OVERVIEW OF **OCULAR MANAGEMENT** IN MARFAN SYNDROME

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OCULAR FEATURES OF MARFAN SYNDROME

Marfan syndrome is a dominantly inherited disorder of connective tissue caused by mutations in the gene encoding fibrillin-1 (FBN-1).[1] The zonule of the eye consists of radial fibers which connect the ciliary body to the crystalline lens. Zonules consist primarily of FBN-1 and therefore mutations lead to progressive ectopia lentis, which is seen in up to 65 percent of patients with Marfan syndrome.[1-6] Aortic root aneurysm (z-score $\geq$ 2) or dissection and ectopia lentis are considered the two cardinal features of Marfan syndrome as agreed upon in the 2010 Ghent nosology.[7] For the full diagnostic criteria, please visit MarfanDX.org.

Lens dislocation

The major diagnostic feature in the eye of the Marfan patient is lens dislocation, which may be uni- or bilateral and vary in severity from absent to total. Note that the dislocation, though most often superior, can occur in all directions, including posteriorly. The onset varies from infancy to all ages with most cases being diagnosed in the first two decades of life. The progression may be insidious, but also can be acute when the onset of dislocation is late. Approximately 65 percent of patients with Marfan syndrome develop lens dislocation during their lifetime.

Additional ophthalmologic features suggestive of Marfan syndrome

- Flattened corneal curvatures[8]
- Enlarged corneal diameters[8]
- Astigmatism
- Increased axial lengths
- Miotic pupils
- Difficulty in completely dilating the pupils
- Hypoplastic iris with peripheral iris transillumination
- Enophthalmos

Ocular problems for which Marfan patients are at increased risk

- Presenile cataracts
- Glaucoma[9]
- Retinal detachments[10]
- Mild to severe vitreous degeneration[11]

Potential long-term ocular complications

- High refractive errors
- Uni- or bilateral amblyopia
- Strabismus[12]
- Total lens dislocation
- Intercalary staphyloma
- Inadvertent bleb—wound herniation
- Chronic intraocular inflammation
- Secondary glaucoma
- Chronic retinal detachments
- Buphthalmos
- Phthisis

Ocular features of clinical sub-types of Marfan syndrome

Severe form of Marfan syndrome

Diagnosis typically is made based on severe Marfan features at birth or within the first two years of life, without presence of Marfan syndrome in a parent. There are specific ocular findings in these children, including:

- Microspherophakia which is typically observed in the Weill Marchesani syndrome
- High refractive error at a young age
- Congenital or infantile glaucoma
- Retinal detachments
- Uveitis
- Enophthalmos secondary to absence of retrobulbar fat

Late onset ocular complications in patients with Marfan syndrome

- Presenile cataracts
- Open angle glaucoma
- Rapid and total lens dislocation in sixth or seventh decades in the absence of prior diagnosis of lens dislocation
- Retinal detachments without lens dislocation

EVALUATION OF THE MARFAN EYE

The diagnosis of lens dislocation is made on slit-lamp examination after full dilation of the pupil. Note that posterior dislocation of the lens may best be appreciated in down gaze and checking for separation of iris and lens with retropositioning of the lens being obvious. Retinoscopy prior to dilation may be helpful in assessing the position of the lens and size of the aphakic versus the phakic space.

The presence of presenile nuclear sclerotic cataracts should be noted on slit-lamp examination.

Keratometry is used to diagnose aberrations of the corneal curvature. Note that keratoconus is not a feature of Marfan syndrome; in fact, Marfan syndrome leads to flattened corneas.

Pachymetry is used to assess the thickness of the cornea. It is normal in Marfan syndrome.

Ultrasonography is used to measure the axial length of the globe and to search for the presence of shallow retinal detachments, which are not easily detected.

Ocular coherence tomography (OCT) is used to assess the structure of the neurosensory retina.

MANAGEMENT OF THE MARFAN EYE

The goals of ocular management

- Excellent and equal vision in both eyes
- Straight eyes
- Controlled glaucoma
- Prevention or treatment of retinal detachments
- Informed patients and families

Basic management includes

- Careful and thorough refraction and the use of contact lenses and/or glasses
- Topical dilating agents for chronic dilation of the eye to increase pupillary size for aphakic correction
- Treatment of amblyopia

Removal of the dislocated lens and cataract surgery

The indications for, and techniques of, removal of a clear subluxated lens in patients with Marfan syndrome continue to be the subject of controversy, and each case must be evaluated on an individual basis. The following indications may be given:

- Inability to achieve good corrected visual acuity in the presence of a clear dislocated lens is the most commonly given indication. The prescription of an optical correction in the presence of a dislocated lens requires considerable skills. Every patient ought to be given a careful refraction and a trial of corrective lenses. A second opinion may be indicated. Myopic astigmatism is the most frequently seen refractive error, when correcting through the lens. The cylinder often combines a corneal with a lenticular component and may exceed 6 diopters.

- Risk of amblyopia. Deep seated amblyopia is rare, given that lens dislocation is typically not congenital but acquired, and, therefore, most patients have experienced years of good near vision, albeit not distance vision. A trial of lenses ought to be given after careful retinoscopy to eliminate the effect of some refractive amblyopia. Asymmetry of lens dislocation, and hence vision loss, is also common and a period of patching may be required to achieve bilaterally normal acuity.
- Presenile nuclear sclerotic cataracts are common and require surgical management.
- Phacolytic glaucoma is common and may require lens removal, from the posterior chamber or the vitreous cavity.
- Pupillary block is very rare in Marfan syndrome and is typically prevented by the miotic pupil and deep anterior chamber. It may be seen in severely affected young children.
- Congenital microspherophakia may be seen in severely affected young children. Phacodonesis (or tremulosity of the lens) may be striking, but is usually not appreciated by the patient. Removal of the dislocated lens in severely affected young children carries a high risk of secondary retinal detachment. Prolapse of a tilted lens into the anterior chamber with corneal touch is seen in severely affected young children, where the lens diameter is typically smaller.
- Imminent total lens dislocation may be considered an indication for lens removal, even though dislocation of the lens into the vitreous cavity may be tolerated for decades. A dislocated lens may be suspended by few superior zonular fibers and appear centered in the pupil but tilted backward when a patient is supine.
- Bisection of the pupil by the edge of the dislocated lens. This is not a good indication for surgery because either a phakic or aphakic prescription can be given to match the fellow eye. Patients typically are the most difficult to refract when the lens edge is at the pupillary margin and not when it bisects the pupillary axis, when conversion to an aphakic prescription may be easily achieved.

Other Considerations

- Note that many patients have a normal axial length and, following lens removal, may require high power aphakic contact lenses or glasses. Glasses cause restriction of the visual field and may lead to ridicule.
- The timing of lens removal in children should be individualized based on age, asymmetry in lens dislocation, severity of the ocular and systemic disease, and risk of surgical complications.
- Intraocular surgery should not be undertaken before exhausting optical corrective measures (glasses, contact lenses). Patients rarely have deep-seated amblyopia because lens dislocation is not congenital, but slowly progressive with onset in the first decades of life. Excellent recovery of acuity may occur in patients who have apparent amblyopia because they had never worn adequate corrective lenses.
- Surgical difficulties are often induced by the unexpected persistence of Weigert's ligament. Even a markedly dislocated lens may have a strong attachment to the anterior vitreous face.

- Either limbal or pars plana surgical approaches can be used.
- Some patients may benefit from primary intraocular lens insertion, but it probably should not be done prior to full growth of the eye. Some physicians are hesitant to insert an anterior chamber lens because the angle is recessed and there is an increased AC diameter with difficulties in sizing of an anterior chamber lens and endothelial cell loss. Other lens styles need to be suture-fixated to the sclera or iris, or require pupillary support. Because lens dislocation is progressive and may occur at all ages, a lens implant should be suture-fixated in patients with Marfan syndrome, even when the lens to be removed is not dislocated. This is due to the fact that dislocation is likely to occur post-operatively.
- Marfan patients often have a hypoplastic iris, which may not be compatible with iris fixation. Every attempt needs to be made to not compromise the possibility of pupillary dilation because good visualization of the retina is needed over the patient's lifetime.
- Scleral fixation of the implant under a scleral flap is an option for lens fixation. A lens with a large optic and a large overall diameter can be used.
- Alternatively, a capsular extension ring can be inserted into the capsular bag, followed by insertion of a foldable IOL and two-point suture fixation of the IOL-capsular bag complex. Most surgeons have switched to the use of 9-O Prolene sutures rather than the previously recommended 10-O Prolene sutures because their durability is not likely to extend beyond 10 to 20 years.
- Cataracts develop 10 to 20 years earlier in patients with Marfan syndrome than in the general population.

Management of glaucoma[9]

Glaucoma is common in Marfan syndrome. More than 30 percent of patients develop this ocular complication.

- When using medical treatment of glaucoma, note that topical beta-blocker agents may have only minimal effect if a patient is using a systemic beta-blocker, a common treatment for prevention of aortic enlargement in patients with Marfan syndrome.
- If a filtering procedure is indicated because of poor control of intraocular pressure, then a lensectomy may be indicated. This can be done as an initial procedure because phakolytic glaucoma may be present and the sole cause of the glaucoma.
- Open angle glaucoma is more common in Marfan syndrome than in the general population and may occur at a younger age. Visual field loss may be rapidly progressive if the glaucoma is poorly controlled.
- Angle closure glaucoma and pupillary block are rare in Marfan syndrome, but common in Weill Marchesani syndrome and homocystinuria.
- Prolapse of the dislocated lens into the anterior chamber with resulting lens touch is very rare in Marfan syndrome; the long-term use of Pilocarpine is rarely required.

Strabismus surgery[12]

- The indications for strabismus surgery for Marfan patients are the same as for those in the general population. Exotropia is more common than esotropia. It may be self-limited with spontaneous resolution after recovery of equal acuity when wearing appropriate refractions with management of amblyopia. Beware of fragile conjunctiva and conjunctival vessels at the time of surgery.

Management of retinal detachments[10]

- Spontaneous retinal detachments occur in 10 percent of patients with Marfan syndrome.
- There is an increased risk of retinal detachment after anterior segment surgery.
- The indications for sclera buckling versus vitrectomy are the same as for the general population.

Refractive corneal surgery[8]

Refractive corneal surgery is currently not recommended because patients with Marfan syndrome have progressive lens dislocation with secondary myopia. Refractive corneal surgery leads to transient increases in intraocular pressure, which can place additional stress on the zonules with resulting additional iatrogenic myopia.

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