M icrospherophakia (MSP) is a rare congenital disease where the crystalline lens has a spherical shape with an increased anteroposterior distance and a reduced equatorial diameter (ED). During months 5 to 6 of embryonic development, there is a lack of nutritional support of the tunica vasculosa lentis, leading to arrested development of the secondary lens fibers. Consequently, the existing zonular fibers become weak and lack tension, directly resulting in the presence of a small spherical crystalline lens without corticonuclear demarcation.

MSP is mainly characterized as follows: it usually occurs bilaterally; the crystalline lens resembles a sphere with a reduced ED and an increased anteroposterior distance; the entire lenticular equator is visible when the pupil is fully dilated; because of the abnormal laxity of the lens zonular fibers, the crystalline lens might move as the position of the body or the eyeball changes; lens dislocation or subluxation might occur; glaucoma is a common complication; accommodation might be defective.

The spherical lens pushes the central iris forward, leading to decreased anterior chamber depth (ACD). Measured by ultrasonographic A-scan biometry, the ACD is from the corneal endothelium to the anterior surface of the lens; in this case, ACD is 1.75 mm. Measured by ultrasound biomicroscopy and Scheimpflug imaging, the ACD is from the corneal endothelium to the anterior surface of the lens; in these cases, ACD ranges from 0.55 to 2.87 mm. If the dislocated spherical lens moves into the anterior chamber (AC) and touches the corneal endothelium, ACD will be reduced to zero.

The crystalline lens shape is nearly spherical. Therefore, the anterior lens radius and posterior lens radius are smaller compared with the normal lens. The radii of anterior lens and posterior lens are both near 6.0 mm in an existing case report. It can be seen from Table 1 that the curvatures of the anterior and posterior surfaces of the lenses are steep, and the radii of anterior lens and posterior lens are similar, proving that the lens is approximately spherical.

The lenticular ED of MSP is between 6.5 mm and 8.0 mm in the existing case reports (Table 1). Compared with the ED of normal eyes, which is about 9.0 mm, the ED in patients with MSP is significantly smaller. The abnormal laxity of the lens zonular fibers arrests the development of lenses, thus the lens remains spherical with the ED of the lens similar to that in normal eyes at birth.

The mean anteroposterior lenticular distance in a normal young adult is 3.7 mm ± 0.26 SD; spheroophakic lenses range from 4.06 to 6.75 mm. In normal eyes, the anteroposterior distance is 3.5 to 4.0 mm at birth, 3.7 mm at 20 years, 4.0 mm at 50 years, and 4.75–5.0 mm at 80 to 90 years. Therefore, the anteroposterior distance of the lens is closely correlated with age. In the same age group, the anteroposterior distance of the lenses in patients with MSP is greater when compared with normal patients. It has been reported that the anteroposterior diameter of these small and spherically shaped lenses is 25% greater compared with that of normal lenses.

The axial length and keratometry of MSP are within a normal range or even less than normal range because of congenital and developmental reasons. The axial length is between 21.5 mm and 25 mm, and keratometry is between 39.4 and 45.6 in the existing case reports (Table 1).
COMPLICATIONS
MSP is associated with the following complications: high lenticular myopia, lens dislocation or subluxation, and secondary glaucoma. The incidence of lens subluxation is 44.4%, and the incidence of glaucoma ranges from 44.4% to 51% in the existing literature.4,16 Because of the spherical shape, the refractive index of the lens is obviously higher compared with that of a normal lens, leading to high lenticular myopia. The lens position is unstable due to abnormal laxity of the lens zonular fibers, often causing lens dislocation or subluxation.10 The small lens is often displaced into the AC, which can lead to the loss of corneal endothelial cells and even corneal endothelial dysfunction.17 Glaucoma in MSP can occur through several mechanisms. A high anterior lens curvature and loosening of the zonular fibers allow the spherical lens to move forward, leading to iridolenticular contact and pupil block.7 Chronic pupillary block can result in the formation of peripheral anterior synechiae; secondary reverse angle-closure glaucoma, also known as malignant glaucoma, might occur due to the use of miotics, causing ciliary muscle contraction, loosening the zonular support, allowing the forward movement of the lens, shallowing the AC, and increasing the pupillary block.7,12 The other reported mechanisms include crowding of the trabeculae by the spherophakic lens, the chronic pupillary block without complete angle closure, and angle abnormalities with agenesis of the angle structures.4,10

GENETIC DIAGNOSIS
MSP is usually a genetic disorder that can occur in Weill-Marchesani syndrome, Marfan syndrome, Alport syndrome, and Klinefelter syndrome. It is most common in Weill-Marchesani syndrome, where it has clinical homoegenity but genetic heterogeneity.18 MSP can be seen in autosomal dominant (AD) or autosomal recessive (AR) familial anomaly or in isolation.18,19 AD pedigrees possibly link to chromosome 15q21.1.19 There is an observation of an in-frame fibrillin-1 gene deletion in AD Weill-Marchesani syndrome.20 AR inheritance links to chromosome 19p13.3-p13.2.21 Null mutations in ADAMTSL0 and ADAMTSL7 are responsible for the AR formation of Weill-Marchesani syndrome with major impairment of the extracellular matrix.22-25 Homozygous mutations in latent TGF-β-binding protein-2, which plays an essential role in the formation of microfibril bundles and structural stability in ciliary zonular fibers, have been found in patients with AR MSP.26,27 Latent TGF-β-binding protein-2 gene analysis in these patients might help the diagnosis of MSP.28

THERAPY
Because of the particularity of its morphology and the complexity of its complications, MSP is treated in a variety of ways, including conservative treatment and surgical treatment.

CONSERVATIVE TREATMENT
High Lenticular Myopia
When patients with MSP seem to have only high myopia with decreased vision, spectacles or corneal contact lens can be used to improve the visual quality.

Lens Subluxation
The abnormal lens might shift anteriorly and block the pupil, under which condition the status of the zonular fibers is usually unknown. If the zonule is intact, the lens can be moved back by measures such as pupil dilation, hyperosmolar treatment to shrink the vitreous, and supine

Table 1. Morphological characteristics of microspherophakia in the existing literature.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age (y)</th>
<th>ACD</th>
<th>ALR*</th>
<th>PLR</th>
<th>Eq Dia¹</th>
<th>APD²</th>
<th>AL§</th>
<th>K⁵ (RE/LE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan and Collin¹</td>
<td>9</td>
<td>1.57</td>
<td>6.2/6.3</td>
<td>6.3/5.6</td>
<td>—</td>
<td>4.77/4.89</td>
<td>21.68/21.79</td>
<td>—</td>
</tr>
<tr>
<td>Burakgazi et al.¹²</td>
<td>26</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>7.6/8</td>
<td>—</td>
<td>23.3/25</td>
<td>—</td>
</tr>
<tr>
<td>Willoughby and Wishart⁷</td>
<td>42</td>
<td>-1.75</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>-4.90</td>
<td>21.53/21.55</td>
<td>—</td>
</tr>
<tr>
<td>Lim et al.¹³</td>
<td>37</td>
<td>—</td>
<td>—</td>
<td>6.75/6.5</td>
<td>7.0/6.75</td>
<td>22.03/21.74</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Ram et al.⁹</td>
<td>42</td>
<td>1.1/0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>5.1/5.24</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Shakrawal et al.⁸</td>
<td>13</td>
<td>0.97/0.55</td>
<td>—</td>
<td>6.6/6.87</td>
<td>4.06/4.09</td>
<td>22.87/23.01</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Knokhar et al.¹⁰</td>
<td>14</td>
<td>2.04/2.18</td>
<td>—</td>
<td>—</td>
<td>5.98/5.69</td>
<td>24.32/24.06</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Moshinlar et al.¹¹</td>
<td>23</td>
<td>2.87/2.80</td>
<td>—</td>
<td>—</td>
<td>4.82/4.82</td>
<td>23.32/24.06</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Yang et al.⁹</td>
<td>mean ± SD</td>
<td>34 ± 23</td>
<td>1.32 ± 0.22</td>
<td>—</td>
<td>—</td>
<td>4.99 ± 0.11</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

ACD = anterior chamber depth; AL = axial length; ALR = anterior lens radius; APD = anteroposterior diameter; Eq Dia = equatorial diameter; K = keratometry; LE = left eye; MSP = microspherophakia; PLR = posterior lens radius; RE = right eye

Each radius of curvature (r) is given by: r = (rᵇ² + s²) / 2s, where rᶜ is one half of the chord length, and s is the sag. Both chord length and sag are measured by Nidek Anterior Eye Segment Analysis System EAS-1000.

1Tested by ultrasound biomicroscopy or removed lens measurement by ruler.
2Tested by ultrasonographic A-scan biometry, ultrasonographic A-scan biometry, Scheimpflug imaging, or removed lens measurement by ruler.
3Tested by ultrasonographic A-scan biomicroscopy.
4Tested by ultrasonographic A-scan biomicroscopy.
positioning.\textsuperscript{5,29} If the zonule is not intact, pupil dilation might have risk to induce lenticular displacement to the posterior pole.\textsuperscript{7} Therefore, under this condition, surgical treatment is usually required.

\textbf{Secondary Glaucoma}

These spherical lenses might result in a narrow AC angle and lead to angle-closure glaucoma, and laser peripheral iridotomy is often recommended early in management to control intraocular pressure (IOP).\textsuperscript{5} When IOP is elevated, antiglaucoma medications can be used early to reduce IOP. It should be noted that miotic agents can worsen the condition, and mydriatic agents are required to relieve the symptoms because spherical lenses can frequently block the pupils and miotics might even cause malignant glaucoma.\textsuperscript{10} After a peripheral iridectomy is performed, if miotics can be used to prevent lenticular dislocation into the AC, thymoxamine is recommended rather than pilocarpine because thymoxamine is an \(\alpha\)-adrenergic blocker that causes miosis by sympathetically inhibiting pupil dilation without affecting ciliary muscle contraction.\textsuperscript{7} Thymoxamine will not loosen the zonular tension, shallow the AC, or increase the pupillary block, thus decreasing the risk of malignant glaucoma.

\textbf{SURGERY}

In the cases of secondary glaucoma, cataract, and lens subluxation in MSP, surgery should be performed to remove the abnormal lens.\textsuperscript{77}

\textbf{Lens Removal}

Lens aspiration (phacoemulsification if necessary) and lensectomy with a limbal approach or pars plana lensectomy are the common approaches to remove the lens.

\textbf{Lens Aspiration}

Khokhar et al. reported a 14-year-old girl with MSP.\textsuperscript{10} Lens aspiration was arranged. To avoid excess zonular stress, after capsulorhexis was completed with an Utrata capsulorhexis forceps, nylon iris hooks are used to hook the capsulorhexis margin to stabilize the capsular bag during lens aspiration to avoid inadvertent collapse of the peripheral capsule, thereby preventing capsule aspiration. Aspiration is performed by keeping the irrigation/aspiration (I/A) mode in the Alcon Universal II phacoemulsification system. Because of the zonular weakness, low-flow parameters are specially set, including reduced bottle height (50 cm) and aspiration (30 mm Hg).

\textbf{Lensectomy and Anterior Vitrectomy}

Lensectomy is a common choice to manage secondary glaucoma in MSP. Khokhar et al. have performed lensectomy and anterior vitrectomy in patients.\textsuperscript{30} Two clear corneal incisions are made using a 23-gauge microvitreoretinal blade at the 10 and 2 o’clock positions, and then, the tip of the blade is inserted into the anterior capsule of the lens. To prevent vitreous entry into the AC, a viscodispersive agent (Viscoat) is injected at the site of the zonular stretch. Vitrectomy cutter of Centurion system (25 gauge) and irrigation cannula are introduced through 2 incisions within the capsular bag, and the cutter in I/A cut mode is maintained. The lens matter is aspirated by keeping vacuum at 400 mm Hg, aspiration flow rate at 50 ccs/min, and cut rate at 100 cpm. The capsular bag is then removed by keeping the cutter vacuum at 250 mm Hg, aspiration flow rate at 20 ccs/min, and cut rate at 4000 cpm, and a limited anterior vitrectomy is performed in cut I/A mode to prevent vitreous entry into the AC.

\textbf{INTRAOCULAR LENS IMPLANTATION}

It is common to combine lens removal with intraocular lens (IOL) implantation for the rehabilitation of vision. Because of the small capsular bag and the stretched zonular fibers, surgeries such as phacoemulsification and posterior chamber IOL (PC IOL) implantation are usually difficult to complete. Various procedures have been adopted in a few cases of MSP reported in the literature to date.

\textbf{Scleral-Fixed IOL Implantation}

Scleral-fixed IOL (SF IOL) implantation includes sutured and sutureless IOLs. Sutured SF IOL implantation has been successfully established in some cases.\textsuperscript{2,31} Yang et al. performed 17 surgeries of SF IOL implantation, and Subbiah et al. performed 8 surgeries of SF IOL implantation.\textsuperscript{2,32} After lensectomy and anterior vitrectomy using pars plana are performed, partial-thickness scleral incision and grooves are then made 1.5 mm posterior to the limbus at the 12 o’clock position, and 2 triangular scleral flaps are constructed at 2 symmetric positions. A needle with 10-0 polyglycan suture is inserted into the PC beneath the scleral flaps. Subsequently, 10-0 polyglycan suture is pulled out of the eyeball by a special hook through the super scleral tunnel incision. After suture is cut, the ends are tied to the haptics of an IOL, which is then inserted into the PC. At the end of the surgery, the sutures are knotted within the bed of the scleral tunnel, and conjunctival incisions are also closed.

Sutured transscleral fixation of a PC IOL has some postoperative complications, such as suture exposure, IOL tilting, IOL decentration, and pupillary capture of the IOL.\textsuperscript{33} Suture rupture is an important long-term complication, particularly in young patients.\textsuperscript{34} Vote et al have found that breakage of polypropylene sutures accounts for 17 (57\%) of 30 cases with a mean follow-up of 6 years.\textsuperscript{35} Younger patients and longer follow-up are significantly associated with suture breakage with the mean time to breakage of approximately 4 years postoperatively.

Sutureless SF IOL is an alternative way to avoid the complication of suture. After a pars plana vitrectomy is performed and a corneal incision is made, 2 sclerotomes are performed at 1.5 to 2.0 mm posterior to the limbus at 2 symmetric positions with a 24-gauge needle. Scleral tunnels of 2.0 to 3.0 mm in length and parallel to the limbus are formed from these sclerotomy sites with a 24-gauge needle. A 3-piece foldable IOL is injected through the corneal incision. While holding onto the IOL, each of the haptics is removed from the eye through the sclerotomy site with 25-gauge
forces and inserted into the scleral tunnel. Short-term postoperative complications include transient corneal edema, elevated IOP, and spontaneous IOL dislocation. Long-term postoperative complications still need further observation.

PC IOL Implantation With Capsular Tension Ring and Capsular Tension Segment
Khokhar et al. described a case of MSP in a 9-year-old boy presenting with high myopia, uncontrolled IOP, and recurrent glaucoma, for which he has been treated with Nd: YAG laser peripheral iridotomy in both eyes. Because of progressive zonular insufficiency in such case, the implantation of PC IOL might confer a possibility of IOL decentration. Khokhar et al. found that the standard 10.0/12.0 mm sized capsular tension ring (CTR) can be easily placed into capsular bag of small spherical lens. The ED of capsular bag can be enlarged by CTR. However, CTR alone cannot solve the problem of zonular weakness, which might cause the CTR–capsular bag–PC IOL complex subsequently dislocating posteriorly into the vitreous cavity. To solve the problem, capsular tension segment (CTS) is used to be sutured to the sclera. Therefore, the dual support provided by the placement of CTR along with CTS provides adequate capsular stabilization. CTR (10.0/12.0 mm) is implanted into the capsular bag after lens removal during surgery. A scleral flap is made in the direction of maximum subluxation. The 10-0 Prolene suture passing through a standard Ahmed CTS is sutured to the sclera in that direction. Then, a hydrophobic acrylic foldable PC IOL is implanted.

Canabrava et al. also performed PC IOL implantation with CTR and CTS. The differences between 2 surgeries are the use of 5-0 suture and a new double-flanged method. The 5-0 suture is heated and shaped into a flange using a bipolar portable cautery between the suturing eyelet of the CTS and external scleral side to fix the CTS. The absence of tied sutures and flaps in this approach saves the operation time and induces less ocular tissue trauma.

AC IOL Implantation
The surgical options for AC IOL implantation include angle-supported AC IOL and iris-claw–supported AC IOL implantation. An angle-supported AC IOL implantation was successfully completed by Willoughby and Wishart. A 42-year-old woman with MSP presented with uncontrolled glaucoma. Lens extraction in the right eye was planned, but no IOL was implanted because the capsular bag was too small and no suitable CTR and PC IOL were available. From the experience of the right eye, the left eye underwent phacoemulsification, with the removal of the capsular bag, anterior vitrectomy, and insertion of an angle-supported AC IOL. At 4 months postoperatively, the uncorrected visual acuity was 6/9, and the IOP was normal without glaucoma therapy, whereas close follow-up is required due to the potential complications of the angle-supported AC IOL. Angle-supported AC IOLs have been reported to be associated with corneal endothelial cell loss, peripheral anterior synechiae formation, and glaucoma due to chronic anterior chamber irritation. Furthermore, patients with MSP are at risk of corneal endothelial decompensation and secondary glaucoma, and the loss of corneal endothelial cell and peripheral anterior synechiae formation caused by angle-supported AC IOL might exacerbate the corneal endothelial decompensation and formation of peripheral anterior synechiae in those patients.

Iris-claw–supported AC IOLs have been reported in some studies. Moshirfar et al. reported a 23-year-old man with bilateral MSP and high myopia. Bilateral iris-fixed phakic IOL implantation was performed because of inadequate optical correction with spectacles and patient intolerance to contact lenses. A Verisyse IOL was inserted through a 6.0 mm corneoscleral incision centered on the steep axis. Enclavations were obtained at the 3 and 9 o’clock positions of the midperipheral iris. To decrease the rate of the postoperative complication of corneal endothelial cell loss, appropriate ACD and no history of lens dislocation should be checked before operation. Follow-up is required to monitor the endothelial cell count and changes in location of IOL. Another study has reported the long-term complications of iris-claw–supported AC-IOL implantation in a patient with MSP who developed corneal decompensation and chronic angle-closure glaucoma 10 years later. In addition, there is a risk of iris chafing, pigment dispersion, and chronic inflammation after iris-claw–supported AC-IOL implantation.

MANAGEMENT OF SECONDARY GLAUCOMA
Secondary glaucoma is the primary cause of visual loss in patients with MSP. There are some surgical options for glaucoma in MSP, including lensectomy, goniosynechialysis, trabeculectomy, drainage implants, or a combination of these procedures. Lensectomy plays an important role in the treatment of angle-closure glaucoma caused by spherical lens. Rao et al. found that lensectomy is effective in controlling IOP without antiglaucoma medications in 69% eyes with spheroaphakia and secondary glaucoma at 1 year and 51% at 5 years postoperatively. Moreover, 40% eyes need antiglaucoma medications, and only 7.7% eyes need glaucoma surgery for IOP control postoperatively, which might be associated with developmental angle anomaly. Therefore, if MSP was is found with developmental angle anomaly, lens removal alone is not enough. Satana et al. reported that a 1-year-old girl with MSP accompanied by developmental angle anomaly was successfully treated with a combination surgery consisting of pars plana lensectomy and goniotomy. Trabeculectomy achieved good results in the treatment of secondary glaucoma in MSP, whereas postoperative shallow AC is a common complication. Nearly half of the eyes require lensectomy during the follow-up. Higher IOP and larger cup-to-disc ratio at presentation are risk factors of poor glaucoma control after lensectomy. Goel et al. recommend lensectomy, vitrectomy, and transvitreal ciliary body photocoagulation as the primary treatment for glaucoma in MSP.

The diagnosis of MSP is difficult. The morphological characteristic determination and genetic analysis can help
the diagnosis. Because of the particular shape of the spherical lens and weakness of zonular fibers, MSP and its complications often bring difficulties in treatment. Conservative treatment can be used in early management, whereas surgery should be arranged when serious complications occur. A variety of operations can be performed. Lens aspiration or lensectomy is the main choice to remove the lens. After that, IOL implantation is required. IOL implantation includes different methods, including SF IOL, PC IOL with CTR and CTS, and AC IOL implantation. Sutured SF IOL and sutureless SF IOL have been widely performed in patients with MSP. However, long-term complications should be noticed in sutured SF IOL implantation, such as suture rupture. Long-term post-operative complications in sutureless SF IOL implantation still need further observation. PC IOL implantation is difficult to perform because of the small capsular bag and weak zonular fibers. Therefore, CTR and CTS are required to help stabilize the capsular bag. There are two types of AC IOL, including angle-supported AC IOL and iris-claw-supported AC IOL implantation. However, both of them have the risk of corneal endothelial cell loss. The choice of AC IOL implantation in MSP needs careful consideration.

REFERENCES


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Ophthalmic Photographers’ Society Exhibit, May 2019

Category: Fundus Photography, Normal—3rd Place

NERVE COLOBOMA

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