

Ocular Features of Marfan Syndrome: Diagnosis and Management

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The main ocular features of Marfan syndrome, all of which can result in decreased vision, include bilateral ectopia lentis (lens dislocation), myopia and retinal detachment [1]. About 50% of patients with Marfan syndrome are diagnosed by an ophthalmologist; some individuals may present with isolated ocular signs suggestive of this syndrome [2]. Recent advances in diagnosis, together with improved surgical techniques for the repair of ocular complications and the application of prophylaxis have contributed to the preservation of sight in Marfan patients [2]. We present here an updated review of the main clinical ocular features of this disorder, their role in the diagnosis of the syndrome, and their management.

Diagnosis

In 1991 the fibrillin-1 (FBN1) gene mutation on chromosome 15 was identified as a cause of Marfan syndrome. Fibrillin, a glycoprotein, provides force-bearing structural support and elasticity of the ocular connective tissues. It is found in multiple structures in the eye and plays an integral role in maintaining the integrity of the healthy eye [3]. Owing to locus heterogeneity as well as the large size of the FBN1 gene and the lack of family history in about one-third of the cases, molecular testing is of limited help in diagnosing Marfan syndrome and clinical evaluation remains fundamental to its diagnosis [1]. Clinical diagnosis depends on a combination of major and minor signs, as defined in the revised 1996 Ghent nosology [4]. The existence of ectopia lentis is considered a major criterion for the diagnosis of Marfan syndrome in

this nosology, which unequivocally diagnoses or excludes Marfan in 86% of cases [5].

Slit-lamp examination with fully dilated pupil for the detection of ectopia lentis and other ocular abnormalities should be a part of every initial evaluation of Marfan syndrome, and all people with non-traumatic lens dislocation should be referred to a pediatrician or internist, medical geneticist and cardiologist for a complete evaluation and a definitive diagnosis [6]. When there is a family history, initial examination by an ophthalmologist should take place in children at 3 to 6 months of age. To detect later refraction changes such as those caused by childhood lens subluxation, and to prevent amblyopia which can be present in up to 50% of patients [2], an annual examination by a pediatric ophthalmologist is recommended until age 12.

Crystalline lens disorders

Of the many ocular abnormalities seen in Marfan patients, by far the most common is ectopia lentis, occurring in 50–80% of affected individuals [7]. Ectopia lentis is defined as displacement or malposition of the crystalline lens [Figure 1]. The most common cause of ectopia lentis is trauma, which accounts for nearly one-half of all cases of lens dislocation. Marfan syndrome is the most frequent cause of heritable ectopia lentis [8]. When associated with this syndrome, ectopia lentis is usually bilateral, symmetric and non-progressive [7]. Other systemic conditions associated with ectopia lentis include homocystinuria, Weil-Marchesani syndrome, hyperlysinemia, sulfite oxidase deficiency and isolated familial ectopia lentis [9].

Abnormal production, distribution and attachment functions of fibrillin-rich zonules, as well as their increased susceptibility to proteolytic cleavage have been proposed to play a role in the pathogenesis of ectopia lentis in Marfan syndrome [2,10]. Preferential focusing of ultraviolet B light on the inferonasal quadrant of the crystalline lens was hypothesized to explain the observed supero-temporal predominance in the direction of lens dislocation in Marfan syndrome [10].

The dislocation may be subtle and detectable only by observing phacodonesis or iridodonesis (tremulousness of the lens or iris, respectively) sometimes visible by gonioscopy [7]. It may vary from an asymptomatic mild displacement seen only in post-pupillary dilation, to significant subluxation that places the equator of the lens in the pupillary axis and causes monocular diplopia (or quadropia if the condition is bilateral). A forward dislocation of

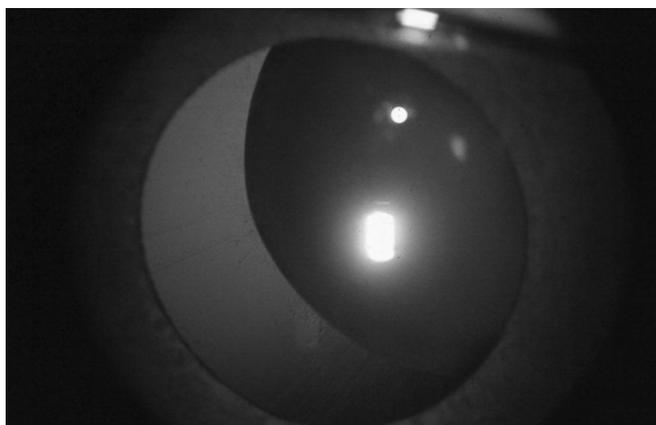


Figure 1. Ectopia lentis bisecting the pupil in a patient with Marfan syndrome. Sparse zonular fibers can be seen.

the lens into the pupil or anterior chamber may cause pupillary block with acute glaucoma or chronic angle-closure glaucoma. Posterior dislocation can cause harmful vitreous traction on the retina with leakage of lens proteins into the vitreous, which may cause chronic vitreitis and chorioretinal inflammation [9].

Premature cataracts and other lens and capsule opacities can also be found in Marfan syndrome patients, and tend to present at a younger age (thirties to fifties) compared to the general population [2].

Common non-surgical interventions in ectopia lentis include refractive aids and pharmacological manipulation of the pupil. Indications for surgical lens extraction include lens opacity with poor visual function, anisometropia or refractive error not amenable to optical correction, impending complete luxation and lens-induced glaucoma or uveitis [8,9].

In the past, surgery for the subluxated lens was associated with serious intraoperative and postoperative complications that resulted in poor visual outcome [9]. With the development of new techniques and instruments in recent years, a number of surgical options are now available to improve visual acuity in patients with ectopia lentis:

Long-term follow-up after lensectomy with limited anterior vitrectomy and subsequent correction of aphakia with glasses or contact lens showed this procedure to be safe and rewarding for children with hereditary ectopia lentis [9]. Mechanized vitrectomy, used in almost all lensectomy operations in Marfan patients, has significantly improved in the last few years with the introduction of small caliber 25 gauge surgical systems.

Because of zonular weakness and the resultant capsular instability, correction of aphakia with implantation of an intraocular lens in ectopia lentis is challenging. Options include anterior chamber IOL, ciliary sulcus posterior chamber IOL fixed to the sclera and/or to the iris, and scleral fixated capsular tension rings [11]:

ACIOL implantation in young eyes is associated with a high rate of postoperative complications such as corneal endothelial damage, peripheral anterior synechia, and glaucoma [12]. This is the result of growth of the pediatric eye and free movement of the lens in the anterior chamber. However, encouraging reports from small series on the use of Artisan iris claw ACIOL in cases of Marfan syndrome and isolated familial ectopia lentis were recently published [13,14]. In this method the IOL is fixated to the iris and its position is not affected by growth of the anterior chamber in the child.

Transscleral or iris suturing of PCIOL is considered a well-established option for fixation of PCIOL in the absence of sufficient capsular support [11]. However, a recently published report of long-term results after scleral fixation of PCIOL in 25 eyes of children showed a high incidence of complications [12] and in most medical centers this method is no longer used in children.

Capsular tension rings, a 270 degree open PMMA ring invented in 1991, evenly distribute centrifugal forces throughout the zonules

by applying gentle pressure throughout the lens equator and allow the preservation of the capsular bag and primary implantation of IOL inside it in cases of insufficient support. These rings contain holes that allow the centering and fixation of the capsule bag to the scleral wall. Recent reports show good visual outcomes with no serious complications in surgery for ectopia lentis in patients with Marfan syndrome that includes sclera-fixated capsular tension rings and primary implantation of an IOL in the capsular bag [15,16].

A new Israeli-developed intraocular anchoring device for re-centering and securing the capsular bag to the scleral wall was recently shown to be safe and effective on porcine and rabbit models of lens subluxation, and was successfully implanted in two patients with Marfan syndrome [17,18].

Myopia

The second most common ocular manifestation in Marfan syndrome is myopia, which is found in 34–44% of Marfan patients as compared to 4.8% in the general population in one study [2]. In Marfan syndrome, an increased ocular axial length can be observed. It is higher in patients with ectopia lentis and even higher in patients with retinal detachment, and is considered a minor criterion for ocular involvement in the Ghent Nosology [4,7].

Retinal detachment

Of all the ocular complications of Marfan syndrome, retinal detachment continues to be the most serious, occurring in 5–11% of patients. However, the incidence of retinal detachment increases to 8–38% in the presence of ectopia lentis. There is also a high incidence of bilateral retinal detachment, occurring in up to 69% of patients with retinal detachment. Retinal detachment in Marfan syndrome generally occurs in the mid-twenties, predominantly affects men, and can be missed on routine examination owing to poor visualization secondary to small pupils and lens abnormalities [3,19,20].

Marfan patients are more prone to develop retinal detachment for the following reasons. Unstable subluxated or dislocated lens capsule exerts traction on the vitreous base, leading to small tears or holes in the retinal periphery. Globe elongation and axial myopia common in Marfan syndrome are associated with early vitreous liquefaction and posterior vitreous detachment, retinal thinning, lattice degeneration, and peripheral breaks – all of which predispose patients to multiple large or even giant retinal breaks [19,20].

Although modern surgical techniques for lens extraction described earlier have dramatically decreased the incidence of postoperative retinal detachment, a history of previous intraocular surgery is still a major risk factor for retinal detachment and poorer outcomes of retinal detachment surgery in Marfan syndrome [20].

Retinal detachment surgery in Marfan syndrome is difficult and challenging because these young patients have thin sclera, poorly dilating pupils, possible ectopia lentis, and multiple breaks in different meridians, both anterior and posterior in location.

Scleral buckling is recommended as a first surgical procedure if the clear lens is normally placed, if the clear subluxated lens does not interfere with the fundus details, or if the retinal breaks are

IOL = intraocular lens

ACIOL = anterior chamber IOL

PCIOL = posterior chamber IOL

located at or anterior to the equator. Vitreous surgery in retinal detachment, however, is required in the following situations: failed scleral buckling, proliferative vitreoretinopathy, a posteriorly dislocated lens, a subluxated or cataractous lens not allowing an adequate evaluation of the fundus periphery, and giant retinal tears [19,20]. With appropriate surgical intervention, an excellent anatomic reattachment rate and good visual outcome can be achieved in Marfan patients with retinal detachment regardless of lens status [3,19].

Strabismus

Strabismus is a frequent feature in Marfan syndrome, and if uncorrected in children can result in amblyopia. It is present in 19–45% of individuals with Marfan syndrome (compared to 3–5% in the general population) and may be a presenting sign of the disorder [6]. Delayed and inadequate correction of refractive errors that compromise visual input, and deficient fibrillin in extraocular muscle pulleys that cause their instability may explain the high incidence of strabismus in Marfan patients [2,7]. Correction of strabismus is done by extraocular muscle surgery. Since many patients have binocular function potential, good surgical alignment can be achieved. In adult patients an adjustable suture technique is used allowing for better correction of the ocular deviation.

Glaucoma

Glaucoma will develop in about 35% of people with the syndrome during their lifetime, often at an earlier age than in the general population [6]. Primary open-angle glaucoma is most common, but glaucoma can also be secondary to anterior lens dislocation, anterior chamber angle abnormalities, or surgery [2]. If medical management is not successful, surgery – whose results are excellent – is an option [6].

Other features

Patients with Marfan syndrome may have flatter than average corneas, and megalocornea may also be present [7]. Hypoplastic iris or ciliary muscle causing decreased miosis can be seen and are considered minor criteria for ocular system involvement in the Ghent nosology [4]. An abundance of other histopathological findings can be found in almost every part of the ocular system in patients with Marfan syndrome.

Conclusion

Eye-care professionals play a significant role in detecting Marfan syndrome. The diagnosis and management of the many associated ocular disorders is challenging: it involves routine ophthalmic examination of patients that includes refraction, intraocular pressure measurement, and evaluation of the peripheral retina and optic nerve head. Patients should be instructed to seek immediate ophthalmological consultation if light flashes, floaters or any sudden decrease of vision occur. Timely diagnosis and treatment of refractive problems, retinal detachment and glaucoma can prevent amblyopia and help to preserve sight in patients with this syndrome.

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