ultrasound biomicroscopy (UBM) to look for ciliary body abnormalities. CBD in eyes without surgery or trauma could be marker for DM.</td>
</tr>
<tr>
<td>Reticular/butterfly Maculopathy</td>
<td>Most common retinal feature.</td>
<td>Both</td>
<td>OCT, fundus photography, FA, EOG, ERG.</td>
</tr>
<tr>
<td>Uveal melanoma</td>
<td>Case report of 6 DM eyes found majority (83%) had choroidal versus iris (17%) melanoma.</td>
<td>Both</td>
<td>27-fold increase in risk of ocular melanoma in DM patients than general population. Ensure a thorough dilated exam of entire choroid and iris.</td>
</tr>
</tbody>
</table>
photography, FA, ERG, EOG) (Table 1). Patients who are suspected of having DM should all be referred for proper genetic testing and counseling.

**Ocular Surgery Considerations**

As cataracts are the most common ocular finding in both DM1 and DM2, evaluating patients for cataract extraction may be necessary. Certain precautions need to be taken in the operating room as these individuals often have systemic issues associated with their disease; most pertinently, cardiac, and endocrine issues. These patients are also very sensitive to muscle relaxants and opioids. Ropivacaine HCl (naropin), a local amino amide-based anesthetic, has been shown to have successful anesthetic outcomes in DM patients compared to lidocaine and bupivacaine. The advantage lies in its ability to have similar deep motor and sensory nerve block functionality with a rapid onset but minimal cardiac effects. Thus, reducing the risk of cardiac arrhythmias intra and post-operatively.

Following cataract extraction and intraocular lens (IOL) placement in DM patients, there is an increased risk of posterior capsule opacity (PCO) and anterior capsular phimosis. Garrott et al reported eight posterior YAG capsulotomies between 2 eyes of one 28-year-old patient and another 49 year-old requiring seven anterior and seven posterior YAG procedures. Others have described similar results in these patients. Anterior capsule phimosis and capsular block syndrome have also been described as having resistance to the use of a YAG laser for immediate pressure relief. The DMPK gene is present in crystalline lens epithelial cells which could play a role in the degree of recurrent fibrosis that occurs in some individuals with DM. It is important to ensure meticulous polishing of both the posterior and the anterior capsule with a selected irrigation device during surgery to remove as many residual epithelial cells as possible. This should help prevent capsular contraction and recurrent PCO formation. Lastly, surgeons should avoid the creation of a small capsulorrhexis as the creation of a larger rhexis that remains within the IOLs optic margin will allow for the least degree of obstruction in the visual axis if some phimosis does occur.

An area not discussed significantly in the literature is intraocular lens selection in patients with myotonic dystrophy. Due to the risk of anterior capsular contraction syndrome (ACCS) and PCO formation, the type of IOL may prevent these outcomes. Using silicone, acrylic, plate haptic and polyHEMA IOLs have been associated with a higher incidence of ACCS when compared to polymethyl methacrylate (PMMA) IOLs. However, more recent studies have shown a decrease in anterior capsular contraction and PCO formation in hydrophobic acrylic IOLs like many of the current monofocal models. Therefore, most modern IOLs would be sufficient in DM patients to pose the lowest risk of capsular contraction and fibrosis. When it comes to multifocal (MF) or extended depth of focus (EDoF) lenses, centration is crucial to maintain optimal results. The use of these lenses should be weighed by the risk of capsular contraction which has been known to cause decentration of IOLs. Baur et al discuss a case where an EDoF lens was used in a patient with DM and reported reassuring outcomes without decentration or capsular phimosis. They attributed this to the hydrophobic acrylic lens material and that EDoF lenses are more resistant to decentration than multifocal lenses. At this time, the literature is not expansive on the opinion of MFL or EDoF lenses being used in patients with DM. It is important for a surgeon to thoroughly discuss the risks and benefits of these and other IOLs with their patients.

Those undergoing visually significant ptosis repair utilizing a frontalis sling technique should also be aware of the potential risks. If there is decreased levator function or severe frontalis/orbicularis muscle weakness due to their progressive dystrophy, this could lead to exposure keratopathy, and potential visual impairment if left untreated.

There may be those individuals who present requesting evaluation of other refractive procedures, such as LASIK, PRK, and SMILE. No literature could be found on patients with DM undergoing LASIK or other corneal refractive procedures specifically, but studies exist on the outcomes of these procedures on FECD patients. Laser refractive procedures are generally not recommended in patients with known FECD due to the risk of corneal decompensation. Further discussion of FECD and laser refractive surgery is beyond the scope of this article and has been published elsewhere in the literature. Due to the increased risk of Fuch's dystrophy in patients with DM1 a thorough exam is warranted on all patients searching for subtle guttae and obtaining endothelial cell counts with specular microscopy. LASIK and other corneal refractive procedures can be done in patients with DM1 or DM2 if the corneal and endothelial architecture is intact, with a normal endothelial cell count, lack of polymegathism, no central guttata, and reassuring coefficient of variation percentage (CV%) less than 33%. The lack of corneal pathology in healthy, stable endothelial cells can offer reassurance in these individuals;
however, more research is needed to identify the risks associated with these corneal refractive procedures in patients with myotonic dystrophy. With cataract formation being so common in this disease, considering cataract or lens extraction, if visually significant, may take precedence, thus, outweighing any benefits to alternative refractive options.

**Conclusion**

Myotonic dystrophy is an autosomal dominant disease that causes muscle weakness, atrophy and myotonia. The most common ocular findings are Christmas tree cataracts, ptosis, lower IOP, FECD and reticular maculopathies, with a rare occurrence of choroidal melanoma. Bilateral CTC in patients with muscle weakness may support the diagnosis of DM. In patients with incidental CTC discovery as the only presenting sign, further workup with genetic testing can be offered. Cataract extraction may be warranted if visually significant with the assurance that hydrophobic IOLs will provide the lowest risk of capsular contraction and PCO formation. Systemic complications most commonly affect the cardiac and endocrine organs, and special considerations need to be taken when anesthetics and opioids are used. Ropivacaine HCL is the recommended local anesthetic used during ocular procedures as they pose the smallest cardiac risk profile. Hydrophobic acrylic IOLs display the lowest risk of capsular phimosis and fibrosis and may be better for these patients. Corneal refractive procedures can potentially be considered after an extensive evaluation of the corneal integrity and endothelial architecture.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**


