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EDITORIAL

Widya Artini Wiyogo

Each year, World Sight Day serves as a global call to action for eye health. In 2025, the International Agency for the Prevention of Blindness (IAPB) leads the campaign under the theme "Love Your Eyes", urging individuals, communities, and governments to prioritize people-centered eye care. Spanning from July 1st to the second Thursday of October, this initiative seeks to mobilize responsibility at every level of society.[1]

Indonesia continues to face one of the highest blindness prevalence rates in the region—3.0%[2], compared to Singapore (0.2%)[3], the Philippines (0.58%)[4], Malaysia (1.2%)[5], Vietnam (2.5%)[4]. These figures underscore a critical truth: avoidable blindness remains a national crisis. It is only fitting that ophthalmologists receive greater government support in tackling this burden.

Among the many contributors to the country's blindness rate, one stands out as both urgent and often overlooked: cataract in children. One article in this issue highlights findings from Indonesia's National Eye Center in Bandung, reporting that a staggering 93.8% of 118 children with cataract presented with bilateral blindness. This is not just a clinical statistic; it is a resounding alarm. This is not just a statistic—it is an urgent call for action. Pediatric cataract requires timely surgery, whether unilateral or bilateral, to prevent irreversible visual loss. Early intervention is especially critical for bilateral cases, where visual outcomes tend to be better due to preserved binocular vision and stereopsis.[6]

Yet, the journey does not end at surgery. Children who undergo congenital or developmental cataract removal face long-term visual and psychosocial challenges.[7] Postoperative complications such as nystagmus, strabismus, and amblyopia frequently persist and can severely degrade quality of life and functional vision.8 Optimal outcomes depend on proper refractive correction—ideally with pediatric contact lenses, even in aphakic or IOL-implanted eyes.[9,10] However, access to contact lenses is limited in many regions, making well-fitted spectacles a necessary alternative.

The psychosocial toll is just as significant. Preschool-aged children undergoing patching therapy or those visibly affected by strabismus often suffer from behavioral issues and social stigma.[11] They are vulnerable not only to vision-related limitations but also to negative social attention, poor self-image, and reduced participation in age-appropriate activities.[12]

Meanwhile, caregivers—often parents balancing work, finances, and emotional strain—face a heavy burden. Early treatment requires significant time, energy, and cost. Children treated with IOLs often need multiple follow-up surgeries, especially in the first year, adding to family stress and reducing quality of life. Over time, evolving visual needs necessitate consistent outpatient care, placing continued pressure on families. Their understanding of the child's condition, along with long-term expectations, deeply affects their overall quality of life and ability to sustain care.[13,14]

As clinicians, researchers, policymakers, and citizens alike, we must confront childhood cataract not merely as a medical issue but as a multidimensional social, economic, and public health challenge. Left untreated or inadequately managed, it compromises education, social inclusion, and independence, deepening cycles of poverty and limiting community potential.

As we observe World Sight Day 2025, let us reaffirm our commitment: a child's future should never be dimmed by delayed cataract care. If we truly "Love Your Eyes," this love must extend with urgency, empathy, and decisive action to protect the vision and lives of the youngest among us.

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ORIGINAL ARTICLE

THE RELATIONSHIP BETWEEN TUMOR NECROSIS FACTOR-ALPHA (TNF- α) WITH RETINAL NERVE FIBER LAYER (RNFL) THICKNESS IN DIABETIC RETINOPATHY PATIENTS AT PROF. CPL UNIVERSITAS SUMATERA UTARA GENERAL HOSPITAL AND AFFILIATED HOSPITAL

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ABSTRACT

Introduction: *Retinal neurodegeneration may be an early indicator of diabetic retinopathy, the second most common complication after nephropathy. Tumor Necrosis Factor-Alpha (TNF-α) plays a role in the pathogenesis of inflammatory and neovascular eye disorders and is associated with intraocular inflammatory diseases like macular edema and proliferative diabetic retinopathy. This study aims to find the relationship between TNF-α levels and Retinal Nerve Fiber Layer (RNFL) thickness in diabetic retinopathy patients at Prof. CPL Universitas Sumatera Utara General Hospital and affiliated hospital.*

Methods: *This cross-sectional study included 45 patients with type 2 DM and diabetic retinopathy at Prof. CPL Universitas Sumatera Utara General Hospital and affiliated hospital from March to June 2024. RNFL and posterior segment examinations were conducted. TNF-α levels were measured from blood samples.Blood sugar data were taken from medical records..*

Results: *Of the 45 participants, 24 were men (53.3%) and 21 women (46.7%). 32 (71.1%) had DM for >5 years, and 27 (60%) experienced PDR. Highest location for RNFL thickness examination was superior (19, 42.2%). Average TNF-α with thin RNFL was 65.67 ng/L, and with thick RNFL was 64.78 ng/L. Mean TNF-α with thin superior RNFL was 65.74 ng/L, and thick was 63.70 ng/L. Mean TNF-α with thin inferior RNFL was 65.73 ng/L, and thick was 63.9 ng/L. Mean TNF-α with thin temporal RNFL was 68.73 ng/L, and thick was 67.19 ng/L. Mean TNF-α with thick nasal RNFL was 67.06 ng/L.*

Conclusion: *There was no statistically significant relationship between TNF-α and RNFL thickness in diabetic retinopathy patients.*

Keywords: *Diabetes mellitus, diabetic retinopathy, TNF-α, RNFL layer*

INTRODUCTION

Diabetes mellitus is a common medical condition that has increased in prevalence over the past few decades, becoming a major health challenge in the twenty-first century. Complications traditionally associated with diabetes mellitus include macrovascular conditions such as coronary heart disease, stroke, and peripheral artery disease, and microvascular conditions including diabetic nephropathy, retinopathy, and peripheral neuropathy.[1]

Diabetic retinopathy (DR) is a common microvascular complication of diabetes mellitus and is the leading cause of vision loss in the elderly.[2,3] In Indonesia, diabetic retinopathy is the

second most common complication after nephropathy. The overall prevalence of diabetic retinopathy is 43.1%, with sight-threatening diabetic retinopathy accounting for 26.1%.[4,5] Meanwhile, in Taiwan, the prevalence of diabetic eye disease ranges from 3.75% to 3.95%, and the prevalence of visual impairment and blindness ranges from 0.29% to 0.35% from 2005 to 2014.[2,6] In Korea, the prevalence of diabetic retinopathy increased from 14.3% in 2006 to 15.9% in 2013.[2,7] Both studies revealed that women with type 2 diabetes have a higher prevalence of diabetic retinopathy than men, but men suffer from more severe retinopathy, poor vision, or blindness. The severity of diabetic retinopathy not only impacts quality of life but also predicts all-cause, vascular, and non-cancer mortality.[2]

The early stages of diabetic retinopathy, such as non-proliferative diabetic retinopathy, may not cause severe visual impairment. Diabetic macular edema and proliferative diabetic retinopathy are collectively known as sight-threatening diabetic retinopathy. If untreated, 26.5% of the population with sight-threatening diabetic retinopathy tends to experience severe visual impairment within 1-2 years. According to the National Diabetic Retinopathy Survey, India, from 2015-2019, diabetic retinopathy occurred in 17% of patients over 50 years old. Timely diagnosis and management of diabetic retinopathy can reduce the risk of severe vision loss by up to 90%, as evaluated by the Early Treatment Diabetic Retinopathy Study (ETDRS). There is a very complex relationship between an individual's socioeconomic status and disease. Unawareness and delays by patients lead to further complications, ultimately increasing the cost of diabetic eye care.[8]

Vascular abnormalities and microvasculopathy are widely accepted factors in diabetic retinopathy. Recent research has found that neurodegeneration, which should be considered a very important component in the pathogenesis of diabetic retinopathy, correlates with microvascular dysfunction. This is supported by evidence from animal studies showing that retinal nerve cell degeneration occurs early in the course of diabetes.[9] Increasing evidence indicates that retinal neurodegeneration plays a crucial role in the pathogenesis of diabetic retinopathy. Cross-sectional studies using OCT have reported a decrease in retinal nerve fiber layer (RNFL) thickness in diabetic patients with or without mild diabetic retinopathy compared to normal controls.[10] Research conducted by Lim et al. found greater peripapillary retinal nerve fiber layer (pRNFL) loss in 103 patients with type 2 DM compared to 63 healthy individuals over 3 years, with even more pronounced reductions in patients with mild diabetic retinopathy.11 Another study by Lee et al. also found greater reductions over 3 years in 85 diabetic patients without diabetic retinopathy compared to 55 normal participants.[12]

Several cross-sectional studies have reported a decrease in RNFL thickness in diabetic patients compared to normal controls. Additionally, it has been reported that diabetic patients without signs of diabetic retinopathy have a larger RNFL, indicating that retinal neurodegeneration may be an early indicator of the development of diabetic retinopathy. In diabetic patients, various molecular pathways have been identified that may mediate retinal nerve damage.[10]

Studies have found that a significant number of inflammatory cytokines are involved in the early stages of diabetic retinopathy, and the expression of inflammatory cytokines in the retina of DM patients is significantly increased. Therefore, inflammation likely plays a crucial role in the development of diabetic retinopathy.[13]

Tumor Necrosis Factor-alpha (TNF-α) is a cytokine produced by macrophages and T-cells, with a major regulatory role in the inflammatory response. Dysregulation of TNF-α has been implicated in the pathogenesis of inflammatory, edematous, neovascular, and neurodegenerative conditions. Blocking the action of TNF-α has been used in the treatment of chronic inflammatory conditions.[14] TNF-α has been found to play a role in the pathogenesis of inflammatory and neovascular disorders in the eye. In vivo retinal injury models indicate that TNF-α plays a detrimental role in ischemia-reperfusion injury, and retinal function is partially protected by direct neutralization of this cytokine.[15]

TNF-α inhibitors are widely used in ophthalmology as off-label alternatives to traditional immunosuppressive and immunomodulatory treatments for non-infectious uveitis. Preliminary studies have shown positive effects of intravenously administered TNF-α inhibitors, especially infliximab, in treating refractory diabetic macular edema and neovascular age-related macular degeneration. Currently, many studies are focusing on the relationship between TNF-α and diabetic retinopathy. Research conducted by Roy et al. found that TNF-α is independently associated with the occurrence of proliferative diabetic retinopathy and macular edema.[13,16] Research by Hang et al. reported that TNF-α levels are significantly increased in patients with proliferative diabetic retinopathy compared to those with non-proliferative diabetic retinopathy and those without diabetic retinopathy.[13,17] Meta-analysis results indicate that TNF-α levels in the proliferative diabetic retinopathy group are higher than in the control group. When interpreting these results, the following issues should be considered. First, TNF-α can stimulate the synergistic release and proliferation of IL-6, IL-8, VEGF, and platelet-derived growth factor (PDGF). Second, TNF-α can inhibit the formation and development of retinal vascular endothelial cells, promote endothelial cell apoptosis, destroy

the normal function of the vascular wall, and affect retinal vascular permeability. Third, TNF-α can induce neovascularization in the eye.[13]

TNF-α has been shown to be associated with various intraocular inflammatory diseases, such as macular edema and proliferative diabetic retinopathy, through its actions as a pro-inflammatory cytokine. Research conducted by Yao et al. suggests that TNF-α can be used as a biomarker for diabetic retinopathy and as a potential therapeutic target.13 Based on the above background, researchers are interested in understanding the relationship between TNF-α and RNFL thickness in diabetic retinopathy patients at Prof. CPL Universitas Sumatera Utara General Hospital and affiliated hospital.

METHODS

RESEARCH DESIGN

This study was conducted using an observational analytic research design with data collection carried out cross-sectionally at the Vitreo-Retina Division Eye Clinic of Prof. CPL Universitas Sumatera Utara General Hospital and affiliated hospital.

DATA COLLECTION

TNF-α was measured from blood samples. The ELISA (Enzyme-Linked Immunosorbent Assay) kit was used to measure TNF-α levels. RNFL was measured using Optical Coherence Tomography (OCT). This device is commonly used to assess RNFL thickness in similar studies. The research sample size was determined using the consecutive sampling method, which includes all patients visiting the eye clinic at Prof. CPL Universitas Sumatera Utara General Hospital and affiliated hospital. The estimated sample size for this study was calculated using the following formula:

$$n = 3 + \left[\frac{(Z\alpha + Z\beta)}{ln\, 0{,}5\left(\frac{1+r}{1-r}\right)} \right]^2$$

Figure 1. Formula to calculate sample size

n = Number of patients

α = Type I error, set at 5%

Zα = Standard value for alpha 5%, which is 1.96

β = Type II error, set at 20%

Zβ = Standard value for beta 20%, which is 0.84

r = Correlation value = 0.612 (Li and Wang, 2020)[70]

$$n = 3 + \left[\frac{1{,}96 + 0{,}84}{\ln 0{,}5\left(\frac{1+0{,}612}{1-0{,}612}\right)} \right]^2$$

$$n = 3 + \left[\frac{2{,}8}{\ln 0{,}5\left(\frac{1{,}612}{0{,}388}\right)} \right]^2$$

$$n = 3 + \left[\frac{2{,}8}{0{,}729} \right]^2$$

$$n = 17{,}7 \sim 18 \text{ sample}$$

Figure 2. Calculation of sample size

The total number of subjects required is 18, and estimating a 10% drop-out rate, the minimum number of subjects needed for this study is 20.

POPULATION AND SAMPLE

The study population consisted of all type-2 DM patients with and without diabetic retinopathy who visited the eye clinic at Prof. CPL Universitas Sumatera Utara General Hospital from March 2024 to June 2024. The research sample included a portion of type-2 DM patients with diabetic retinopathy who visited the eye clinic at Prof. CPL Universitas Sumatera Utara General Hospital and affiliated hospital from March 2024 to June 2024.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria for the study included patients diagnosed with type 2 diabetes mellitus, those diagnosed with diabetic retinopathy, patients with clear refractive media, and those willing to participate in the study. Exclusion criteria included patients with anterior segment abnormalities, diabetic retinopathy with increased intraocular pressure, those diagnosed with any type of glaucoma or having a family history of glaucoma, patients with a history of orbital tumors, eye surgery, anti-VEGF injections, or laser therapy on the eyes.

DATA ANALYSIS

Data analysis was conducted analytically and presented in tabulated form, displaying frequency and percentage values for categorical data. Numerical data were presented by showing the mean, median, minimum, and maximum values. To analyze the relationship between TNF-α, the degree of diabetic retinopathy, and the duration of DM with Retinal Nerve Fiber Layer (RNFL) thickness, Pearson correlation test was used if the data were normally distributed. If the data were not normally distributed, the Spearman test was used. Data were considered significant if a P value of <0.05 was obtained.

RESULTS

DEMOGRAPHIC CHARACTERISTICS OF STUDY SUBJECTS

This study included 45 type-2 DM patients with diabetic retinopathy who visited the eye clinic at Prof. CPL Universitas Sumatera Utara General Hospital. All patients involved in the study met the inclusion criteria. Table 1 presents the demographic characteristics of the study subjects.

Table 1. Demographic Characteristics of Study Subjects

Demographic Characteristics	n = 45
Gender, n (%)	
Male	24 (53,3)
Female	21 (46,7)
Duration of disease course, n (%)	
≤ 5 years	13 (28,9)
6 – 10 years	16 (35,6)
> 10 years	16 (35,6)
Degree of Retinopathy, n (%)	
NPDR	18 (40)
PDR	27 (60)
Location, n (%)	
Superior	19 (42,2)
Inferior	17 (37,8)
Temporal	5 (11,1)
Nasal	4 (8,9)
RNFL thickness, n (%)	
Thinning	22 (48,9)
Thickening	23 (51,1)

The number of male patients was 24 (53.3%). Most patients had DM for more than 5 years, totaling 32 patients (71.1%). A total of 27 patients (60%) had a degree of PDR. The most common location for RNFL thickness examination was the superior region in 19 patients (42.2%), followed by the inferior region in 17 patients (37.8%).

Table 2. The Relationship Between Tumor Necrosis Factor-Alpha (TNF-α) Levels and the Degree of Diabetic Retinopathy with Retinal Nerve Fiber Layer (RNFL) Thickness in Diabetic Retinopathy Patients

	RNFL Thickness		p
	Thinning (n=22)	Thickening (n=23)	
TNF-α, ng/L			
Mean (SD)	65,87 (9,45)	64,78 (11,40)	0,729[a]
Median (Min – Max)	67,34 (50,67-87,34)	64,9 (48,07-85,9)	
Degree of Retinopathy			
NPDR	10 (55,6)	8 (44,4)	0,465[b]
PDR	12 (44,4)	15 (55,6)	

[a]*T Independent,* [b]*Chi Square*

Table 2 presents the results of the analysis of the relationship between TNF-α levels and the degree of retinopathy with RNFL thickness in all diabetic retinopathy patients in this study.

The mean TNF-α level in diabetic retinopathy patients with thin RNFL thickness was 65.87 ng/L (SD = 9.45 ng/L). Meanwhile, in diabetic retinopathy patients with thick RNFL thickness, the mean TNF-α level was 64.78 ng/L (SD = 11.4 ng/L). Using the Independent T-test, no significant relationship was found between TNF-α levels and RNFL thickness in diabetic retinopathy patients.

Among the 18 diabetic retinopathy patients with NPDR, 10 patients (55.6%) had thin RNFL thickness. Meanwhile, among the 27 retinopathy patients with PDR, 12 patients (44.4%) had thin RNFL thickness. Using the Chi-Square test, no significant relationship was found between the degree of retinopathy and RNFL thickness in diabetic retinopathy patients.

Table 3. The Relationship Between Tumor Necrosis Factor-Alpha (TNF-α) Levels and the Degree of Diabetic Retinopathy with Retinal Nerve Fiber Layer (RNFL) Thickness in Diabetic Retinopathy Patients

	Superior RNFL thickness		p
	Thinning (n=12)	Thickening (n=7)	
TNF-α, ng/L			
Mean (SD)	65,74 (9,53)	63,70 (11,03)	0,676[a]
Median (Min – Max)	67,99 (50,67-77,54)	59,89 (50,39-81,04)	
Degree of Retinopathy			
NPDR	5 (71,4)	2 (28,6)	0,656[b]
PDR	7 (58,3)	5 (41,7)	

[a]*T Independent,* [b]*Fischer's Exact*

The mean TNF-α level in diabetic retinopathy patients with thin superior RNFL thickness was 65.74 ng/L (SD = 9.53 ng/L). Meanwhile, in diabetic retinopathy patients with thick superior RNFL thickness, the mean TNF-α level was 63.70 ng/L (SD = 11.03 ng/L). Using the independent T-test, no significant relationship was found between TNF-α levels and superior RNFL thickness in diabetic retinopathy patients.

Among the 7 diabetic retinopathy patients with NPDR, 5 patients (71.4%) had thin

superior RNFL thickness. Meanwhile, among the 12 retinopathy patients with PDR, 7 patients (58.3%) had thin superior RNFL thickness. Using Fischer's Exact test, no significant relationship was found between the degree of retinopathy and superior RNFL thickness in diabetic retinopathy patients.

Table 4. The Relationship Between Tumor Necrosis Factor-Alpha (TNF-α) Levels and the Degree of Diabetic Retinopathy with Inferior Retinal Nerve Fiber Layer (RNFL) Thickness in Diabetic Retinopathy Patients

	Inferior RNFL thickness		p
	Thinning (n=9)	Thickening (n=8)	
TNF-α, ng/L			
Mean (SD)	65,73 (10,41)	63,9 (11,23)	0,662[a]
Median (Min – Max)	66,78 (55,65-87,34)	65,67 (48,07-78,99)	
Degree of Retinopathy			
NPDR	4 (66,7)	2 (33,3)	0,620[b]
PDR	5 (45,5)	6 (54,5)	

[a]*T Independent,* [b]*Fischer's Exact*

The mean TNF-α level in diabetic retinopathy patients with thin inferior RNFL thickness was 65.73 ng/L (SD = 10.41 ng/L). Meanwhile, in diabetic retinopathy patients with thick inferior RNFL thickness, the mean TNF-α level was 63.9 ng/L (SD = 11.23 ng/L). Using the Independent T-test, no significant relationship was found (p = 0.662) between TNF-α levels and inferior RNFL thickness in diabetic retinopathy patients.

Among the 6 diabetic retinopathy patients with NPDR, 4 patients (66.7%) had thin inferior RNFL thickness. Meanwhile, among the 11 retinopathy patients with PDR, 5 patients (45.5%) had thin inferior RNFL thickness. Using Fischer's Exact test, no significant relationship was found (p = 0.620) between the degree of retinopathy and inferior RNFL thickness in diabetic retinopathy patients.

Table 5. The Relationship Between Tumor Necrosis Factor-Alpha (TNF-α) Levels and the Degree of Diabetic Retinopathy with Temporal Retinal Nerve Fiber Layer (RNFL) Thickness in Diabetic Retinopathy Patients

	Temporal RNFL thickness		p
	Thinning (n=1)	Thickening (n=4)	
TNF-α, ng/L			
Mean (SD)	68,73	67,19 (16,45)	-
Median (Min – Max)	-	66,24 (50,39-85,9)	
Degree of Retinopathy			
NPDR	1 (100)	0	0,200*
PDR	0	4 (100)	

**Fischer's Exact*

Only one patient had thin temporal RNFL thickness with a TNF-α level of 68.73 ng/L. Meanwhile, four patients had thick temporal RNFL thickness with a mean TNF-α level of 67.19 ng/L (SD = 16.45 ng/L). Analysis could not be performed because only one patient had thin temporal RNFL thickness. For statistical analysis, at least two data points are required to

calculate the mean value.

One diabetic retinopathy patient with thin temporal RNFL thickness had NPDR, while all four diabetic retinopathy patients with thick temporal RNFL thickness had PDR. Using Fischer's Exact test, no significant relationship was found (p = 0.200) between the degree of retinopathy and temporal RNFL thickness in diabetic retinopathy patients.

Table 6. The Relationship Between Tumor Necrosis Factor-Alpha (TNF-α) Levels and the Degree of Diabetic Retinopathy with Nasal Retinal Nerve Fiber Layer (RNFL) Thickness in Diabetic Retinopathy Patients

	Nasal RNFL thickness		p
	Thinning (n=0)	Thickness (n=4)	
TNF-α, ng/L			
Mean (SD)	-	67,06 (11,04)	-
Median (Min – Max)	-	66,3 (57,55-78,05)	
Degree of Retinopathy			
NPDR	0	0	-
PDR	0	4 (100)	

[a]*T Independent,* [b]*Chi Square*

Among the 4 diabetic retinopathy patients with thick temporal RNFL thickness, the mean TNF-α level was 67.06 ng/L (SD = 11.04 ng/L). Based on the degree of retinopathy, all patients had PDR. Statistical analysis could not be performed due to the homogeneity of the data, as all nasal RNFL layers examined showed thick results and were associated with PDR.

DISCUSSION

The results of this study indicate that the demographic characteristics that can be found in the majority of research patients are male, this is not in accordance with several studies such as those conducted by Sentani et al[18] which stated that diabetic retinopathy sufferers are often found in female patients and in a study conducted by Novianti which stated that female patients have a greater risk of developing diabetic retinopathy.[19]

The results of this study showed that many patients had suffered from DM for 5 years, this is in accordance with research conducted by Novianti in her study which stated that patients with diabetic retinopathy on average suffered from diabetes with a time span of 5-10 years.[19] However, the results of this study do not match the research conducted by Primaputri et al, which stated that diabetic retinopathy sufferers are often found in DM sufferers with a duration of <5 years.[20]

The results of this study also showed that the distribution of RNFL thickness was often found in the superior quadrant, this is in accordance with research conducted by Mehboob et al which stated that RNFL thickness was often found in the superior quadrant in patients with a degree of retinopathy PDR.[21] This is in line with research conducted by Dwijayanti which stated

that there was a positive correlation between RNFL thickness in the superior quadrant.[22] The results of this study showed insignificant results, there was insufficient evidence to state that TNF-α levels were related to RNFL thickness in diabetic retinopathy patients in the samples studied. This is likely due to the condition of the patients in this study being patients with chronic diseases who have received treatment, which allows for suppression of the response to inflammatory stimuli, as stated in a study conducted by Swapan K. De et al.[23] This was also proven in a study conducted by Panchenko M.V et al which stated that increased levels of TNF-α can significantly occur in patients who have a strong drive to induce autoimmune retinal diseases such as autoimmune uveoretinitis.[24] This study also found no significant relationship between TNF-α levels and the level of RNFL thickness with the superior and inferior quadrants in patients with diabetic retinopathy, which is in line with a study conducted by Mehboob, which stated that the thickness of retinopathy cannot be linked regardless of the degree of diabetic retinopathy itself. These results indicate that TNF-α levels may not directly affect superior RNFL thickness in patients in this study.[21]

As for the relationship between TNF-α levels and RNFL thickness levels with the temporal and nasal quadrants, analysis could not be performed so that insignificant results were obtained, this was due to the limited research sample and the available research time. This indicates that TNF-α levels may not play a major role in determining RNFL thickness in the patients studied. Clinically, one patient with thin temporal RNFL thickness was also known to suffer from diabetic retinopathy at the Non-Proliferative Diabetic Retinopathy (NPDR) level, while the other four patients with thick temporal RNFL thickness all experienced Proliferative Diabetic Retinopathy (PDR). This suggests a potential relationship between temporal RNFL thickness and the degree of diabetic retinopathy, although it was not statistically significant in this limited sample.

This indicates the need for further research with a larger sample to confirm these results, given the possible influence of individual variation in response to changes in RNFL thickness and diabetic retinopathy. This highlights the importance of considering additional factors that may influence RNFL thickness, such as other assessments of retinal structure or biomolecular factors other than TNF-α, to obtain a more complete picture of the role of RNFL in the pathophysiology of diabetic retinopathy.

CONCLUSION

In this study, the demographic characteristics of diabetic retinopathy patients at Prof. CPL Universitas Sumatera Utara General Hospital and affiliated hospital were predominantly

male. The frequency distribution of diabetic retinopathy patients by degree in this study showed that the degree of PDR was the most frequently encountered. The duration of diabetes in diabetic retinopathy patients in this study was generally more than 5 years.

The average TNF-α levels in diabetic retinopathy patients with thin and thick RNFL did not show a significant difference (65.87 ng/L vs 64.78 ng/L). Independent T-test results indicated no significant relationship between TNF-α levels and RNFL thickness in the temporal, superior, or inferior regions in diabetic retinopathy patients. Additionally, analysis based on the degree of retinopathy (NPDR vs PDR) showed no significant relationship between the degree of retinopathy and thin RNFL thickness in the temporal, superior, and inferior regions.

Chi-Square and Fischer's Exact tests confirmed that there was no significant relationship between the degree of diabetic retinopathy and RNFL thickness in various layers. These findings suggest that RNFL thickness in diabetic retinopathy patients is not directly related to TNF-α levels or the degree of retinopathy. Differences in RNFL thickness between patients with NPDR and PDR may be influenced by other factors that need to be considered in further research, such as genetic factors, blood sugar control, or therapy use.

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ORIGINAL ARTICLE

REFRACTIVE AND VISUAL OUTCOMES OF PEDIATRIC CATARACT SURGERY IN INDONESIAN TERTIARY EYE CENTER

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ABSTRACT

Introduction: *Cataract remains as a leading cause of visual impairment in children. Surgical intervention and post-operative refractive correction remain fundamental. This study aims to describe the refractive and visual outcome of pediatric cataract surgery in a tertiary eye center in Indonesia.*

Methods: *This retrospective study was conducted utilizing medical records of all congenital and developmental cataracts patients undergoing cataract extraction procedures with or without primary IOL implantation between January and December 2022. Exclusion criteria included patients who did not undergo visual acuity and objective refraction examination 1-month post-cataract surgery and those with incomplete medical records data.*

Results: *A total of 118 eyes from 65 patients was included in this study. Most patients had bilateral cataracts (93.80%) and operated at the median age of 18 (0.96-212.64) months. Post-operatively, there were 71 (60.19%) aphakic and 47 (39.81%) pseudophakic eyes with a respective refractive status of +18.00 (12.00 – 21.13) D and +0.60 (±2.37) D. Prediction error (PE) and absolute prediction error (APE) were obtained within 1.00 D. Most aphakic eyes had unquantifiable visual acuity both before (91.50%) and after (83%) surgery. Among pseudophakic eyes, nine (19.16%) had visual acuity of ≥ 6/12 and seven (14.89%) had visual acuity of <6/12 - 6/18 post-operatively. No patients had visual acuity ≥ 6/12 and <6/12 - 6/18 before surgery.*

Conclusion: *Post-operative refractive status of both aphakic and pseudophakic patients were well within correctable range. There was an improvement of vision after surgery. Limited visual potential may be attributed to the presence of amblyopia.*

Keywords: *cataract extraction, congenital cataract, visual acuity*

INTRODUCTION

Cataract remains as a leading cause of visual impairment in children. It was estimated that the prevalence of congenital cataract is 0.6 to 9.3 per 10,000 live births. They account for 10% of pediatric visual impairment worldwide. Four percent of childhood blindness could be attributed to cataract due to inoperable bilateral condition, amblyopia, postoperative complications, and associated ocular conditions.[1–3]

Lens extraction procedure remains the mainstay of treatment for congenital cataract. Discussions regarding several aspects of congenital cataract surgery, such as the optimal age for primary intraocular lens (IOL) implantation and the target refraction for IOL implantation, were

still ongoing. However, timely surgery for clinically significant cataracts and postoperative refractive correction remains critical to prevent amblyopia.[1,3,4]

Pediatric cataract surgery is one of the initiatives to reduce the prevalence of childhood visual impairment and blindness. Post-operative evaluations are crucial to determine the quality of surgical service. In Indonesia, some of the barriers to cataract surgical services include cost, community awareness, and willingness to undergo surgery. Similar barriers are also faced in the implementation of cataract surgical services for children in developing countries. Performing pediatric cataract surgery in a timely manner in developing countries may still be challenging.[5,6] This study aims to describe the refractive and visual outcome of pediatric cataract surgery in a tertiary eye center in Indonesia.

METHODS

This study employed a single-center retrospective design, analyzing medical records of patients diagnosed with congenital or developmental cataracts who underwent surgery between January and December 2022. The study included children who underwent cataract extraction procedure with or without primary IOL implantation. Patients who loss to follow up and did not undergo objective refraction examination 1 month post operatively or lacked complete medical records were excluded.

Data collected from medical records included child's age at recognition (when signs of cataract were first noticed by the parents or caregiver), age at surgery (when the first surgery was done), gender, place of resident, cataract laterality, pre-operative biometry and keratometry, and associated ocular and systemic disorder. Pre-operative and post-operative presenting visual acuity (PVA), post-operative lens status, and post-operative objective refraction were also documented. In uncooperative patients, keratometry (Autokeratometer KM-500, Nidek Co. Ltd., Japan) and A-scan biometry (Biometer AL-100, Tomey, Japan) measurements were done in general anaesthesia before surgery. IOL Master® 700 (Carl Zeiss, Germany) were done in cooperative patient. To determine refractive target, Enyedi's Rule of Seven were used for children under 7 years. In cases of unilateral cataract or pseudophakic fellow eye, refractive target adjusted according to the objective refraction of the fellow eye.

All lens extraction procedures, with or without primary IOL implantation, were performed under general anaesthesia. Primary posterior capsulotomy with or without anterior vitrectomy were done in children under 5 years or deemed uncooperative for post-operative in-office Nd:Yag capsulotomy laser due to posterior capsule opacification (PCO) or visual axis opacification (VAO). Primary IOL implantation was done in children aged at least 2 years old

and sufficient corneal diameter. IOL may be implanted in-the-bag or in sulcus. At the end of the procedure, corneal incision was sutured using non-absorbable 10–0 nylon. Five experienced pediatric ophthalmology consultants performed all of the surgeries.

All participants were examined after surgery with follow-up appointments at 1 day, 1 week, and 1 month. Visual acuity and objective refraction measurement at the 1-month mark were used for the study's analysis. Visual acuity assessment methods were varied depending on the child's age, ability to communicate verbally, and overall cooperation, using Snellen chart, Cardiff cards, cake decoration, toys, or pen light. Patients aged 5 years old and/or able to communicate properly were assessed using Snellen Chart. Those aged below 5 years were assessed with Cardiff card or Cake Decoration if the patient is not cooperative enough. Infant patients were assessed with blink reflex or light/object fixation examination.

Objective refraction measurement is conducted using an autokeratorefractometer (TONOREFTM III; Nidek Co. Ltd., Japan) on cooperative patients and streak retinoscopy on uncooperative patients. Refractive status is then converted into spherical equivalent (SE). Subsequently, prediction error (PE) is calculated by subtracting the predicted refractive status from the actual postoperative refractive status and absolute prediction error (APE) is calculated by subtracting the predicted refractive status from the actual postoperative refractive status in absolute value.

Data processing and analysis were conducted using Microsoft® Excel (Microsoft, Washington, USA) and Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corporation, New York, USA). To determine the normality of distribution within variable, the Shapiro-Wilk tests and the Kolmogorov-Smirnov tests were used where the sample size was either smaller or larger than 50 in each group, respectively. Mean and standard deviation were used to describe normally distributed data, while median and range were used to describe non-normally distributed data. This study adhered to the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of our institution (No.:DP.04.03/D.XXIV.16/5400/2024; April 1,2024).

RESULTS

Congenital and developmental cataract surgery was performed on 71 pediatric patients at our institution during the period of January-December 2022. Six patients were excluded due to incomplete follow-up data, resulting in 118 eyes from 65 patients who were used as the sample for this study.

Demographic and clinical characteristics were presented in Table 1. The median age at where cataract signs were recognized was quite early at 1.92 months with several patients were recognized not long after birth. However, there was a delay before patients present to our institution and subsequently, surgery was performed at median age of 18.00 months. Males were slightly more prevalent, making up 56.9% of the patients. Bilateral cataracts were present in the vast majority (93.8%) of patients. Nystagmus (53.85%) and congenital heart disease (7.7%) was the most frequently found associated ocular and systemic disorder, respectively. In addition, 3 cases (4.6%) were linked to congenital rubella syndrome.

Table 1. Clinical And Demographic Profile

Profile	n=65 (patients)
Age, recognized (months)	1.92(0.00-123.00)*
Age, surgery (months)	18.00(0.96-212.64)*
Sex	
Male	37(56.90%)
Female	28(43.10%)
Laterality	
Bilateral	61(93.80%)
Unilateral	4(6.20%)
Associated Ocular Disorder	
Nystagmus	35(53.85%)
Strabismus	7(10.77%)
Microcornea	5(7.69%)
Persistent fetal vasculature	4(6.15%)
Microphtalmia	2(3.08%)
Anterior segment dysgenesis	1(1.54%)
Optic nerve hypoplasia	1(1.54%)
Microspherophakia	1(1.54%)
Retinopathy of prematurity	1(1.54%)
Associated Systemic Disorder	
Congenital heart disease	5(7.70%)
Down syndrome	4(6.20%)
Microcephaly	3(4.60%)
Congenital rubella syndrome	3(4.60%)
Congenital hypothyroid	1(1.50%)
Hearing impairment	1(1.50%)
Epilepsy	1(1.50%)

*Median (range)

Preoperative biometry was performed before surgery under anaesthesia in 94 (79.7%) eyes of uncooperative patients using A-scan biometry. The results of preoperative biometry for all eyes are shown in Table 2. The median of axial length (20.72 mm), corneal diameter (11.00 mm), and mean K (44.26 D) were within normal range. Based on the post-operative lens status, 71 patients (60.19%) were aphakic and the remaining 47 patients (39.81%) were pseudophakic. The details regarding post-operative refractive status, including PE and APE, can be found in Table 3. Both the PE and APE was found within the range of 1.00 D.

Table 2. Pre-operative Biometry

Parameter	n=118 (eyes)
Axial length (mm)	20.72(15.59-28.20)*
Keratometry	
Corneal diameter (mm)	11.00(8.00-12.80)*
K1 (D)	43.51(37.30-52.28)*
K2 (D)	45.59(39.43-53.55)*
Mean K (D)	44.26(39.11-52.72)*

*Median (range)

Pre-operative and post-operative PVA were detailed in Figure 1. A significant portion of the aphakic eyes had unquantifiable visual acuity both before (91.50%) and after (83%) surgery which may be attributed to the young age of the patients. However, in pseudophakic group, 34.05% eyes achieved post-operative visual acuity of ≥ 6/18. Notably, no eye in this group had pre-operative visual acuity of ≥ 6/18.

Table 3. Post-operative Refractive Status

Variables	Mean/Median
Aphakic (n=71 eyes)	
Actual refraction (D)	18.00(12.00 – 21.13)*
Pseudophakic (n=47 eyes)	
Actual refraction (D)	0,60 (±2,37)†
Predicted refraction (D)	0,61 (-0,30 - 6,03)*
PE (D)	0,83 (±1,37)†
APE (D)	1,00 (0,04 - 3,96)†

*Median (range); †Mean (standard deviation); PE: prediction error; APE: absolute prediction error.

DISCUSSION

Bilateral congenital cataracts are more commonly encountered than unilateral ones. These cataracts may present with or without associated systemic conditions. In a previous study conducted in Guatemala, it was also found that the majority of congenital cataract cases presented bilaterally (70%).[2] Bilateral presentation generally occurs due to mutations of gene that regulate proteins in the crystalline lens. As much as 70% of bilateral congenital cataract cases etiology in developed countries can be identified due to adequate available diagnostic modalities, including genetic testing. These findings differ with studies conducted in developing countries, where the etiology could be identified in only 37% of cases, consisting of 34% genetic cases and 3% infection-related cases.[1,2,7] In this study, it was also found that the majority of cases involved bilaterally. Infection-related etiology was identified in 4.60% of cases which was attributed to congenital rubella syndrome. Unfortunately, identification of gene mutations of pediatric cataract cases in this study were implausible due to the absence of genetic testing modalities in our institution.

Figure 1. Presenting Visual Acuity Based on Post-Operative Lens Status.
*Unquantifiable visual acuity status includes blink reflex, fix & follow the light, and fix & follow the object

Nystagmus is one of the most commonly found associated ocular conditions in pediatric cataract. In Wilhelm's study, the prevalence of nystagmus in congenital cataracts was found to be 61%.[2] Significant bilateral cataracts can cause limited visual input on the retina, thus disrupting the normal development of ability to fixate. This leads to observable nystagmus within the first 3 months of life, although the onset of nystagmus can occur up to 2 years of age. The presence of nystagmus indicates a poorer visual prognosis in patients with bilateral congenital cataracts as nystagmus may be used as a marker for deprivation amblyopia.[3,8,9] Early

intervention is critical, but remains a challenge in developing countries. Data on the age at surgery for congenital cataracts in developing countries have been obtained from Kabylbekova et al.'s study in Kazakhstan, which found a median age at surgery for bilateral congenital cataracts at 52 months, and from Liu et al.'s study in China, which found a mean age of 0.92 years for aphakic group and 4.9 years for pseudophakic group.[8,10] In this study, nystagmus was observed in 35 (53.85%) patients and the median age at surgery was 18 months. This is quite unfortunate considering that the median age when cataract signs were noticed by the caregivers was 1.92 months, and for some patients, shortly after birth. Delay in surgical intervention may be attributed to several factors including existing healthcare systems and family knowledge regarding pediatric cataract signs. Previous study by Ratnaningsih et al showed that cost, both direct and indirect, is the major barrier for cataract surgery for adults in West Java Province in Indonesia.[5] Further research is needed to assess the factors causing such delays for pediatric cataract surgery in Indonesia.

A newborn infant undergoes significant physiological axial length growth up to the age of 2 years. Axial length increases from an average of 16.78 mm at birth to an average of 20.69 mm by 1-2 years of age. The rate of axial length growth then decreases as the patient ages from 2 to 5 years, with a total increase in axial length of 1.1-1.2 mm. A phase of slow axial length growth continues until approximately 13 years of age, with an increase in axial length of 1.1-1.2 mm. The rate of axial length increases then diminish until around 18 years of age. These changes in axial length are important considerations in determining refractive targets and selecting IOL for pediatric cataract surgery. Additionally, changes in corneal status as a child grows also need to be considered. In newborns, the physiological horizontal corneal diameter ranges between 9.5-10.5 mm with a mean K reading of 52.00 D. As age progresses, corneal diameter increases and corneal curvature flattens, reaching an average of 11-12 mm for horizontal corneal diameter and 42.00-44.00 D for mean K readings.[3,7] However, changes in refractive status of patients with pediatric cataracts undergoing surgical intervention, with or without IOL implantation, differ from children without history of aforementioned surgery as the patient ages. Studies by McClatchey et al. indicate a higher rate of refractive growth (RRG) variation in eyes that have undergone congenital cataract surgery compared to normal eyes in a 10-year follow-up post-operation. Thus, predicting refractive status changes in aphakic and pseudophakic children is more challenging.[11] Pre-operative median axial length (20.72 mm) and mean K readings (44.26 D) obtained in this study was in accordance with physiological axial length growth and corneal curvature changes in children. Several associated ocular disorder which may affect refractive status also present in this study, including microphthalmia

(7.69%), microcornea (3.08%), anterior segment dysgenesis (1.54%), microspherophakia (1.54%), retinopathy of prematurity (1.54%), and persistent fetal vasculature (6.15%), although in insignificant numbers.

Based on previous studies, primary IOL implantation is recommended when the patient is at least 2 years old. However, the ongoing development of the eye makes determining the refractive target and the accuracy of IOL calculation more challenging compared to adults. There is a high risk of complications and significant PE/APE for primary IOL implantation in younger patients.[4,10,12] A study conducted by Oke et al. indicates that the accuracy of IOL calculations increases as the patients age with a statistically significant result.[13] A review by Muslim and Barliana found that most studies on IOL accuracy in children assess outcomes 4-8 weeks post-operatively. The same study also found no superior formula for determining IOL power in pediatric patients.[12] In this study, 47 (39.81%) pseudophakic patients had a mean PE value of 0.83 D and median APE value of 1.00 D at the 1-month follow-up. This indicates good refractive outcomes of pediatric cataract surgery and in accordance with the follow-up examination timeframe for assessing PE and APE in previous studies. These results are also consistent with our prior research, which found an average APE of 1.34 D using the SRK/T formula.[14] The median age of patients undergoing primary IOL implantation in this study was 6.66 years, may also possibly contributing to the observed good accuracy.

WHO recommends pediatric cataract surgery as a means to reduce preventable blindness in children population. A study conducted by Asferaw et al. in Ethiopia showed improvement from 4% of eyes with visual acuity of 6/6-6/18 and 92% of eyes with visual acuity <6/60, to 37% of eyes with visual acuity 6/6-6/18 and 43% of eyes with visual acuity <6/60 post-operatively.[15] Higher RRG values and myopic shift in eyes that have undergone pediatric cataract surgery need to be considered during follow-up examinations to adjust refractive correction according to the patient's needs as they age. This is important to prevent a decrease in visual acuity, especially as patients reach school age.[11,16] Most aphakic patients in this study had PVA that could not be quantified either before (91.50%) or after (83%) surgery. This is due to the very young age of the patients, making it difficult to perform quantifiable visual acuity examinations. Improvement in visual status can be observed in patients undergoing primary IOL implantation. There was a decrease in the percentage of patients with visual acuity <3/60 post-operative (17.02%) compared to pre-operative (42.56%). The number of patients with visual acuity ≥6/18 also increased to 34.05% post-operatively, which was none in this category pre-operatively. Long-term follow-up is necessary for all patients, considering the dynamic changes in refractive status that occur in pediatric patients and the refractive adjustments for

ongoing visual needs.

In this study, there was an improvement in visual acuity after surgery, especially in the pseudophakic group. However, limited improvement may be attributed to deprivation amblyopia that had already occurred in the patients. The median age at surgery at 18 months and median age at recognition at 1.92 months may indicate a barrier that prevented the patients from being brought to our institution earlier. Literatures suggested that patients with unilateral cataract undergo surgery at 4-6 weeks of age and bilateral cataract before 10 weeks of age. The presence of cataract at this critical period causes limited visual input resulting in visual cortex deficiency. The prognosis of amblyopia due to deprivation is known to be worse. However, with appropriate post-operative occlusion therapy and refractive correction, the patient's visual function may be steadily improved during follow-up examinations.[3,6,7]

This study has several limitations. Regarding the nature of its retrospective design, several potential variables that could be analyzed such as cataract morphologies could not be documented due to incomplete medical records. Additionally, standardized examination protocols could not be implemented as in prospective studies. Some variables in this study showed non-normal distributions, suggesting a need for a larger sample size. This study was conducted at a national ophthalmology referral center in Indonesia with a relatively sufficient resources, thus the findings may not be generalizable to other healthcare facilities in Indonesia. However, to our knowledge, this is the first published reports regarding the outcomes of pediatric cataract surgery in Indonesia which includes both aphakic and pseudophakic group.

CONCLUSION

The majority of pediatric cataract patients who underwent surgery at an Indonesian tertiary eye referral center had bilateral cataracts. Post-operative lens status was predominantly aphakic, with a mean postoperative refractive power of 18.00 D. In patients with post-operative pseudophakia, a refractive power of 0.60 D was obtained. Both the PE and APE were within acceptable range. There was an improvement in visual acuity after surgery. However, a large number of the patients was not cooperative enough to be evaluated with quantifiable methods of visual acuity measurements. Limited visual potential may be attributed to the presence of amblyopia due to the late presentation.

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CASE REPORT

UNUSUAL CASE OF A METAL FOREIGN OBJECT IN ORBITOCRANIAL INJURY: UNLOCKING THE MACCARTY KEYHOLE

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ABSTRACT

***Introduction**: Penetrating orbitocranial injuries are quite rare but very fatal if left untreated. Various metal objects have been reported as foreign bodies that have penetrated the orbit. However, unusual objects such as motorcycle locks have never been reported before.*

***Case Illustration:** A 14-year-old boy was brought to the emergency room with a motorcycle lock embedded in his left temporal region. Examination of the left eye showed decreased vision, clear serous ciliary secretions, conjunctival hyperemia, chemosis, and relative afferent pupillary defect. Investigations using a 3D Head MSCT Scan revealed the presence of a metal object that penetrates the left optic nerve, the rectus lateralis muscle, and the frontal process of the left zygoma bone in the left temporal region, which is located around the MacCarty keyhole. The operation in the form of exploration and foreign object removal was then carried out in collaboration with the neurosurgeon. No postoperative complications were reported, but the patient had restricted movement of the left eye.*

***Discussion:** Penetrating orbitocranial injury should be treated as an emergency. Diagnosis should include comprehensive ophthalmological and neurological examinations. CT Scan continues to be the best cranial imaging technique. In this case, the motorcycle lock penetration was around the MacCarty keyhole, a structure that is frequently used to enter both the orbit and the frontal fossa, which located 7 mm superior and 5 mm posterior to the frontozygomatic suture. An appropriate surgical strategy is mandatory for removing the object because it may lead to serious consequences, including cerebral, infectious, vascular complications, and even death.*

***Conclusion**: Metal foreign objects such as motorcycle lock was considered unusual, particulary when it unlock an important landmark such as MacCarty keyhole. This case emphasizes the significance of a surgical strategy based on accurate anatomical tracking.*

***Keywords:** penetrating orbitocranial injury, unusual foreign objects, motorcycle lock, MacCarty keyhole.*

INTRODUCTION

Injuries to the orbitocranium (orbitocranial injuries) that penetrate the skull account for just 0.4% of all head injuries in the general population, yet they are extremely deadly.[4] Approximately 45% of penetrating head injuries in children and 24% of penetrating head injuries in adults result from these traumas.[5,6] Despite being rare, penetrating orbitocranial injuries frequently result in serious brain damage if left untreated.[7] Additionally, these injuries may result in eyeball abrasions, retrobulbar hematoma, prolapse, injury to the optic nerve (visual abnormalities), intracranial consequences (neurological deficits), vascular complications

(hemorrhage, thrombosis, or occlusion) and infection.[4] The mechanisms by which this type of trauma occurs are falls, motorcycle crashes, accidents, suicides, murder attempts, and explosions.[6,8] Knives, nails, spikes, iron rods, pencils, scissors, fan blades, and screwdrivers are examples of foreign objects that can result in stab wounds that penetrate the orbit and skull.[5,7]

Lacerations from trauma should be examined since they may contain foreign objects.[8] Penetrating orbitocranial injuries might have pronounced clinical signs when they present.[6] Large penetrating object needs specialized care given as soon as possible.[10] The removal of foreign objects in penetrating orbitocranial injuries may increase the risk of further neural, vascular, and cerebral damage. Therefore, surgical therapy strategies may be considered according to the location, type, and size of the traumatic agent.[6] The most common route of foreign objects entry is through the superior orbital roof due to its thin structure and the fragility of the superior orbital plate of the frontal bone in the anterior cranial fossa floor. Another route that relatively common reported is through the superior orbital fissure due to its conical shape, inferior orbital fissure, and optic canal.[9,17,18] Herein, we report a case of penetrating orbitocranial injury in a 14-year-old boy which was caused by a motorcycle lock located right at the keyhole which is very rare where in the last 10 years there have been no similar cases reported in the literature.

CASE ILLUSTRATION

A 14-year-old boy was brought to the emergency room after being stabbed with a motorcycle lock that was embedded to his left temporal region (Figure 1A, 1B). The patient complained of pain and blurring in the left eye accompanied by red and watery eyes since the incident.

Figure 1. Clinical photograph of the patient showing a motorcycle lock embedded in the left temporal region (A,B) with proptosis, chemosis, and hyperemia of the conjunctiva (C).

Airway, breathing, and circulation were within normal limits. An examination of the left eye revealed the visual acuity was 20/40 with normal intraocular pressure. There was lagophthalmos, hyperemia and chemosis of the conjunctiva with minimal clear serous discharge, and mild relative afferent pupillary defect (Figure 1C). The remaining structures were normal. Examination of the right eye revealed no abnormalities.

Supporting examination in the form of a 3D Head MSCT Scan was performed, which revealed the presence of metal density (foreign object) from the frontal process of the left zygoma bone to the posterior of the orbital cavity, with a depth of ± 5cm from the skin, which penetrates the frontal process of the left zygoma bone, the rectus lateralis muscle, and the left optic nerve (Figure 2, Figure 3). There was also fracture of the frontal process of the left zygoma; beam hardening (metal artifact) in the left temporal region; and retention cyst of the right maxillary sinus and left sphenoid sinus. It appeared that the trauma has an impact on an anatomical structure known as the MacCarty keyhole (Figure 3).

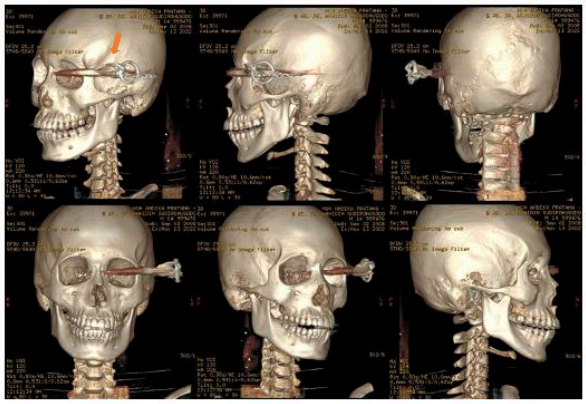

Figure 2. Head MSCT Scan (without contrast) examination showing a metal artifact in the left temporal region

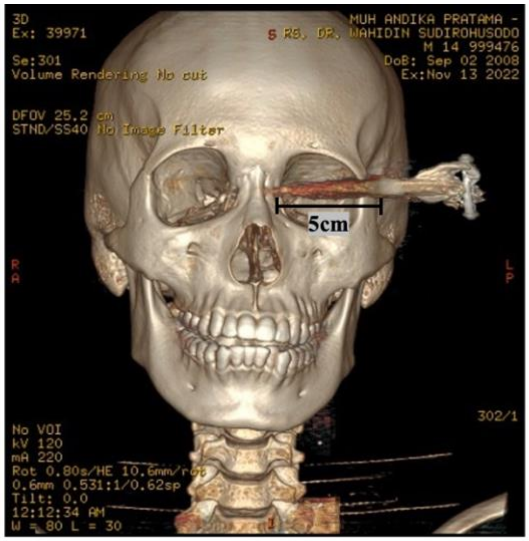

Figure 3. The metal density from the frontal process of the left zygoma bone to the posterior of the orbital cavity, with a depth of ± 5cm from the skin

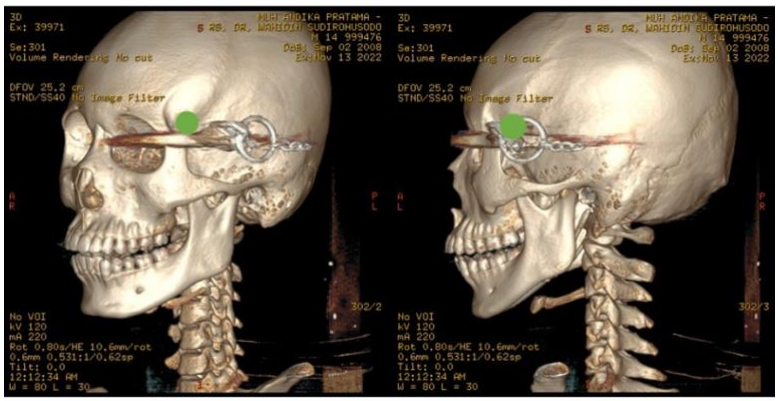

Figure 4. The foreign object impact the MacCarty keyhole (green circle)

The laboratory examination results showed leukocytosis. The diagnosis of penetrating trauma in the left temporal region with orbital involvement was made. The patient was given intravenous Ceftriaxone 1 gram per 12 hours, Metamizole 1 gram per 8 hours, and Ranitidine 50 milligrams per 12 hours.

Exploration and removal of the foreign object was performed in collaboration with neurosurgeon. A lazy S incision is made parallel to the zygoma through the insertion point of the foreign object and deepened, penetrate the cranium. A temporal conjunctival peritomy was made, the tenon was released, then the lateral rectus muscle identified and fixated with 5.0 non absorbable suture. The neurosurgeon then performed craniotomy to remove the foreign object from the lateral wall of the orbital cavity. Forced duction test was done to evaluate the extraocular muscle's function and revealed no restriction at any directions. Evaluation of orbital cavity was normal. The lateral rectus fixation was removed, and conjunctival suture was performed with 8.0 absorbable suture.

The patient was given Polygran eye ointment three times daily, Posop eye drop four times daily, eye compress with Vasacon eye drop four times daily, and oral Methylprednisolone 8mg three times daily.

After surgery, the visual acuity of the left eye decreases to 20/60, there was swelling and hematoma of the eyelid (Figure 5). Examination of the eye movement showed restriction to the superotemporal, temporal, and inferotemporal direction, with interpretation -2, -1, and -2, respectively (Figure 6). The lagophthalmos and relative afferent pupillary defect persisted. The patient was referred to Neuro-ophthalmology division. However, the patient refused funduscopy examination so the optic nerve could not be evaluated and refused the high-dose steroid therapy.

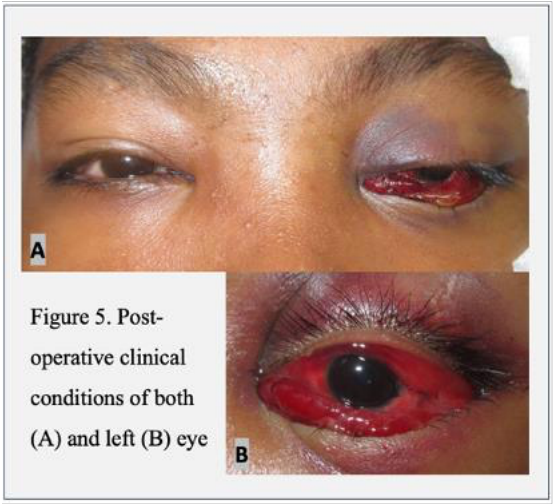

Figure 5. Post-operative clinical conditions of both (A) and left (B) eye

Figure 6. Evaluation of eye movements post-operatively

DISCUSSION

The orbit is a bony cavity that resembles a quadrangular pyramid, with the base located in front and the apex in the back. This anatomical feature has the ability to deflect objects in the direction of the apex, where the superior orbital fissure and optic canal serve as access points to the skull. Additionally, the frontal bone's thin plate and the lesser wing of the sphenoid that make up the roof of the orbit are both easily fractured.[13] The MacCarty keyhole (Figure 7), which is drilled 1 cm behind the frontozygomatic junction (between the zygomatic process of the frontal bone and the frontal process of the zygomatic bone), as the first connecting point between all orbital cuts of the roof and the lateral wall.[20] Tubbs et al. (2010) concluded that the most precise placement of the MacCarty keyhole was at a location approximately 7 mm superior and 5 mm posterior to the frontozygomatic suture.[12]

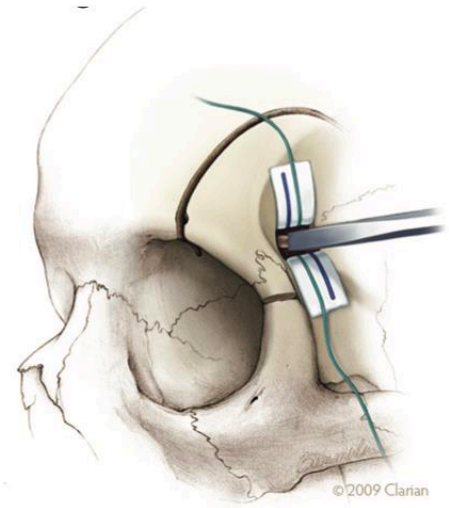

Figure 7. The site of MacCarty keyhole[12]

The MacCarty keyhole and the surgical anatomy of the inferior orbital fissure must be understood to perform a frontotemporal orbitozygomatic approach safely and successfully. Additionally, making use of the MacCarty burr hole aids in maintaining the orbit's lateral wall, which is crucial for avoiding postoperative enophthalmos.[11,20] Accordingly, we accounted this structure when choosing the surgical procedures on patient.

A literature review by Amaral et al. (2020) involving 33 cases with penetrating orbital trauma between 1997 to 2018 reported the main cause for the orbital penetration by foreign objects was assaults (36.3%), followed by falling over blunt objects (33.3%), and motor vehicle accident (12.1%).[8] In our case, the cause of the penetration of the foreign object was an assault.

According to reports, this case accounts for 24% of in adults and 45% in children, and it affects boys more frequently than girls.[11] This was evident in our case, where the patient is a boy.

Prior cases have reported unusual foreign objects like house key (Sarkar et al., 2015) and pressure cookers nozzle (Bhattacharyya et al., 2022) causing penetrating ocular injuries.[9,14] In our case, the foreign object was a motorcycle lock. To the best of our knowledge, we considered this report as a rare and unusual case.

The diagnosis was based on physical examination where there was evidence of lagophthalmos, hyperemia and chemosis of the conjunctiva, clear serous discharge, and the presence of relative afferent pupillary defect, indicating involvement of orbital structures. These findings were classically similar with previous studies. Yin et al. (2020) reported a 66-year-old male patient with a coat hook penetrated his left orbit through the lower lid. The ophthalmologic exam revealed an edematous left lower eyelid, decreased visual acuity, and relative afferent pupillary defect.[16] Hansen et al. (2020) described a 75-year-old man with left upper cheek laceration with a lodged wooden object. The examination revealed periorbital swelling, blepharoptosis, conjunctival hyperemia, exophthalmos, and relative afferent pupillary defect.[19]

Radiographic studies are crucial for making a proper diagnosis, selecting an appropriate surgical protocol, and determining the size, shape, and trajectory of the foreign object penetration.[15,16] The use of simple facial X-rays for the identification of orbital fractures is debatable in specific situations where there is a possibility of an intraocular foreign body.[10,16] This is particularly true in our case because the foreign object can be seen clearly and the mechanism of injury can be foreseen, eliminating the need for a plain x-ray. Complaints of blurred vision and limited eye movement raise our suspicions of damage to the orbital structures and optic nerve. Because of the metallic property of the foreign object, we chose to perform a 3D Head MSCT Scan to determine the impacted orbitocranial structures and severity of the

injury, which is also the gold standard test for penetrating orbitocranial injury.[10,11,13,16]

In our case, the penetration of the foreign object was through the frontal process of the left zygoma bone and the CT scan revealed the wound is located around the MacCarty keyhole. This structure is regarded as the foundation of orbitozygomatic approaches, which were used in our case and are frequently employed by skull base neurosurgeons.

Additional laboratory tests for preoperative evaluation were performed with results of leucocytosis. According to the literature, broad-spectrum antibiotics with good central nervous system penetration, such as metronidazole, ciprofloxacin, and ceftriaxone, should be administered as soon as possible after admission to begin treatment. Although the visual outcome has not been established, high dose steroids are recommended for traumatic optic neuropathy.[10] In our case, the administration of high dose steroids was not done because the patient refused to undergo funduscopy examination causing the optic nerve could not be evaluated.

Penetrating orbitocranial injury patients are at a high risk for intracranial infections. Brain abscess, encephalitis, meningitis, osteomyelitis, and scalp wound sepsis can happen. Monitoring infection indicators and prompt prophylactic antibiotic administration for 7 to 14 days are advised.[16] In our case, the patient showed no symptoms of infection or vascular complications, which may have been prevented by the rapid and accurate removal of the foreign object during surgery. However, signs of eye disorders caused by lockkey trauma to the surrounding muscles, nerves, or directly to the eye organs persist after surgery. A long-term follow up is mandatory. Nevertheless, our patient had a poor compliance which limited us in assessing long-term outcomes.

CONCLUSION

Penetrating orbitocranial injury cases caused by unusual foreign objects such as motorcycle lock are uncommon. In such cases, suspicion of involvement of the orbital structures should be tracked with a 3D CT-Scan. The clinical outcome is strongly influenced by the object's entry point, trajectory, involvement of the paranasal sinuses, degree of brain parenchymal injury, and complications. This case emphasizes the significance of a surgical strategy based on accurate anatomical tracking.

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CASE REPORT

NON METALLIC ANTERIOR CHAMBER FOREIGN BODY: A CASE REPORT

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ABSTRACT

Introduction: *Intraocular foreign body (IOFB) is a serious form of open-globe injury that can cause a serious ocular trauma that lead to blindness (10–40% of all open eye injuries). This case report is aimed to report a challenging management of anterior chamber foreign body.*

Case Report: *A 41 year-old man presented with discomfort on his right eye 4 days prior to visit. The slit lamp biomicroscopic examination revealed inferior anterior chamber foreign body (stone), measuring 5 x 2 mm and 5 mm scar at the area of a full thickness self-sealed corneal laceration. The corneal edema was localized hence it was possible to visualize the foreign body's entire path through the cornea. The foreign body was removed with forceps from superior limbal incision. Post operative visual acuity was improved and the inflammation was decreased.*

Discussion: *Management of such cases is not always easy because certain ACFB made of inert materials (stone, plastic, glass, and inert metals such as gold, silver, or platinum) excite minimal inflammation and may remain quiescent for a long period of time. An anterior IOFB is usually associated with a better final BCVA than a posterior IOFB. The self-sealing wounds were limited to the paracentral or peripheral cornea, resulting in no significant astigmatism*

Conclusion: *The risk of intraocular foreign body is associated with mechanism of injury and history taking must be accurate. Intraocular foreign bodies must have surgical removal to prevent of ocular inflammation and complication.*

Keywords: *Anterior Chamber Foreign Bodies (ACFB), IOFB, Open Globe Injury, Penetrating Injury.*

INTRODUCTION

IOFBs are the worldwide problems and represent a serious form of open-globe injuries that can result in visual loss. Intraocular foreign bodies (IOFB) cause a serious ocular trauma that can lead to blindness (10–40% of all open eye injuries). IOFB is closely related to the living and working environment, as well as the individual awareness of protection and protective measures. [1,2]

The most eye injuries with IOFBs are work related. The three most common causes of eye injuries were grass trimming, chiselling, and hammering. [3] Penetrating ocular trauma is a

potentially vision-threatening injury. The extent of injury depends on factors that include size and composition of the foreign body, force of entry into the eye, location of the resulting wound, and the final location of the foreign body. Other important factors that might influence the final prognosis are initial visual acuity, presence of an afferent pupillary defect, perforation of the globe, and endophthalmitis.[4]

We report a case of an adult male with a retained intraocular stone foreign body in the anterior chamber of the eye and discuss the various considerations in the management of such cases.

CASE ILLUSTRATION

A 41-year-old man was referred to the outpatient clinic of the Cataract and Refractive Surgery Department in Dr. Saiful Anwar Hospital, Malang, Indonesia, with discomfort in his right eye (RE) for the past 4 days while hammering the stone. The patient had a past history of ocular trauma to the left eye (LE) while hammering stone four days before his visit. He didn't wear any protective glasses at that time. The patient was treated by local ophthalmologist using amoxicillin 500 mg t.i.d., sodium diclofenac 50 mg b.i.d., gatifloxacin q.6h, a combination of hydrocortisone acetate 5 mg and chloramphenicol 2 mg eye drop q.6h on RE for 4 days. There was no improvement, but a detailed examination revealed a foreign body, and he was referred to our hospital for further evaluation and management.

The chief complaint was accompanied by redness, blurred vision, and watering on his RE. There were no complaints of nausea or vomiting. In his past medical history, there was no significant eye disease, history of previous eye surgery, or history of systemic disease.

Upon examination, the patient's best corrected visual acuity (BCVA) was 6/30 for the RE and 6/6 for the LE. In the RE, there was a 5 mm of a full thickness self-sealed corneal laceration proven by negative seidel test. Slit-lamp examination showed anterior chamber single black foreign body (FB) residing in the angle inferiorly (Figure 1). Inflammatory reaction showed inferior corneal oedema, conjunctival injection, pericorneal injection cornea,. The iris sphincter was regular. Moderate anterior chamber reaction was found (flare +2 and cell +3). The pupil showed a slightly non-round diameter of 4 mm, sluggish pupillary reflex, and negative RAPD. Lens was clear (Figure 2). The intraocular pressure (IOP) was 20 mmHg for the right eye. The anterior and posterior segments of the left eye were normal.

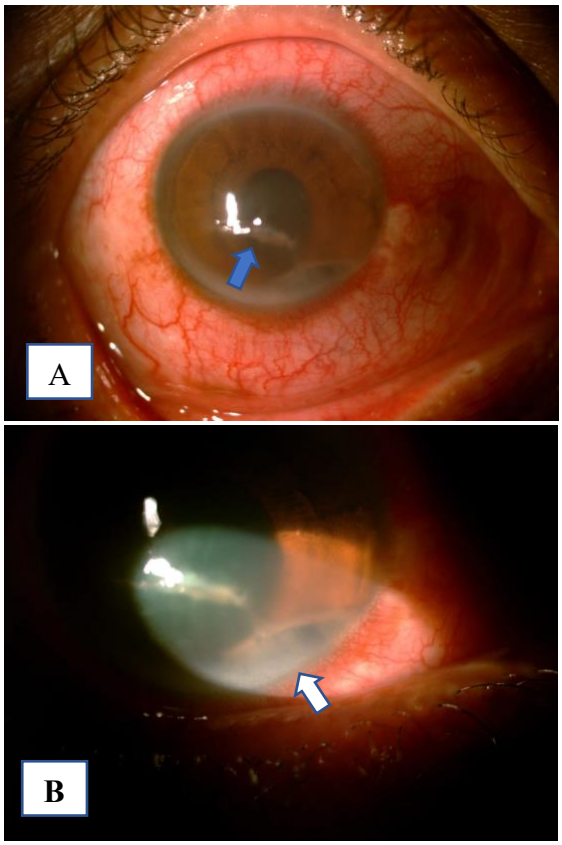

Figure 1. Anterior segment of RE : **A**. Ocular surface of the RE showing macula cornea (blue arrow) and anterior chamber foreign body (white arrow). **B**. Anterior chamber foreign body in 25x magnification.

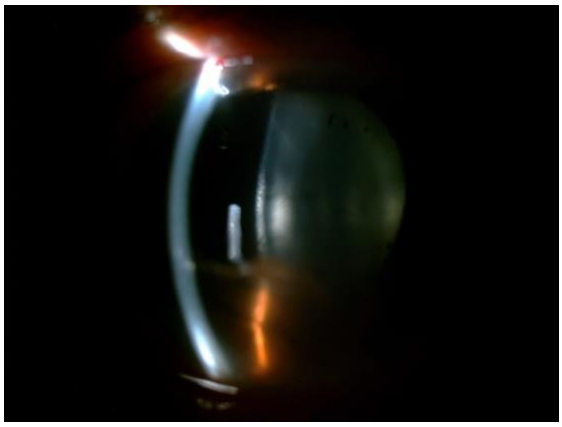

Figure 2. Clear lens showed no injury to the lens.

The ultrasound B scan reported no acoustic shadowing or reverberations, as would be expected. B-scan ocular ultrasonography of the posterior segment for the RE showed a clear vitreous cavity with an attached retina in both eyes and did not reveal any abnormality in the posterior segment (Figure 3). The patient was diagnosed with an anterior chamber foreign body (ACFB).

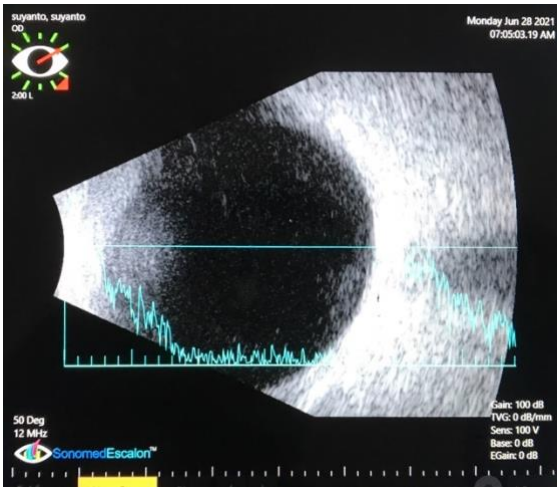

Figure 3. Ultrasound B scan did not reveal any abnormality in the posterior segment.

The ACFB was planned to be removed surgically with local anaesthesia. Levofloxacin eye drop q.4h and 1% atropine sulphate eye drop q.8h are given as preoperative medicine.

The superior limbus incision was made at 5 o'clock with a 2.8 mm keratome blade. The anterior chamber was filled with 2% methylcellulose, and the foreign body (Figure 4) was removed *in toto* with forceps. The remaining refractile particles were aspirated out with irrigation and an aspiration instrument Intracameral cefuroxime was given before suturing and incision was then closed with 10-0 nylon.

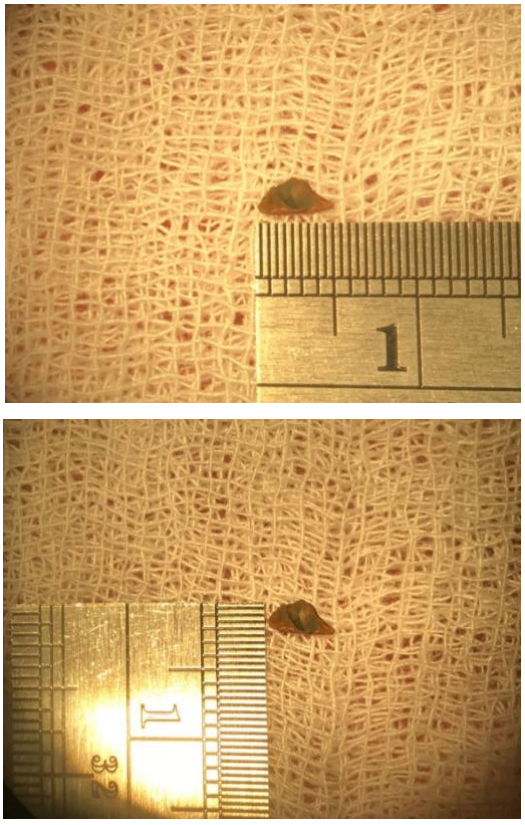

Figure 4. The size of the removed stone was 5 x 2 mm.

During postoperative period, the patient was given oral ciprofloxacin 500 mg b.i.d., oral paracetamol 500 mg t.i.d., oral metilprednisolon 8 mg t.i.d., topical levofloxacin eye drop q.4h, and atropine sulphate eye drop q.8h on RE.

The first day postoperatively, RE visual acuity was decreased to 6/60 due to corneal edema (Figure 5). Conjunctival injection, pericorneal injection, and two sutures with a negative seidel test at the superior limbus were noted. Flare +2 and cell +3 were seen in the anterior chamber. The pupil was not round with a negative pupillary reflex due to cycloplegia. The intraocular pressure was 18 mmHg. Fundus examination was performed post-operatively, and there wasn't any retained intraocular foreign body, and the detail was normal.

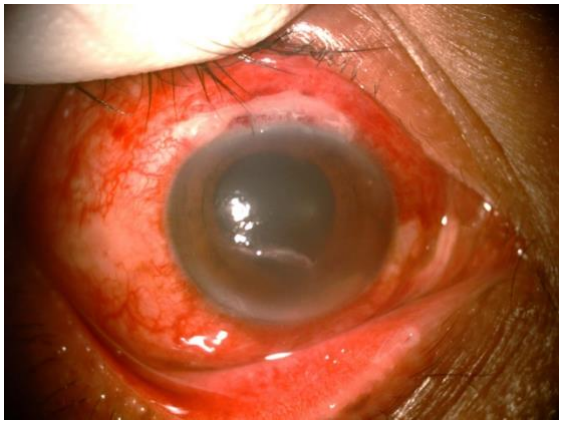

Figure 5. Day 1 post-op: corneal edema with conjunctival and pericorneal injection.

One week after the surgery, RE visual acuity had improved to 6/12 with a correction of S-1.00 C−4.00 ×60. Reduction of conjunctival injection, pericorneal injection, and corneal edema was significant (Figure 6). Anterior chamber flare and cell were negative. Pupil was still not round with a negative pupillary reflex due to cycloplegia. Intraocular pressure was 16 mmHg and the posterior segment was within the normal limit.

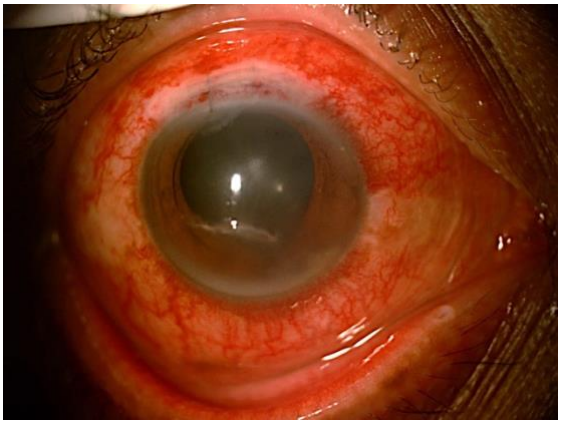

Figure 6. 1 week post-op: corneal edema, conjunctival, and pericorneal injection were reduced.

Two weeks after surgery, RE VA improved to 6/6 with a correction of C−3.00 ×60. Conjunctival injection was minimum and there was negative anterior chamber reaction (Figure 7). The pupil was still not round with a negative pupillary reflex due to cycloplegia. Intraocular pressure was 14 mmHg and the posterior segment was normal.

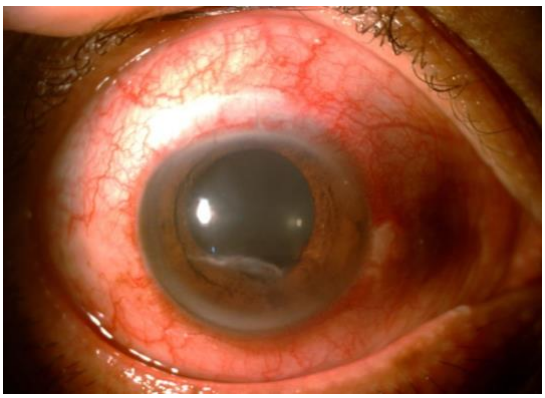

Figure 6. 2 week post-op: corneal edema, conjunctival, and pericorneal injection were significantly reduced.

DISCUSSION

Intraocular foreign body, a kind of ophthalmic emergency, accounts for about 6 % of the ocular trauma and is commonly seen in young male. Splashing of foreign bodies appears most commonly during hammering the foreign object; polishing, welding, drilling, and so forth are also common situations. The IOFBs is one of the leading causes of monocular blindness. The longer foreign bodies stay in the eyes, the greater damage they make. For those reasons, early diagnosis and treatment of IOFBs is important. [1,5]

AC FBs are rare accounting for only 15% of all intraocular IOFBs. Common ACFBs include metallic iron, lead, copper, and nonmetallic FBs such as stone, glass, plastic, cilia, wood, or other vegetative matter. The nonmetallic FBs often have a lower velocity and tend to remain in the AC.[6]

Our patient had a stone foreign body entering through the cornea and resting in the inferior angle making it difficult to detect on slit-lamp examination. Therefore, after taking a thorough history of any ocular or orbital trauma, foreign body must be ruled out even when not observed on initial examination.

The CT scan with thin slices is currently considered the gold standard for the detection, localization, and characterization of both metallic and non-metallic IOFBs. Ultrasonography can be used to detect metallic IOFB but sensitivity is user dependent. It is also contraindicated in cases where globe rupture is suspected. Plain X-ray may be used as a screening modality for IOFBs. MRI is contraindicated in cases of suspected metallic IOFB. It may be considered when

there is a strong suspicion of a non-metallic foreign body not seen with CT scan or ultrasonography.[7]

Primary removal of a small nonmagnetic foreign body can be very challenging. Once the decision to remove is made, surgery should be performed as early as possible.[8] Removal of ACFB through the entry wound is generally not recommended. Foreign body was removed using an intraocular magnet or forceps through a secondary corneal limbal incision, which can also be used for the removal of intralenticular foreign bodies.[9]

In this case, incision was made at superior limbus because it gave surgeon easier access. Sinskey was firstly used to release the FB from the surrounding tissue. It was hard to release because of the surrounding inflammatory membrane. FB was removed from anterior chamber with forceps after widening the wound. Repeated viscoelastic injections were given during the procedure to maintain its stability and to protect corneal endothelium.

Intracameral cefuroxime was given before closing the wound. Bowen, et al. reported that intracameral cefuroxime and moxifloxacin reduced endophthalmitis rates compared to controls with minimal or no toxicity events at standard doses. [10]

Management of such cases is not always easy because certain ACFB made of inert materials (stone, plastic, glass, and other metals such as gold, silver, or platinum) excite minimal inflammation and may remain quiescent for a long period of time. Furthermore, decreased visibility through the cornea due to severe whole corneal edema and lots of KPs with pigmentation imposes an even greater challenge for many surgeons in ACFB removal procedures. [11] In other journal, *Jastaneiah, et al.* reported despite the long duration of the corneal edema it resolved after removal of the FB, the endothelial damage will always be there. [12] In this case, the corneal edema was appeared 1 day after surgery and reduced in one week.

Clinicians administer antibiotics, such as third and fourth generation fluoroquinolones for 7 to 10 days following surgery as prophylaxis against post-traumatic endophthalmitis.[13] We gave ciprofloxacin in this case as a prophylaxis and we added methyl prednisolone to reduce inflammation.

An anterior IOFB is usually associated with a better final BCVA and prognosis than a posterior IOFB. The self-sealing wounds were limited to the paracentral or peripheral cornea, resulting in no significant astigmatism. [14] The Ocular Trauma Classification Group has developed the Ocular Trauma Score (OTS) system to help the ophthalmologists prognosticate the outcomes of eye trauma, OTS show 77% chance to predict the final functional outcome within one visual category shortly after the eye injury.[15] Ocular Trauma Score (OTS) in this

case has a prognosis of visual acuity were 94% ≥20/40 and the visual acuity after one week surgery was improved

CONCLUSION

In conclusion, prognosis of anterior chamber foreign body is greatly associated with mechanism of injury and accurate history-taking. Anterior chamber foreign bodies must be removed surgically to prevent further ocular inflammation and complication.

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CASE REPORT

EMERGING CHALLENGES OF ACUTE BILATERAL DIABETIC CATARACT IN PEDIATRIC: INSIGHT TO EARLY DETECTION AND MANAGEMENT– A CASE REPORT

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ABSTRACT

Introduction: *Intraocular foreign body (IOFB) is a serious form of open-globe injury that can cause a serious ocular trauma that lead to blindness (10–40% of all open eye injuries). This case report is aimed to report a challenging management of anterior chamber foreign body.*

Case Report: *A 17-year-old male patient complained of blurry vision and glare in both eyes(BE) since 3 months in newly diagnosed T1DM (HbA1c 10% → now 6.3%). Visual Acuity(VA) was 6/45PH6/21f2, with correction S-1.50 advancing to 6/18 in BE. Slitlamp examination revealed lens opacity(P3),central,3mm, retinometri 0.32. Posterior segment evaluation and intraocular pressure (IOP) were within normal limits. Right eye(RE) was underwent lensectomy with IOL under GA(General Anesthesia).*

Discussion: *Postoperative RE with final VA of 6/18 PHNI and IOP of 43 mmHg. Patient was given antiinflammation eyedrops, oral and topical antiglaucoma, and achieved final IOP of 8mmHg within 3 days and remains stable without antiglaucoma. Result was satisfying despite of uncomplicated secondary glaucoma as short-term complication that resolved with therapy.*

Conclusion: *Early detection for ocular complication in DM is needed as cataract genesis process still progressing despite of good glycemic control. Ocular manifestation may present as early sign of undiagnosed T1DM or as its complications. Comprehensive multidiscipline treatment, glycemic control, and routine evaluation is essential for the success of metabolic cataract therapy and progression of microvascular complications due to DM. Lensectomy with IOL implantation still the mainstay therapy in pediatric cataract. Awareness play vital role as it possibly cause decreased vision and or amblyopia, leading to blindness.*

Keywords: *Lensectomy, Type I Diabetes Mellitus, Posterior Subcapsular Cataract, Acute Bilateral Cataract*

INTRODUCTION

IOFBs are the worldwide problems and represent a serious form of open-globe injuries that can result in visual loss. Intraocular foreign bodies (IOFB) cause a serious ocular trauma that can lead to blindness (10–40% of all open eye injuries). IOFB is closely related to the living

and working environment, as well as the individual awareness of protection and protective measures. [1,2]

The most eye injuries with IOFBs are work related. The three most common causes of eye injuries were grass trimming, chiselling, and hammering. [3] Penetrating ocular trauma is a potentially vision-threatening injury. The extent of injury depends on factors that include size and composition of the foreign body, force of entry into the eye, location of the resulting wound, and the final location of the foreign body. Other important factors that might influence the final prognosis are initial visual acuity, presence of an afferent pupillary defect, perforation of the globe, and endophthalmitis.[4]

We report a case of an adult male with a retained intraocular stone foreign body in the anterior chamber of the eye and discuss the various considerations in the management of such cases.

CASE ILLUSTRATION

A male patient, 17 years old was consulted for eye evaluation from Endocrine Department with diagnosis of T1DM and AKI (Acute Kidney Injury) prerenal stage. The patient has received insulin therapy.

He complained of blurry vision in both eyes (BE) and glare since diagnosed with T1DM 4 months ago and get worsened since the last 1 month. Complaints of blurry vision didn't improve with wearing glasses and glares especially during the day. Other complaints in BE such as red eye and pain, headache, nausea, and vomiting were denied. History of wearing glasses since 3 years ago with S-1.00 in RE and S -0.75 in LE but felt uncomfortable since the last 4 months.

History of previous eye pain, eye surgery, drug allergies, and trauma were denied. Confirmed history of Diabetic Ketoacidosis (DKA) on DMTI with HbA1c 10%, currently controlled to 6.3% and random blood glucose 115 mg/dl with insulin therapy. History of malaise and unconscious in intensive room and underwent hemodialysis. History of grandmother with DM (+) but the detail is unknown.

On ophthalmological examination, it was found that the visual acuity in BE was 6/45 PH 6/21f2, with spherical correction in BE -1.50 progressing to 6/18. Refraction examination with cycloplegic was obtained in BE 6/45 PH 6/21 with binocular vision of 6/18, hirschberg was orthotrophia, and nystagmus was negative. Examination of the anterior segments of BE showed normal conjunctiva, clear cornea, AC VH4, cells (-) flare (-), posterior lens opacity (P3), central, 3 mm in diameter, was found on retro illumination examination. The pupillary reflex of both

eyes, both direct and indirect light reflex, and RAPD were within normal limits.

On examination of the posterior segments : papil N II were round, well defined, CDR 0.3, a/v 2/3, good retina, dot (-) blot (-) microaneurysm (-) intraretinal microvascular abnormality (IRMA) (-) neovascularization (-) and positive macular reflex. IOP of 14 mmHg in RE and 11 mmHg in LE. The patient's eye movements and confrontation tests were within normal limits in both eyes.

The biometry results of the RE showed that the lens size with the IOL Avansee 21 D (right eye) had a refraction target of -0.34 and Avansee 20.5 D had a refraction target of -0.39 using the SRK/T formula. Specular examination of RE: NUM 253, CD 3529, CV 27, MAX 1062, HEX 64, CT 610 and LE NUM 284, CD 3753, CV 26, MAX 681, HEX 66, CT 611. The patient was then planned for RE pro lens mass aspiration with IOL (Avansee 21 D) under GA. Patients and families are educated about the eye condition, visual prognosis, risks, and complications of surgery. The patient was also consulted to the Cataract and Refractive Surgery (CRS) division for evaluation and assistance for surgery. The paediatric endocrine department and anesthesia department stated that surgery was feasible.

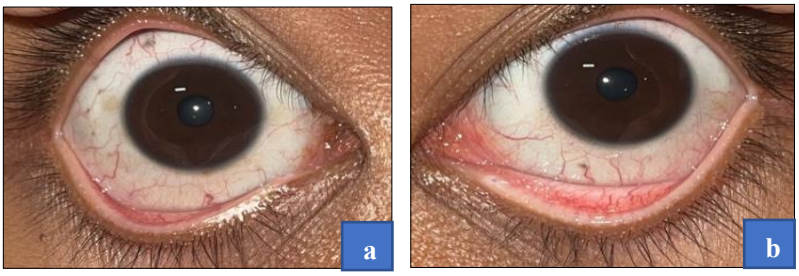

Figure 1a and 1b. both eyes in the time of presentation

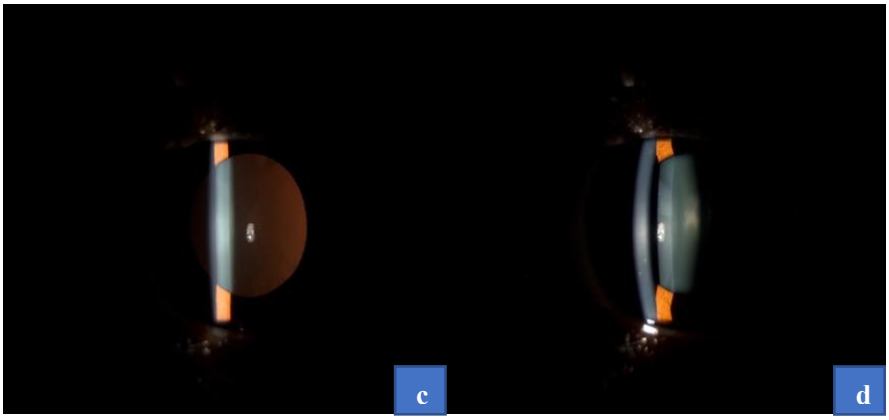

Figure 1c and 1d. Slit lamp image of the right eye with retroillumination

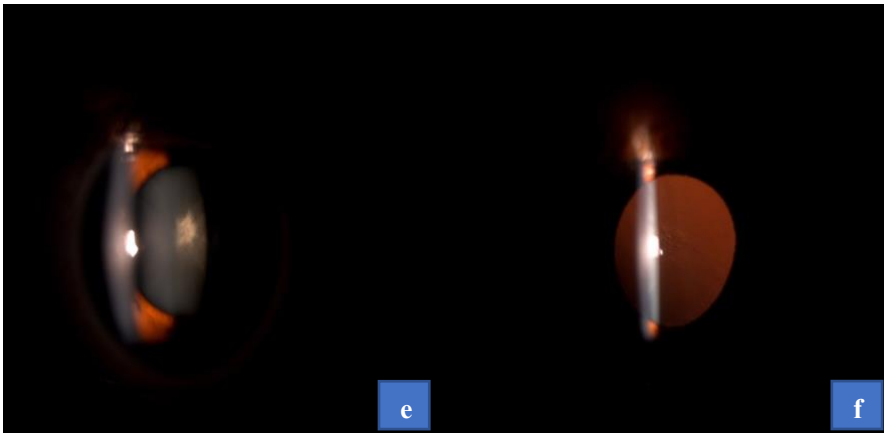

Figure 1e and f. Slit lamp image of the left eye with retroillumination

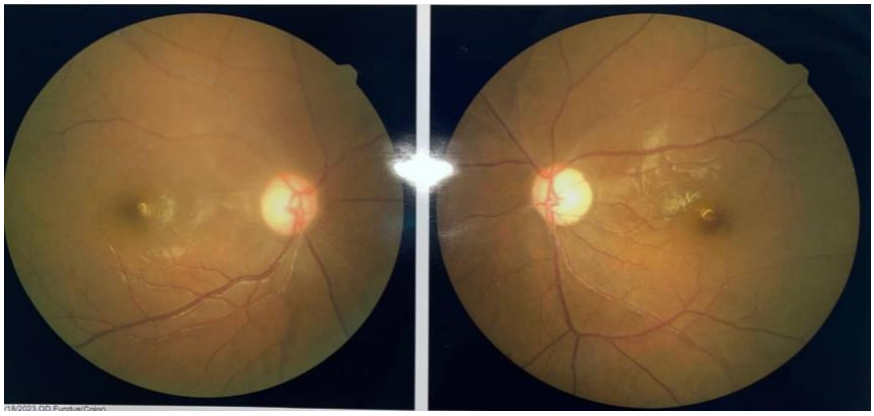

Figure 2. Fundus photo of both eyes

The patient was then diagnosed with RLE Acute Metabolic Cataract (PSC) ec T1DM + susp. Amblyopia Deprivation and planned for RLE lensectomy with IOL implantation under GA (RE first).

After general anaesthesia and disinfection, a blepharostat and eye drape were placed on the right eye. The initial step begins with a lateral corneal incision in the temporal direction at 2 and 5 o'clock and injection of trypan blue to visualize the anterior capsule of the lens and administration of viscoelastic. The operator then performed the capsulorhexis technique with a 27 G needle and microforceps, hydrodissection, and aspiration irrigation of the lens mass. Injection of viscoelastic and IOL placement in the bag followed by aspiration irrigation of remaining visco and intra-cameral and myostat antibiotic injection and corneal hydration. The next steps are bubble and betadine injection to see the tightness of the anterior chamber, subconjunctival anaesthesia + anti-inflammatory injection, betadine wash, and steroid + antibiotics drops in the right eye, and the operation is complete.

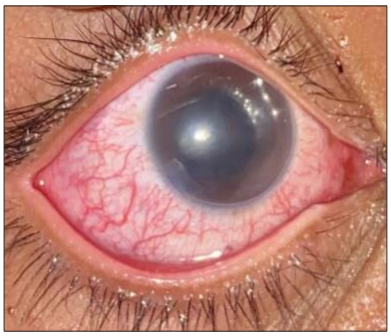

Figure 3. Photo of the right eye after surgery on the first day

The first day after the procedure, the patient complained of blurry vision in RE accompanied with slight pain (+), headache (-), nausea and vomiting (-). On ophthalmological examination, VA of light perception good projection (LPGP) in RE. Conjunctiva CVI (+) PCVI (+), cornea Descemet fold (+) minimal, iris regular (+), pupillary reflex (+/+) RAPD (-), bubble ¾ anterior chamber (AC), AC deep, IOL (+) central. In the posterior segment, the fundus reflex (+) but the details were difficult to evaluate and the IOP of 56 mmHg. The patient was then advised to take a head up position with paracetamol 4x500 mg, xitrol ed 6x1 in RE, lyteers ed 6x1 in RE, acetazolamide 3x250 mg, and kalium aspartate 1x300 mg (IOP dropped to 43mmHg) and was consulted to the Glaucoma Division for management of secondary glaucoma. The Glaucoma Division diagnosed with OD Secondary Glaucoma + Pseudophakia; LE PSC, and recommend continuing the therapy given and observing IOP.

On third day, patient controlled with no significant complaints : no pain in the eyes and head, right eye vision still blurry but brighter than before, nausea (-), vomiting (-). VA in RE was 6/45PHNI with normal eyelids. Calm conjunctiva, minimal descemet fold (+), bubble as high as ½ AC (+),AC VH4, pupillary reflex (+), IOL (+) central, iris pigment (+) in the lens, posterior segment reflex fundus (+) detail is difficult to evaluate, and IOP of 7 mmHg. Treatment of xitrol ed 6x1 in the RE was continued, all antiglaucoma drugs were stopped, and planned for LE pro lensectomy with IOL implantation under GA.

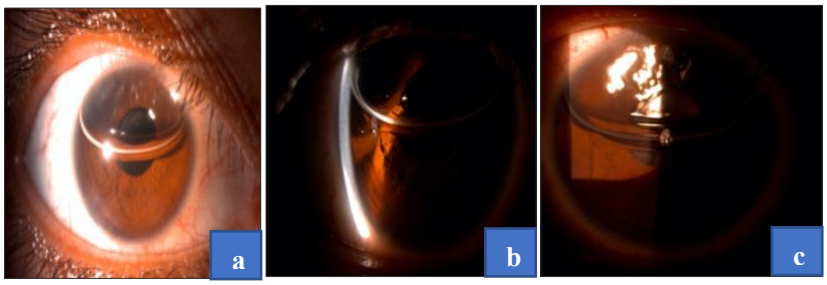

Figure 4 a-c. Photo after lensectomy + IOL surgery on the third day.

The patient came for control 10 days after surgery to the Glaucoma division and admitted that the vision in the RE was brighter and no pain. Red eyes (-), watery (-), discharge (-), headache (-), nausea (-), vomiting (-). On visual examination of the RE, it was found to be 6/21 PH 6/18. Normal eyelids, calm conjunctiva, deep AC, bubble (-), regular iris (+), pupillary reflex (+) IOL (+) in the center, iris pigment (+) in the lens. Posterior segment examination showed fundus reflex (+),NII papil was round, well defined, CDR 0.3-0.4, good retina, macular reflex (+) and IOP of 8 mmHg. The patient was diagnosed with RE Secondary Glaucoma + Pseudophakia post Lensectomy + IOL D+10; OS PSC and receive therapy in the form of observation, control back to the Glaucoma Division if IOP is high, medication according to POS Division, control according to schedule to POS Division; xitrol ed 6x1 in RE and other therapy according to POS Division.

On third week post surgery, the patient came back for control. RE was brighter and no complaints in both eyes. On examination, the visual acuity examination in RE showed 6/18 PHNI. Palpebra normal, conjunctiva calm, AC Van Herick 4, pupillary reflex (+), IOL (+) central position. Posterior segment examination showed fundus reflex (+), NII round, well defined, CDR 0.3, good retina, macular reflex (+) and IOP of 8 mmHg, retinometry of BE was 0.32. The patient was diagnosed with RE Pseudophakia post Lensectomy with IOL D+19; LE PSC and received therapy in the form of Xitrol ed 4x1 and Lyteers ed 4x1 in RE.

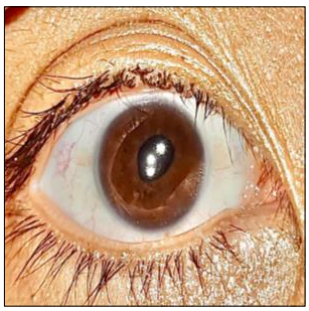

Figure 5. Photo of the right eye after lensectomy + IOL surgery on the 19th day.

DISCUSSION

Cataract is an ocular complication with a prevalence of 0.7%-3.4% and can be an early sign of type I diabetes mellitus (DM) in children and young adults.[3] A person's age when diagnosed with cataracts varies greatly, with the age range being as young as 5 years and there is no gender predilection for T1DM.[7,8] The time span for acute bilateral cataracts after diagnosis of T1DM and initiation of insulin is 3 weeks – 24 months.[9]

The pathophysiology of cataract formation in T1DM still cannot be fully explained, but

there are several hypotheses that are most widely accepted, namely activation of the polyol pathway, osmotic disturbances, increased lens hydration from sorbitol accumulation, glycation of lens proteins, oxidative stress, and currently being studied is autoimmune, due to the condition hyperglycemia which leads to lens opacification in diabetes patients.[9] Hyperglycemia conditions and HbA1c levels of 12.8-14.1% at the time of diagnosis are said to increase the risk of cataracts by 3.6 times.[8]

Several morphologies that can be found in T1DM are posterior subcapsular, lamellar, cortical, snowflake, and milky white cataracts, where posterior subcapsular cataracts are the most common type of diabetic cataract in children.[4] PSC is a type of cataract characterized by causing significant glare and occurring at a younger age than nuclear and cortical cataracts. This type forms in the cortex at the back of the lens and only causes complaints of visual acuity problems if its location covers the visual axis.[5]

The typical early symptoms of T1DM in the form of polyuria, polydipsia, polyphagia and weight loss were alerted and early detection has an important role in reducing lens exposure to hyperglycemia and other consequences of severe metabolic conditions, which might have a positive impact on early diabetic cataract formation in pediatric populations.[10,11]

The American Diabetes Association (ADA) and the International Society for Pediatric and Adolescent Diabetes (ISPAD) are the two main pediatric diabetes expert societies that have issued comprehensive guidelines for the prevention, diagnosis, and treatment of T1DM.[10,12] The ADA does not include recommendations about screening for early diabetic cataract, although it recommends that the first ophthalmologic examination for assessment of retinopathy should be performed when the patient reaches age 10 years, soon after puberty, or when the duration of T1DM is longer than 3–5 years.[12] In addition, ISPAD guidelines recommend that initial eye examination should be considered for early detection of diabetic cataract or major refractive errors, but there is no clear further guidance on expanding screening for diabetic cataract in the pediatric and adolescent population.[10]

In this case, a 17-years-old male patient was detected to have cataracts in both eyes 3 months after being diagnosed with T1DM, which was categorized as an acute case if measured from the duration of cataract formation. The patient complained of blurry vision and glare in BE that did not improve with the use of glasses over the last 3 months. On ophthalmological examination, central PSC type cataract was found to be 3mm, while other anterior segment, posterior segment examinations, and IOP were within normal limits. The patient's complaints was depend on the type, size, and position of the cataract. In younger children under 10 years, which is a critical period of visual development, cataracts removal must be done as soon as

possible. The size, type, and location of the cataract will determine visual prognosis. Cataracts with a diameter of >2 mm, especially central or nuclear cataracts, have the potential to cause amblyopia.[5] In cases of diabetes, posterior examination must also be evaluated considering the high incidence of complications of diabetic retinopathy. Regular diabetic retinopathy screening every three years is recommended for early detection of vascular and retinal changes.

The patient was consulted from TS Pediatric Endocrine for eye evaluation. He had history of hospitalization due to diabetic ketoacidosis on T1DM and a history of dialysis due to prerenal AKI. There were complaints of polydipsia, polyphagia and polyuria at that time, but the patient's parents were not aware of this symptoms because they thought it was normal because he is in growing period. Four months ago an HbA1c test was carried out with a value of 10%, but it has been controlled now with insulin to 6.3%. High levels of HbA1c (>10%) and hyperglycemic conditions are believed to increase the risk of cataract formation. On the other hand, even though the patient has good glycemic control and insulin initiation, the patient still experiences eye complications in the form of cataracts. There have been several similar cases reported where there were cases of 17-years-old and 19-years-old children who were newly diagnosed with T1DM and developed bilateral cataracts within 6 weeks.[13] Another report also reported cases of acute bilateral cataracts within 3 months after diagnosis of T1DM, these three cases occurred even though the patient had good glycemic control.[14]

A case study hypothesizes the possible role of the autoimmune hypothesis where upon initial patient arrival, ophthalmological examination was within normal limits and insulin autoantibody levels were negative, accumulation of sorbitol in the lens via the polyol pathway, causing osmotic stress and influx of aqueous humor resulting in intracellular edema, damaged fibrils or experiencing disruption and turbidity. However, lens disruption due to aldose-reductase alone is not sufficient to explain the development of opacities in patients with acute cataracts. Another suspected mechanism is non-enzymatic glycation of lens proteins related to oxidative stress. Glucose autooxidation and nonenzymatic glycation may contribute to an increase in free radicals in the lens, and loss of antioxidants in the lens under hyperglycemic conditions.[4]

Metabolic changes associated with diabetic ketoacidosis may further reduce antioxidant levels and induce cataract formation. In these various mechanisms, intracellular electrolyte and biochemical changes that occur cause protein damage and cell death and ultimately acute irreversible cataract. However, the reason why all patients with T1DM and irreversible acute bilateral cataracts always develop several months after diagnosis and initiation of insulin therapy, in a period with proven good metabolic control, remains need further study to be

explained.[13]

Some theories hypothesize that hyperglycemia is not the only factor because not all patients with hyperglycemia develop cataracts and good glycemic control is also thought to not prevent cataract formation. Other factors such as autoimmune disease, genetic propensity, nutritional status, and use of drugs such as steroids contribute.

Currently, there are many experimental therapies for the treatment of diabetic cataracts, but cataract surgery remains the gold standard in the treatment of diabetic cataracts.[6] Postoperative vision is generally favorable with good recovery of visual acuity. A study by Wilson, *et al*. reported nineteen of twenty-three operated eyes had postoperative better-corrected visual acuity of 20/40 or better.[4] In the last two decades, phacoemulsification is the most common cataract extraction technique in developed countries. The type of surgery differentiates between younger and older children. Because cataracts are soft at younger ages, the use of phacoemulsification is not mandatory, while in older children and adolescent phacoemulsification is recommended.[15,16]

Lensectomy and IOL insertion provide optimal results in primary IOL implantation considering that his lens nucleus is still soft and his age has passed the emmetropization period, so that the power of the lens installed won't change much. Despite the high success rate of cataract surgery, it is important to remember that cataract surgery is not without complications, and it is important to consider the long-term risk of T1DM and its effect on the growth and development of the anterior eye segment The most common complications after cataract surgery are Posterior Capsular Opacification (PCO), secondary glaucoma, retinal detachment, amblyopia, and acute complications (incision leak, increased intraocular pressure, edema, and uveitis).[17,18]

There are differences in the management of PCO between younger and older children, because PCO occurs more often in younger children. It is generally recommended that Primary Posterior Capsulotomy (PPC) should be performed in children under 4 years of age, as the risk of developing PCO even if the posterior capsule remains intact is very high, due to the more reactive inflammatory response at younger age.[15,19] Even after PPC is performed, there is a substantial risk of secondary visual axis opacification due to migration of lens epithelial cells from the anterior vitreous; thus, it is recommended to perform anterior vitrectomy (AV) along with PPC in infants and young children.[19] Whitman and Vanderveen suggest that older children with simple PCO can undergo laser capsulotomy and those with PCO and secondary visual axis opacification can proceed to surgery.[20] In this patient, inflammatory reaction and incidence of PCO are considered low thereby PPC and AV was not performed. However, if PCO occurs in

the future, this patient is considered cooperative to undergo NdYag laser in the polyclinic.

Complications that occurred after cataract extraction in this case were secondary glaucoma where in the first 2 days after surgery, the patient's IOP in the right eye was quite high, reaching 52 mmHg, but it was controlled on the third day, reduced to 7 mmHg after administering analgesic, anti-inflammatory and antiglaucoma drugs, and head up position. In first day post surgery, VA of RE is still 6/45 due to the presence of a bubble ½ AC and IOP was increased due to suspected bubbles being trapped between the IOL and the iris, but the AC is formed well without significant signs of inflammation and subjective symptoms are only found with minimal pain.

On the tenth day VA of RE improved to 6/21 PH 6/18 and controlled IOP of 8mmHg without antiglaucoma medication, examination of the anterior and posterior segments was within normal limits where the bubble had been absorbed and posterior segment could be evaluated with NII papil was found to be round, well defined, CDR 0.3-0.4, cupping (+), good retina, macular reflex (+).

On the nineteenth day post surgery, VA of RE had improved to 6/18 PHNI, the anterior and posterior segments were within normal limits, the IOP was controlled at 8mmHg, and retinometry showed 0.32 in BE, which is an indicator that the vision will not progressing optimally to normal vision. Overall process of the surgery, from preparation, intra-operatively, and post-operative complications management, has gone well. The next thing that needs attention is education to patient and his family about his eye conditions, monitoring blood glucose regulation, and routine evaluation for ocular complications in DM.

CONCLUSION

Type 1 diabetes often appears early and is manifested in the form of cataracts in children and vice versa, so there is a need for collaboration and screening as well as multidisciplinary therapy between pediatricians, endocrine, eye and other related departments. Metabolic regulation and good glycemic control, educating patient and family, aggressive management and evaluation are very important and play a role in the successful therapy and other complications in DM.

Lensectomy and primary IOL implantation are management that have high success rate in children and adolescents. However routine monitoring and evaluation for cataract (amblyopia, secondary glaucoma) and ocular diabetic complication (metabolic cataracts, diabetic retinopathy), as well as complications from surgery (secondary cataract, macular edema) and planning further therapy are essential to achieve optimal vision and good visual

prognosis.

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CASE REPORT

GIANT INTRACRANIAL ANEURYSM PRESENTING AS TEMPORAL HEMIANOPIA: WHEN THE EYES REVEAL A HIDDEN DANGER

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ABSTRACT

Introduction: *Giant intracranial aneurysms (GIA) are rare and deadly diseases due to the high risk of rupture. The purpose of this report is to describe a case of GIA presenting as temporal hemianopia.*

Case Report: *A 52-year-old male presented with worsening blurry vision three weeks before admission. Visual acuity was light perception in the right eye and 6/18 in the left eye. Neuro-ophthalmic examination revealed a relative afferent pupillary defect in the right eye and bilateral optic atrophy. At the next visit, the visual acuity of the right eye recovered to 6/18. Visual field testing showed temporal hemianopia in the left eye and generalized depression in the right eye. Magnetic resonance imaging demonstrated a 0,4 cm x 2,5 cm x 1,9 cm saccular aneurysm, on the medial side of the left internal carotid artery (ICA).*

Discussion: *A giant (diameter ≥2.5 cm) ICA aneurysm may compress the optic chiasm, leading to various stages of visual loss. Several factors are known to delicate balance between thrombogenesis and thrombolysis within the aneurysmal sac. Spontaneous intra-saccular thrombosis in an unruptured GIA may be induced by calcification within the atherosclerotic wall of the aneurysm and loss of elastic lamina. It is prone to occur in a narrow aneurysm neck (<0.4 cm). Thrombosis reduces the size of the aneurysm sac, in which the accumulated fluid is reabsorbed. This may explain the decompression effect on optic chiasm and spontaneous visual recovery.*

Conclusion: *Intracranial aneurysms are a rare cause of optic chiasm compression but can still be considered in cases of temporal hemianopia.*

Keywords: *Intracranial aneurysm, optic chiasm compression, temporal hemianopia*

INTRODUCTION

Giant intracranial aneurysms (GIAs), which are vascular abnormalities over 25 mm in diameter, represent a small percentage (3%-13.5%) of all intracranial aneurysms, with a typical occurrence of around 5%. They pose a significant risk of rupture, making them rare but life-threatening conditions.[1-4] In a recent case, a GIA mimicked a space-occupying lesion and caused temporal hemianopia.

CASE ILLUSTRATION

A 52-year-old male presented with worsening blurry vision three weeks before admission. He had no complaints of headaches or a history of significant head trauma. Visual acuity was light perception in the right eye and 6/18 in the left eye. Neuro-ophthalmic examination revealed a relative afferent pupillary defect in the right eye, and bilateral optic atrophy (Figure 1 & Figure 2).

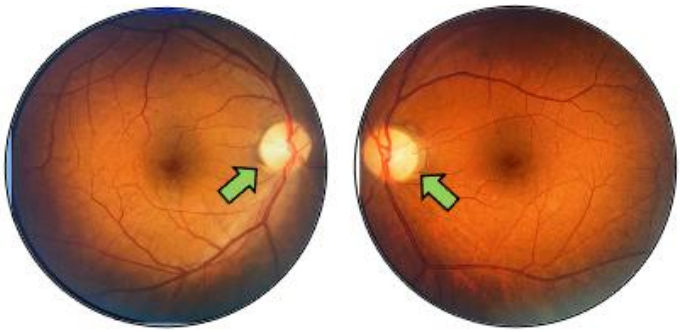

Figure 1. **Fundus photographs showed bilateral optic disc atrophy (green arrows)**

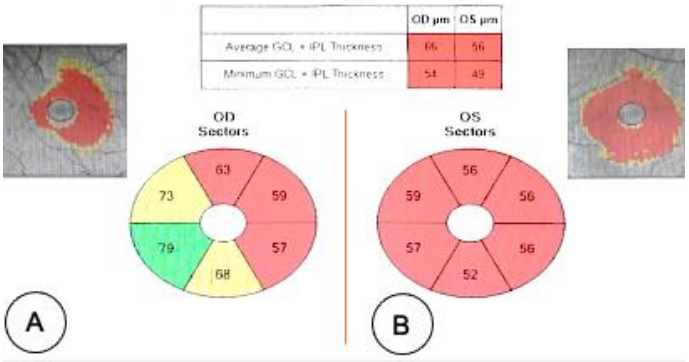

Figure 2. **Optical coherence tomography of macular ganglion cell-inner plexiform layer (GC-IPL) showed (A) GC-IPL thinning predominates in the heminasal retina in the right eye, (B) GC-IPL thinning extends beyond midline crossing to the temporal hemifield in the left eye.**

At the next visit, the visual acuity of the right eye recovered to 6/18. Visual field testing showed temporal hemianopia in the left eye and generalized depression in the right eye (Figure 3). Magnetic resonance imaging (MRI) of the brain demonstrated a saccular aneurysm, measuring 0,4 cm x 2,5 cm x 1,9 cm, on the medial side of the left internal carotid artery (ICA) (Figure 4).

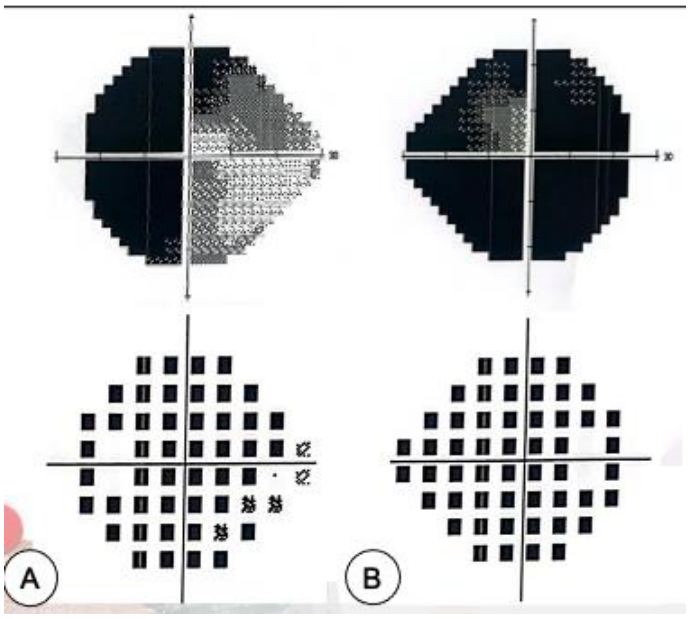

Figure 3. Humphrey visual field 24-2 test showed (A) temporal hemianopia in the left eye (VFI 28%; MD -21.69 dB), (B) generalized depression in the right eye (VFI 6%; MD -31.15 dB).

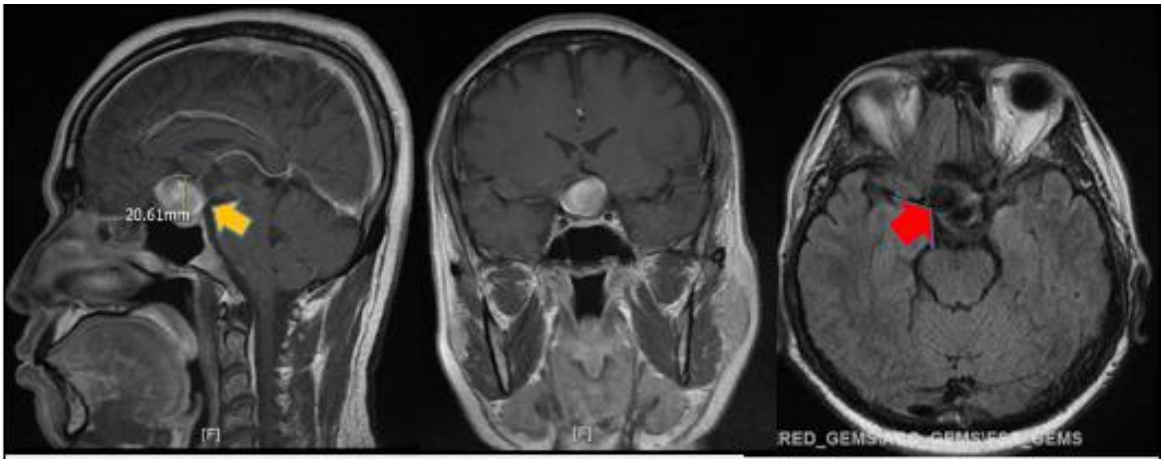

Figure 4. Magnetic resonance imaging of the brain revealed a saccular aneurysm on the medial side of the left ICA pars C7 (neck width: 0,4 cm; dome height 2,5 cm; dome width: 1,9 cm) (yellow arrow), compressing the optic chiasm (red arrow).

The patient was then immediately consulted for neurosurgical treatment. He was planned to undergo digital subtraction angiography (DSA) and installation of a flow diverter device (FDD).

DISCUSSION

Aneurysms typically develop in regions of high hemodynamic stress due to factors such as endothelial dysfunction, turbulent blood flow, and arterial wall damage. They can be

categorized into saccular, fusiform, and dissecting types based on appearance and pathogenesis. Saccular GIAs, the most common type, resemble round or oval malformations with a connecting neck to the vessel. Fusiform aneurysms involve the entire arterial circumference and lack a distinct neck. Carotid artery aneurysms can manifest symptoms through rupture, mass effect on adjacent structures, or compression of nearby vessels, resulting in varying clinical presentations depending on their location and size.[1,4]

Internal carotid artery (ICA) aneurysms, depending on their size and location, can cause various visual pathway disturbances such as hemianopia or loss of acuity. These effects often stem from direct compression on the visual pathway, leading to neurological deficits. Visual impairments linked to intracranial aneurysms typically result from increased pressure on the anterior optic pathway near the Circle of Willis. Symptoms may include unilateral scotoma, blindness, bitemporal hemianopsia, or homonymous hemianopsia, all resulting from compression on the optic nerve, chiasma, or tract. Notably, these symptoms tend to progress gradually. Compressive optic neuropathy from aneurysms can present with diverse visual field defects, often featuring hemianopia visual field defects and progressive visual decline. In our case, temporal hemianopia was attributed to optic nerve compression by an unruptured ICA aneurysm.[1,5-7]

Diagnostic imaging such as computed tomography (CT) scans can reveal calcification and skull base erosion in large or giant aneurysms with mass effect, while MRI aids in assessing ischemia, perianeurysmal hemorrhage, and the aneurysm's relationship with surrounding neurovascular structures. Three-dimensional digital subtraction angiography (3D-DSA) is crucial for surgical planning, providing comprehensive visualization of the aneurysmal sac, neck, parent vessel, and aneurysm itself, facilitating understanding of hemodynamic characteristics related to aneurysm initiation, growth, and rupture. Intraoperative CFD imaging assists surgeons in identifying weaker or thrombosed aneurysmal walls to avoid or handle them with caution. Patients with visual field defects but no apparent ophthalmological abnormalities should undergo intracranial vessel studies like MRI, magnetic resonance angiography (MRA), or CT angiography (CTA).[4,6]

Relief of optic nerve compression through tumor removal or decompression surgery for aneurysms can restore visual function, even in cases of blindness. However, the recovery timeline varies, with some patients experiencing rapid improvement while others require longer periods due to remyelination. Successful decompression doesn't always guarantee full visual recovery, potentially due to vascular insufficiency of the optic nerve. In our case, complete recovery occurred after four weeks of visual deterioration to blindness, although spontaneous

visual recovery is rare in compressive optic neuropathy from aneurysms.[7]

Spontaneous partial thrombosis of giant aneurysms is common, occurring in up to 60% of cases, with complete thrombosis being rarer and potentially associated with parent vessel occlusion. Thrombosed aneurysms likely arise from inflammatory mechanisms triggered by chronic dissections, hematomas of the aneurysmal wall, and the proliferation of vasa vasorum.[1,2] Several factors, such as geometrical configurations, hemodynamics, and biological conditions of the blood vessels around an aneurysm, are known to delicate balance between thrombogenesis and thrombolysis within the aneurysmal sac. Spontaneous intra-saccular thrombosis in an unruptured GIA may be induced by calcification within the atherosclerotic wall of the aneurysm and loss of elastic lamina. Other factors contributing to spontaneous thrombus formation are blood stagnation, increased viscosity, and slow flow. Thrombosis especially in giant aneurysms is prone to occur in narrow aneurysm neck size (<4 mm), as observed in our case. Thrombosis reduced the size of the aneurysm sac, and the fluid accumulated in the sac was reabsorbed. This may cause the decompression effect on optic chiasm and explain the phenomenon of spontaneous visual recovery in our case.[8-9]

Treating giant intracranial aneurysms (GIAs) poses significant challenges due to their high rupture risk and disabling symptoms. Management options include neurosurgical techniques (open surgery), endovascular procedures, or a combination of both. Endovascular methods are increasingly favored for ICA GIAs due to challenging neurosurgical access. Survival and complication rates between the two approaches are comparable, although evidence from large clinical trials is lacking. Treatment decisions hinge on factors like patient age, comorbidities, aneurysm size, location, morphology, neck-to-dome ratio, presence of thrombosis and calcification, collateral circulation, and critical perforating vessels. [1,4,6,10]

Endovascular decisions consider aneurysm localization, anatomy, size, dome-to-neck ratio, thrombus presence, patient health, and material availability. Therapeutic techniques include embolization with platinum coils or flow-diverting stents, aiming to occlude the aneurysm while maintaining parent vessel flow. Parent vessel occlusion (OPV) is another option, associated with reduced aneurysm growth and retreatment rates but requires sufficient collateral circulation.[1,2]

Surgical options involve aneurysmal clipping with thrombectomy, trapping with or without revascularization. Careful surgical handling is crucial to prevent thrombus dislodgment and embolism. Wide necks and intraluminal thrombus can complicate clipping, necessitating revascularization in unfavorable embolization conditions or poor collateral circulation. Patient factors, aneurysm characteristics, and team expertise guide treatment decisions for GIAs.

CONCLUSION

Intracranial aneurysms are a rare cause of optic chiasm compression but can still be considered in cases of temporal hemianopia. Prompt diagnosis and immediate treatment are recommended to prevent serious complications.

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CASE REPORT

SECONDARY GLAUCOMA DUE TO MUCOPOLYSACCHARIDOSIS: A CASE REPORT

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ABSTRACT

Introduction: *Mucopolysaccharidosis (MPS) is a rare, autosomal recessive inherited lysosomal storage disorder involved in glycosaminoglycans (GAG) degradation. Glaucoma, as a leading cause of irreversible blindness, in MPS patients has a very low occurrence rate, indicating that this condition needs attention and more research to improve MPS patients' quality of life.*

Case Report: *A 15-year-old boy came with a chief complaint of progressive onset of blurred vision in both eyes 4 years prior to admission. He was being treated as hypermetropia since then. Opacity was noticed in both eyes in addition to deteriorating vision for the last 3 months. Genetic test supported the possibility of MPS type VI. Hence this patient was diagnosed as secondary glaucoma due to MPS. Glaucoma medications were unable to control the intraocular pressure, thus trabeculectomy was planned. After the surgery, the patient was given antibiotic, analgetic, steroid, and anti-glaucoma medications. Releasable suture was removed on the 14th day post-surgery due to elevated IOP. Unfortunately, the patient did not make any visit afterward for further follow-up.*

Discussion: *Our case faces several difficulties with anterior and posterior ophthalmological examinations. Corneal opacity with corneal thickening often occurs in MPS type VI. The exact mechanisms underlying corneal opacities remain elusive. IOP measurements can be helpful for the diagnosis and monitoring of glaucoma. Changes in corneal thickness can affect IOP measurements, and corneal opacity can prevent accurate visualization of the optic nerve and cornea-sclera angle, as well as supportive diagnostic devices such as Funduscopy, Ultrasound Biomicroscopy (UBM), and Optical Coherence Tomography (OCT), are difficult to perform.*

Conclusion: *The underlying syndrome was suspected only after glaucoma occurred. Early detection and regular assessment play an important role in MPS. Routine follow-up is needed to ensure IOP control and determine the long-term outcome of IOP after trabeculectomy.*

Keywords: *Glaucoma, Mucopolysaccharidosis, trabeculectomy*

INTRODUCTION

Glaucoma is a group of progressive optic neuropathies that is defined by alterations in the optical nerve head caused by degeneration of the retinal ganglion cells and retinal nerve fiber layers. It affects over 79.6 million people worldwide and remains the leading cause of irreversible blindness.[1] Glaucoma in children is a rare condition that has the potential to cause blindness and is characterized by ocular structural damage and visual impairment associated with increased intraocular pressure (IOP) and is caused by a variety of conditions. The clinical

picture may vary depending on the age of onset of the disease.[2]

Impaired outflow through the trabecular meshwork is the fundamental pathophysiology of all pediatric glaucomas. The first step in developing diagnostic and screening tools that could identify individuals at risk for the condition before irreparable optic nerve damage occurs is characterizing the underlying genetic abnormalities that cause glaucoma. Additionally, genetic counseling and the risk assessment of subsequent pregnancies depend on it.[3]

For the rare conditions associated with glaucoma in children, determining the mechanism of glaucoma produces the best therapeutic outcomes. Mucopolysaccharidosis (MPS) is a heterogeneous group of multisystem disorders resulting from the accumulation of glycosaminoglycans in ocular and systemic tissues. MPS is inherited in an autosomal recessive manner except for MPS II, which is inherited in an X-linked manner. Frequent visual disturbances can be caused by corneal opacities, optic neuropathy, retinopathy, or cerebral vision disorders.[3,4]

This case report aims to determine the relationship between clinical symptoms, systemic abnormalities, and supporting examinations to be carried out, as well as establish the correct etiology and diagnosis in the patient.

CASE ILLUSTRATION

A 15-year-old boy came with the main complaint of blurry vision in both eyes. Blurred vision in both eyes has occurred for 4 years. The patient has been examined and treated as a case of hypermetropia since then. Vision became progressively blurry and opacity began to appear in the center of the patient's eyes which became more extensive, which led his family to take him to see a doctor to change glasses 3 months ago. Afterward, the patient was referred to the glaucoma department because of high intraocular pressure (IOP) and was given latanoprost, timolol 0.25%, artificial tears, and eye vitamin.

There is no history of infection or other eye problems. The patient has had a history of growth and development delays since the age of 5 years and started wearing glasses since the 5th grade of elementary school using S + 2.25D glasses. History of using other medications was denied. The patient is a child who was adopted at the age of 3 days so the biological family's medical history is unknown. The patient was born spontaneously vaginally, at term with a birth weight of 1900 grams, and immediately cried at birth. The patient's vaccination history is complete. There was no history of allergies.

On physical examination, his general condition was good, with compos mentis, and adequate nutrition (body weight of 21 kg and height of 106 cm). Vital signs are within normal

limits.

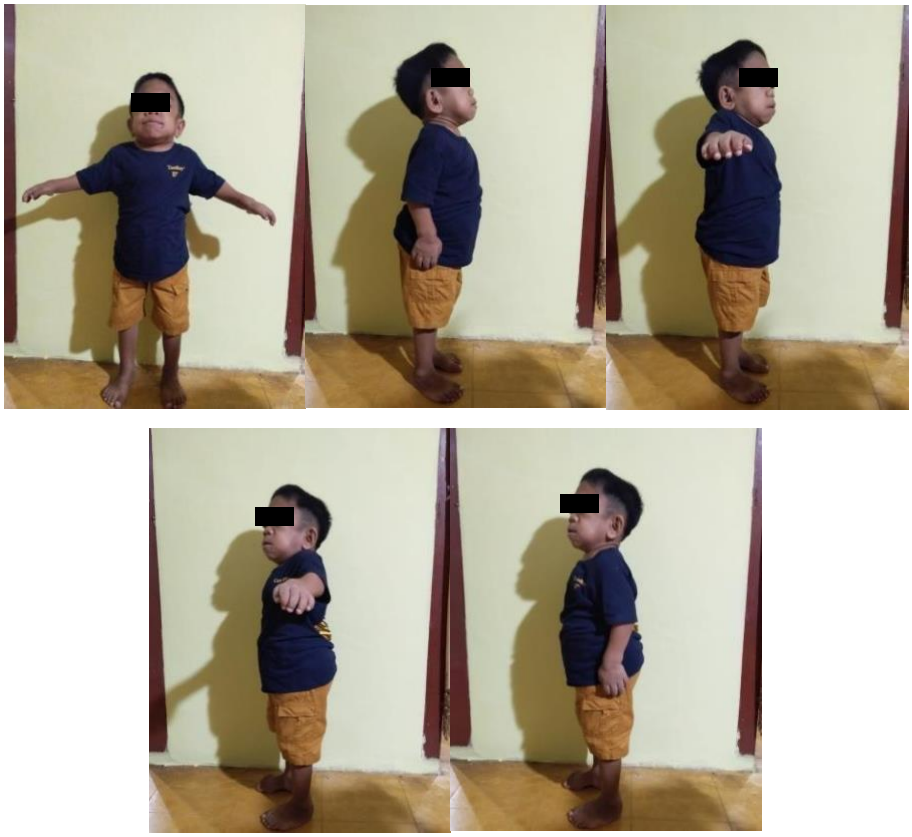

Figure 1. Clinical photo of the patient

On ophthalmological examination of the right eye, visual acuity was 1/60 and intraocular pressure was 20.7 mmHg. Ocular movement was good in all directions. The cornea was cloudy. The anterior chamber depth was Van Herick (VH) I-II. Iris was brown, crypts (+), with minimal iridodonesis. The pupil was round and light reflex (+). The lens was difficult to assess. The palpebra and conjunctiva were both normal. On ophthalmological examination of the left eye, visual acuity was 1/60 and intraocular pressure was 20 mmHg. Ocular movement was good in all directions. The cornea was cloudy. The anterior chamber depth was VH I-II. Iris was brown, crypts (+), with minimal iridodonesis. The pupil was round and light reflex (+). The lens was difficult to assess. The palpebra and conjunctiva were both normal (Figure 2).

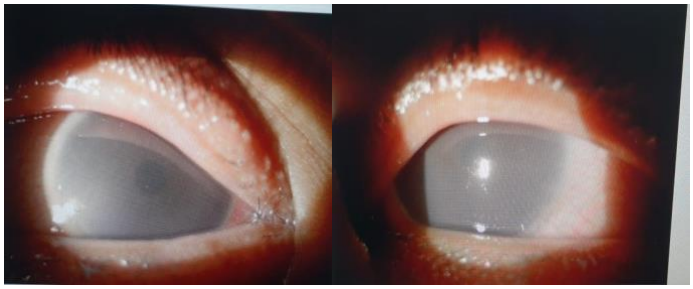

Figure 2. Anterior segment in both eyes

During examination of the posterior segment, fundus reflex, papillary, retina, and macula were all difficult to assess in both eyes (Figure 3).

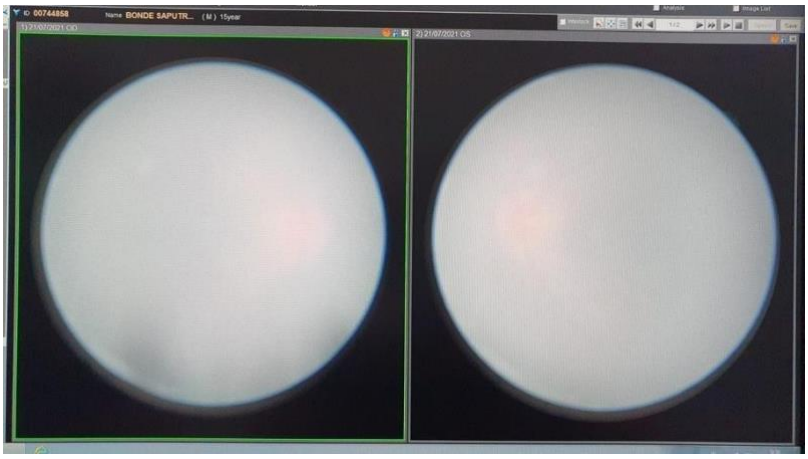

Figure 3. Fundoscopic findings

Gonioscopy was performed and it was difficult to assess in both eyes. Similarly, perimetry, UBM, papillary OCT, macular OCT, and specular microscopy were all difficult to assess. Ocular ultrasound showed echolucent features in vitreous cavity ODS (Figure 4). The biometry result showed that the right eye axial length was 21.87 mm and the left eye 21.61 mm (Figure 5). The CCT was 602 μm and 582 μm in his right and left eye, respectively. The corneal diameter was 12.6 mm in both eyes.

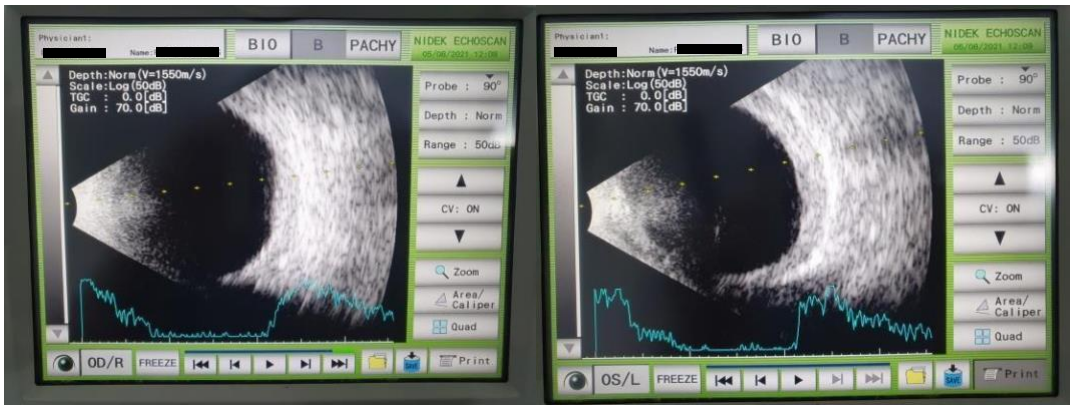

Figure 4. Ocular ultrasound

Figure 5. Biometry result

On laboratory tests, overall was within normal limits. Chest x-ray showed normal cardiac and lung. Echocardiography showed mild mitral regurgitation (MR), tricuspid regurgitation (TR), and pulmonary insufficiency (PI).

A multidisciplinary team was involved in treating our patient, including a pediatrician, otolaryngologist, nutritionist, cardiologist, medical rehabilitation, respirologist, and clinical pathologist. Of all the results, we observed signs and symptoms that may lead to MPS such as growth restriction, facial coarse, dysostosis multiplex, upper airway obstruction, and structural cardiac valvular dysfunction. The genetic test showed the activity of arylsulfatase B decreased at 1.9 μmol/L/H (normal range $\geq$8.8 μmol/L/H) which supports the possibility of MPS type VI. Hence, we concluded that this patient had secondary glaucoma due to MPS VI.

With the medications that have been prescribed before, yet the patient's IOP still had not been under control, instead, he began experiencing complaints such as watery eyes, pain, glare, and headache about 1.5 months ago. Therefore, we decided to perform a trabeculectomy alternately with a releasable suture in both eyes.

On 9th September 2021, the surgery was performed. The patient was laid on the operating table, and then disinfection and subconjunctival anesthesia were performed. Limbus fixation was performed at 12 o'clock. Conjunctival peritomy was performed at approximately 6-8 mm at 12 o'clock. Any bleeding was cauterized. Mitomycin C is placed as a subconjunctival compress for 2-3 minutes. Grooving measuring 4 x 2 mm is made and flaps with crescents on the grooving. The side port was installed at 10 o'clock. A sclerostomy was performed through the COA with a stab knife, then a hole was made with the Kelly Puncher, then an iridectomy was performed with a puncture. The sclera was sutured with a releasable suture using Nylon 10.0. Mattress suture to close the conjunctiva was performed using Vycril 8.0. Intracameral

antibiotic (Levofloxacin) and subconjunctival dexamethasone-gentamycin were administered. Antibiotic ointment was applied and the surgery was completed.

On 1st postoperative day, the patient complained about minimum pain and gritty sensation in the right eye. On ophthalmological examination of the right eye, visual acuity was 1/300, and intraocular pressure was 11.3 mmHg. Ocular movement was good in all directions. Conjunctival injection (+), intact suture, and high bleb were found. The cornea was cloudy with a releasable suture (+). Anterior chamber depth was VH II-III. Iris was brown, crypts (+), with iridodonesis minimal. Pupil was round and light reflex (+). The lens was difficult to assess (Figure 6). On the left eye, visual acuity was 1/60, and intraocular pressure was 23.1 mmHg. Other examinations remain the same.

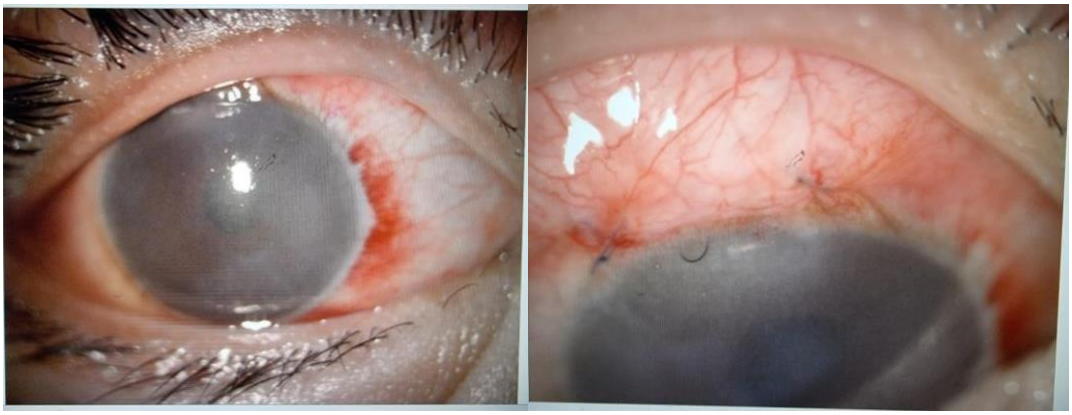

Figure 6. Anterior segment on the right eye day 1 post-trabeculectomy.

The patient was allowed to be discharged and treated as an outpatient, with a scheduled follow-up 1 week post-operative. Post-surgical management includes eye hygiene, amoxicillin 3x250 mg, paracetamol 3x250 mg, methylprednisolone 2x8 mg, prednisone acetate eye drop every 3 hours OD, levofloxacin eye drop every 2 hours OD, timol eye drop 0.25% 2x1 gtt OS, latanoprost eye drop 1x1 gtt OS, and eye vitamin.

On the 7th postoperative day, there was minimum pain on the right eye. On ophthalmological examination of the right eye, visual acuity was 1/300, and intraocular pressure was 17.0 mmHg. Ocular movement was good in all directions. Minimal conjunctival injection (+), intact suture, and high bleb were found. The cornea was cloudy with releasable suture (+). Anterior chamber depth was VH II-III. Iris was brown, crypts (+), with iridodonesis minimal. Pupil was round and light reflex (+). The lens was difficult to assess (Figure 7). On the left eye, visual acuity was 1/60 and intraocular pressure was 21.7 mmHg. Ocular movement was good in all directions. The cornea was cloudy. Anterior chamber depth was VH I-II. Iris was brown, crypts (+), with iridodonesis minimal. Pupil was round and light reflex (+). The lens was difficult to assess. Palpebra and conjunctiva were both normal. The steroid and antibiotic were being tapered off.

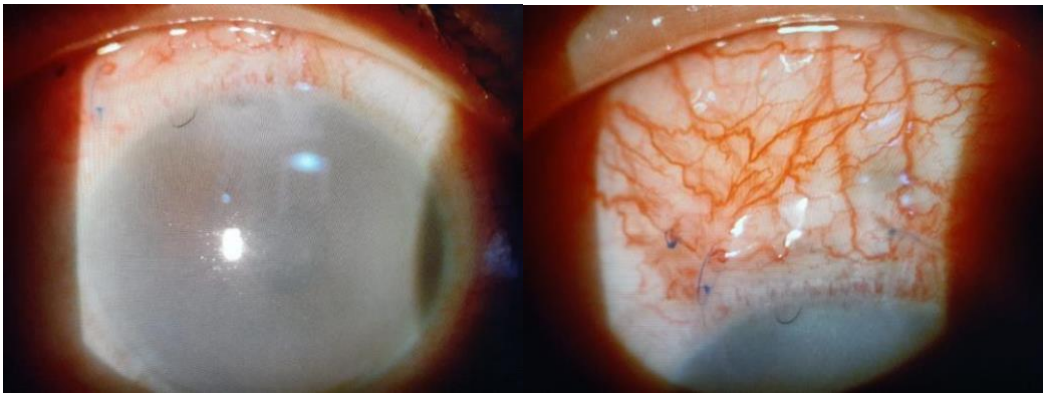

Figure 7. Anterior segment on the right eye on day 7 post-trabeculectomy.

On the 14th postoperative day, the patient complained of watery eye. On ophthalmological examination of the right eye, visual acuity was 1/60, and intraocular pressure was 33.0 mmHg. Ocular movement was good in all directions. Minimal conjunctival injection (+), intact suture, and high bleb were found. The cornea was cloudy with a releasable suture (+). Anterior chamber depth was VH II-III. Iris was brown, crypts (+), with iridodonesis minimal. Pupil was round and light reflex (+). The lens was difficult to assess (Figure 8). On the left eye, visual acuity was 1/60, and intraocular pressure was 24.0 mmHg. Ocular movement was good in all directions. The cornea was cloudy. Anterior chamber depth was VH I-II. Iris was brown, crypts (+), with iridodonesis minimal. Pupil was round and light reflex (+). The lens was difficult to assess. Palpebra and conjunctiva were both normal. We decided to release the releasable suture and did a slight digital pressure on the bleb under topical anesthesia. We then measured his IOP right after and 30 minutes after these procedures. We noticed that there was a reduction in IOP. Moreover, we shifted the steroid to a lower potent group while the timol and latanoprost therapy was continued.

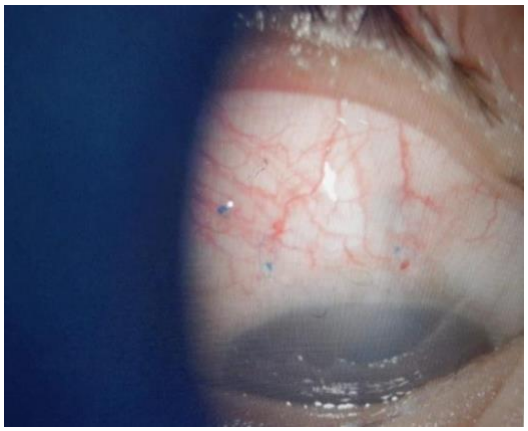

Figure 8. Anterior segment on the right eye on day 12 post-trabeculectomy.

The visual acuity remained the same as before the surgery, but the patient stated that he felt more relief. There was also a deepening of the anterior chamber in his right eye. The next follow-

up was scheduled for every 2 weeks. Unfortunately, the patient did not make any visit afterward for further follow-up.

DISCUSSION

Secondary glaucoma is glaucoma brought on by other ocular abnormalities (acquired or congenital) or linked to systemic illnesses or syndromes. Patients should be referred to a pediatrician for assessment if they have diseases that are known to be linked to systemic abnormalities. For inherited disorders, genetic counseling and family screening are recommended.[3,5]

Similar to adults, uveitis, infection, ocular trauma, and corticosteroids can all lead to secondary glaucoma in children. The age of the child, the extent of the IOP elevation, and the degree of vision loss all influence the presenting signs and symptoms. Patients with Marfan syndrome, homocystinuria, Weill-Marchesani syndrome, and microspherophakia may experience lens-related problems that result in angle-closure glaucoma.[6,7]

A diverse collection of lysosomal storage diseases called mucopolysaccharidosis (MPS) are brought on by the buildup of glycosaminoglycans (GAGs). This substance causes a multi-organ illness with extensive systemic effects that is characterized by a phenotypically diverse condition (Figure 9). In MPS, ophthalmologic abnormalities include retinopathy, optic neuropathy, glaucoma, and corneal opacities. The most prevalent ocular characteristic of MPS, particularly types I, IVA, and VI, is corneal opacification. The use of enzyme replacement therapy (ERT) and hematopoietic stem cell transplantation (HSCT) has significantly raised survival rates in recent years; nonetheless, the best results are obtained when treatment is started during the first 16 months of life. Ophthalmologists are therefore crucial in the accurate diagnosis and treatment of eye disorders by identifying them early on.[8,9]

Disease	Corneal Opacification	Retinopathy	Glaucoma	Optic nerve anomalies
MPS I-H (Hurler)	+	++	+	+
MPS I-HS (Hurler-Scheie)	++	++	++	++
MPS I-S (Scheie)	+++	++	++	++
MPS II (Hunter)	+	++	+	++
MPS III (Sanfilippo)	+	+++	+	+
MPS IV (Morquio)	+	++	+	+
MPS VI (Maroteaux-Lamy)	+++	Unknown	++	++
MPS VII (Sly)	++	Unknown	++	++
MPS IX (Natowicz)	Unknown	Unknown	Unknown	Unknown

MPS—mucopolysaccharidosis; + mild; ++ moderate; +++ severe

Figure 9. Manifestation of MPS type.[10]

Mucopolysaccharidosis I is an autosomal recessive disease caused by α-L-iduronidase deficiency. Heparan sulfate (HS) and dermatan sulfate (DS) build up as a result of an enzyme shortage. Hurler, Hurler-Scheie, and Scheie are the three phenotypic diverse subtypes; Hurler is the most severe variety, while Scheie is the mildest. All three genotypes exhibit ocular symptoms.[8]

The majority of MPS I patients have corneal opacity, which can appear within the first year of life. The opacity, which is frequently characterized as a diffuse ground glass look, is brought on by a disruption of the normal collagen alignment in the corneal stroma, even though GAGs are deposited in all layers of the cornea. GAG deposits thicken the cornea in addition to opacifying the cornea, obstructing vision, and making glaucoma diagnosis and treatment challenging.[8]

IOP readings can be useful in the detection and tracking of glaucoma. IOP measurements may be impacted by changes in corneal thickness, and precise vision of the optic nerve and cornea-sclera angle may be impeded by corneal opacity. According to a cross-sectional study conducted on children with MPS I, IOP readings should be adjusted to prevent needless glaucoma treatments, such as medication or surgery. GAG buildup in the trabecular meshwork can result in both open-angle and closed-angle glaucoma.[8] Refractive errors, particularly hypermetropia, are also common in MPS I because of inelastic reduced scleral axial length and inflexible corneal curvature, both of which are associated with GAG storage. GAG accumulation in the extraocular muscles and decreased corneal opacity are the main causes of anomalies in ocular motility, particularly exotropia. Incidence of retinopathy was discovered in all three MPS I disorders by another investigation. Due to the presence of corneal opacification on top of optic neuropathy and retinopathy, visual abnormalities may go unnoticed.[4,8]

Within the MPS family, mucopolysaccharidosis II (Hunter syndrome) is the only X-linked illness. DS and HS build up when there is a deficiency in iduronate-2 sulfatase, an enzyme that catalyzes the removal of sulfate groups. Hunter syndrome affects between one in 100,000 and one in 170,000 live male newborns. Compared to men, women experience milder clinical symptoms. Many times, phenotypic traits are not understood at birth, but they start to show up between the ages of two and four. Even though ocular symptoms are not the main characteristic of MPS II, posterior chamber abnormalities are more common than anterior chamber problems.[4,8]

In MPS II, corneal opacities are uncommon. The most frequent visual symptoms are exophthalmos and hypertelorism, which can result in long-term problems linked to corneal overexposure. A moderate frequency of retinopathy and anomalies of the optic nerve was also

seen in Hunter's patients. Chronic disc elevation without elevated intracranial pressure is caused by increased pressure on the optic nerve resulting from scleral GAG deposition and thickening, notwithstanding the rarity of glaucoma. The degree of the disease determines the extent of retinopathy; yet, electroretinograms have been helpful in many MPS II individuals exhibiting nyctalopia.[8]

Sanfilippo Syndrome, also known as mucopolysaccharidosis III, is an autosomal recessive condition that has four subtypes: A, B, C, and D. These subtypes are characterized by defects in heparan-N-sulfatase, N-acetylglucosaminidase, α-glucosaminide acetyltransferase, and N-acetylglucosamine-6-sulfatase, respectively. Retinopathy is the most common eye ailment associated with Sanfilippo syndrome. Retinal dysfunction, retinal degeneration, and progressive photoreceptor loss are brought on by the accumulation of heparan sulfate in retinal pigment epithelial cells and the photoreceptor matrix. In clinical settings, patients frequently report impaired vision and nyctalopia. MPS III is typically not linked to corneal opacities.[8]

MPS IVA and MPS IVB are two subtypes of mucopolysaccharidosis IV (Morquio syndrome), an autosomal recessive illness. Refractive errors and widespread corneal opacification are common ophthalmological symptoms. Patients may observe corneal opacity that gets worse with age and can still feel photosensitivity even though the degree of corneal clouding is not as great as it is in MPS I and MPS VI.[8]

Mucopolysaccharidosis VI (Maroteaux-Lamy syndrome) is an autosomal recessive disease. It is known to be caused by a deficiency of N-acetylgalactosamine-4-sulfatase (arylsulfatase B), which leads to the accumulation of DS and chondroitin-4-sulfate (C4S). Corneal opacity with corneal thickening often occurs. Ocular motility issues are another prevalent issue that can result in amblyopia and strabismus. Retinopathy is not linked to MPS VI.[8] Recently, patients with MPS VI may also have a scleral thickening, which is most likely a result of scleral GAG deposits.[11]

Patients typically have a characteristic phenotype early in life, such as respiratory disorders and facial dysmorphias. During growing, additional characteristics such as small stature, heart valve disease, sleep apnea, skeletal degeneration, medullar and peripheral compression, and sensory impairment may manifest. Unlike individuals with other forms of MPS, those with MPS VI typically do not have cognitive impairment. There is a treatment called enzyme replacement therapy (ERT) that can potentially alter the course of the disease if started early.[8,11]

Due to the low frequency and high childhood mortality, the majority of studies on these disorders have concentrated on their fatal symptoms. Glaucoma affects 2.1% to 12.5% of people

with all MPS, with MPS VI having a particularly high frequency of the condition.[11] Nonetheless, these patients' life spans increased and their quality of life improved as a result of the advent of innovative medicines.[12]

Corneal penetrating keratoplasty (PK) is frequently used to treat corneal opacity due to the deposition of GAG.[13] To a limited extent, PK facilitates early vision recovery; nevertheless, most patients experience low visual acuities, which are often related to optic neuropathy and ocular hypertension (OHT).[11]

Optic neuropathy most likely has multiple causes. OHT and glaucoma are prevalent in these individuals. OHT could result from trabecular meshwork infiltration and the inadequate drainage of the aqueous humor as a result. However, because of the elevated corneal thickness brought on by GAG deposition, OHT could also be an artefactual measurement. On the other hand, optic neuropathy and atrophy may also be caused by orbital and retro-orbital causes. The advancement of optic neuropathy may be significantly influenced by the rise in intracranial pressure and the posterior compression of the optic nerve.[8,11]

Figure 10. Corneal clouding in patients with MPS VI.[8]

Mucopolysaccharidosis VII (Sly syndrome) is an autosomal recessive illness caused by β-galactosidase deficiency. Corneal clouding is the most prevalent eye condition, however, it's typically not as bad as MPS I or VI. No abnormalities of the optic nerve were reported. It is still unknown how often retinopathy and glaucoma occur.[8]

With very little information available, mucopolysaccharidosis IX, also known as Natowicz syndrome, is the rarest type of the MPS family. As of right now, no instances of MPS IX have been reported with ocular symptoms. This could also be brought on by the low disease prevalence and the unavailability of data.[8]

Depending on the phenotype, children with MPS have varying prognoses: some may live until their second decade, while others may not make it past 50 or 60 years of age. For patients with severe MPS I, the optimal course of treatment is early (before 2 years of age) hematopoietic stem cell transplantation (HSTC) using compatible bone marrow or cord blood cells. A pediatrician oversees the multidisciplinary management team, which also includes regular evaluations by a pediatric ophthalmologist and input from several other specialties.[9]

Refractive errors are widespread, particularly hypermetropia and astigmatism, however not all patients benefit from standard glasses due to coexisting ocular conditions. Refraction with a retinoscope or autorefractor is strongly advised following cycloplegia with cyclopentolate and phenylephrine. Accommodative fixation targets and stereopsis assessment should be employed in strabismus situations. The symptoms of photophobia may be alleviated using photochromatic lenses.[8]

Assessing the degree of corneal opacification over time and looking for surface alterations or vascularization can be done with slit lamp examination and photos. It might not be possible to apply more exact and objective techniques utilizing Pentacam and iris cameras in every therapeutic situation. At this time, corneal transplantation is the only available treatment for corneal opacities. Patients with MPS have had deep anterior lamella keratoplasty (DALK) and penetrating keratoplasty (PK). Whereas DALK simply replaces the corneal epithelium and stroma, PK is a full-thickness corneal transplant that involves the removal of the corneal endothelium, stroma, and epithelium.[2,8,13]

It is common for patients who have had HSCT to experience dry eye syndrome. Topical lubricants are advised in these cases of keratoconjunctivitis sicca, along with corneal exposure reduction and topical steroids or cyclosporine for more severe cases. Moreover, topical lubricants are advised in cases of pseudoexophthalmos.[8]

Depending on the patient's age and level of intellect, various methods such as finger counting, Humphrey field analyzer, and Goldmann visual field perimetry are employed for visual field evaluation. Methods beyond standard gonioscopy and slit lamp examination are employed to enhance anterior chamber and optic nerve visualization to conduct a comprehensive glaucoma evaluation. In order to help with the diagnosis and treatment of glaucoma, advanced segment optical coherence tomography (OCT) and ultrasound biomicroscopy offer precise pictures of the anatomy behind a potentially clouded cornea. The increased corneal stiffness in MPS may cause a spurious increase in IOP. OCT facilitates the imaging of the optic nerve, photoreceptor layer, retinal nerve fiber layer (RNFL), corneal layers, and retinal thickness. When measuring intraocular pressure (IOP), Goldmann applanation

tonometry and ocular response analyzers may be more accurate because they rely less on corneal characteristics. The microendoscope is another instrument that aids in resolving the issue of clouded corneas during trabecular surgery.[8]

A thorough fundus examination is necessary for posterior chamber disease to detect retinal and optic nerve pathologies. Even though corneal opacification makes it difficult to manually visualize the retina, fundus photography can nonetheless yield better-than-expected photographs. A-scan ultrasonography helps determine axial length, while echography aids in the examination of the vitreous and retina.[8]

The precise processes that cause corneal opacities are still unknown. A well-known notion proposes that type 1 collagen is not properly organized. Diffuse corneal opacification and decreased corneal transparency are caused by a deficiency in the decorin gene. Decorin is a dermatan proteoglycan that controls collagen fibrogenesis. Patients with MPS I and age-matched controls with healthy corneas were compared for variations in corneal collagen expression. Furthermore, MPS I corneas exhibit elevated smooth muscle actin expression, a sign of stromal cell conversion to myofibroblasts. As demonstrated by corneal opacities and injuries, this conversion is linked to increased corneal collagen synthesis. It is yet unknown if collagen organization is impacted or if myofibroblast conversion has a direct impact on GAG deposition. Understanding how GAGs impact corneal transparency has also been made easier by typical age-related changes in the cornea. Compared to younger subjects, elderly subjects had a 30% higher overall GAG. Reduced antioxidant enzymes in aging eyes are thought to be the cause of these age-related changes in GAG, raising the risk of oxidative stress and slowing the healing of corneal injury.[8]

One of the biggest problems in the realm of glaucoma treatment is managing childhood glaucoma. For the majority of glaucomas, medication is the primary line of treatment; however, sustained efficacy is less common in newborns and infants, particularly in PCG (Primary Congenital Glaucoma). In their lifetime, the majority of youngsters with glaucoma will require surgery. Since there is no cure, lifelong monitoring is necessary to guarantee IOP management and identify any consequences. It is advisable to use protective eyewear, particularly for monocular individuals.[3]

Topical application of medication increases the risk of possibly fatal systemic side effects in children. It is best to avoid using beta-blockers in premature or newborn babies, children with asthma, or children with other heart conditions, such as arrhythmias. First-line treatment options for β blockers are timolol 0.1% and timolol maleate 0.25% because of their superior risk profile and effectiveness. While oral acetazolamide is more effective than dorzolamide in

decreasing intraocular pressure (IOP), its use in children is restricted due to severe systemic adverse effects, including altered hyperactive behavior, failure to thrive, and bedwetting. The first medication authorized for usage in children was latanoprost. Brimonidine can cause drowsiness, unconsciousness, and apnea in newborns. It can also penetrate the blood-brain barrier. The literature suggests against using it on children younger than six years old or under 20 kg in weight. Because parasympathomimetic drugs can enhance aqueous outflow and decrease anterior synechiae development, they are helpful in the postoperative therapy of PCG following angle surgery.[2,14]

Surgery is the primary therapeutic option for pediatric glaucoma. The chosen procedure of treatment is mostly determined by the type of glaucoma; additional factors that may be relevant include the age at which the condition first manifests, the degree of optic nerve damage, corneal clarity, coexisting eye diseases, surgical experience, and surgical history.[3]

The success rate following several goniotomies typically ranges from 70% to 90% with medium-term follow-up, indicating that goniotomy is an effective procedure. Trabeculotomy is more commonly used than goniotomy; nonetheless, it is a more intrusive procedure that may result in conjunctival scarring. For trabeculotomy to be successful, Schlemm's canal (SC) localization must be precise.[3]

Failure of the surgical angle is one of the primary indications for Mitomycin C-treated trabeculectomy. When a very low target pressure is needed, the glaucoma is primarily secondary, the presentation is either very early or very late, and the surgeon lacks the competence to conduct angle surgery, this operation is the first choice. Due to their powerful wound-healing response, children are more likely to have a failed outcome from this technically more challenging surgery. Subconjunctival 5-fluorouracil (5-FU) (0.1–2 ml 5-FU 50 mg/ml) and a steroid, like betamethasone, can be temporarily administered next to the bleb if there is noticeable conjunctival inflammation near the drainage site under anesthesia (EUA).[3,14,15,16]

In order to help control long-term IOP, glaucoma drainage devices, or GDDs, are an essential component of the therapeutic arsenal for pediatric glaucoma. Children with aphakic or pseudophakic uveitis, glaucoma following cataract surgery, cataracts that need to be removed right away, and extremely serious conditions that start at birth are among the indications.[3]

Every child with glaucoma within the vulnerable age range has to have their amblyopia evaluated regularly. When the cornea is clear, refraction should be included in routine exams along with the prescription for glasses as needed. For amblyopia, occlusion therapy ought to be attempted on all children who may benefit from improved vision.[3]

In this patient, signs and symptoms were found that were consistent with secondary glaucoma associated with systemic disorders, namely Mucopolysaccharidosis. The level of visual impairment depends on the severity and/or combination of existing eye disorders.[15] Visual disturbances in Mucopolysaccharidoses type VI are common and can be caused by corneal opacities, optic neuropathy, or cerebral visual impairment. The majority of patients with MPS are hypermetropic due to altered corneal refraction and reduced axial length.[17]

Physical examination revealed short stature, short and stubby fingers and toes, and facial coarse features. Visual acuity was reduced in the right and left eyes. The cornea appeared cloudy and the anterior chamber angle was shallow in both eyes. The lens and posterior segment are difficult to evaluate due to the cloudy cornea. The description is consistent with MPS.[14] Corneal opacity is a characteristic of several MPS disorders (MPS I, MPS IV, MPS VI, and MPS VII), and can appear in infancy. A patient with mild corneal opacities may be asymptomatic, but photophobia and decreased vision occur as the opacities worsen.[17] For the majority of patients, corneal opacity can be resolved with PK, improving vision at least right after surgery. Nevertheless, following successful PK, MPS VI patients typically have extremely low visual acuities.[11,18]

Intraocular pressure in this patient may appear within normal limits, but it should be noted that the patient has received previous anti-glaucoma therapy. Corneal clouding affected the measurement of intraocular pressure (IOP) by altering corneal thickness and stiffening the cornea, in addition to obstructing the inspection of the lens and posterior segment (vitreous and retina).[11,12] According to Ashworth et al., MPS type VI has ophthalmologic characteristics and is predisposed to glaucoma in 50% of cases and corneal clouding in 95% of cases.[19]

Gonioscopy, perimetry, OCT, fundoscopy, CCT, and UBM examinations are difficult to perform due to the deposition of GAG in the cornea which leads to poor refractive media. The ultrasound results showed an echolucent image in both eyes. Chest x-ray examination concluded that there were no visible abnormalities in the heart and lungs. On a simple laboratory examination, no significant abnormalities were found. On echocardiography examination, mild MR, mild TR, and mild PI were found. One important characteristic of MPS VI is the increasing deterioration in cardiorespiratory function. All individuals had cardiac involvement to varying degrees of severity; the most pertinent findings were mitral and aortic thickening/dysplasia.[11] Aortic valve disease is seen in 43% of cases, mitral valve disease in 96% of cases, and tricuspid valve disease in 71% of cases, according to Azak and Golda. As a result, cardiac examinations, which should include an electrocardiogram, echocardiogram, and blood pressure measurement to evaluate any abnormalities in cardiac rhythm or conduction, as well as any changes in the

structure or function of the heart, are advised to be performed every one to two years.[19,20] Additionally, patients may exhibit spinal stenosis and hydrocephalus.[21]

The treatment for this patient was trabeculectomy for both eyes. In eyes that have undergone multiple procedures, it is important to make the next surgery definitive. Some of the advantages of trabeculectomy are postoperative IOP titration with removable sutures, lower mean IOP can be achieved compared with GDD, less reliance on drugs for IOP control compared with GDD, fewer postoperative surgical revisions compared with GDD, significantly clear cloudy corneas, and avoids potential corneal surgery.[3] Unfortunately, the patient's visual acuity remains the same as before surgery. Spartalis et al., stated that in addition to helping with the early diagnosis and treatment of posterior segment ophthalmologic disorders, keratoplasty can enhance vision.[18]

The MPS is still a significant medical issue that requires early detection and timely treatment. When patients exhibit significant clinical symptoms (respiratory symptoms, mental retardation, eyes and ears problem), along with an abnormal appearance (short stature, coarse face, short neck, short nasal bridge, wide nose, swollen eyelids, shortened forearm, genu valgum, and coarse face), it is time to suspect MPS. Enzyme assays are required for these people to diagnose themselves.

CONCLUSION

Any suspicion of glaucoma in children should always be treated seriously and immediately to minimize visual impairment. The goal of the initial assessment is to make a diagnosis of glaucoma and determine its type. Ocular management of Mucopolysaccharidosis is challenging given the complexity of the condition in conjunction with the limited available studies. Despite their challenging management, these patients should have their visual acuity maximized to give them the best quality of life possible. Future eye management is expected to prevent eye abnormalities, such as corneal opacities.

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CASE REPORT

DIFFUSE GRANULOMATOUS CONJUNCTIVITIS AS AN OCULAR MANIFESTATION OF ANCA-NEGATIVE LIMITED WEGENER'S GRANULOMATOSIS

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ABSTRACT

Introduction: *Necrotizing granulomatous vasculitis, which is commonly known as Wegener's Granulomatosis (WG), frequently affects small to medium-sized blood vessels and is associated with anti-neutrophil cytoplasmic antibodies (ANCA). Despite ocular manifestations being prevalent in the disease, initial symptoms involving the eyelid and conjunctiva are infrequent. While most of WG cases shows ANCA positivity, this study report an unusual case of ANCA-negative, but biopsy-proven WG presenting only localized in conjunctiva*

Case Report: *An 11-year-old girl presented a red membrane covering the entire ocular surface and diminished vision in the left eye seven months before admission. At presentation, hand motion in the left eye was the best corrected visual acuity. There were granuloma formations in the palpebral and bulbar conjunctival, covering the entire ocular surface in the left eye. An incisional biopsy was performed in the conjunctiva, which revealed an ulcerative mucous membrane, prominent vasculitis, and necrotizing granulomas with giant cells and massive leukocyte infiltrate consistent with WG diagnosis.*

Discussion: *There is a need to consider the clinical manifestations suggesting the presence of vasculitis, ANCA determination, and histopathological evidence of the compromised organ to confirm the diagnosis. Overall, 82-94% of patients with WG were ANCA positive, leaving approximately 10% who tested negative, particularly those with limited WG. Moreover, a biopsy can confirm the diagnosis, specifically in ANCA-negative cases.*

Conclusion: *This case illustrated the consideration for WG diagnosis in limited form and negative ANCA-test. The clinical suspicion of WG based on symptoms and signs and alternative diagnostic criteria using tissue biopsy might be helpful in such cases for starting the treatment.*

Keywords: *Wegener's Granulomatosis, ANCA-negative, granulomatous conjunctivitis*

INTRODUCTION

Wegener's Granulomatosis (WG), which is also known as Granulomatosis Polyangiitis (GPA), is a type of pauci-immune necrotizing granulomatous vasculitis that typically affects small to medium-sized blood vessels, and often associated with anti-neutrophil cytoplasmic antibodies (ANCA). The disease primarily affects the kidneys and upper and lower airways. Although the condition frequently presents with symptoms in the eyes, incidences with eyelid and conjunctival involvement as the earliest symptoms of the disease are rare.[4] While the exact cause of WG remains unknown, previous studies have suggested the pathogenic role of

ANCA in the disease's progression.[1-3] Positive ANCA results are observed in 82-94% of WG patients, while approximately 10% of individuals tested negative, leading to the potential for misdiagnosis and delayed treatment. The absence of ANCA can obscure the clinical presentation, particularly in atypical cases, making histopathological confirmation through biopsy become crucial for accurate diagnosis. This case report highlights a case of an eleven-year-old girl diagnosed with localized WG in the conjunctiva, a rare site of involvement, with a negative ANCA test and biopsy strongly suggesting WG. We would like to emphasize the importance of considering WG as differential diagnosis of granulomatous conjunctival lesion, even in the absence of ANCA, and demonstrates the critical role of biopsy in confirming the diagnosis.

CASE ILUSTRATION

In June 2021, an 11-year-old girl was referred to the Rumah Sakit Umum Pusat Dr. Wahidin Sudirohusodo due to a conjunctival mass in her left eye. The patient had experienced a red membrane covering the entire ocular surface and diminished vision for seven months before admission. Two years prior to admission, the left eye had been red with excessive tearing, eye discharge, and itchiness, but no pain was reported. Despite being initially treated with antibiotic eye ointment, there was no improvement, and there was no previous history of any systemic autoimmune diseases. Six months later, the patient noticed a mass-like lesion in the upper region of the conjunctiva that progressively spread to the entire ocular surface.

During the patient's presentation, her best-corrected visual acuity for the right eye was 1.0, while for the left eye, it was limited to hand motions. The results of the slit-lamp test indicated that the anterior segment of the right eye was within normal limits. However, in the left eye, ectropion was observed in the lower eyelid, and granuloma formations were present in the palpebral and bulbar conjunctiva, which covered the entire ocular surface as shown in Figure 1. The conjunctiva was observed to bleed easily with friction, and there was a presence of white mucopurulent eye discharge. However, evaluation of other structures of the anterior segment was not conducted.

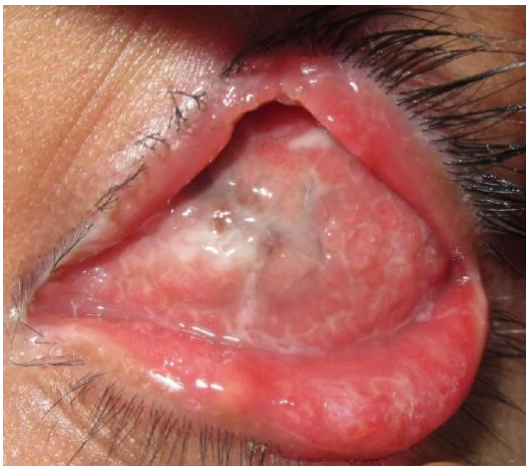

Figure 1. Granuloma formation in palpebral and bulbar conjunctival that covers the entire ocular surface

Blood testing revealed normal renal as well as liver function tests and unremarkable complete blood count. Furthermore, the urinalysis was negative, except for bacteria and mucus. Chest X-Ray examination was within the normal limit. Brain MRI without contrast showed a conjunctival mass in the left eye that infiltrated the cornea, suggestive of basal cell carcinoma or squamous cell carcinoma, bilateral ethmoidal and maxillary sinusitis, atrophicans rhinitis, and nasal septum deviation to the right side, as presented in Figure 2.

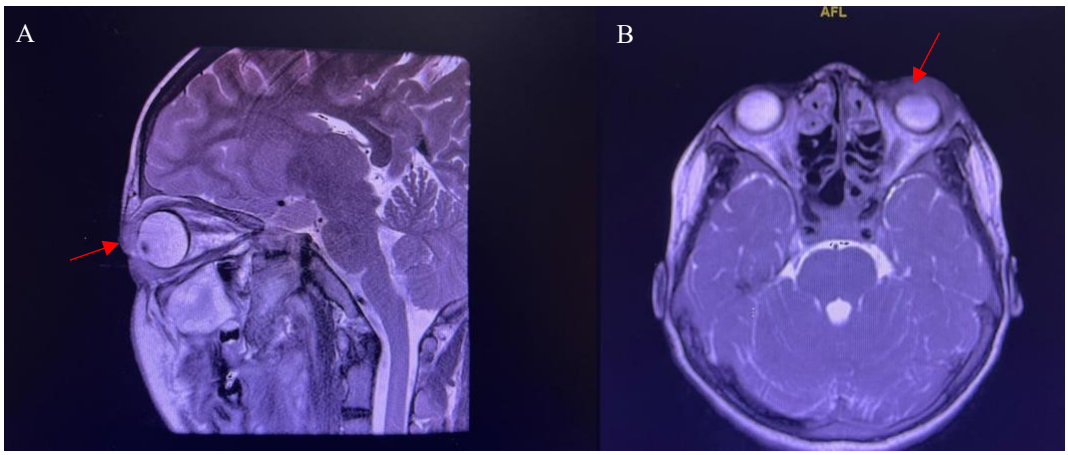

Figure 2. MRI brain without contrast. Red arrow shows conjunctival mass in the left eye infiltrated the cornea, (a) sagittal view ; (b) axial view

An incisional biopsy was carried out on the conjunctiva to collect specimens for anatomic pathology examination. The report showed an ulcerative mucous membrane, prominent vasculitis, and necrotizing granulomas with giant cells and massive leukocyte infiltrate consistent with a Wegener's Granulomatosis diagnosis. ANCA Test was performed to support the WG diagnosis, however, the result was negative.

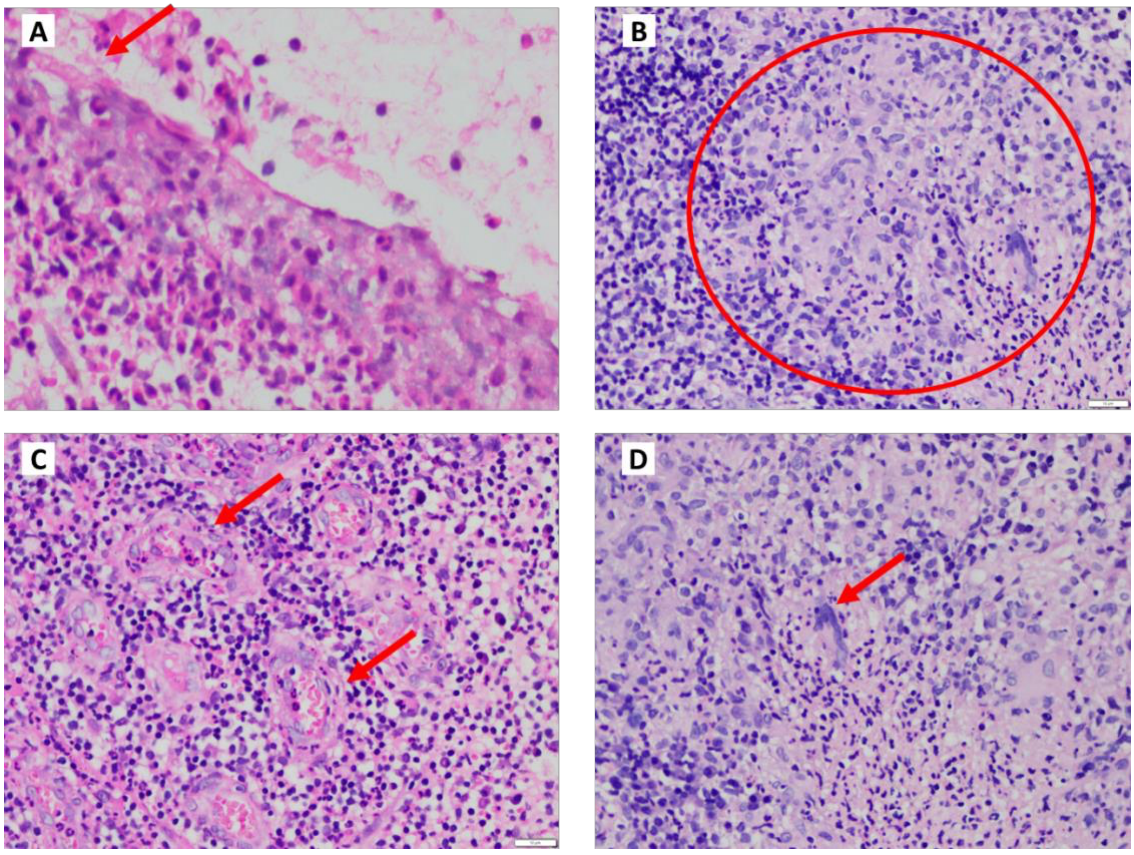

Figure 3. The conjunctival biopsy histopathology showed A) Ulcerated mucous membrane; B) Necrotizing with granuloma area; C) Vasculitis suggestive of a Wegener's Granulomatosis; D) Multinucleated giant cells

DISCUSSION

Wegener Granulomatosis is a necrotizing granulomatous inflammation of small to medium-sized vessels associated with ANCA. This disease is often presented in the classic form, which involves the kidney and the respiratory tract. It can also affect one or two organ systems and typically spares the kidneys. In this study, we found interesting that Wegener's Granulomatosis in children can present as a solitary, localized form, as in this case, which only affected the conjunctiva. Moreover, the most prevalent clinical manifestations of WG included necrotizing glomerulonephritis, sinusitis, and pulmonary infiltrates. Sinusitis that was identified through MRI was one typical manifestation found in the patient presented in this study. However, the Ear, Nose, and Throat Department found no anomaly during their consultations.[5, 6]

Almost half of the patients experienced ocular and orbital involvement, which may be the first signs of WG. These symptoms include inflammatory conditions of the orbit, episcleritis, scleritis, uveitis, nasolacrimal duct obstruction, peripheral ulcerative keratitis, dacryoadenitis, and optic nerve illness, as well as retinal vasculitis. Moreover, conjunctival

involvement also occurred in approximately 16% of WG patients and the early sign often manifested as conjunctival hyperemia. Further cicatrizing conjunctivitis may result from granuloma necrosis and ulceration. Progressive conjunctival cicatrization may also lead to symblepharon, which is the formation of fibrovascular tissue that covers the ocular surface. Symptoms of conjunctival involvement include eye redness, blurred vision, foreign body sensation, as well as bloody tears in some cases. As we found in our case, there was granuloma formations in the palpebral and bulbar conjunctiva which bleed easily with friction along with white mucopurulent eye discharge. Ectropion was also observed in the lower eyelid.[7, 8]

Nejebat et al. noted a case of protracted conjunctivitis in a 37-year-old guy with Wegener's granulomatosis. After receiving treatment for conjunctivitis for a month, the patient unexpectedly started experiencing photophobia, ocular pain, as well as diminished visual acuity in the left eye. According to immunologic tests, the patient had cytoplasmic anti-neutrophil cytoplasmic antibodies (C-ANCA). Subsequently, the patient experienced worsening Peripheral Ulcerative Keratitis (PUK), scleritis, and scleromalacia, which was treated with oral cyclophosphamide, followed by pulse treatment of intravenous (IV) methylprednisolone. Although prolonged conjunctivitis in WG was thought to be uncommon, a delay in identification can lead to blindness and death.[9]

Conjunctivitis in Wagener's granulomatosis may become ulcerative and necrotic, leading to cicatricial alterations to the ocular surface. Tarsal conjunctivitis can also cause areas of necrosis, active fibrovascular alterations, and fibrovascular scarring. Subglottic stenosis and nasolacrimal duct obstruction may both cause tarsal conjunctivitis. Robinson et al. conducted a study examining all patients who were referred to the eye clinic with the diagnosis of WG. Among the 82 WG patients investigated for 6.5 years, 13 (16%) patients developed a tarsal-conjunctival illness. The median age of these patients at diagnosis of the illness was 47 years, and 11 patients were male. All the patients had at least one eyelid affected by tarsal-conjunctival illness, only two had a bulbar conjunctival disease, and 5 patients had a bilateral tarsal-conjunctival illness. Furthermore, among patients with upper eyelid involvement, 5 also had lower eyelid involvement. The most frequent locations for tarsal-conjunctival lesions were the superior border of the upper eyelid and the inferior border of the lower eyelid.[10]

A better understanding of the etiology of tarsal-conjunctival lesions can clarify the disease's predominant distribution in the superior and inferior borders of the upper as well as lower eyelids, respectively. The terminal branches of the marginal and peripheral arcade vessels provide the upper and lower eyelid tissues with their circulatory supplies. The mostly avascular superior part of the tarsus of the upper eyelid may, however, be a factor in the

occlusive vasculitis of the peripheral arcade arteries and branches. This may result in ischemia, and infarction, as well as ultimately provide an explanation for the pattern of horizontal tissue destruction in the area of the posterior eyelid. Due to a richer blood vessel supply, the lower eyelid may be less prone to tissue infarction.[10]

Conjunctival hyperemia with or without granuloma formation and areas of apparent necrosis were the disease's initial symptoms in patients with early disease at presentation who had long-term follow-up. Among six patients with active disease, four had entropion in one or both eyes due to contracture deformities of the tarsus. Moreover, two of these patients exhibited trichiasis symptoms in both eyes. The histopathologic results from eyelid biopsies found conjunctival and tarsal scarring, granulomatous inflammation, and necrosis, as well as occlusive vasculitis. Therefore, in order to fully analyze the palpebral area, it is advised to routinely eversion the upper and lower eyelids during the assessment of patients with WG. This is because the tarsal-conjunctival involvement was most commonly found on this location.[10]

A case of persistent cicatrizing conjunctivitis with negative antineutrophil cytoplasm antibodies was also described in the study by Miserocchi et al (ANCA). The patient had been experiencing redness, itchiness, and a foreign body sensation in both eyes for two years. Epilation as well as topical corticosteroids were used in the treatment, but there was no change. An external examination revealed trichiasis, diffuse conjunctival injection, mucous strands in the inferior fornix, bilateral fornix foreshortening, as well as symblepharon development. Histopathology analysis of a conjunctival sample revealed striking microangiopathy with vaso-occlusion and extensive inflammatory cell infiltration of the conjunctival stroma. The patient's Wegener granulomatosis caused catastrophic lung problems, which led to the death. Despite receiving methotrexate, the patient's ocular and extraocular mucosal inflammation persisted, leading to the development of peripheral ulcerative keratitis.[11]

Non-specific conjunctival inflammation is a possible conjunctival symptom of Wagener's granulomatosis with or without cicatricial changes. In a case study by Jordan et al., an enlarged left upper eyelid exhibited trichiasis and an eyelid notch affecting the medial 20% of the eyelid edge. The entire palpebral surface displayed pronounced conjunctival inflammation, cicatricial alterations, and surface abnormalities. During the follow-up care 7.5 months later, a spontaneous conjunctival adhesion was found to have formed in the lateral canthus and the patient tested positive for c-ANCA. The patient had cyclophosphamide and prednisone treatment. Eyelid biopsy results showed perivascular inflammation areas as well

as chronic granulomatous inflammation suggestive of WG. For the past years, the prognosis has improved due to the combined use of prednisone and cyclophosphamide.[12]

Orbital inflammatory illness or pseudotumor is a typical WG ocular symptom. The rare presentation of painless bulbar-conjunctival ulcer without underlying episcleritis or scleritis described by Toh et al. showed the possibility of a dangerous underlying pathology, even in the presence of a painless ulcer. The patient also experienced a transient left visual loss that lasted for 15 minutes before full recovery. Upon examination, the patient was found to have a modest 2 mm right proptosis, engorged right eye, and twisted episcleral blood vessels. The patient also encountered a sudden and complete loss of vision in the left eye as well as a fundus examination showed a left central retinal artery occlusion (CRAO). Serum antineutrophil cytoplasmic antibodies (c-ANCA) were significantly elevated. For the first three days of treatment, the patient received 1000 mg/day of intravenous methylprednisolone. The vast clinical and pathological spectrum of WG was highlighted by this case, underscoring the need to maintain a high index of suspicion for this condition. This is due to the fact that the disease can advance quickly, as seen by the emergence of the left CRAO soon after the presentation.[13]

Considerations for diagnosis workups include the histological evidence of the damaged organ, the ANCA result, and the clinical signs that suggest the existence of vasculitis. In 1990, the American College of Rheumatology (ACR) defined 4 criteria, at least 2 of which should be met to diagnose WG, including 1) alterations in urine sediments like hematuria and hematic cylinders, 2) histology with perivascular granulomas presence 3) alterations in pulmonary radiology, and 4) sinus involvement. Approximately 82–94% of WG patients had positive ANCA results, leaving only 10% of individuals with negative results. Patients with specific disorders, as reflected in our study, were more frequently discovered to be ANCA-negative. Although it was recommended to repeat the ANCA test six months after the first test, there was no agreement on how often and according to what procedures ANCA testing should be repeated. According to Kemna et al., longitudinal ANCA measures are less valuable in individuals with the nonrenal disease but may be helpful in those with renal involvement. [5, 14, 15]

Tissue diagnosis of active sites plays a crucial role in confirming WG. In most cases of ANCA positivity, treatment may be initiated without a biopsy result. However, a biopsy is required to verify the diagnosis when the ANCA test is negative. Histological findings are comparable between ANCA-positive and ANCA-negative diseases.[5, 14]

A biopsy can confirm the diagnosis, particularly in cases of orbital WG and conjunctival involvement. When a granuloma is present, the conjunctiva is a potential site for biopsy. According to Ursea et al., a conjunctival biopsy is an easy and minimally invasive procedure to support granulomatosis with polyangiitis diagnosis. Isa et al. stated that vasculitis, necrosis, neutrophil, eosinophil, and macrophage infiltration of orbital tissue are all related to a clinical diagnosis of WG. Recommendations by EULAR has stated that positive biopsy is strongly supportive of diagnosis of vasculitis, therefore, biopsy can be used to support a new diagnosis and for further evaluation for patients suspected of having relapsing vasculitis. [8, 16, 17,18]

The treatment of Wegener's Granulomatosis consists of two phases, namely the induction phase, from 6 to 12 months to achieve remission. Secondly, the maintenance phase, which lasts from 24 to 48 months to consolidate the remission and avoids relapses. For induction of remission in patients with new-onset or relapsing WG with organ-threatening or life-threatening disease, EULAR recommends treatment with a combination of glucocorticoids (GCs) and either Rituximab (RTX) or Cyclophosphamide (CYC). RTX is more preferred in relapsing disease. The recommended starting dose of oral GCs is 50-75 mg prednisolone equivalent/day, depending on body weight. For the non-organ-threatening or non-life-threatening WG, treatment with a combination of GCs and RTX is recommended. Methotrexate (MTX) or Mycophenolate Mofetil (MMF) can be considered as alternatives to RTX. For the maintenance phase, EULAR recommends treatment with RTX. Azathioprine (ZA) or MTX can be considered as alternative. In patients with signs and/or symptoms raising suspicion of a WG diagnosis, supported by ANCA or tissue biopsy, the initiation of treatment should not be delayed. However, due to communication issues, the patient in this study has not received treatment until now.[18]

CONCLUSION

In conclusion, this study showed the consideration for Wegener's Granulomatosis diagnosis in limited form, despite the normal lung and kidney function and negative ANCA-test. The clinical suspicion of WG based on symptoms and signs and alternative diagnostic criteria using tissue biopsy might be helpful in such cases for starting the treatment.

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LITERATURE REVIEW

ROLE OF OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY (OCTA) IN ANTERIOR ISCHEMIC OPTIC NEUROPATHY

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ABSTRACT

Introduction: *Anterior ischemic optic neuropathy (AION) is the most common type of optic neuropathy with symptoms of sudden and painless visual field defect and vision loss. Although evaluating the nonperfusion areas of the vascular ischemia have traditionally been visualized through fluorescein angiography, OCTA has proven to be effective in noninvasively representing the retinal vascular network. This literature review aims to evaluate the quantitaive OCTA assessment of peripapillary vessel density (VD) changes in AION.*

Methods: *Literature search was performed in four databases (PubMed, ScienceDirect, ProQuest, and Cochrane Library) from 2018 to 2022 to identify relevant articles. Five studies were included in this review.*

Results: *All five studies on OCTA findings of NAION eyes reported a reduction in the vessel density of peripapillary capillary plexus when compared to either the healthy control eyes or the fellow unaffected eyes. OCTA reveals vascular changes in both forms, aiding prognosis and treatment. One study comparing NAION and AAION indicates reduced vessel density in NAION and AAION, with more severe abnormalities and reduction of vessel density in AAION.*

Conclusion: *OCTA can visualize alterations in vascular density in both types of AION, AAION and NAION, with a notably more pronounced reduction in peripapillary vessel density observed in AAION.*

Keywords: *anterior ischemic optic neuropathy, optical coherence tomography angiography, peripapillary vessel density*

INTRODUCTION

Anterior ischemic optic neuropathy (AION) is the most common type of optic neuropathy that affects elder people. AION includes both arteritic and non-arteritic forms[1,2] 90% of AION cases are Non-arteritic AION (NAION) with an annual incidence of approximately 10.3 per 100,000 individuals and a median age of 72, more commonly affecting males and whites. It is characterized by sudden and painless visual field defect and vision loss. Examination of the fundus typically reveals ONH edema at the acute stage, which could be diffuse or segmental, and resolves over 6-11 weeks, then replaced by disc pallor. Although the underlying mechanism of NAION remains unknown, the available evidence reveals that it may

be associated with perfusion deficiency of optic nerve head (ONH) microcirculation that is predominantly supplied by the short ciliary arteries. Probable risk factors that increase the onset includes hypertension, hypercholesterolemia, diabetes mellitus, nocturnal hypotension, and obstruction sleep apnea.[3,4] Arteritic AION (AAION), on the other hand, which occurs most commonly in association with giant cell arteritis (GCA), a large vessel vasculitis occurring in people older than 50, since it is the most common manifestation of end-organ ischemia in GCA (up to 20% of patients). It is caused by inflammatory and thrombotic occlusion of short posterior ciliary arteries (PCA).[3,4] Nerve fibers from the optic nerve head travel through the lamina cribrosa into the extraocular space. The optic nerve then gets a myelin sheath covering just posterior to the sclera. From then on, it traverses through the orbital apex into the intracranial space, where the right and left optic nerve cross each other at the optic chiasm and ending its journey at the visual cortex of the occipital lobe. The optic nerve may experience ischemia anywhere along this route.[4]

Optical coherence tomography angiography (OCTA) is a noninvasive, rapid, and simple imaging modality that provides a 3-dimensional image of the structural and microvascular information of the posterior pole of the retina in vivo. It was first made commercially available in 2014. This technology was developed as an extension of optical coherence tomography (OCT) imaging and utilizes motion contrast to detect blood flow. When two successive images are taken, stationary objects will appear the same, while moving objects will change. OCTA captures successive A-scans of the same retinal location, with each scan capture separated by a brief lapse in time, hence there will be a difference in the signals detected between the two scans due to motions happening between the scans. This difference in the detected signals is termed decorrelation signal. Since the retina is a static structure, the decorrelation signal is caused by the movement of blood throughout the retinal vasculature, and thus enabling the generation of a decorrelation map that mirrors the blood flow and represents the vascular networks in the back of the eye. Traditionally, nonperfusion areas are visualized through fluorescein angiography and indocyanine green angiography, but OCTA allows representation of the retinal vascular network especially peripapillary blood supply noninvasively without the need for contrast dye administration. Since the recent development of OCTA, this technique has been used in several fields in ophthalmology inculding in AION. [5,6]

It is only recently that OCTA is vastly studied in optical neuropathy, with various and sometimes contradicting results. Moreover, its role in the evaluating vessel density in AION has yet to be established. This literature review aims to evaluate the OCTA assessment of peripapillary vessel density (VD) and optic nerve head flow changes found in AION patients.

METHODS

Literature search was done in four online databases (PubMed, ScienceDirect, ProQuest, and Cochrane Library) from 2018 to 2022. Search terms such as "arteritic anterior ischemic optic neuropathy", "non-arteritic anterior ischemic optic neuropathy", "optical coherence tomography angiography", "OCTA", along with other relevant synonyms and derivatives were included (Table 1). The search was then limited to articles with full text availability and English as the publication language.

Based on search results in the previous section, articles were considered eligible to be reviewed if these inclusion criteria are met: (1) Subjects were patients diagnosed with AION; (2) Studies included the evaluation of OCTA as a diagnostic tool in AION cases; (3) Study outcomes include peripapillary vessel density and optic nerve head flow area. On the other hand, exclusion criteria were studies not written in English, conducted in non-human subjects, not applying OCTA, inaccessible full text, and articles in form of editorial publication. The flow of literature search was reported using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). All reviewed studies were rated based on the Oxford Center of Evidence-Based Medicine 2011 Level of Evidence on diagnostic studies.[7] As this review highlights cross-sectional studies, validity assessment of selected articles will be conducted with Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). Information extracted from each study includes the following: authors, publication year, the location and year in which the study is conducted, study design, number of subjects involved, variables examined, and outcome data.

RESULTS

The search term used in the previous chapter resulted in 153 studies. 5 duplicates were then removed and a total of 148 studies were screened based on their respective titles and abstracts. 131 articles were excluded because of unmet inclusion criteria or irrelevant outcomes for this literature review. Full-test review was then done on the remaining 17 articles, excluding 12 articles. In total, 5 articles were included in this review. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart on Figure 1 illustrates the process of article selection.

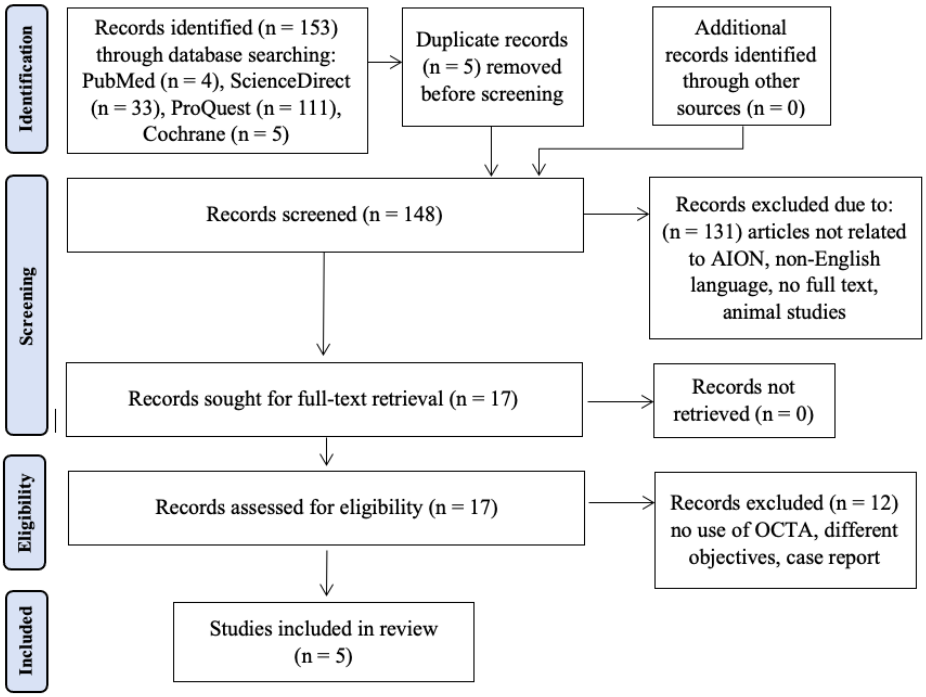

Figure 1. PRISMA flow chart

A total of 5 studies, ranging from 2018-2022, reporting outcomes of 236 eyes were included in this review. Two of the included studies were cross-sectional observational studies (Haitham et al[12], Pierro et al[14]), achieving a Level II Evidence based on the Oxford Center of Evidence Based Medicine (OCEBM). The other studies consisted of retrospective cohort studies (Liu et al[15]) retrospective comparative case series (Gaier et al[11]), and prospective comparative observational study (Aghdam et al[13]), hence the level of evidence assessment according to OCEBM was not applicable (N/A). Three of the studies (Gaier et al[11], Haitham et al[12], Liu et al[15]) compared OCTA findings in eyes with non-arteritic anterior ischemic optic neuropathy (NAION) with unaffected fellow eyes, and three among the studies (Haitham et al[12], Aghdam et al[13], Pierro et al[14]) also comparing OCTA findings with the eyes of healthy controls. One studies compared NAION eyes with AAION eyes (Pierro et al[14]). When it comes to the study outcomes, all studies reported that eyes with optic neuritis showed either microvascular impairment in comparison to fellow unaffected eyes or healthy controls, or progressively worsening microvascular impairment over time. The summary of the studies' characteristics is presented in Table 1

Table 1. Overview of the included studies

Author (Year)	Study Design (Level of Evidence)	Year Conducted	Country	Types of Diseases	Number of Subjects	Gender (M/F)	PDP
Gaier et al[11] (2018)	Retrospective comparative case series (N/A)	2016-2017	United States	NAION	25 eyes (7 acute and 18 non-acute) in 19 patients with NAION, 6 unaffected fellow eyes	19/5	Ac & chr
Haitham et al[12] (2020)	Cross-sectional observastional study (II)	2020	Egypt	NAION	25 eyes with unilateral acute NAION, 25 unaffected fellow eyes used as a control group	14/11	Ac
Aghdam et al[13] (2018)	Prospective comparative observational study (N/A)	2016-2017	Iran	NAION	10 eyes with ONHD, 10 eyes with NAION, and 10 normal eyes	4/6	Ac
Pierro et al[14] (2020)	Cross-sectional observational study (II)	2020	Italy	NAION & AAION	15 eyes with AAION & 15 eyes with NAION, 15 healthy controls	9/6 & 8/7	Ac
Liu et al[15] (2020)	Retrospective cohort study (N/A)	2017-2019	China	NAION	21 eyes with NAION & 19 unaffected fellow eyes	12/9	Ac & Chr

AAION: arteritic anterior ischemic optic neuropathy; Ac: acute; Chr: chronic; M: male, F: female, N/A: not available; NAION: non-arteritic anterior ischemic optic neuropathy, PDP: patient disease phase

Table 2. presents the demographics of the patients in the included studies. The mean age of the NAION patients involved is 47 years and above. Gender distribution of the patients are also quite heterogenous, with the male/female ratio ranging from 4/6 up to 19/5. OCTA devices across the studies are also variable, with a total of four different kinds of devices.

Table 2. Demographics of the patients in the included studies

Study	Age (Mean ± SD)	Gender (M/F)	OCTA Device
Gaier et al[11]	58.71 ± 13.19	19/5	Optovue, Zeiss
Haitham et al[12]	60.2 ± 3.5	14/11	Optovue
Aghdam et al[13]	56.80 ± 6.81	4/6	Optovue
Pierro et al[14]	47.7 ± 11.35	8/7	Topcon
Liu et al[15]	54.67 ± 7.55	12/9	Optovue
Lee et al[16]	63 ± 11	14/7	Heidelberg

N/A: not available; OCTA: optical coherence tomography angiography; SD: standard deviation; M: male; F: female

Findings on vessel density of the peripapillary capillary is shown on Table 3. All studies unanimously reported reduction of both vessel densities in patients with NAION at the various fields examined by OCTA. Peripapillary vessel density values highest in the study by Aghdam et al[13], which is 49.47 ± 5.42.

Table 3. Vessel density findings from each study

Study	Peripapillary VD (WMD or mean ± SD)
Gaier et al[11]	N/A
Haitham et al[12]	Whole: 44.7 ± 2.1 (p<0.001) Inside: 42.9 ± 3.5 (p<0.001) Superior: 42.1 ± 2.4 (p<0.001) Inferior: 43.7 ± 1.8 (p<0.001) Nasal: 46.1 ± 3.3 (p<0.001) Temporal: 47.6 ± 2.9 (p<0.001)
Aghdam et al[13]	49.47 ± 5.42 (p<0.001)
Pierro et al[14]	AAION vs NAION: 37 ± 1 vs 40 ± 1 (p<0.01)
Liu et al[15]	Whole baseline: 46.32 ± 2.63 Whole 1-2 weeks: 44.29 ± 3.28 Whole 1-2 months: 41.45 ± 3.43 Whole 3-6 months: 38.22 ± 4.00

N/A: not available; SD: standard deviation; WMD: weighted mean difference; VD: vessel density

In the study by Gaier et al[11] (Figure 2), there was a 4-5-fold greater amount of major retinal vessels in the superficial lamina in comparison to the superficial capillaries of the unaffected eyes, both at the disc and peripapillary. There were also more amounts of patent capillary vessel density in the peripapillary area compared to the papillary area in the unaffected eye and acutely affected eye ($p < 0.005$), but not for non-acutely affected eyes ($p = 0.745$). Quantitative analysis showed that there was a significant reduction in the angiographic signal from acutely affected eyes in comparison to the unaffected eyes in the papillary and peripapillary regions ($p < 0.022$). The difference in the major vessel density between non-acutely affected and unaffected eyes was not statistically significant ($p > 0.209$) in both sampling regions.

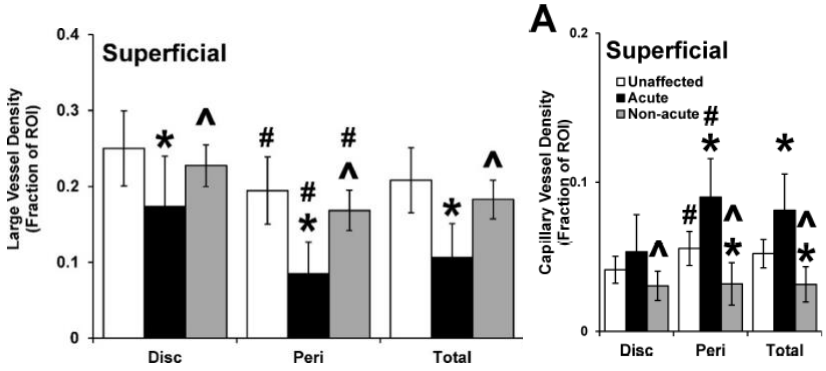

Figure 2. Quantitative analysis results of OCTA data and comparison in unaffected, acutely affected, and non-acutely affected eyes[11]

Only one study (Pierro et al[14]) analyzed the difference between AAION and NAION. 15 eyes of 15 AAION patients, 15 eyes of 15 NAION patients and 15 eyes of healthy controls were evaluated. OCTA quantitative analysis from this study revealed significant differences between patients and control. VD values for RPC and SCP for AAION and NAION eyes showed significant differences compared to controls ($p<0.01$). VD value were significantly lower both in AAION and NAION eyes compared to contralateral and control eyes ($p<0.01$).

DISCUSSION

OCTA is a non-invasive imaging modality that can provide three-dimensional visualization of perfused vasculature of the retina and choroid. In addition to the ability of optical coherence tomography (OCT) to analyze the intensity of the reflected light, OCTA is also able to analyze the temporal changes of the OCT signal based on repeated OCT section images from the same location of the retina. Through this method, it is possible to separate the temporal signal changes due to moving particles (i.e., erythrocyte flow through the blood vessels) from other possible causes of signal change such as noise in the OCT signal or eye

motion. As it is non-invasive, OCTA is regularly seen superior to fluorescein angiography. But this seems not to be the case, since FA and ICGA are able to display dynamic phenomena namely dye leakage, pooling, and staining, that are not observable with OCTA because they involve no blood cells in motion. Though this phenomena are useful in clinical diagnosis, retinal pathology can sometimes be obscured by hemorrhage or leakage, hence the ability of OCTA to generate high definition images of the microvasculature are able to work hand in hand with the information provided from dye-based angiography.[17]

AION is a term used to describe optic neuropathies due to a transient or permanent interruption of the optic nerve blood supply in any of its portion. AIONs are basically classified into AION and NAION.[1,2,3,4] This review explored the role of OCTA as a diagnostic tool for AION. From a total of the five studies screened in this review, all studies discussed the role of OCTA in patients with non-arteritic anterior ischemic optic neuropathy (NAION), with one study also discussing AAION. The availability of OCTA have enabled the identification of early and late structural changes in the retina and optic nerve head, therefore may assist the prediction of visual outcomes and the expansion of knowledge regarding the pathogenesis, also the development of more effective medical interventions.[18]

NAION is also one of the ischemic differential diagnoses of optic disc edema, along with inflammatory and papilledema. Patients with this disease typically report sudden onset of painless vision loss, and hallmarks signs include decreased visual acuity and/or visual field loss along with a relative afferent pupillary defect (RAPD) on the affected side (if the fellow eye is normal). The occurrence of optic disc edema at the acute phase of NAION is thought to be from ischemia due to hypoperfusion of the small vessels supplying the anterior portion of the optic nerve. This acute swelling of the disc may progress in the first 2-3 weeks after symptom onset and will start to remit by 6 weeks. In time, the optic disc becomes pale, either partly or globally.[18,19]

Arteritic anterior ischemic optic neuropathy, on the other hand, is most frequently caused by giant-cell arteritis (GCA) and often results in more severe visual loss. In contrast to NAION, OCT has not been extensively used in AAION, both in acute or chronic phases. With OCTA, findings of AAION are similar to NAION, showing defects of the radial peripapillary capillary (RPC).[18] Both NAION and AAION are characterized by the presence of optic nerve ischemia and inflammation, in which both contributed to the manifestation of symptoms like visual acuity reduction and visual field defects.

The relatively novel non-invasive OCTA has allowed the quantitative assessment of the circulation peripapillary and retinal vessels in different ophthalmic diseases. OCTA provides

useful information on the ongoing vascular impairment of AION. To be exact, remarkable perfusion reductions have been identified, and also localized and well-matched to the area of visual field defects.[14]

Several studies have reported the results of peripapillary OCTA in NAION eyes, both in the acute and post-acute stages. Those studies reported both a reduced radial peripapillary capillary (RPC) density in acute NAION and a progressive reduction of vessels within 3 months. Another study has also shown flow impairment in the RPC corresponds to structural OCT deficits of the peripapillary retinal nerve fiber layer (p-RNFL) in 80% of eyes.[18] These are in sync with the findings of this review, in which all studies on OCTA findings of NAION eyes reported a reduction in the vessel density of peripapillary capillary plexus when compared to either the healthy control eyes or the fellow unaffected eyes.

Peripapillary vessel density loss in post-acute NAION has also been reported in other studies, but this does not necessarily mean that OCTA directly displays the optic nerve ischemia in NAION. This is because NAION is known to be resulted from acute infarction of the retrolaminar segments of the optic nerve head, which are primarily sourced from the short posterior ciliary arteries. The current technology of OCTA is not yet able to show those deep-located vessels. Another reason is that the location of decreased peripapillary vessel density in post-acute NAION is similar to the locations of defected visual field and also correlates with the severity of p-RNFL thinning. This information indicates that RPC reduction (RPC dropouts) is not specifically due to NAION, and that p-RNFL loss may have also contributed. NAION patients are more prone to have diabetes, hypertension, and even sleep apnea, which is another possible cause of RPC reduction.[18,19]

The study by Pierro et al discovered the presence of vascular tortuosity together with reduced vessel density in AAION eyes, which was significantly more severe in comparison to NAION eyes, particularly in terms of vessel density (VD) for RPC and SCP ($p<0.01$). Quantitative analysis by OCTA has displayed more vascular abnormalities in AAION than NAION, which is expected since AAION is characterized by more optic disc swelling. However, further studies are still needed to determine quantitative values as possible cut-offs to distinguish AAION from NAION eyes.[14,20]

CONCLUSION

In conclusion, this review demonstrated that OCTA can display vascular density changes, mainly showing a reduction in peripapillary vessel density thickness in cases of AION both arteritic and non-arteritic which was found significantly more severe in AAION than

NAION. On the other hand, though the methodology of this review is thorough, the studies included presents different limitations and should not be ignored, and the risk of bias and variability of data collected should be regarded meticulously. Further study is recommended to assess differences regarding vascular impairment in AION.

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