A Case of Pediatric Ectopia Lentis: Systemic Associations and Management Options
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ABSTRACT

Background: Ectopia lentis is a subluxation, displacement, or malposition of the crystalline lens of the eye. It can be a congenitally inherited condition or it can be acquired and there are several etiologies. Systemic conditions should be considered when a patient presents with ectopia lentis of unknown etiology, including Marfan Syndrome, Weill-Marchesani Syndrome, Ehlers-Danlos Syndrome, and homocystinuria. Surgical management of ectopia lentis is often indicated, as potential benefits outweigh possible risks and complications secondary to surgical intervention. However, the condition can also be non-surgically managed. It is crucial that the optometrist first makes an accurate diagnosis in these patients, then appropriately refers them to other professionals for further consultation and management, and finally continues to monitor the visual development of these patients over the course of their lives.

Case Report: A three-year-old black male presented with bilateral lens subluxation of unknown etiology, in addition to high myopia, strabismus, and decreased visual acuity. He is being managed for refractive amblyopia and strabismus and was referred for a consultation for surgical management of ectopia lentis.

Conclusion: Ectopia lentis has numerous etiologies and a variety of management considerations that optometrists need to be cognizant of when they encounter a pediatric patient with this condition.

INTRODUCTION

Ectopia lentis is a subluxation, displacement, or malposition of the crystalline lens of the eye. It can be congenital or acquired at any point during one’s lifetime. Patients with ectopia lentis will typically present with symptoms consistent with decreased visual acuity. They may complain of blurry vision, which can be variable due to any movement of the ectopic lens. Monocular diplopia may also be present. An ectopic lens will be evident during ocular examination, but other signs of the condition include high refractive error or irregular astigmatism, irregular red reflexes, and phacodonesis, or a trembling, vibrating lens with eye movement. There are a wide variety of etiologies for this condition. When a patient presents with ectopia lentis, it is prudent for the optometrist to consider all the possible etiologies and systemic conditions associated with the ocular presentation because it will aid in forming differential diagnoses and ultimately aid in the management of the patient.
Etiology

Ectopia lentis can occur both with and without systemic associations. If the condition is present without a systemic association but another family member also has ectopia lentis, it is often considered familial. If there is no positive family history of the condition and it is without a systemic association, it is commonly referred to as simple ectopia lentis. More frequently, however, an underlying systemic condition can be uncovered that causes this condition. Common among the systemic associations are Marfan Syndrome, homocystinuria, Ehlers-Danlos Syndrome, and Weill-Marchesani Syndrome. These conditions all result in an inability of the zonules to hold the crystalline lens in its proper position. There are genetic variations that are associated with each of these conditions. What many of the genetic variations have in common are defects in microfibril assembly necessary to create the zonules holding the crystalline lens in its proper position. Congenital ectopia lentis can be inherited with or without an association with one of these conditions. If ectopia lentis is not congenital, it can be acquired. Most often, it is acquired secondary to trauma. It can also be iatrogenic, if zonular dehiscence is induced during cataract surgery. Other secondary causes include high myopia and buphthalmos, pseudoexfoliation syndrome, cataracts, and some tumors. Ectopia lentis is almost always bilateral if there is a systemic association, but can be asymmetric in some cases of Marfan Syndrome. Acquired cases of ectopia lentis such as those due to trauma are more likely to be unilateral. The epidemiological statistics of ectopia lentis will vary depending on the underlying etiology of the condition. The treatment and management of these patients can also vary depending on the etiology.

Regardless of the cause of ectopia lentis, there are serious visual consequences of its presence. There are refractive error changes that will occur when the crystalline lens loses its zonular support and no longer occupies its proper anatomical position. Often, non-traumatic ectopia lentis is revealed in childhood. This is important to note because there are risks for the patient’s visual development during this critical period. Ametropia and any changes in the amount of refractive error are risk factors for the development of amblyopia. The degree of functional vision and how patients can capitalize on their best level of vision needs to be taken into account for appropriate optometric management.

CASE REPORT

A three year old black male presented with his mother to the University Eye Center for his first comprehensive eye exam. Chief complaints were an eye turning out, squinting with both eyes, and holding objects very close to see them. His mother went on to explain that the patient would hold objects close to one eye, usually his right, and would often close one eye when looking at an object. He had no known medical conditions, did not take any medications, and had no known allergies. Pregnancy was reported to be full term with no complications at birth and his birth weight was over seven pounds. Development was reported to be normal as well, as the patient walked around 15 months and talked around 12 months of age. His mother reported that the pediatrician did not express any concerns regarding an eye turn or any ocular problems, but recommended an eye exam given her stated concerns.

Family history was given by the patient’s mother. She reported that she has high hyperopia and felt that her son was acting similarly to the way she did as a child. She also reported that she has subluxated lenses, but was unable to provide any further information regarding her ocular condition. She denied having surgery on either eye. The family history was not significant for any other ocular or medical conditions.

At the initial exam, unaided distance visual acuities were 20/150 in the right eye and
20/350 in the left eye with HOTV matching. Extraocular motility was full in both eyes, but with poor fixation and supportive head and body movement. There was a >40 prism diopter intermittent left exotropia present at both distance and near with occasional alignment noted. No random dot stereogram shapes or Wirt Circles were appreciated with stereopsis testing. Pupillary testing was normal. The Bruckner reflex was unequal, with the left eye bright and white relative to the right. Confrontation visual fields were grossly full. Retinoscopy revealed -17.00sph in the right eye and -14.00sph in the left eye but was variable and with a very dull reflex in each eye. Anterior segment evaluation was initially unremarkable, including normal corneal diameters. However, upon dilation, it was noted that lenses were subluxated inferiorly in both eyes. It was difficult to assess the posterior pole given the lens dislocation in addition to poor patient cooperation at this point during the exam. He was given a spectacle prescription of -15.00sph OU, which was estimated based on the fluctuating reflex caused by on intraocular lens movement. Ultimately this patient was referred for a consultation in the Pediatric Ocular Disease Unit. The aided visual acuity, binocular alignment, fixation abilities, and lens condition and position would all be re-assessed.

The consultation was performed within the week, and distance acuities with correction in a trial frame were 20/100+ in the right eye and OS 20/300 in the left. There was only a mild improvement in the aided acuity, likely secondary to some degree of refractive amblyopia in addition to any inherent image degradation or distortion due to lens movement. The dilation at this exam provided slightly better posterior segment views due to more complete dilation and improved patient cooperation. It was determined that the lenses were subluxated inferior and temporal in each eye. The patient was then referred to an ophthalmologist for evaluation under anesthesia to better assess ocular health and determine if surgical removal of both crystalline lenses would be appropriate.

The patient’s mother was extensively educated on the importance of full-time spectacle correction for her son. Additionally, a strong emphasis was placed on consultation with an ophthalmologist regarding possible surgical management for the patient’s condition. Regardless of whether surgical intervention was deemed appropriate, the patient was going to need visual rehabilitation in addition to the spectacle correction to address amblyopia and strabismus. The patient’s mother was informed that occlusion therapy as well as vision therapy would be indicated and started after the results of the surgical consultation were obtained. Despite this, there was relative non-compliance. The patient was seen in the Pediatric Ocular Disease clinic for follow up four months later and while glasses had been ordered, they had not been picked up and the patient remained uncorrected. An appointment for the consultation with the ophthalmologist was never scheduled. Examination findings, including best-corrected visual acuity, refraction, and position of the subluxated lenses in each eye, were stable. Again, the appropriate referral was made to the ophthalmologist. At this point, no direct referral was made to the pediatrician, but the possible hereditary etiologies were discussed with the patient’s mother. Given the possible systemic conditions serving as an etiology for lens subluxation and their possible adverse effects on overall systemic health, a more thorough systemic work-up should have been emphasized even further.

One year after his initial presentation, he presented to the clinic again for follow up. At this time, he had obtained his spectacle prescription and had been wearing them full-time for the past nine months. However, he still had not been to the referred ophthalmologist for consultation. At this point, the patient was in kindergarten and his mother noted that he was having difficulty learning letters,
and she potentially attributed this to his poor vision. A variable head tilt was noted during acuity testing possibly because the patient was attempting to align his eyes or even his intraocular lenses in a manner that allowed him to look through a more clear visual axis. A constant alternating exotropia of 45 prism diopters was noted at distance and near with right eye fixation preference. Stereopsis was tested with random dot stereograms and the Lang stereotest, but the patient was not able to appreciate any of the shapes. The lens subluxation remained stable in each eye. B-scan ultrasonography (See Figure 1) was performed due to poor visualization of the fundus at this exam. It revealed clear vitreous with a flat and intact retina in both eyes. The patient was yet again referred to an ophthalmologist and it was confirmed that he was scheduled for a surgical consultation. He was to return in three months for further optometric management. Unfortunately, he has not been back to our clinic, so the results of the consultation, if it was attended, are unknown.

DISCUSSION
Causes of Ectopia Lentis with Systemic Associations

Since ectopia lentis can present both with and without systemic associations, it is important to keep the systemic associations in mind as we make differential diagnoses for the etiology. These patients may present for eye care first, and may require additional medical evaluation and treatment if they are found to have a systemic cause underlying ectopia lentis. The proper referrals need to be made after the eye examination is complete, especially if there is high suspicion of any of the common systemic associations. The most common systemic condition associated with subluxated lenses is Marfan Syndrome, and others include Weill-Marchesani Syndrome, Ehlers-Danlos Syndrome, and homocystinuria.

Marfan Syndrome is a connective tissue disorder that has an effect on many systems in the body, notably the ocular, cardiovascular, and skeletal systems. It can be autosomal dominant in inheritance with the presence of a mutation of the FBN1 gene, coding for a fibrillin protein. These patients will often have a positive family history of the Syndrome. Marfan Syndrome can also occur from a spontaneous mutation. Overall, it is estimated to occur in 1 in 5000 people. Lens subluxation occurs in about 50-80% of patients with Marfan Syndrome. It is a main feature in the established guidelines for diagnosing Marfan Syndrome, known as the Ghent criteria. There is a high degree of clinical variability across all ocular and systemic manifestations of Marfan Syndrome. While some signs of the Syndrome...
can be detected early, the formal diagnosis is not usually made until the patient is around 20 years old.\textsuperscript{7}

Marfan Syndrome has other ocular associations that can be useful to aid in diagnosis. A study showed that mean keratometry values were significantly lower in patients with Marfan Syndrome than in control eyes.\textsuperscript{8} Similarly, the mean corneal thickness at the thinnest point was significantly lower in patients with Marfan Syndrome than in control eyes. Patients with ectopia lentis and confirmed Marfan Syndrome also demonstrated significantly higher amounts of corneal astigmatism. Ultimately, there are tests that can be performed on patients in-office to further support Marfan Syndrome as a differential diagnosis for the patient, requiring a referral to a pediatrician or primary care physician.

Skeletal abnormalities are common in Marfan Syndrome, including overgrown long bones of the limbs. Typical facial characteristics include down slanting palpebral fissures and enophthalmia. Cardiac complications are an important cause of morbidity and mortality for these patients. Aortic root aneurysm, dissection, or rupture can have serious consequences. Mitral valve dysfunction is seen in about two thirds of patients.\textsuperscript{3} The patient in this case did not exhibit any of the typical characteristics of Marfan Syndrome upon gross observation, patient medical history, or family history.

Weill-Marchesani Syndrome is a more rarely occurring connective tissue disorder. Lens subluxation is a notable feature of this syndrome and can be due to a lack of microfibrils. The microfibrils are not present to properly form the zonules that support the lens.\textsuperscript{3} An additional ocular feature of Weill-Marchesani Syndrome is spherophakia, where the zonules are in fact present but they do not have the proper tension to support the lens due to this structural defect. The lack of support can cause a host of other complications, such as increased myopia, narrowing of the anterior chamber, formation of peripheral anterior synechiae, and pupillary block.\textsuperscript{9} These patients can have a range of joint problems and the function of cardiac tissue can also be negatively affected.\textsuperscript{3} Diagnosis typically relies on clinical findings, which in addition to lens subluxation, include short stature and joint stiffness. Molecular genetic tests can be performed to help confirm the diagnosis of Weill-Marchesani Syndrome in the presence of these clinical findings. The mean age of diagnosis of an ocular manifestation attributed to Weill-Marchesani Syndrome is 7.5 years old.\textsuperscript{10} There was no history of joint problems in the patient presented in this case, which moved Weill-Marchesani Syndrome lower on a list of differential diagnoses for ectopia lentis in this patient.

Ehlers-Danlos Syndrome has ocular manifestations that include not only ectopia lentis, but also myopia, keratoconus, and scleral fragility.\textsuperscript{3} In this syndrome, there is a mutation for type V collagen. This is required for fibrillogenesis. Other systemic findings in patients with Ehlers-Danlos Syndrome include joint hypermobility, easy bruising, and delayed wound healing with scarring. The overextensibility of the abnormal connective tissue can lead to lens subluxation as well as subluxation of other joints in the body.\textsuperscript{11} Children with Ehlers-Danlos Syndrome are often diagnosed based on clinical examination and family history. There is variability in the amount and degree of clinical manifestations, but children will often initially present with delayed motor development and joint instability.\textsuperscript{12} The patient in this case did not have any history of these types of systemic health complications, such as easy bruising or delayed wound healing, and this rare syndrome moved down on a list of differential diagnoses for the etiology of the patient’s subluxated lenses.

Patients with homocystinuria can also present with ectopia lentis. This rare metabolic abnormality can be inherited in an autosomal recessive pattern. Ultimately, it leads to
degenerative changes in the zonular fibers. The building blocks of these fibers are microfibrils, which are rich in half-cystine residues. If the homocysteine levels are elevated, there is loss of the structure of these proteins, which will therefore not support the crystalline lens. Other systemic manifestations of homocystinuria include developmental delays, intellectual disability, and skeletal or vascular abnormalities. Newborns can be screened for homocystinuria with a blood test, and then additional plasma or urine analysis is used to confirm the diagnosis. In patients who have homocystinuria, ectopia lentis is not usually present in infancy, and developmental delays may be the first notable abnormality prompting further assessment for the condition.

There are several underlying systemic disease processes that include ectopia lentis as one of their clinical manifestations. While all of them are rather rare, Marfan Syndrome is the most prevalent among the systemic associations discussed. While the patient in this case did not demonstrate any visible skeletal manifestations consistent with the Syndrome, it is still highest on the list of differential diagnoses regarding the etiology of the patient’s subluxated lenses. It is the most prevalent condition of those discussed and it is often not formally diagnosed until the patient is around 20 years old. The lens subluxation in this patient may very well be the first clinical manifestation of this patient’s systemic disease. The patient should be regularly followed by an optometrist or ophthalmologist for lens subluxation, refractive amblyopia, strabismus, and overall visual development. He also should be referred to a primary care physician, cardiologist, and orthopedist for baseline evaluations. These professionals can also monitor the patient over time to confirm or reject the tentative diagnosis as the patient develops.

Surgical Management

Often surgery is indicated for patients with ectopia lentis. Historically, this was considered a challenging surgery, with several intra- and post-operative complications. Zonular pathology and other peripheral retinal changes inherent to the anatomy of these eyes are predisposing factors for potential surgical complications. In the past, it was considered high-risk surgery and other more conservative approaches to management were taken. Today, the surgical approach is considered less daunting given the improvements in surgical techniques and developments in technology.

During the surgical evaluation, the degree of zonular loss is taken into consideration by the surgeon. If the ectopia lentis is associated with a certain systemic condition, there can be global weakness of the zonular fibers. Surgical techniques will vary given the state of the zonules at the time of the surgical consultation.

Surgical management for ectopia lentis can include lensectomy, thus leaving the patient aphakic and requiring optical correction post-surgery. An intraocular lens (IOL) can also be inserted to replace the crystalline lens. If this is the case, one of the goals of the surgery needs to be to stabilize the IOL and minimize intra-operative and post-operative complications.

With zonular compromise, it can be more difficult to secure an intraocular lens, so modifications can be made to traditional IOL placement. A capsular tension ring (CTR) may be used to promote capsular bag and IOL stability. A posterior chamber IOL can also be fixed to the sclera to promote security. An IOL can also be fixed to the iris and supported by the structures in the angle, either in the anterior or posterior chambers.

In one study of pediatric patients, 37 eyes with non-traumatic ectopia lentis underwent lens extraction surgery. An IOL was inserted with a capsular tension ring which was then sutured to the sclera anterior the capsular plane in the ciliary sulcus. No eyes participating in the study were left aphakic. The causes of the ectopia lentis in patients in this study varied. Most patients had Marfan Syndrome,
some had another systemic association causing ectopia lentis, some had inherited lens dislocation without systemic associations, and some had idiopathic lens dislocation. Many of the post-surgical eyes developed visual axis opacification of the IOL, which required additional surgical procedures for the patient to achieve clear vision. Additionally, in a small number of patients the IOL became dislocated, requiring additional suturing for stability. It was concluded, however, that this type of scleral-fixed CTR with an IOL can be safe and effective to use in children with ectopia lentis. This system provided adequate centration control of the IOL and a positive visual outcome.4

Another study evaluated children with hereditary lens subluxation and managed these cases with lensectomy and aphakic correction. The criteria used for surgical intervention included progressive subluxation of the lens with bisection of the pupil, best corrected visual acuity of 20/60 or worse at distance or less than J5 for near, and development of cataract that would interfere with daily visual functions. The average age of children at the time of surgery was 6.4 +/- 4.6 years. The study found that there was significant improvement in visual acuity post-operatively in all patients except those who had deep amblyopia preoperatively. Over eighty four percent of patients achieved 20/40 or better. Long-term post-surgical outcomes were measured, with IOP remaining stable for up to 19 years after surgery in some cases. One patient developed a peripheral retinal tear 12 years post-operatively, but the authors argued that this complication could have happened in an eye that did not have surgical intervention.16

Ectopia lentis due to Marfan syndrome poses a unique challenge due to the mutation in the fibrillin gene, which is present in several ocular tissues. The fibrillin is deficient in not only the lens capsule and zonules leading to ectopia lentis, but it is also deficient in the iris and sclera. If an IOL is secured to either of these tissues, further complications have been reported, including pupillary block, lens decentration, and retinal detachment.14 Some studies show that use of an IOL in these types of cases can be advantageous and lead to better visual acuity outcomes, as compliance with spectacles or contact lenses does not become an issue.14 However, further studies with long-term follow up results are needed to determine the safety of using an IOL in patients with ectopia lentis due to Marfan Syndrome.

Risks and Benefits of Surgical Management
A common complication of lens removal in pediatric patients is the development of glaucoma or ocular hypertension. Many studies have examined the frequency and prevalence of these conditions occurring after surgery secondary to a pediatric cataract. One evaluated pediatric patients undergoing cataract extraction and leaving them aphakic. It found that there was a high prevalence of ocular hypertension and glaucoma at the 5 and 10 year post-surgical state.16 Another study examined pediatric subjects with cataracts that underwent lensectomies without IOL implantation. It found somewhat of a threshold, where glaucoma was more common if the surgery was performed after the patient was 9 months old.17 This demonstrates the potential importance of early intervention to minimize a major sight-threatening complication.

The patient in the case presented also had high myopia contributing to his reduced vision. One method for treating high myopia in an otherwise unremarkable eye is by clear lens extraction. One study looked at the effect of this type of surgery on patients with high myopia and neurobehavioral disorders.18 Children with neurobehavioral disorders may be non-compliant with other management options for high bilateral myopia, such as spectacles or contact lenses. This leads to refractive amblyopia and the poor vision
can exacerbate any behavioral issues. Their visual attention and visual cues necessary for learning, recognizing others, and navigating around space will be limited. In the study, uncorrected acuity improved in all 26 eyes of the 13 patients. Myopic regression was noted in 69% of the patients at an average rate of -0.16D per year with younger age of surgery positively correlating to this change. The study discussed their low complication rate, making this procedure an effective option for improving visual function in these types of patients. In the patient case presented, this type of lensectomy may be considered.

Non-surgical Management

Despite potential difficulties of surgical management in cases with a systemic etiology, there are potential complications of deferring surgery. If the lens is dislocated, it has the ability to move around within the globe. This could cause an unusual change in refractive error, often with varying amounts of astigmatism. The lens could move forward, more anteriorly into the anterior chamber. This could lead to pupillary block with angle closure. When this occurs, the patient will have increased intraocular pressure and ultimately angle closure glaucoma. The lens may move backward, more posterior into the vitreous. This backward motion could cause dangerous traction on the retina. The lens proteins may also leak, causing inflammation in the posterior segment. These problems can often be treated, but prior surgical intervention may have prevented any unnecessary complications. Fortunately, the patient in this case did not experience any of these complications to our knowledge. However, it was considered extremely important to at least rule out the need for surgical intervention first in order to minimize any more serious sight-threatening conditions.

The optometrist must consider several other non-surgical means of managing a patient such as the one described in this case. The patient will clearly need continued optometric care to promote optimal visual development. In cases of refractive amblyopia, optical correction alone can improve visual acuity to a certain degree. From there, the patient should be prescribed some form of occlusion therapy as well as active in-office vision therapy. The young patient in this case would certainly need to improve acuity, fixation, and oculomotor control. In addition, his ocular alignment should be addressed. His binocularity can be developed and improved with anti-suppression or diplopia awareness techniques in addition to vergence activities. Based on the nature of ectopia lentis, patients diagnosed with the condition will likely have reduced or possibly non-existent accommodative abilities. If phakic, patients can work to improve the quality of their accommodative skills with therapy techniques and ultimately additional plus lens power at near may be beneficial.

Young patients with multiple factors affecting their visual performance may need special attention to their developing vision as they enter school. Optometrists managing these patients should advocate for services that can benefit the patient in the classroom, such as large print materials, preferred seating, or additional time for testing. A referral to a pediatric low vision specialist would also be critical to ensure that these types of patients maximize the level of vision that they do have. These doctors will be able to ensure that the patient can recognize people and objects, safely navigate through space, and successfully function in the educational environment. In addition to the best refraction and vision therapy, optical aids can be prescribed to these children to enhance their functional vision. A dome magnifier, for example, would be a simple and effective device for a child with low vision to use, as it sits directly on a page of text, is sturdy, and can be easily manipulated. Tablet devices can also be useful, as it is simple to magnify or zoom in on text or pictures. While there may be a team
of professionals managing different aspects of a complicated case, the optometrist will best understand how the patient is taking in, processing, and then using visual information. They will therefore play a critical role in addressing the visual needs of the patient to promote proper development and success in an academic setting.

CONCLUSION

Ectopia lentis has both several etiologies and several management considerations that optometrists need to be cognizant of when they encounter a patient with this condition. As health care professionals, optometrists need to consider possible systemic health associations with ectopia lentis and make the proper referrals to other specialized doctors. Surgical intervention for lens subluxation needs to be seriously considered and co-management with an ophthalmologist will be necessary. Pediatric patients with ectopia lentis need to be closely monitored, as their vision is still developing. They will be seeing the world differently regardless of the management option selected. Optometrists will need to re-assess these patients’ visual status regularly and manage amblyopia appropriately. Patients’ visual skills such as their oculomotor control and vergence abilities should also be assessed. These patients may be at a disadvantage in terms of their visual acuity, so optometrists should encourage high quality visual skills. Disease processes such as glaucoma are a serious complication for many of these patients, reinforcing the need for regular monitoring. Treating patients with ectopia lentis involves treating more than just their crystalline lenses, and they can be lifelong patients.

Disclosure

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