A 42-year-old patient presented with loss of visual acuity in the right eye (OD) that she has had for approximately one year. She was diagnosed with lens subluxation in the OD. She has myopia magna and has been using contact lenses since she was 15 years old. Her mother has Marfan syndrome, but the patient does not have any signs of this disease on full physical examination. Six months previously, she had an episode of intense ocular pain with high intraocular pressure. This was treated with YAG laser iridotomy and topical ocular hypotensive agents (timolol 0.5%, 1 drop every 12 hours). She has not had any subsequent episode of ocular pain, but she continues to use ocular hypotensive drops. Surgical intervention has not been proposed by her ophthalmologist, who suspects amblyopia in the OD.

Refraction by ophthalmic examination in our clinic:
CDVA: OD: +8.5 −2.25 × 160 = 0.4 (diplopia); OS: −12 −1.75 × 10 = 0.6.

Anterior biomicroscopy:
OD: Clear cornea. Inferior lens subluxation. Shallow anterior chamber depth. Inferior laser iridotomy (Figure 1); OS: Shallow anterior Chamber depth. No phacodonesis.

Intraocular pressure:
OD: 18 mmHg (timolol 0.5% 1/12 h); OI: 14 mmHg.

Fundoscopy: OD: Myopic choroidosis OU. Cup-to-disc ratio: 0.4 in OD and 0.3 in OS.


Endothelial cell count: OD: 653 cells/mm²; CV: 28%; OS: 2,226 cells/mm² CV: 35% (Figure 2).

Biometry: OD: AXL: 27.19 mm, Km: 42.56, ACD: 2.08 mm, LT: 4.35 mm (not reliable measure); OS: AXL: 25.70 mm, Km: 42.43, ACD: 2.18 mm, LT: 5.01 mm.

Ultrasound biomicroscopy (UBM) (Figure 3).

What would be your diagnosis?
Are these cases common in family members of patients with Marfan syndrome?
What type of surgery would you perform in the OD? Would you use only one type of surgery or several?
How would you manage the ocular hypertension?
How would you manage the endothelial cell situation?
What type of lens would you implant?
What calculation would you use?
What would be your residual refractive goal?
What would be your implantation site of choice?
What would you do with the left eye?
This is a patient with bilateral microspherophakia. Microspherophakia is a malformation of the lens, normally bilateral, in which the lens is smaller than normal and is spherical, with increased anteroposterior thickness and increased curvature in both the anterior and posterior aspects. Microspherophakia is associated with hypoplasia and zonular apparatus failure, but is not clear if the spherical shape of the hypoplastic lens is due to lack of zonular traction or if the zonular fibres are hypoplastic because the lens is small.

Microspherophakia can present without other ocular or systemic manifestations. Its mode of inheritance is generally recessive autosomal or it can be associated with systemic diseases, including Marfan syndrome, Weill-Marchesani syndrome, or other ocular malformations, such as iridocorneal dysgenetic syndromes, such as Peter's anomaly or Axenfeld-Rieger syndrome. Isolated microspherophakia is caused by a homozygotic LTBP2 gene mutation (13q24.1-q32.12)\(^1\).

Given the patient's family history, the differential diagnosis of this patient must include Marfan syndrome. To diagnose Marfan syndrome relying exclusively on the ocular findings, one major criterion (lens subluxation) and at least two minor criteria (increased axial length, abnormally flat anterior corneal surface or poorly developed iris with hypoplasia, eccentric pupil or problems with pupil dilation). Lens subluxation in Marfan syndrome occurs in two-thirds of patients, it is generally supero-temporal and normally bilateral and asymmetric. In microspherophakia, the lens generally dislocated downwards, unlike Marfan syndrome in which lens displacement is upwards.

The surgical options in lens subluxation are the following: (a) intracapsular extraction with anterior vitrectomy; (b) lensectomy and pars plana vitrectomy; and (c) extracapsular extraction with phacoemulsification using mechanisms that fixate the capsular bag (capsular rings, Cionni ring, anchoring systems). The latter option is the least traumatic, but it can only be used when the surgeon is sufficiently sure that the remaining zonular fibers will allow for a safe intervention and good long-term intraocular lens (IOL) stability. The IOL implanted will depend on the technique used for extracting the lens and could be: (a) in-the-bag IOL; (b) sulcus-fixed IOL normally sutured to the sclera, or fixated using biological glue and scleral tunnels; (c) pre or retro-pupillary iris-fixed IOL; or (d) angle-supported anterior chamber IOL.

In the case discussed here, in the right eye I would perform an intracapsular extraction with anterior vitrectomy (if necessary) using retentive viscoelastics to protect the corneal endothelium as far as possible. I would use an iris-fixed IOL (Artisan\textsuperscript{\textregistered} Aphakia lens), placing it in a retro-pupillary position to keep it as far away as possible from the corneal endothelium and to minimize endothelial loss, which is already considerable in this patient's right eye. The Artisan\textsuperscript{\textregistered} Aphakia IOL has already demonstrated long-term stability in eyes with insufficient capsular support, in both the prepupillary and retro-pupillary positions\(^2\).\(^4\).

For calculating the IOL for the right eye, in which the lens subluxation is affecting the visual axis (hypermetropic refraction), I would use IOLMaster immersion ultrasound biometry, which the biometric technique I use in normal eyes. In the right eye, with its axial length of 27.19 mm, IOL can be calculated with a third generation formula, such as SRK-T or Hoffer Q. I would recommend a value of 116.8 for the A constant of the Artisan\textsuperscript{\textregistered} Aphakia IOL in the retro-pupillary position. The aim would be to achieve a residual myopia of −1.50 diopters. Logically, this would affect the approach to be taken in the contralateral eye to avoid diplopia due to aniseikonia, in view of the patient's myopia magna. The patient could be temporarily managed...
with a contact lens in her left eye, but I would insist on carrying out a similar surgical intervention in the left eye as in the right, because there is a high risk that that eye will have a similar pupillary block as occurred in the right. It should be taken into account that, for an eye such the left eye in this case, with an axial length of 25.70 mm, a very shallow anterior chamber of 2.18 mm indicates anterior dislocation of an already thick lens (5.01 mm), so this eye would need surgical intervention. This would also involve intracapsular extraction with or without anterior vitrectomy and retropupillary implantation of an Artisan® Aphakia IOL. While the patient is waiting for surgery, laser iridotomy would be essential to reduce the risk of pupillary block.

Initially, I would not undertake any type of antiglaucomatous surgery, since presumably the removal of the lens dislocated towards the anterior chamber and anterior vitrectomy (if necessary) would be sufficient to deepen the anterior chamber and provide a clear hypotensor effect. If necessary, filtration surgery or canalicular rehabilitation could be carried out at a second stage: non-perforating deep sclerectomy or canalooplasty, respectively. These techniques must always be performed without vitreous in the anterior chamber. Perforating filtration surgery in the form of trabeculectomy or Express™ device implantation may also be a good alternative.

The mechanism by which microspherophakia causes glaucoma is generally anterior lens luxation with permanent or intermittent pupillary block and secondary angle closure. The lens may also dislocate towards the vitreous cavity. When the lens dislocates towards the anterior chamber, it closes the cameralar angle, narrows the anterior chamber and may cause critical pupillary block and acute glaucoma. Glaucoma is a common cause of blindness in microspherophakic eyes, so it must be treated actively and prevented, if possible. The acute glaucoma presented by this patient, together with the lens possibly coming into contact with the cornea, could be the reason for the low endothelial cell count in the right eye.

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In patients with Marfan syndrome, superior lens subluxation occurs in around 85% of the cases, although inferior subluxation is not unknown. The factor complicating the surgical decision in this case is the severe endothelial cell loss presented by the patient, which is an unusual problem in the planning of surgery in a young subject with subluxation. This significant endothelial cell loss is probably related with the acute episode of glaucoma, which must have involved severe corneal edema.

In view of the patient’s age, such severe endothelial cell loss will probably lead to corneal decompensation over time, even though surgery may not be necessary. Thus, the big question in this case is if endothelial transplantation should be carried out at the same time as lens surgery or if it should be done in a second stage.

a) Lens surgery

If the endothelial cell loss were less (>1,000 cells/mm²), I believe that the best approach would be for an expert vitreous surgeon to carry out pars plana lensectomy, followed by implantation of a retro-iridian Artisan® lens. However I would rule out this approach if the patient, due to her myopia, showed a spherical equivalent between +1 and −2 diopters in aphakia, in which case I would probably recommend the aphakia.

However, as an anterior segment surgeon, I would always prefer, as far as possible, to keep the anterior chamber compartment separate from the vitreous, so my recommendation would be to first carry out phacoemulsification after implanting a Cionni ring with two sutures at 6 and 12 o’clock and then to insert an open C-loop intraocular lens (IOL) in the sulcus, capturing the optic disk if possible through the continuous circular capsulorhexis (CCC), or if this is impossible, above both capsules.

This is complex surgery, but with protection with dispersive viscoelastic and a lens that should be soft, given the patient’s age, this would be my first choice.

In my opinion, the calculation of the IOL is not so critical, given the case. I would use a formula that does not take into account the anterior chamber depth in the calculation, probably the SRK-T, aiming for −1 diopter.

b) Corneal surgery

Our current proposal for this patient would be to carry out a corneal endothelium transplant (DSEAEK), but we would have to evaluate if this should be done at the same time as the lens surgery, or in a subsequent intervention. In this case, the possibility of endothelial detachment may be less if surgery is performed in two stages. We should remember that she has already had an inferior iridotomy.
The inconvenient aspect of the option of leaving the patient aphakic is that the DSAEK is greatly complicated by the gas, as the two chambers are not compartmentalized. For this reason, this would be an option only if we think that there is a good chance that the cornea will not end up decompensated, but this does not seem to be very likely here.

To conclude, my clinical recommendation would be the following:

1. **Lens surgery, phacoaspiration with suturing of the bag with a Cionni ring in the sulcus and sulcus-fixated open C-loop IOL implantation, capturing the optic disk through the CCC.**

2. **Depending on the progression of the cornea, carry out DSAEK 5-7 days after lens surgery, or possibly longer, depending on corneal transparency.**

3. **Continue with topical hypotensor treatment, monitoring intraocular pressure stability before undertaking DSAEK, if permitted by corneal transparency.**

4. **I would maintain the contralateral eye with a contact lens, or if this is intolerable, propose an iris-sutured IOL implant, probably an Artisan®.**

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The patient has been diagnosed of lens subluxation. Ectopia lentis or lens subluxation can occur with or without associated systemic disorders. Thus, in the pathogenesis of lens subluxation as the only genetic alteration in a patient with family history, there might be a genetic mutation that could be associated with Marfan syndrome or Weill Marchesani syndrome. However, she could also present a simple ectopia lentis, ectopia lentis et pupillae, Ehlers Danlos syndrome, homocystinuria, or sulphite oxidase deficiency. So we cannot affirm that the lens subluxation is associated with other syndromic characteristics.

In this patient, the lens subluxation is causing instability and refractive changes that require surgical intervention.

The patient’s first generation family history of Marfan syndrome might explain the monolateral lens subluxation, although none of the other defining symptoms of Marfan syndrome are present. Moreover, the patient presents inferior subluxation, while in Marfan syndrome, subluxations tend to be superior and symmetrical. In diagnosing the patient, we can also take into account the fact that she presents all the ocular criteria, including myopia magna and glaucoma, but she does not have any of the systemic, vascular or dermatological features typical of Marfan syndrome.

The patient had acute glaucoma that was resolved with YAG laser iridotomy. However, she is still using beta-blocker treatment to control intraocular pressure. Accordingly, chronic angle-closure glaucoma could be suspected, as suggested by the need for beta-blockers for controlling pressure, in addition to the asymmetrical intraocular pressure in the contralateral eye. In the future, this asymmetry will require close monitoring to look out for even the slightest change.

On the other hand, the refraction in the right eye suggests that the patient does not have severe amblyopia, although significant anisometropia is observed, which, if not resolved, could cause problems, so this is another issue that must be taken into account in this case.

It is worth remarking that the patient has a very shallow anterior chamber depth (ACD) in the left eye, while the axial length and Km are similar. This would be another reason for using latest generation formulae which would allow the inclusion of values such as ACD and lens thickness, or alternatively the IOL power could be determined using ray tracing systems.

If possible, the surgical approach in this case would be femtosecond-assisted phacoemulsification with a device that would allow us to perform a non-centered capsulorhexis. It is important to avoid the use of ultrasound energy during phacoemulsification, and to reduce significantly the number of surgical maneuvers required to eliminate the nucleus, and thus preserve the zonular fibers as much as possible.

This technique would also permit a significantly lower increase in intraocular pressure during the procedure. We would use the shield technique described by Steve Arshinoff, consisting of a layer of dispersive viscoelastic that would protect the endothelium, and a central layer of cohesive viscoelastic for performing the central maneuvers, although this would not be necessary if capsulotomy has been performed with laser. During the irrigation and aspiration phase, the bottle must be lowered to prevent the fluids affecting the endothelium during the surgery. We would then implant a three-piece monofocal in-the-bag lens with Cionni ring fixation or similar for the appropriate positioning of the bag-lens complex.

If irreversible endothelial cell decompensation should occur, we would recommend carrying out DMEK or DSAEK in a second intervention.

Another surgical possibility would be to reduce as far as possible any manipulation in the anterior chamber by carrying out pars plana vitrectomy with lensectomy and implantation of a phakic iris-sutured retropupillary lens.

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The mother’s history of Marfan syndrome would suggest that the patient may have an incomplete expression of the same syndrome, since no systemic signs of the disease are present. This should be confirmed with a genetic study to determine if there is an FBN1 gene mutation on chromosome 15. This could be useful for defining a clinical correlation with phenotype and appropriate treatment.

Ectopia lentis and family history are two main criteria in the diagnosis of Marfan syndrome, along with a tall, slim figure, long limbs and arachnodactyly, chest deformities and scoliosis and possible cardiac complications, such as mitral valve prolapse and aortic elongation that are the main cause of death in this disease entity.

In addition to the family history, lens subluxation and myopia magna (minor criteria) are common in these patients, who also often present other ocular complications, such as retinal detachment, strabismus, glaucoma, cataracts, iris abnormalities, microspherophakia and corneal flattening.

This patient had a previous episode of ocular hypertension secondary to pupillary block which was managed effectively and resolved with YAG-laser assisted cataract surgery using a fluid-filled interface. However, the patient’s history of Marfan syndrome would suggest that the patient may have an incomplete expression of the same syndrome, since no systemic signs of the disease are present. This should be confirmed with a genetic study to determine if there is an FBN1 gene mutation on chromosome 15. This could be useful for defining a clinical correlation with phenotype and appropriate treatment.

1. Lens phacoemulsification:

Evaluation should be made whether to use general or loco-regional anesthesia, depending on the criteria and experience of the surgeon and patient collaboration. Topical anesthesia is ruled out due to the high risk of complications, the length of the surgery and because it would prevent the performance of scleral surgery for ring fixation or IOL scleral fixation, should it be required.

Two scleral incisions would be made at 12 and 6 o’clock for insertion of a Cionni ring.

Incisions: first we would carry out microincision surgery as it is easier to make the incisions in the opposite area to the detachment, to avoid vitreous traction. In this case, as the subluxation is superior, we would make the principal incision in the temporal zone and the auxiliary incision as nasal as possible. Alternatively, we would enter laterally, making a lower temporal incision, which would be the main incision for a skilled surgeon, and the other in the upper temporal zone. Making a microincision would make it easier to switch to pars plana lensectomy, if necessary.

We would use dispersive viscoelastic to cover the subluxation area, offering good corneal endothelial protection. This would have to be injected repeatedly during emulsification if the nucleus turns out to be hard, although this is not expected, given the age of the patient.

If any anterior vitreous is present, this would have to be removed by anterior vitrectomy.

Capsulorhexis: this is perhaps the most difficult step. Its success will determine whether we continue with the surgery as planned or switch to pars plana vitrectomy. Using a cystotome, we would begin in the side furthest from the subluxation, continuing with a microincision capsulorhexis forceps. The capsulorhexis would be fixed with iris claws in at least two superior points, followed by careful and complete hydrodissection.

Insertion of the capsular ring: two options are available: a conventional sclera-sutured ring or a...
Cionni ring. In the latter case, we would have to extend the incision by at least 2.4 mm to allow the insertion of the scleral fixation branches of the ring.

Nucleus phacoemulsification can be carried out with the dislocated nucleus in the anterior chamber, but this is not advisable due to the condition of the endothelium. If necessary, the endothelium should be repeatedly protected with dispersive viscoelastic.

The cortex would then be aspirated.

Implantation of intraocular lens (IOL): my choice in these cases is a 3-piece IOL with a 6 mm optic and PMMA haptics fixated in the zonular dialysis zone.

2. Pars plana lensectomy

If surgery is impossible or some complication occurs, it would be advisable to perform a pars plana lensectomy with IOL scleral fixation with PMMA haptics, or else suturing, or even better, scleral tunnel fixation.

The IOL of choice is an aspherical hydrophobic lens with PMMA haptics. The calculation would be made using the SRK-T formula, with a refractive goal of between −0.75 and −1.00 D.

For the contralateral eye, I would propose carrying out phacoemulsification with ring implantation, with the same type of IOL as in the OD, to prevent any future subluxation of the IOL/bag complex and making scleral fixation easier. In this case, the refractive goal would be the same.

Regarding the glaucoma in the OD, I would continue with the medical treatment as long as it remained controlled, since, if the subluxation is resolved and an iridectomy is in place, it should not get any worse, unless open-angle glaucoma develops in the future, which would not be uncommon in eyes of this kind.

If there is corneal decompensation due to the loss of cell density, which would not be unusual after such complicated surgery, I would propose a DMEK to be performed in a second intervention.

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This is a case of unilateral inferior lens subluxation, with a history of angle block caused by a shallow chamber, associated with lens subluxation1. It can be seen in the tomography that the subluxation with anteversion of the lens has caused a loss of endothelial cells in the eye, caused by episodes of hypothalamia2. Although the most common cause of unilateral subluxation is injury, the high myopia and family history of Marfan syndrome give some clinical orientation, since it may be that the syndrome is presenting in a rather late, atypical form, the more common manifestation being bilateral, asymmetric temporal superior ectopia lentis. Ectopia lentis is the most common ocular indication of Marfan syndrome (76%)3.

Marfan syndrome is inherited in a dominant autosomal form, with 50% chance of symptoms appearing. It is associated with a fibrillin 1 or ADAMTSL4 gene mutation, the latter being related with isolated ectopia lentis5. Genetic testing could confirm this mutation and would help in determining the diagnosis.

Lens surgery would be required in the right eye for the subluxation. In view of the condition of the endothelium, we would choose femtosecond laser-assisted lens surgery, which could help achieve a well-centered capsulorhexis, as mentioned by Schultz et al, although this is not always possible if the lens is very displaced6. In any case, femtosecond laser permits a faster procedure with less use of pulsed ultrasound energy7, minimizing endothelial cell damage8. Although the patient has a history of angle closure, which is currently controlled with iridotomy and timolol 0.5% eye drops, we would carry out the lens surgery separately, with close post-operative monitoring of intraocular pressure and endothelial cell count.

New phacoemulsification techniques and careful surgery mean that the rate of loss of endothelial cells is less than 11.5%5. Even so, with the patient’s current endothelial cell count, early endothelial decompensation is a real possibility, and in this case, endothelial transplantation should be performed.

As for the type of lens, if we manage to stabilize the capsular bag with a Cionni capsular ring, indicated for displacements greater than 150°9, we would implant a monofocal lens-in-the-bag or a toric monofocal lens, depending on the corneal astigmatism. If this is not possible, we would use an iris-claw lens fixed in the posterior aspect of the iris10. The aim is always to achieve emmetropia. Given the high risk of retinal detachment, a full periphery study would be required.

Since the other eye has myopia magna, there will be significant anisometropia after surgery. We rule out phakic lens implantation due to the insufficient length of the anterior chamber. We would propose carrying out clear lens surgery with implantation of a monofocal or toric monofocal lens, depending on corneal astigmatism, with the aim of achieving emmetropia. The need for optical correction for near sight after surgery would be explained to the patient.
If the patient rejects this option, correction with a contact lens would be necessary and prophylactic iridotomy would be required to prevent capsular block caused by a shallow chamber.

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