Ophthal Focus

Dear Doctor,

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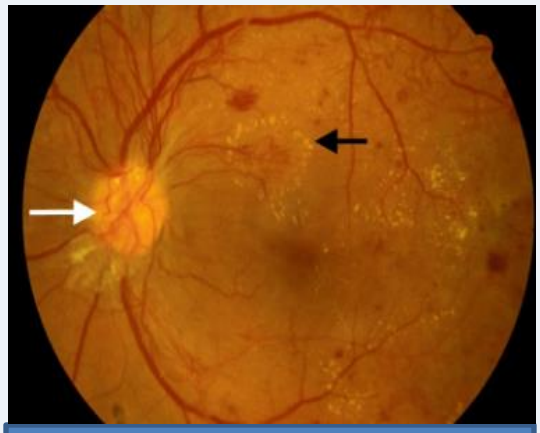
Evaluation of Globulin Levels and Albumin-to-Globulin Ratio in Individuals with Diabetic Retinopathy: A Single-center Retrospective Study

INTRODUCTION



DIABETIC RETINOPATHY

The study emphasises the potential use of regular blood biomarkers as useful markers for DR in type 2 diabetes.

Diabetes mellitus (DM) has become a global epidemic, and diabetic retinopathy (DR), a severe and vision-threatening condition, stands among the most prevalent diabetes-related complications. Current understanding identifies diabetic retinopathy as an inflammatory neurovascular complication, where neuronal injury or dysfunction precedes observable microvascular damage.[1] DR was associated with persistent low-grade inflammation, oxidative stress, and changes in retinal microvasculature. Serum albumin, a key component of blood proteins, shows an inverse relationship with inflammation, with hypoalbuminemia serving as an inflammation biomarker. In contrast, serum globulin, encompassing complements, Interleukin 6 (IL-6), and immunoglobulins, was intricately connected to inflammation. While the albumin-to-globulin ratio has been suggested as an inflammation marker, its specific role in detecting diabetic retinopathy requires further comprehensive investigation.[2] This study aimed to assess inflammation-related routine blood biomarkers in individuals with DR.

METHODS

A retrospective cross-sectional investigation was carried out on individuals with type 2 diabetes (T2D) receiving care at a tertiary care hospital's outpatient clinic. Encrypted data from 139 diabetic patients (70 with DR and 69 without DR) were collected and analyzed. Cases were categorized based on the presence (DR) or absence (non-DR) of retinopathy. Selection criteria included patients with comprehensive medical records, incorporating eye examinations and laboratory results. Data encompassing patient demographics (age and gender) and laboratory parameters (HbA1c, C-reactive protein (CRP), serum total protein levels, albumin, and globulin) were extracted from patient files. Statistical analyses, using SPSS software, involved descriptive statistics for categorical variables (frequencies and percentages) and quantitative variables (means

and standard deviations). Chi-square tests compared frequencies, while Pearson's correlation test evaluated factor correlations. The significance threshold was set at $p \leq 0.05$.

RESULTS

Mean and standard deviation calculations revealed the following parameters: HbA1c (mean=7.7%, SD=1.56), albumin (mean=38.6g/L, SD=6.60), total protein (mean=70.1g/L, SD=7.95), and globulin (mean=24.1g/L, SD=9.52). The mean CRP level was 29.5mg/L. No significant differences were observed in total protein, albumin, and CRP levels between the two groups. However, a significant difference in globulin levels was evident (no retinopathy: mean 18.0g/L, SD 9.14; retinopathy: mean 30.1g/L, SD 5.04; P <0.001). The albumin-to-globulin ratio also varied significantly between the two groups (no retinopathy: mean 2.8, SD 2.06; retinopathy: mean 1.3, SD 0.33; P <0.001). Moreover, HbA1c levels were significantly higher in individuals with retinopathy compared to those without retinopathy (no retinopathy: mean 7.4%, SD 1.58; retinopathy: mean 8.0%, SD 1.49; P = 0.020). Comparison of total protein levels in diabetic patients with and without retinopathy yielded no significant differences among male groups (p=0.323), female groups (p=0.281), and male versus female (p=0.373) based on a t-test. Regarding globulin levels, a statistically significant difference was observed between the two groups (p<0.001), with mean values of 18 g/L for no retinopathy and 30.1 g/L for retinopathy (Figure 1). Both male and female patients with retinopathy exhibited similar elevated globulin levels. In patients without retinopathy, there was a weak negative correlation between globulin and albumin levels (Pearson's correlation coefficient: -0.146, p=0.231). Similarly, in patients with retinopathy, a weak negative correlation between globulin and albumin levels was noted (Pearson's

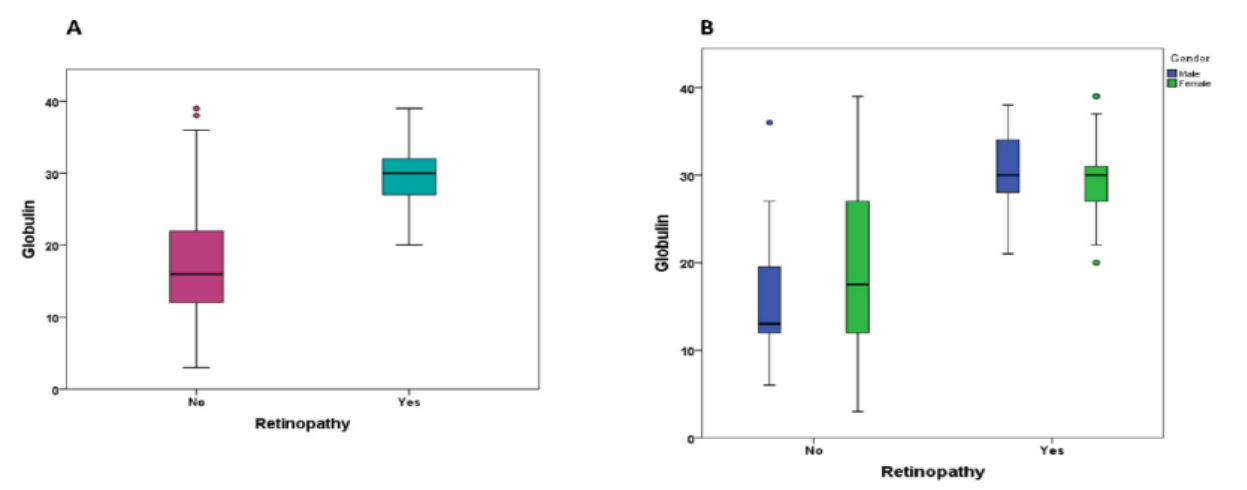


Figure 1. Distribution of globulin levels (g/L) in diabetic individuals with and without retinopathy. The data's range, median, and interquartile range were displayed in boxplots. A) The mean value was 30.1 mg/dL for the group with retinopathy and 18 mg/dL for the group without retinopathy. B) Both male and female patients with retinopathy had elevated globulin levels at similar levels.

correlation coefficient: -0.085, p=0.482), although these correlations were not statistically significant.

DISCUSSION

Limited studies has indicated an association between the severity of diabetes mellitus and total serum protein levels.[3] However, this study found no significant disparity in total protein and albumin levels between the two groups, with all mean values falling within the established reference range for adults and the elderly. This observation might be attributed to the majority of patients being in the early stages of non-proliferative retinopathy. The study focused on comparing diabetic individuals with and without DR. Notably, the study emphasized the noteworthy increase in serum globulin levels and the observed negative correlation with albumin, providing valuable insights into the pathophysiology of DR. As per Nakazawa D et al., heightened globulin levels can potentially trigger neutrophil secretion, constituting a risk factor for complications in diabetes.[4]

CONCLUSION

The study underscored the possible effectiveness of routine blood biomarkers as markers for retinopathy in type 2 diabetes, notably the documented rise in serum globulin levels, HbA1c, and the decline in the albumin-to-globulin ratio. These results implied that both inflammation and inadequate glycemic control may play roles in the progression of DR. Nevertheless, additional investigations were essential to elucidate the underlying mechanisms and clinical significance of these biomarkers.

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Incidence, Characteristics, Management, and Outcome of Endophthalmitis Following Intravitreal Injection

INTRODUCTION

The majority of individuals with post-IVI endophthalmitis do not restore their original VA, making it an uncommon consequence. A number of criteria, including clinical, microbiological, and therapeutic ones, can be used to predict results and direct therapy and diagnostic decisions.

The extensive use of intravitreal injection (IVI) for pharmacotherapy has revolutionized the treatment of numerous ocular conditions. Nevertheless, each injection entails a slight risk of endophthalmitis. Published rates of endophthalmitis post-IVI vary between 0.016% and 0.056%. In contrast to the well-studied postoperative endophthalmitis after cataract surgery spanning decades, information on the clinical progression, microbial causes, and treatment results for endophthalmitis following IVI has only started to emerge in the past decade.[1] Endophthalmitis occurring after IVI typically manifests with symptoms like redness, pain, diminished vision, and vitritis. Patients commonly seek medical attention within 3 days of the injection, although some may present weeks later. Management involves obtaining a vitreous sample through vitreous tap or pars plana vitrectomy (PPV), followed by administering intravitreal antimicrobial agents. Visual outcomes in post-IVI endophthalmitis vary significantly. Predictors of a less favorable prognosis include positive culture results, particularly when caused by Streptococcus and Enterococcus species, which were associated with the poorest outcomes.[2] This study aimed to document the occurrence, clinical and microbiological attributes, visual prognosis, and disease activity in cases of post-IVI endophthalmitis. Additionally, the goal was to assess the correlation between clinical and therapeutic factors with culture results and visual outcomes. Furthermore, the study sought to investigate the impact of endophthalmitis on disease activity within the subgroup of patients with neovascular age-related macular degeneration (nAMD) experiencing post-IVI endophthalmitis.

METHODS

This retrospective case series involved patients diagnosed with post-IVI endophthalmitis from January 2018 to December 2019 at two major medical centers. Inclusion criteria encompassed eyes diagnosed with infectious endophthalmitis within 6 weeks of IVI of any agent, with a minimum 12-month follow-up. Eyes with presumed infectious endophthalmitis underwent either tap and inject (TAI) or early PPV. The study assessed medical records to identify patients treated for endophthalmitis within 6 weeks post-IVI during the specified period. The primary outcomes measured were best-corrected visual acuity (BCVA) at 6 and 12 months' post-treatment, along with the change in BCVA at these time points compared to baseline and presentation BCVA. Secondary outcomes included the incidence of post-IVI endophthalmitis, BCVA, clinical findings at presentation, and microbiological characteristics. Additionally, the study explored the association of various demographic, clinical, laboratory, and management factors with visual outcomes, including the return to baseline BCVA, improvement in BCVA from presentation, and relatively low BCVA (defined as 6/60 or lower).

RESULTS

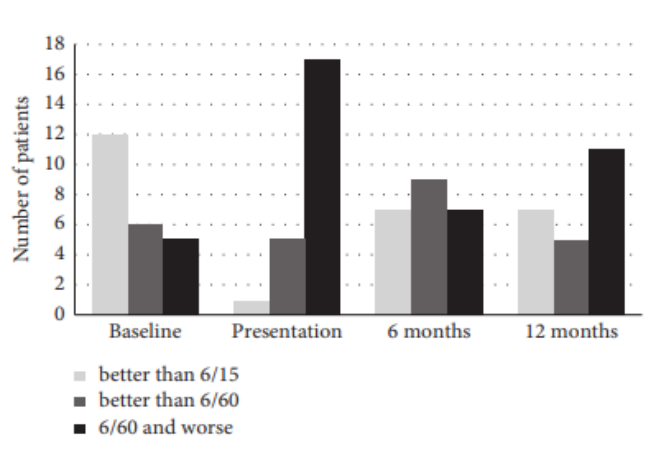

Figure 1. BCVA distribution throughout the study period

Within the study timeframe, a total of 51,356 IVIs were administered, resulting in the diagnosis of 23 cases of post-IVI endophthalmitis. The predominant presenting symptom was decreased vision in 20 (87%) patients, with anterior chamber cells and vitritis being the most prevalent clinical signs, observed in all patients (100%). The median interval from IVI to symptom onset was 2 days (IQR: 1–5), from symptom onset to the first procedure was 1 day (IQR: 0–3), and from IVI to the first procedure was 4 days (IQR: 2–7). Direct smear of vitreous samples (from TAI or PPV) revealed white blood cells (WBCs) in 12 (52%) patients, of which 11/12 (92%) eventually had positive culture results (positive predictive value of 92%). WBCs on direct smear were associated with a higher rate of positive culture results (91.7% vs. 18.2%, P = 0.001). PPV (as an early or late procedure) exhibited a higher culture-positive rate compared to TAI-only cases (76.9% vs. 30.0%, P = 0.04). All pathogens (100%) were Gram-positive bacteria, predominantly coagulase-negative staphylococcus (CoNS) in 11 cases (76.2%). A higher culture-positive rate was observed in cases with a longer time interval from IVI to any first procedure (median 7, IQR: 4–10 vs. median 3.5, IQR: 2–4, P = 0.007). Of the patients, 20 (87%) experienced vision loss compared to baseline BCVA. BCVA improvement from presentation was documented in 18 (78%) and 17 (74%) patients at the 6- and 12-month follow-up, respectively. Eight (35%) and nine (39%) patients returned to their baseline vision (within one line from the baseline BCVA) at the 6- and 12-month follow-up, respectively. BCVA distribution throughout the study period was illustrated in Figure 1. Younger age was associated with a higher rate of return to the baseline BCVA. Among the presenting signs and symptoms, better BCVA on presentation was correlated with higher rates of return to the baseline BCVA. In terms of laboratory findings, positive culture results were linked to a worse visual outcome (BCVA of 6/60 and worse, 53.9% vs. 0%, P = 0.017). Patients who received systemic steroids treatment demonstrated a lower rate of improvement in visual acuity along the follow-up (54.6% vs. 100%, P = 0.035).

DISCUSSION

In the present study, it was observed that the cumulative number of IVIs within the 12 months preceding endophthalmitis did not correlate with an elevated culture-positive rate. A prior investigation by Dossarps et al. involving a series of 65 endophthalmitis cases post-IVI, similarly reported no notable difference in the median number of IVIs before endophthalmitis between cases with positive cultures and those with negative cultures.[3] The percentage of patients experiencing

vision improvement (within one line from the baseline BCVA) in comparison to the presentation was 78% and 74% at the 6- and 12-month follow-up, respectively. Additionally, 35% and 39% of patients reverted to their baseline vision at the 6- and 12-month follow-up, respectively. These rates align with those reported in similar studies.[4] Among the examined demographic factors, a younger age exhibited a correlation with improved visual outcomes. This observation aligns with a recent study by Xu et al. which investigated 40 patients with endophthalmitis following anti-VEGF intravitreal injections and similarly found that younger age was associated with better visual outcomes.[4] Patients who underwent systemic steroid treatment exhibited poorer visual outcomes in our study. The literature lacks consensus on the utility of systemic corticosteroids in endophthalmitis. A retrospective trial conducted by Robbins et al. involving 133 eyes with endophthalmitis (23 post-IVI) reported a higher rate of vision improvement of three lines or more among the 25% of patients treated with systemic steroids.[5]

CONCLUSION

Endophthalmitis following IVI was an uncommon complication, and the majority of patients do not recover their initial visual acuity. Specific parameters (clinical, microbiological, and therapeutic) can assist in predicting the outcome and informing decisions related to diagnosis and treatment.

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Comparison of the efficacy and safety of Low-Level Red Light in controlling Myopia progression at 3 different powers

INTRODUCTION

Myopia is a prevalent eye condition of global concern, particularly reaching high prevalence rates, ranging from 80% to 90%, among high school students in certain regions of East and Southeast Asia. The correction of refractive errors due to myopia imposes a substantial burden on individuals and society. Moreover, early-onset myopia has an increased likelihood of progressing to high myopia, which elevates the risk of potential vision-threatening conditions, such as myopic macular degeneration. Consequently, the prevention of myopia holds significant importance. Presently, various interventions, including increased outdoor time, reduced engagement in activities at a short working distance, eye exercises, and low-dose atropine, have been suggested to prevent the onset of myopia. The efficacy rates of these interventions in preventing myopia within one year range from 11.0% to 54.3%. As an alternative myopia control intervention, repeated therapy involving low-level red-light (RLRL) delivered by a device emitting 650-nm visible red light has been proposed.[1] Recent research indicates that exposure to low-level red light (LRL) has the potential to induce hyperopia and slow down the progression of myopia. The hypothesis suggested that LRL might enhance choroidal blood flow, addressing the relative oxygen supply deficiency in the myopic fundus and impeding the rapid increase in axial length (AL). By increasing choroidal blood flow through LRL therapy, it was speculated that this approach may help alleviate potential consequences associated with reduced choroidal perfusion. However, the precise molecular pathways underlying the effects of LRL and its impact on choroidal and scleral responses, blood flow regulation, and cellular processes implicated in myopia development were not fully understood. Additionally, the power range used in previous studies varies from 0.35 to 2.0 mW, and the difference in LRL power could be a crucial factor contributing to the diverse results observed in these studies. Despite this, there were no study confirming which power of LRL was most effective in controlling myopia, and there was no consensus on the standard power of LRL.[2] Hence, the objective of this study was to assess the effectiveness of LRL for myopia control at power levels of 0.37 mW, 0.60 mW, and 1.20 mW.

At 0.37 mW, 0.60 mW, and 1.20 mW, LRL successfully inhibited the progression of myopia. Additional investigation is needed.

METHODS

This prospective, single-center, 6-month randomized clinical trial involved a parallel-group design. A total of 200 participants, aged 6 to 15 years, with myopic refraction of at least -0.50 diopter (D) in both eyes, astigmatism less than 2.50 D, intraocular pressure between 10 and 21 mmHg, and best-corrected visual acuity (BCVA) of 20/25 or better in both eyes were enrolled. Participants were randomly assigned to four groups: 0.37-mW, 0.60-mW, 1.20-mW, and a control group (n=50 each). Children in the intervention groups wore single-vision spectacles (SVS) throughout the day and received LRL therapy twice daily for 3 minutes per session, with a minimum 4-hour interval between sessions, using the sky-n1201 device (Beijing Ming Ren Shi Kang Science & Technology Co., Ltd.). All participants were prescribed best-corrected spectacles

throughout the study and underwent detailed eye examinations at baseline, 1, 3, and 6 months. The examination included measurements of best-corrected visual acuity, spherical equivalent (SE), axial length (AL), and subfoveal choroidal thickness (SFCT). The 200 participants were evenly distributed into four groups: 0.37-mW, 0.60-mW, 1.2-mW, and control groups. The intervention groups received LRL at three different powers twice daily for 3 minutes per session, with a minimum 4-hour interval. The main outcome measures focused on changes in SE, AL, and SFCT.

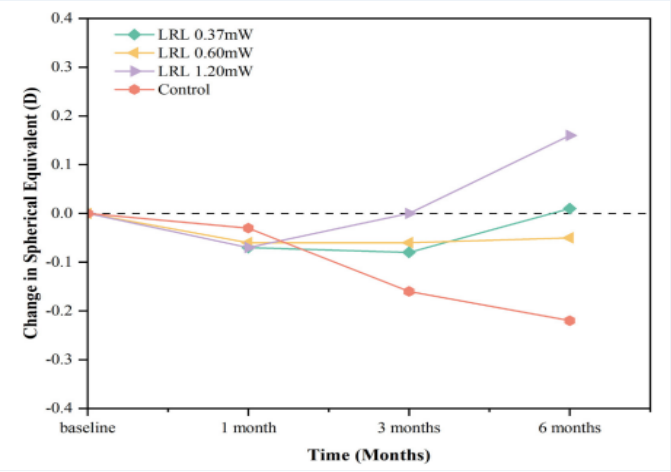

Figure 1. Line graph illustrating change in spherical equivalent (SE) across treatment groups throughout time. D = diopter

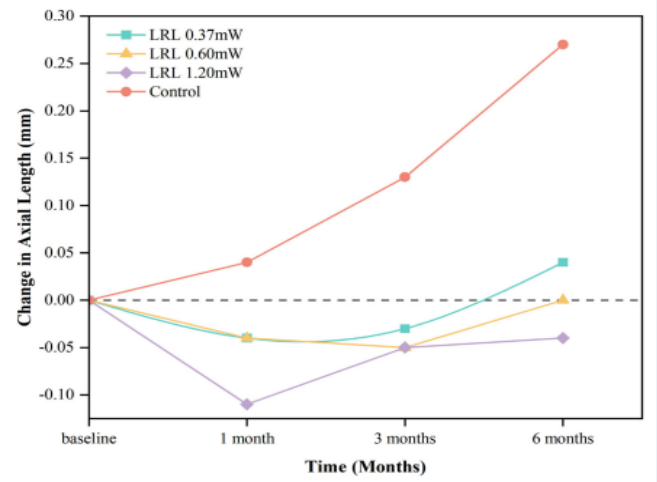

Figure 2. A line graph illustrating the axial length changes over time in each treatment group. LRL= low-level red light.

RESULTS

During the first month monitoring visit, none of the four groups experienced an initial hyperopic shift. However, at the end of 3 months, a hyperopic shift occurred in the 1.20-mW group (adjusted P = 0.04). At the 6-month mark, changes in spherical equivalent (SE) were 0.01 D (95% CI, -0.12 to 0.15), -0.05 D (95% CI, -0.18 to 0.07), 0.16 D (95% CI, 0.03 to 0.30), and -0.22 D (95% CI, -0.50 to 0.30) in the 0.37-mW, 0.60-mW, 1.20-mW, and control groups, respectively (P < 0.001). The differences in SE among the three LRL groups and the control group were statistically significant (adjusted P <0.001 for all). Notably, the higher-power group (1.20 mW) exhibited the greatest hyperopic shift at the 6-month follow-up (Figure 1). However, no significant differences in SE were observed among the three LRL groups at any of the evaluated time points. Regarding axial length (AL), the control group showed a more significant change at 6 months (0.27 mm; 95% CI, 0.22 to 0.33) than the 0.37-mW group (0.04 mm; 95% CI, -0.01 to 0.08), 0.60-mW group (0.00 mm; 95% CI, -0.05 to 0.05), and 1.20-mW group (-0.04 mm; 95% CI, -0.08 to 0.01; P < 0.001; Figure 2). The differences in AL among the three LRL groups and the control group were statistically significant in terms of different follow-up times and the interaction between follow-up time and different intervention methods (F = 0.273 for main effect; P < 0.001; F = 0.179 for crossover effect; P < 0.001). The fastest decline in AL was observed in

the 1.20-mW group, after which the downward trend started to slow down and persisted until the end of the 6 months (Figure 2). However, at any of the follow-up times, no significant differences were found in AL among the three LRL groups. At the end of 6 months, the increase in SFCT had lessened significantly in the control group (-5.07 mm; 95% CI, -10.32 to -0.13) than in the 0.37-mW group (22.63 mm; 95% CI, 12.13 to 33.34), 0.60-mW group (36.17 mm; 95% CI, 24.37 to 48.25), and 1.20-mW group (42.59 mm; 95% CI, 23.43 to 66.24; adjusted $P < 0.001$ for all). No significant differences in SFCT were observed among the three LRL groups. Participants did not report any adverse events during the study, and best-corrected visual acuity remained normal at each follow-up visit, with no abnormalities observed in the retinal or choroidal structure.

DISCUSSION

This study found that low-level red light (LRL) at powers of 0.37 mW, 0.60 mW, and 1.20 mW effectively controlled the progression of myopia. A recently conducted meta-analysis also indicated the substantial efficacy of both low-power (0.35 mW) and relatively high-power (2 mW) LRL in controlling myopia progression and slowing AL elongation in children within a 6-month intervention period.[3] Furthermore, the results suggested potential variations in the trends among the three LRL powers in terms of myopia control. Notably, the effectiveness of 1.20 mW (115%) surpassed that of 0.60 mW (100%) and 0.37 mW (85.2%). Dong et al. demonstrated that LRL therapy at 100% power significantly decreased myopia progression over six months compared to 10% of the original power.[4]

CONCLUSION

LRL therapy at 0.37 mW, 0.60 mW, and 1.20 mW effectively managed myopia progression. While no statistically significant variances were observed among the three LRL power settings, a potential trend indicated that higher powers might exhibit increased efficacy. Larger-scale samples and extended follow-up studies were essential for determining the optimal power settings for LRL therapy.

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Case Report on the Yokoyama Procedure for Managing Cyclic Strabismus in Individuals with Axial High Myopia

INTRODUCTION

In cases when axial high myopia coexists with cyclic strabismus, the Yokoyama technique was efficacious in ending cycles without overcorrection on days when squinting was absent.

Cyclic strabismus is an uncommon condition characterized by alternating days of strabismus and orthotropia within a 24-hour cycle. While it has been linked to factors such as trauma, strabismus surgery, central nervous system disorders, or reduced vision, the exact cause of this phenomenon remains unclear, and it is often considered idiopathic.[1] There have been no reported cases of cyclic strabismus accompanied by axial high myopia. Despite multiple efforts to elucidate the pathophysiology of this condition, the precise mechanisms behind it remain elusive.[2] This study presented a case involving cyclic esohypotropia and axial high myopia. The patient underwent medial rectus (MR) recession and lateral rectus (LR) muscle resection. An orbital CT revealed supertemporal dislocation of the elongated globe's posterior portion outside the muscle cone. Consequently, the Yokoyama procedure was performed on the left eye, yielding positive outcomes.

CASE PRESENTATION

A 43-year-old woman presented with esohypotropia and axial high myopia in her left eye four years ago. Two years prior, she had undergone MR muscle recession and LR muscle resection on her left eye elsewhere. Twelve months' post-surgery, she experienced a recurrence of left eye esohypotropia in a cyclic pattern, squinting one day (Figure 1a) and not squinting the next (Figure 1b). Her right best-corrected visual acuity was 20/20, and the refractive error was -0.75 diopter sphere/-2.25 diopter cylinder at 117°. The left eye had poor corrected vision due to myopic maculopathy, with a refractive error of -24.00 diopter sphere/-2.00 diopter cylinder at 115°. The worth 4-dot test revealed left suppression on both squint and non-squint days. Axial lengths were 22.35 mm (right globe) and 28.37 mm (left globe). She exhibited left esotropia of 60 prism diopters (PD) and hypotropia of 30 PD in the primary position with mild left eye abduction limitation (Fig. 1a). Orbital CT revealed supertemporal dislocation of the elongated globe's posterior portion from the muscle cone (Figure 1c and d). After six examinations over 6 months, the patient underwent extraocular muscle surgery eight months into the cyclic phase, based on measurements on a squint day. During surgery, the forced duction test (FDT) showed no restriction in the left eye. The distance from the limbus to the MR muscle insertion was 10 mm. A 12 mm left medial rectus recession from the limbus was performed, combined with uniting the muscle bellies of the superior rectus and lateral rectus muscles to restore the dislocated globe back into the muscle cone. In the

first postoperative week, the patient achieved orthotropia. Orbital CT confirmed the dislocated globe's relocation into the muscle cone. At the 6-month postoperative follow-up, no recurrence of esohypotropia was observed.

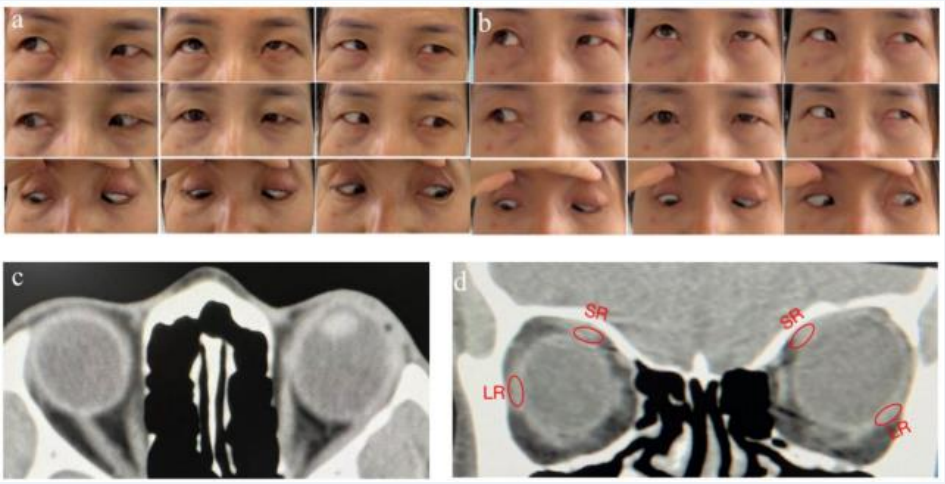

Figure 1. Patient's pictures on a "bad" day and a "good" day, with computed tomography (CT) scans. A) "Bad" day. In main position, the patient showed signs of 30 PD hypotropia and 60 PD esotropia, along with a slight restriction in her left eye's ability to abduct. B) Orthotropia on Good Day. C) and D) supertemporal displacement of the left eye's muscular cone outward from the posterior part of the elongated globe on a CT scan.

DISCUSSION

In this particular case, the patient exhibited esohypotropia along with axial high myopia in her left eye.[2] Myopic strabismus fixus was characterized by a gradually worsening, often significant esotropia and hypotropia, leading to restricted abduction and supraduction. This condition was commonly observed in eyes with elevated axial lengths, indicative of high myopia, typically exceeding 25 diopters.[3] The primary approach for managing cyclic strabismus involves extraocular muscle surgery, determined by assessing the maximal deviation on days when the squinting was apparent. Additionally, other documented interventions include botulinum injections[4] and the use of prismatic corrections.[5] In this case, the Yokoyama procedure was conducted by uniting the superior and lateral rectus muscles, alongside medial rectus recession, due to the supertemporal dislocation of the posterior most part of the globe outside the muscle cone. The procedure proved effective, successfully breaking the cyclic pattern without causing overcorrection on days without squinting. A 6-month postoperative follow-up revealed no reappearance of esohypotropia.

CONCLUSION

In cases where cyclic strabismus coincides with axial high myopia, the Yokoyama procedure has proven effective, successfully ending the cycles without causing overcorrection on days without squinting. The objective of this procedure was to reposition the dislocated globe within its muscle cone by connecting the muscle bellies of the superior rectus and lateral rectus.

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