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CASE REPORT

Isolated Ectopia Lentis in Suspect of Weill-Marchesani Syndrome (WMS)

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Abstract

Introduction: The prevalence of Weill-Marchesani syndrome (WMS) is estimated to be 1:100.000 proportion of the population. Knowledge of the clinical and therapy of WMS is expected to improve the ability to diagnose this disease. In this case report, we will present a case of WMS in a tertiary hospital because our findings are rare and essential concerning the symptomatic treatment and visual rehabilitation. **Case Presentation:** A 7-year-old child presented with blurred vision in the left eye. The patient showed an abnormal facial appearance with short stature and brachydactyly on both hands. The patient had a history of Intracapsular cataract extraction (ICCE) surgery on the right eye with an indication of anterior lens subluxation. The patient then suffered aphakic glaucoma in the right eye after surgery. Anterior segment examination of the right eye found an aphakic lens, conjunctival sclerectasia, atrophic iris, and mid-dilation pupil. Anterior segment of the left eye found an atrophic iris and lens subluxation. From the clinical appearance and the ocular disturbance, such as brachydactyly and short stature, the patient was diagnosed with suspected WMS. The patient was treated with ICCE surgery on the left eye and micropulse transscleral cyclophotocoagulation (MP-TSCPC) surgery on the right eye. **Conclusion:** WMS is a rare disease. It is essential to make an early diagnosis of glaucoma and ectopia lentis in WMS patients because it will affect their vision.

Keywords: weill-marchesani syndrome (WMS); ectopia lentis; aphakic lens; refractory glaucoma; MP-TSCPC

Introduction

Weill-Marchesani syndrome (WMS) is a genetic disease that can be inherited through autosomal recessive and autosomal dominant traits. Another name for WMS is a microspherophakia-brachydactyly syndrome. This disorder is caused by a rare and generally inherited connective tissue disorder.[1] The prevalence of WMS is estimated to be 1:100.000 proportion of the population.[2]

Genetic mutations are the leading cause of WMS. The most common mutations were found in ADAMTS10 and fibrillin-1 (FBN1). The a disintegrin and metalloproteinase with thrombospondin motifs 10 (ADAMTS10) protein is essential for the extracellular matrix and is involved in the human eye, heart, and skeletal development. The FBN1 protein has been identified as a structural macromolecule that polymerizes micro-fibrils and helps provide resilience and flexibility to connective tissue. The a disintegrin and metalloproteinase with thrombospondin motifs type 1 motif 17 (ADAMTS17) protein can cause disorders associated with WMS by binding to the extracellular matrix.[3],[4]

An ectopic lens, short stature, brachydactyly, and stiff joints characterize patients with WMS. Spherofakia is caused by an abnormality in the zonular fibers, which causes an increase in the anteroposterior diameter of the lens so that the lens looks spherical. The lens's thickening causes the eye's anterior chamber to become smaller and the angle narrower. As a result of the relaxation of the zonules, the lens will tend to move forward, causing blockage of the pupil and an increase in intraocular pressure (IOP) so which causes glaucoma.[5]

Early detection and removal of an ectopic lens to decrease the possibility of pupillary block and glaucoma. Glaucoma surgery can include laser peripheral

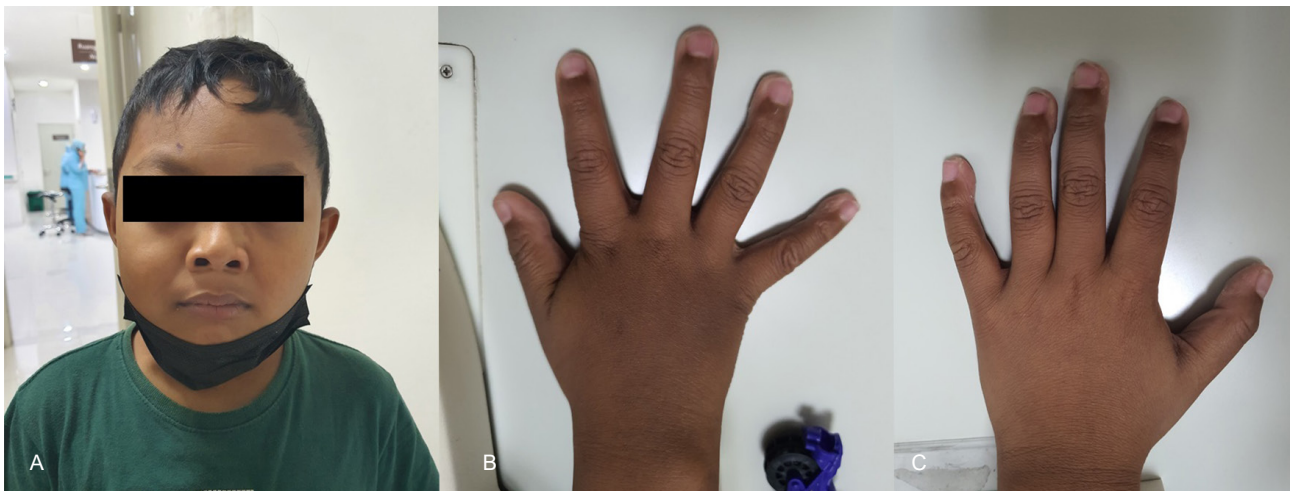

Figure 1. Patient clinical appearance. (A) Clinical appearance of the patient; (B) Brachydactyly on the right palm, and (C) Brachydactyly on the left palm.

iridectomy or iridectomy and trabeculectomy; medical treatment of glaucoma is complex because of the paradoxical response to miotics and mydriatics. Consider physical therapy for joint issues. Careful evaluation prior to anesthesia because of stiff joints, poorly aligned teeth, and maxillary hypoplasia. Treatment of cardiac anomalies per cardiologist.[2]

Knowledge of the clinical and therapy of WMS is expected to improve the ability to treat this disease. In this case report, we present a case of WMS in a network hospital because our findings are rare and essential concerning the symptomatic treatment and visual rehabilitation.

Case presentation

A 7-year-old Javanese boy complained of blurred vision in his left eye. The patient was 112 cm in height and 24 kg in weight. Blurred vision complaint was manifest since the patient fell from bike four months prior to the hospital visit. The patient's parents also complained that the patient had visual disturbance three years prior to the trauma. The patient had a history of the same complaint in the right eye and underwent intracapsular cataract extraction (ICCE) surgery on the right eye with the indication of anterior lens subluxation. The patient had aphakic glaucoma in the right eye following the surgery. The patient's physical appearance showed abnormal facial appearance and had short stature and brachydactyly (Figure 1).

On physical examination, it was found that the patient had right eye proptosis. Visual acuity of the right eye was 1/60 with a correction of S +8.00 became 1/10. Visual acuity of the left eye was 1/60 without correction. The result of the IOP examination of the left eye was 15 mmHg and the right eye was 25 mmHg. The patient got timolol maleate 0.25% eye drops twice a day in the right eye, tobramycin dexamethasone, sodium phosphate eye, drops six times a day in the right eye, and acetazolamide 125 mg three times a day orally. Examination of the anterior segment of the right eye found an aphakic lens, conjunctival sclerectasia, atrophic iris, and mid-dilation pupil. In the left eye, we found an atrophic iris and posterior lens subluxation (Figure 2). No abnormalities were found on posterior segment examination. From the complaints and physical examination, the patient was diagnosed with suspected WMS.

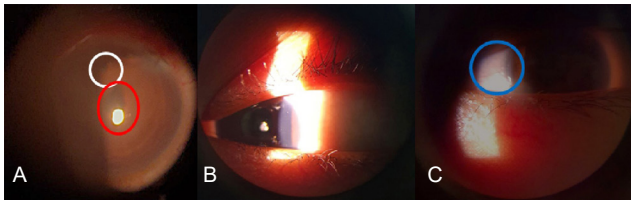

Figure 2. Anterior segment examination. (A) White circle: Post iridectomy and red circle: Irregular pupil; (B) Slit lamp examination of the left eye, and (C) blue circle: Sclerectasia.

The patient underwent ICCE surgery on the left eye with anterior vitrectomy and iridectomy (Figure 3). Furthermore, the surgery was continued with micropulse transscleral cyclophotocoagulation (MP-TSCPC) on the right eye, scheduled after the left eye's ICCE recovery period was completed. The selection of MP-TSCPC is due to refractory glaucoma, which had been found. After the ICCE surgery in the left eye, the patient was given timolol maleate 0.25% eye drops two times daily in the right eye, tobramycin dexamethasone, sodium phosphate eye drops four times daily in the left eye, levofloxacin eye drop four times, and paracetamol syrup 5 ml three times daily.

Post-ICCE surgery, the patient was followed for 15 days to assess the improvement and response to the surgery performed on the left eye. On the first day, the right eye visual acuity was 1/60, with lens correction of S +8.00 became 1/10. Left eye visual acuity was 1/60. The IOP of the right eye was 17 mmHg on timolol maleate 0.25% eye drop, and the left eye was 14 mmHg.

In the second follow-up (one week later), the right eye visual acuity was 1/60 with lens correction of S+8.00 became 3/60. Left eye visual acuity was 1/60 with

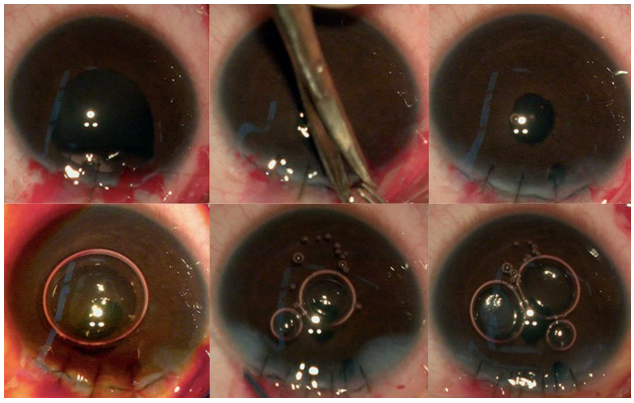

Figure 3. Intra capsular cataract extraction ICCE surgery with anterior vitrectomy and iridectomy on the right eye.

correction of S+10.00 became 4/10. The IOP of the right eye was 39 mmHg on timolol maleate 0.25 mg eye drop, and the left eye was 16 mmHg.

In the third follow-up (two weeks later), the right eye visual acuity was 2/60 with lens correction of S+6.00 became 2/10. Left eye visual acuity was 1/60 with lens correction of S+10.00 became 4/10. The IOP of the right eye was 27 mmHg on timolol maleate 0.25mg eye drop and the left eye was 13 mmHg. The patient was given latanoprost 0.005% eye drop in the right eye, timolol maleate 0.25 mg eye drop in the right eye, and tobramycin dexamethasone eye drop in the left eye.

The patient was scheduled for MP-TSCPC surgery on his right eye (Figure 4). After follow-up, right eye visual acuity without correction was 2/60, and left eye visual acuity without correction was 1/60. The IOP of the right eye was 18.3 mmHg on timolol maleate 0.25 mg eye drop, and the left eye was 15.5 mmHg.

Discussion and conclusions

WMS is a connective tissue disorder with an incidence of 1:100.000 proportion of the population. This syndrome is characterized by brachydactyly, short stature, joint stiffness, cardiovascular abnormalities, and eye anomalies, including microspherophakia, cataracts, ectopia lentis, myopia, and secondary glaucoma. Patients with incomplete signs of WMS were diagnosed with Weill-Marchesani-like Syndrome (WMS-like).[2] In this patient, we found abnormal facial appearance, brachydactyly, aphakia lens in the right eye, conjunctival scleretasia, iris atrophy, and mild pupil dilation, while in the left eye, we found iris atrophy and posterior lens subluxation. This patient was 112 cm in height; according to the Centers for Disease Control and Prevention (CDC)[6], this patient was short stature because the stature for age was in the 10th percentile. However, further collaboration from pediatricians, cardiologists, and radiologists to find abnormalities such as ductus arteriosus and pulmonary stenosis as well as shortened tubular bone and delayed bone age.[2] Other present clinical and biochemical findings excluded endocrine diseases in particular hypothyroidism, primary or secondary hypogonadism and pituitary nanism, homocystinuria, and other heritable disorders of connective tissue such as mucopolysaccharidosis, oligosaccharidosis, chondrodysplasias, and osteogenesis imperfecta. Identification of biallelic pathogenic variants in ADAMTS10, ADAMTS17, or latent transforming growth factor beta binding protein 2 (LTBP2) or heterozygous pathogenic variants in FBN1 by molecular genetic testing can confirm the diagnosis of WMS if the clinical picture is inconclusive.[7],[8] In this case, we did not do genetic testing because of the limited insurance in our country. So, from that clinical examination, we suspected the patient was WMS2.

Management of the WMS is very comprehensive. Prevention and therapy of post-ICCE secondary glaucoma are one of them. Early detection and removal of the ectopic lens are essential to reduce the possibility of pupillary block and glaucoma.[2] In this case, the patient had a history of ICCE surgery of the right eye indicating a massive anterior subluxation. Subsequently, ICCE surgery was also performed on the left eye due to posterior lens subluxation. Lens subluxation in children is more often performed using ICCE surgery.[9] ICCE is the leading choice in cases of bilateral subluxation due to several syndromes in children. Myopia can develop from increased lens curvature caused by subluxated lenses. The shifting of the lens position can also result in irregular astigmatism that cannot be corrected with cylindrical lenses, as well as amblyopia, strabismus, or monocular diplopia. In addition to causing anterior uveitis, a lens that is anteriorly displaced raises intraocular pressure and lowers endothelial cell count. If the lens is inside the vitreous body, it may move freely and cause retinal ablation, or it may rupture and cause uveitis (lens-induced uveitis) and phacolytic glaucoma.[10] Slit lamp examinations can be used to determine whether iridodonesis or phacodonesis is present. To assess the lens equator and determine which area has zonule weakening or rupture, the pupil's dilatation must be examined. However, the exams that are performed need to be exhaustive. Comprehensive eye exams and history-taking include checking the best-corrected visual

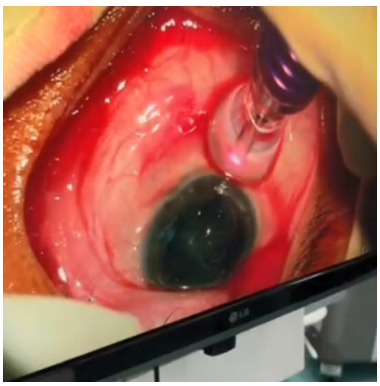

Figure 4. During micropulse transscleral cyclophotocoagulation (MP-TSCPC) procedure on the right eye.

acuity, intraocular pressure, the anterior and posterior segments, the USG, and another systemic testing (chest plain radiograph, laboratory, and echocardiography).[11]

The goal of treatment for childhood ocular diseases is vision rehabilitation. This makes it possible to treat amblyopia, prevent it from happening, and restore fusion and stereoscopic function in patients, all of which will help their vision's prognosis. Pediatric patients receive visual rehabilitation that is very different from adult patients since children's eyes are still developing. This enables the axial and curvature elongation of the corneas, which are the refractive components of their eyes. Children with visual impairments such as best-corrected visual acuity (BCVA) 20/40 on the best eye, decreased field of vision, central field loss, decreased contrast sensitivity, and trouble seeing in dimly light environments are candidates for visual rehabilitation.[12]

Both conservative and surgical treatments are options for treating a displaced lens. Spectacles or contact lenses may be prescribed as part of conservative therapy. Despite the variations in risk levels, techniques for operating on displaced lenses in children advanced to some extent at the same time that techniques and surgical equipment for cataracts did. When the displaced lens causes severe visual impairment or conservative (non-operative) therapy no longer works, one may need to turn to surgical techniques. Following a thorough examination that considers the level of lens opacity, the severity of zonular abnormality, visual function, patient age, equipment accessibility, operator skill, and parental desire, the decision of therapy for children is made.[13]

Children with signs of binocular aphakia, contact lens sensitivity, or when an intraocular lens (IOL) implant is not viable can be given glasses. If a youngster has monocular aphakia, contact lenses or glasses may be a better option than glasses as the primary option. The preferred refractive correction for babies and kids with binocular aphakia is still glasses. Some advantages of wearing glasses include more convenient refractive eye exams, low prices, safe use, simplicity of maintenance, and customizable lens designs based on the required distance (monofocal and bifocal). However, wearing glasses also has a number of disadvantages, such as hefty and thick lenses that might reduce compliance. Due to the size of the lens on the glasses, they can also cause magnification, a disturbing field of vision, and ring scotoma. They lack aesthetic appeal as well. The treatment of choice for people with monocular aphakia maybe contact lenses. Their comfort during usage, greater aesthetic appeal than spectacles, lack of magnification, and lack of field-of-vision disruption make them preferable to spectacles. However, the drawbacks of utilizing contact lenses include that it can be challenging to determine their correct size because kids can be uncooperative sometimes and easily get lost. They are significantly more expensive due to their more complicated manufacturing process. Infections of the conjunctiva or cornea and hypersensitive reactions may become more common when wearing contact lenses. Soft contact lenses and rigid gas permeable (RGP) contacts are two different types of lenses that can be worn. Soft contact lenses are more comfortable and adapt faster than RGP because they are more elastic and can cover the entire corneal surface.[14]

In this case, we used MP-TSCPC on the right eye. Indications for MP-TSCPC are to reduce IOP and the number of drugs used.[15] The choice of MP-TSCPC over trabeculectomy or glaucoma drainage device (GDD) implant was based on the considerations we found in this patient: 1) had refractory glaucoma or glaucoma that was not controlled by medication and 2) had sclerectasia or sclera ectasia (thin sclera) which was a contraindication to trabeculectomy or GDD implant placement.

Using MP-TSCPC therapy in primary or secondary refractory glaucoma surgery has a good outcome.[16] Tan et al.[17] reported that MP-TSCPC therapy in refractory glaucoma showed an 80% success rate in maintaining IOP between 6-21 mmHg without eye hypotony post-surgery or visual loss after 16.3 ± 4.5 months follow-up. Another study by Lee et al.[18] compared IOP after MP-TSCPC in adult versus pediatric glaucoma patients. They reported a success rate (defined as IOP 5 mmHg - 21 mmHg and 20% reduction from baseline at 12-month follow-up) of 72.22% vs. 22.22% at 12-month follow-up. Seven of nine pediatric patients required another surgery during 12 months of follow-up; however, no significant complications were noted in either treatment group.[18]

Research by Emanuel et al.[19] reported that MP-TSCPC therapy was able to reduce the average postoperative IOP to 14.6 mmHg (SD, 8.8 mmHg), 13.0 mmHg (SD, 6.9 mmHg), and 1.1 mmHg (SD, 4.4 mmHg). At three, six, and twelve months, a decrease in antiglaucoma drug usage 20 also accompanied this.

After surgery, an IOL will be placed on the patient's eyes. However, this is not always possible due to complications such as loosened zonula, IOL luxation, or other complications that occur intraoperatively (anterior or posterior capsule tear). In children older than two years, IOL insertion is usually done because it has a good outcome. Likely, many of these patients with aphakia will later require secondary IOL implantation. Secondary IOL implantation is recommended when traditional eyeglasses or contact lens correction are unsuccessful.[11],[20],[21] In this case, the placement of secondary IOL was not possible because the patient had wide pupil, iris atrophy, and sclerectasia in the right eye.

The patient's vision was corrected using glasses to restore visual acuity after ICCE surgery. Visual acuity recovery in pediatric patients can be made using contact

lenses, glasses, and IOL installation.[13] Aphakia or pseudophakia may occur in post-ICCE patients. Aphakia must be corrected immediately because it can cause secondary glaucoma.[22] The IOP of the right eye exceeded the standard limit, reaching 25 mmHg, which means that the patient obtained secondary glaucoma after ICCE surgery.

WMS can be present in a patient with short stature, abnormal facial appearance, brachydactyly with ocular abnormalities shown in this patient. Discussion and collaboration with a cardiologist, pediatrician, and radiologist should be done to establish the syndrome phenotype and genotype. A multidisciplinary approach is required to treat the syndrome comprehensively. The outcome of both surgeries was good for this patient. We followed this patient until day 15, with an improvement in her visual acuity. Follow-up should still be done until about 6-12 months. Children with bilateral posterior lens luxation can receive conservative visual rehabilitation to stop amblyopia. The use of operational techniques is required to avoid any difficulties. Aphakic eyewear is part of the conservative care for this patient while waiting for additional surgical procedures. The allelic examination is also essential and will be the prerequisite for diagnosing the WMS

References

[1] Guo H, Wu X, Cai K, Qiao Z. Weill-Marchesani syndrome with advanced glaucoma and corneal endothelial dysfunction: A case report and literature review. BMC Ophthalmol 2015;15:3. https://doi.org/10.1186/1471-2415-15-3.

[2] Marzin P, Cormier-Daire V, Tsilou E. Weill-Marchesani Syndrome. GeneReviews® 2007. https://www.ncbi.nlm.nih.gov/books/NBK1114/ (accessed October 1, 2022).

[3] Yi H, Zha X, Zhu Y, Lv J, Hu S, Kong Y, et al. A novel nonsense mutation in ADAMTS17 caused autosomal recessive inheritance Weill–Marchesani syndrome from a Chinese family. J Hum Genet 2019;64:681–687. https://doi.org/10.1038/s10038-019-0608-2.

[4] Steinkellner H, Etzler J, Gogoll L, Neesen J, Stifter E, Brandau O, et al. Identification and molecular characterisation of a homozygous missense mutation in the ADAMTS10 gene in a patient with Weill-Marchesani syndrome. Eur J Hum Genet 2015;23:1186–1191. https://doi.org/10.1038/ejhg.2014.264.

[5] Satana B, Altan C, Basarir B, Alkin Z, Yilmaz OF. A new combined surgical approach in a patient with microspherophakia and developmental iridocorneal angle anomaly. Nepal J Ophthalmol a Biannu Peer-Reviewed Acad J Nepal Ophthalmic Soc NEPJOPH 2015;7:85–89. https://doi.org/10.3126/nepjoph.v7i1.13178.

[6] National Center for Health Statistics. Clinical Growth Charts. Centers Dis Control Prev 2009. https://www.cdc.gov/growthcharts/clinical_charts.htm#Set1 (accessed August 15, 2022).

[7] Misra S, Parthasarathi G, Vilanilam GC. The effect of gabapentin premedication on postoperative nausea, vomiting, and pain in patients on preoperative dexamethasone undergoing craniotomy for intracranial tumors. J Neurosurg Anesthesiol 2013;25:386–391. https://doi.org/10.1097/ANA.0b013e31829327eb.

[8] Akram H, Aragon-Martin JA, Chandra A. Marfan syndrome and the eye clinic: From diagnosis to management. Ther Adv Rare Dis 2021;2:26330040211055736. https://doi.org/10.1177/26330040211055738.

[9] Sahay P, Maharana PK, Shaikh N, Goel S, Sinha R, Agarwal T, et al. Intra-lenticular lens aspiration in paediatric cases with anterior dislocation of lens. Eye (Lond) 2019;33:1411–1417. https://doi.org/10.1038/s41433-019-0426-y.

[10] Vasavada AR, Praveen MR, Desai C. Management of bilateral anterior dislocation of a lens in a child with Marfan's syndrome. J Cataract Refract Surg 2003;29:609–613. https://doi.org/10.1016/s0886-3350(02)01529-8.

[11] Nihalani BR, Vanderveen DK. Secondary intraocular lens implantation after pediatric aphakia. J AAPOS Off Publ Am Assoc Pediatr Ophthalmol Strabismus 2011;15:435–440. https://doi.org/10.1016/j.jaapos.2011.05.019.

[12] Deng D, Li J, Yu M. Postoperative Visual Rehabilitation in Children with Lens Diseases BT. In: Liu Y, editor. Pediatric Lens Diseases. Singapore: Springer Singapore; 2017, p. 353–369. https://doi.org/10.1007/978-981-10-2627-0_26.

[13] Baradaran-Rafii A, Shirzadeh E, Eslani M, Akbari M. Optical correction of aphakia in children. J Ophthalmic Vis Res 2014;9:71–82.

[14] Repka MX. Visual Rehabilitation in Pediatric Aphakia. Dev Ophthalmol 2016;57:49–68. https://doi.org/10.1159/000442501.

[15] Landry DW, Oliver JA. The pathogenesis of vasodilatory shock. N Engl J Med 2001;345:588–595. https://doi.org/10.1056/NEJMra002709.

[16] Ndulue JK, Rahmatnejad K, Sanvicente C, Wizov SS, Moster MR. Evolution of Cyclophotocoagulation. J Ophthalmic Vis Res 2018;13:55–61.

[17] Tan AM, Chockalingam M, Aquino MC, Lim ZI-L, See JL-S, Chew PT. Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. Clin Experiment Ophthalmol 2010;38:266–272. https://doi.org/10.1111/j.1442-9071.2010.02238.x.

[18] Lee JH, Shi Y, Amoozgar B, Aderman C, De Alba Campomanes A, Lin S, et al. Outcome of micropulse laser transscleral cyclophotocoagulation on pediatric versus adult glaucoma patients. J Glaucoma 2017;26:936–939. https://doi.org/10.1097/IJG.0000000000000757.

[19] Emanuel ME, Grover DS, Fellman RL, Godfrey DG, Smith O, Butler MR, et al. Micropulse cyclophotocoagulation: Initial results in refractory glaucoma. J Glaucoma 2017;26:726–729. https://doi.org/10.1097/IJG.0000000000000715.

[20] Trivedi RH, Wilson MEJ, Facciani J. Secondary intraocular lens implantation for pediatric aphakia. J AAPOS Off Publ

Am Assoc Pediatr Ophthalmol Strabismus 2005;9:346–352. https://doi.org/10.1016/j.jaapos.2005.02.010.

[21] Wood KS, Tadros D, Trivedi RH, Wilson ME. Secondary intraocular lens implantation following infantile cataract surgery: intraoperative indications, postoperative outcomes. Eye (Lond) 2016;30:1182–1186. https://doi.org/10.1038/eye.2016.131.

[22] Turlapati N, Salim S. Aphakic and Pseudophakic Glaucoma After Congenital Cataract Surgery. Eyenet Mag 2015. https://www.aao.org/eyenet/article/aphakic-pseudophakic-glaucoma-after-congenital-cat (accessed October 13, 2022).