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Original Article

Clinical Findings, Follow-up and Treatment Results in Patients with Ocular Rosacea

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Summary

Objectives: To report the clinical features, treatment options and complications in patients with ocular rosacea.

Materials and Methods: The records of 48 eyes of 24 patients with ocular rosacea were retrospectively reviewed. Patients' ocular signs and symptoms were scored between 1 and 4 points according to disease severity; tear film break-up time (BUT) and Schirmer's test results were recorded before and after the treatment. Preservative-free artificial tears, topical antibiotic eye drops/ointments, short-term topical corticosteroids, topical 0.05% cyclosporine and oral doxycycline treatment were applied as a standard therapy to all patients. Additional treatments were given as needed. Complications were recorded.

Results: Twenty-four patients with a mean age of 48.5±35.4 (32-54) years were followed for a mean 15±9.4 (8-36) months. Ocular findings included meibomitis in 100% of cases, anterior blepharitis in 83% (40 eyes), punctate keratopathy in 67% (32 eyes), chalazia in 50% (24 eyes), corneal neovascularization in 50% (24 eyes) and subepithelial infiltrates in 16.6% (8 eyes). Significant improvement of symptoms and clinical findings were achieved in all patients with treatment. The increases in Schirmer's test and BUT were 3.3±1.5 and 4.5±2.8, respectively ($p<0.05$). Descemetocele and small corneal perforation occurred in 2 eyes; re-epithelialization was achieved in both eyes with tissue adhesive application (1 eye) and additional amniotic membrane transplantation (1 eye). Four eyes of three patients showed significant regression of corneal neovascularization with topical bevacizumab therapy.

Conclusion: Ocular rosacea may present with a variety of ophthalmic signs. It is possible to control the ophthalmic disease with appropriate therapeutic modalities including topical corticosteroids, topical cyclosporine and systemic doxycycline.

Keywords: Ocular rosacea, treatment, complications, cyclosporine

Introduction

Rosacea is a chronic skin condition affecting the blood vessels and sebaceous glands and is characterized by recurrent erythema, telangiectasia, papules and pustules.[1,2,3] Although usually presenting with skin involvement, ocular involvement is found in 58-72% of patients with acne rosacea.[1] In approximately 20% of patients, ocular signs appear prior to dermatological signs.[1,2] Signs of ocular rosacea include anterior blepharitis, meibomitis, recurrent chalazia, eyelid erythema and telangiectasia, interpalpebral conjunctival hyperemia, and peripheral corneal vascularization.[1,4,5] Complications in cases with severe corneal involvement can also lead to vision loss.[5,6]

Though the etiology of rosacea is not fully understood, immune system dysfunction, inflammatory reaction to cutaneous microorganisms, *Demodex folliculorum* infestation, environmental factors like sunlight, and vascular anomalies have been implicated in its pathogenesis.[2,3] By inducing changes at the vascular level, environmental factors such as sunlight and temperature changes are claimed to lead to vascular dilation, increased capillary permeability and edema, which create an ideal environment for the proliferation of *Demodex folliculorum*.[2,3,6]

Furthermore, it has been shown that proinflammatory cytokine release is triggered in these patients due to immune system dysfunction.[7] This hypothesis is supported by findings of significantly elevated levels of proinflammatory cytokines (interleukin-1 alpha) and the degradative enzyme matrix metalloproteinase-9 in patients' tears, and the subsequent improvement of symptoms after inhibiting these factors.[7,8]

Rosacea patients show increased bacterial lipase activity in their meibomian gland secretions due to increased bacterial

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flora on the eyelids. This causes the release of toxic free fatty acids, which contribute to the pathogenesis of the disease.[2,7]

There are several different approaches and treatment choices available for the treatment of rosacea,[5,6,7,8,9,10] including lubricating agents, topical steroids, topical antibiotic eye drops and ointments, and systemic antibiotics. As these patients often have concomitant dry eye syndrome, dry eye therapy may also be necessary.[9]

In this study, we aimed to report the clinical characteristics, treatment options and complications of ocular rosacea.

Materials and Methods

The records of patients who were followed in the Başkent University Faculty of Medicine and the Ophthalmology Clinic of the Bayındır Kavaklıdere Hospital for ocular rosacea between January 2008 and December 2013 were retrospectively analyzed.

Diagnosis was based on the presence of anterior blepharitis, meibomitis and/or meibomian gland dysfunction (MGD), recurrent chalazion, eyelid telangiectasia, punctate epitheliopathy, corneal infiltrates or neovascularization, particularly in the peripheral cornea. Patients who first presented to the ophthalmology clinic but also exhibited dermatological symptoms were given an initial diagnosis of rosacea and the dermatology clinic was consulted to confirm the diagnosis. Patients who presented to the dermatology clinic due to skin symptoms and were diagnosed with acne rosacea were evaluated for ocular involvement in our clinic. Patients received topical metronidazole prescribed by the dermatology clinic and our standard ophthalmologic treatment regimen, with no additional systemic treatments.

At each visit, all patients underwent a detailed ophthalmologic examination including best corrected visual acuity measurement, slit-lamp anterior segment examination, and tear film break-up time (BUT) and Schirmer's tests. Patients' signs and symptoms were scored on a scale of 0-4 points based on their severity before treatment and at their last follow-up visit. Table 1 shows the scoring scale of ocular symptoms; Table 2 shows the scoring scale of ocular findings.

All patients were treated with hot compresses, eyelash base cleansing, preservative-free artificial tear drops (Tears Naturale Free, Alcon, Fort Worth, Texas, USA or Refresh, Allergan Inc, Irvine, CA, USA), artificial tear gel (Thilotears SE, Liba Lab., İstanbul, Turkey), topical antibiotic ointment (Ciloxan ophthalmic ointment, Alcon), short-term low-dose topical corticosteroid drops (loteprednol etabonate or fluorometholone) four times daily, 100 mg oral doxycycline once daily, and topical 0.05% cyclosporine drops (Restasis, Allergan) four times daily. Fluorometholone (FML, Allergan) was used as the topical corticosteroid drops between January 2008 and December 2010, and loteprednol etabonate drops (Lotemax, Bausch&Lomb, Bridgewater, NJ, USA) were used after December 2010. Additional medical and/or surgical treatments applied when necessary and complications were recorded.

Patients with structural abnormalities of the eyelids, aqueous-deficient dry eye, inflammatory or infectious keratitis, or previous intraocular surgery were not included in the study.

The Wilcoxon signed rank test was used to evaluate the patients' pre- and post-treatment signs and symptoms due to their nonparametric values.

Results

Forty-eight eyes of 24 patients (18 women, 6 men) with a mean age of 48.5±35.4 (32-54) years were included in the study. The mean follow-up time was 15±9.4 (8-36) months.

At the time of diagnosis, meibomitis/MGD was present in all eyes (100%), anterior blepharitis in 40 eyes (83.3%), punctate keratopathy in 32 eyes (67%), chalazion in 24 eyes (50%), corneal neovascularization in 24 eyes (50%), and peripheral subepithelial infiltrates in 8 eyes (16.6%).

Table 1. Scoring system of the patients' ocular symptoms

Scoring	0	1	2	3	4
Itching	Never	Sometimes	Half of the time	Most of the time	All of the time
Burning/Stinging	Never	Sometimes	Half of the time	Most of the time	All of the time
Redness	Never	Sometimes	Half of the time	Most of the time	All of the time

0: The symptom is not present at any time of day, 1: The symptom is present less than 1/4 of the day, 2: The symptom is present between 1/4-1/2 of the day, 3: The symptom is present for more than 1/2 of the day, 4: The symptom is present throughout the day

Table 2. Scoring system of the patients' ocular signs

Scoring	0	1	2	3	4
Eyelid telangiectasia	None	Mild	Moderate	Severe	Extremely Severe
Meibomitis	Minimal, Clear	Cloudy	Granular	Pasty	Not expressible
Conjunctival hyperemia	None	Mild	Moderate	Severe	Extremely Severe
Corneal neovascularization	None	1 clock hour, in the peripheral cornea	1-3 clock hours	>3 clock hours, and/or affecting the mid-peripheral cornea	>3 clock hours, affecting the central cornea

Figure 1 and Figure 2 show anterior segment photographs of patients with anterior and posterior blepharitis, and peripheral sterile corneal infiltrates, respectively. Figure 3 and Figure 4 show anterior segment photographs of patients with corneal neovascularization and peripheral corneal infiltrates, and descemetocele, respectively.

Hot compresses and massage were recommended to all patients as initial treatment. All patients were administered preservative-free artificial tears four times daily; artificial tear gel once daily if necessary; topical corticosteroid eye drops four times daily, decreasing by one drop each week for four weeks; topical antibiotic ointment for 10 days; 100 mg/day systemic doxycycline once daily for a mean of 6.8±2.1 (4-13) months; and 0.05% topical cyclosporine eye drops four times daily for a mean 9.7±3.0 (5-13) months. Topical corticosteroid eye drops were reintroduced in two patients who had exacerbations of their signs and symptoms in the third and fourth months of treatment. Their corticosteroid treatment consisted of four drops daily decreasing by one drop each week for four weeks, followed by one drop every other day for a week and one drop every third day for another week. Peripheral sterile infiltrates were observed during follow-up in 8 eyes of 8 patients; these eyes were treated with topical steroid eye drops starting four times daily and gradually decreased according to clinical response to treatment.

All patients showed significant improvement in their ocular signs and symptoms at the end of the follow-up period. Compared to pre-treatment values, Schirmer's scores increased 3.3±1.5 mm and BUT increased 4.5±2.8 s ($p<0.05$, $p<0.05$). Patients' mean pre- and post-treatment symptoms scores are shown in Table 3.

Four eyes of 3 patients that did not show sufficient clinical response and/or developed severely sight-threatening choroidal neovascularization despite standard therapies were treated with 5 mg/ml topical bevacizumab eye drops four times daily. The topical bevacizumab treatment was discontinued in each of the 4 eyes when clinical remission of the corneal neovascularization was observed (after 3, 3.5, 4 and 5 months in the four eyes).

Table 3. Comparison of total pre- and post-treatment scores of patients' signs and symptoms

Sign/Symptom	Pre-treatment	Post-treatment	p value*
Burning/Stinging	2.79	2.04	<0.05
Redness	2.67	1.88	<0.05
Meibomitis	2.88	1.92	<0.05
Conjunctival hyperemia	2.75	1.71	<0.05
Corneal NV	1.38	1.13	<0.05

NV: Neovascularization
*Wilcoxon signed rank test

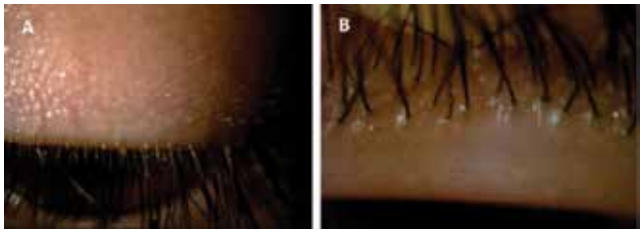

Figure 1. Anterior (A) and posterior (B) signs of blepharitis

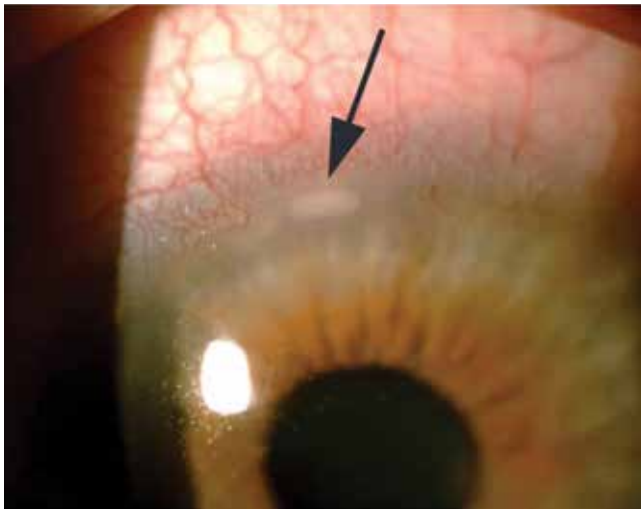

Figure 2. Anterior segment photograph showing peripheral sterile corneal infiltrate

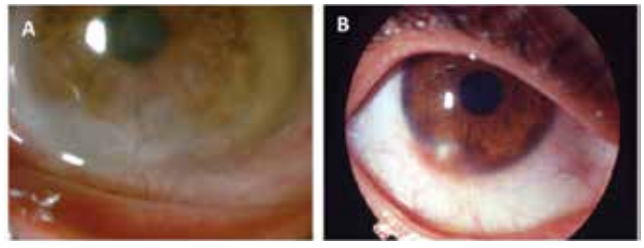

Figure 3. Anterior segment photographs showing corneal neovascularization (A) and peripheral corneal infiltrate (B)

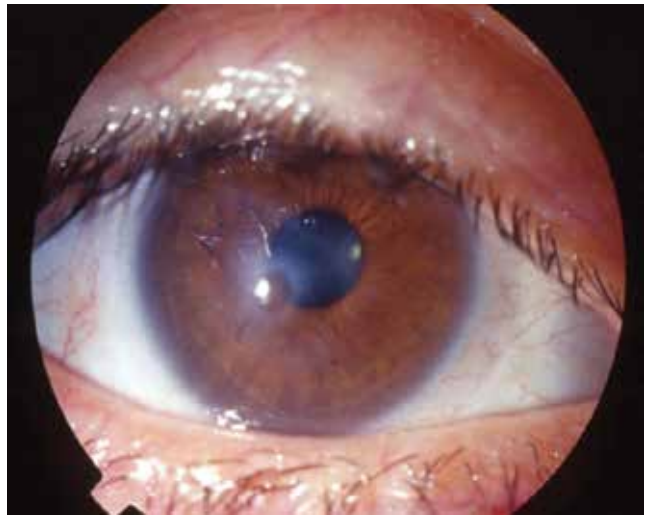

Figure 4. Anterior segment photograph of an ocular rosacea patient with descemetocele

Two patients presented to our clinic with descemetocele formation and corneal perforation; their histories revealed that they had been diagnosed with ocular rosacea and followed at a different center. Corneal re-epithelization was achieved with tissue adhesive and bandage contact lens in one of these patients and with tissue adhesive and amniotic membrane transplantation in the other. After re-epithelization the patients were followed up with the standard treatments (12 months for one patient, 14 for the other). At final examination both patients were stable.

None of the patients developed complications related to the use of steroid, cyclosporine and/or topical bevacizumab eye drops during the follow-up period.

All patients showed improvement of their ocular signs and symptoms at the end of the follow-up period, and recurrence was not observed in any of the patients during follow-up. Ten patients used artificial tears for maintenance therapy as needed.

Discussion

Ocular rosacea may present with various ocular signs.[5,6] However, it is still not entirely clear which treatment approaches are effective.

Mild or moderate ocular rosacea can be treated with hot compresses, baby shampoo for lid hygiene and artificial tears, while a more intense lubricant in the form of a gel or ointment can be used for long-term comfort.[11,12]

Although there are studies showing decreased local inflammation of the meibomian glands with a combination of lid hygiene and topical antibiotic application alone, these agents do not have the desired effect on the ocular surface.[11,12] Therefore we utilize short-term topical steroid and long-term topical cyclosporine and oral doxycycline as adjunct therapies to the standard treatment of lid hygiene and artificial tears. With this treatment we achieved significant improvement in our patients' ocular signs and symptoms.

Doxycycline administered orally to treat rosacea has both antibacterial properties as well as an anti-inflammatory effect. Doxycycline inhibits neutrophil chemotaxis, angiogenesis, lymphocyte proliferation and blocks matrix metalloproteinase activity as well as collagenase and lipase production.[10,11,12,13,14,15] Thus, as in cutaneous rosacea, it has also been successfully used as an adjunct to topical therapies in ocular rosacea.[10,11,12,13,14,15] Compared to other tetracyclines, doxycycline has fewer side effects. In a study including 15 ocular rosacea patients, slow-release doxycycline at a dose of 40 mg once daily resulted in a marked decrease in ocular complaints in 80% of patients.[8] However, studies including larger numbers of patients are necessary to determine the efficacy of doxycycline at low doses. It should also be kept in mind that many patients experience exacerbations when tetracycline use is discontinued. Thus, we prescribed doxycycline for a mean duration of 6 months, and we believe doxycycline also contributed to the clinical improvements observed in our patients. However, long-term use of tetracyclines can result in gastrointestinal system intolerance, which may cause a drug compliance problem and necessitate discontinuation of the drug. Recent studies have shown that topical azithromycin is also effective in the treatment of posterior blepharitis.[16,17]

Episcleritis, scleritis, iritis and sterile keratitis may occur subsequently to persistent ocular inflammation. Nine eyes of 8 patients in our series exhibited sterile peripheral corneal infiltrates. Steroid eye drop treatment was reintroduced in these patients, all of whom showed significant or complete regression of the infiltrates. Because the long-term use of steroids has potential side effects like cataract and glaucoma, they are recommended for acute exacerbations and cases of sterile infiltrates, applied in gradually tapering doses. We did not see any side effects related to topical steroid use in our study.

The pathophysiology of rosacea is still not fully understood, but there are arguments pointing toward the dysregulation of inflammatory and vascular responses to immune agents.[7] Considering the anti-inflammatory effect of cyclosporine A and its efficacy in the treatment of meibomitis, we also prescribed 0.05% topical cyclosporine four times daily as an adjunct therapy. Significant improvement in ocular signs and symptoms was observed with this treatment in particular. Ocular surface inflammation was controlled, and we observed longer BUT and higher Schirmer's test values. These effects were likely due to 0.05% topical cyclosporine inhibiting active lymphocytes in the conjunctiva, thereby decreasing inflammation and increasing tear production. Schechter et al.[9] followed 34 patients with ocular rosacea and found that patients treated with 0.05% topical cyclosporine twice daily had longer BUT, higher Schirmer's test values and corneal staining improvement compared to patients who used artificial tears. These effects suggest that topical cyclosporine has utility in the treatment of ocular rosacea. Cyclosporine is usually applied twice daily in mild cases of dry eye, but more frequent application has been shown to result in greater improvement of ocular signs and symptoms in more severe cases.[15,18,19] We found that topical cyclosporine applied four times daily was well tolerated and effective. Furthermore, the safe anti-inflammatory profile of topical cyclosporine allows it to be used in the long term and while the disease is in remission. The results of our study indicate that topical cyclosporine use in combination with other treatments provides important benefits in the management of ocular rosacea.

Corneal neovascularization, especially in the inferior quadrant, occurs with ocular rosacea. Vessels advancing into the cornea cause corneal inflammation, scarring, edema and lipid accumulation, which can lead to reduction in corneal transparency and impaired vision; therefore, the treatment of these patients is very important. Although systemic antibiotics, cyclosporine and steroids can be applied in corneal neovascularization, the increasing use and reported efficacy of anti-vascular endothelial growth factor (VEGF) agents in the treatment of retinochoroidal

diseases has brought these agents to the fore in the prevention of corneal neovascularization.[20,21,22,23,24] Bevacizumab inhibits vascular endothelial cell migration and proliferation and decreases vascular permeability by blocking VEGF-A.[23,24] Local or topical bevacizumab can be successfully used to treat ocular surface neovascularization when other therapies have been insufficient or to enhance their efficacy.[21,22,23,24] Cheng et al.[25] treated corneal neovascularization with 3 weeks of 1.0% topical bevacizumab and followed the patients for 24 weeks; they found reductions in the area of neovascularization in week 6 and in vessel diameter in week 12. Koenig et al.[26] observed new epithelial defects in 16.7% of their cases and spontaneous corneal perforation in one case after topical bevacizumab treatment. In our study, 4 eyes that developed corneal neovascularization due to ocular rosacea were treated with topical bevacizumab with the primary aim of stabilizing the ocular surface and to avoiding aggravation of corneal epitheliopathy. We started topical bevacizumab treatment 4 weeks after initial presentation in 3 cases and 5 weeks after in 1 case, and we observed significant clinical reduction of the neovascularization with the application of 5 mg/ml 4 times daily. According to our results, we believe that topical bevacizumab may be an effective adjunct therapy in rosacea-related ocular surface neovascularization when required.

The most severe sight-threatening complications of ocular rosacea are stromal thinning and corneal perforation.[27,28,29] The underlying cause of corneal thinning has not been clearly determined, but an elevated level of matrix metalloproteinases (especially type 9) in the inferior tear meniscus is believed to be responsible for stromal thinning and perforation.[5] There is very little information in the literature about corneal perforation in patients with ocular rosacea.[27,28,29] In one of the reported cases keratoplasty was performed to repair an area of perforation extending to the sclera; in other cases, amniotic membrane transplantation was performed after the application of cyanoacrylate tissue adhesive and bandage contact lenses proved insufficient.[27,28,29] In one of our two patients who developed this complication, tissue adhesive and amniotic membrane transplantation were used to repair the perforation and achieve re-epithelization; in the other, only tissue adhesive and bandage contact lens were used. These results suggest that tissue adhesive and, if necessary, amniotic membrane transplantation are effective in the treatment of perforations due to ocular rosacea.

Due to the retrospective nature of this study, it has certain limitations. As there were no controls for the treatment approaches used, it is difficult to clearly determine the effect of each drug or treatment.

Conclusion

Ocular rosacea may affect the ocular surface to varying degrees and can threaten patients' vision, but in most cases ocular surface inflammation can be managed with appropriate medical treatment. It is important to choose treatment approaches according to the patients' clinical characteristics and to follow these patients closely.

Ethics

Ethics Committee Approval: It was taken, Informed Consent: It was taken, Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Yonca Aydın Akova, Concept: Yonca Aydın Akova, Design: İlkay Kılıç Müftüoğlu, Yonca Aydın Akova, Data Collection or Processing: İlkay Kılıç Müftüoğlu, Analysis or Interpretation: İlkay Kılıç Müftüoğlu, Yonca Aydın Akova, Literature Search: İlkay Kılıç Müftüoğlu, Writing: İlkay Kılıç Müftüoğlu, Yonca Aydın Akova.

Conflict of Interest

No conflict of interest was declared by the authors.

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Original Article

Comparison of Different Types of Complications in the Phacoemulsification Surgery Learning Curve According to Number of Operations Performed

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Summary

Objectives: To compare the differences in intraoperative complications rates by the number of resident-performed sequential phacoemulsification surgeries.

Materials and Methods: Preoperative and postoperative ophthalmological examination records and intraoperative data of 180 eyes of 140 patients who underwent cataract surgery by two residents between November 2009 and February 2012 were analyzed retrospectively. The data of 180 eyes were separated into 3 groups based on the number of operations performed: Group A (first 1-60 eyes), group B (61-120 eyes) and group C (last 121-180 eyes). The number of direct supervisor interventions and the rates of different types of complications were compared between the three groups.

Results: The number of direct supervisor interventions was 45, 35 and 19 in group A, B and C, respectively. The number of complications anterior to the iris plane was 3, 4 and 12 in group A, B and C, respectively. The difference in the rate of complications between group B and C was statistically significant (p=0.029). The number of complications posterior to the iris plane was 6, 14 and 3 in group A, B and C, respectively. The difference in the rate of complications between the groups was statistically significant (p=0.042, p=0.004).

Conclusion: This study provides insight into which types of complications might arise during the phacoemulsification training period. The trends in the rates of different complication types in clinics may be analyzed, and this analysis may be used to improve and modify phacoemulsification training programmes according to the needs of residents.

Keywords: Cataract surgery, learning curve, phacoemulsification

Introduction

Phacoemulsification (phaco) is the most commonly performed surgery in ophthalmology and is a must for ophthalmology residents to learn during their training. Declines in intraoperative complications, number of direct supervisor interventions required and operation time are measures of the learning curve of resident phaco surgery.[1,2,3,4,5] According to the many studies performed in this field, operation times and complication rates are reported to change as the resident gains experience in cataract surgery.[1,2,3,4,5,6,7] In several studies, an inverse relationship was observed between the complication rate and residency year.[1,2,6]

One of these studies examined complication rates of residents according to their residency year and although it reports no significant association with overall intraoperative complications, vitreous loss did occur more frequently in surgeries performed by second-year residents.[1] Another study also found no significant difference between second- and third-year resident phaco surgeries.[7] From the residents' point of view, capsulorhexis was the most difficult step for second-year residents and the nuclear emulsification procedure was the most difficult step for third-year residents according to one study.[8]

Recent studies have compared complication rates of residents by their year of residency, but it is well accepted that the phaco learning curve is directly correlated with the number of operations performed and not the residency year. The trend in the rate of different complications in resident-performed phaco surgery might reveal clues about which stages of phaco surgery are most challenging for residents at various surgical skill levels.

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Analysis of this trend may yield a new perspective in resident phaco training. The purpose of this study was to compare the differences in intraoperative complication rates by the number of surgeries residents had performed.

Materials and Methods

The setting of this retrospective study was a tertiary care university hospital. Preoperative and postoperative ophthalmological examination records and intraoperative data of 180 eyes of 140 patients (67 female, 73 male) who underwent cataract surgery at İstanbul University, Cerrahpaşa Faculty of Medicine were analyzed. The study followed the tenets of the Declaration of Helsinki. All patients signed a consent form after receiving an explanation of the nature and possible consequences of the procedure.

Surgeries were performed between November 2009 and February 2012 by two residents. Before their direct attendance to phaco surgeries, these residents had attended several lectures and observed nearly 30 phaco surgeries. The residents had not performed any extracapsular cataract extraction surgery prior to phaco surgery training. Patients were preoperatively informed about the resident contribution to his/her surgery and informed consent was signed by each patient. Cataract surgery was performed by residents under the supervision of a qualified cataract surgeon. Patients were selected randomly from the outpatient clinic with no specific criteria in terms of case difficulty excluding traumatic cases, patients with zonular dehiscence and cases necessitating combined procedures.

The phacoemulsification procedure was performed under topical or retrobulbar anesthesia according to the patient's status and the surgeon's decision. A 3.2 mm clear corneal incision was used and two side ports were created for bimanual phacoemulsification. A continuous curvilinear capsulorhexis was performed with the help of trypan blue when needed. The lens was emulsified using the "divide and conquer" technique in all cases. The surgery was concluded with the insertion of an injectable hydrophobic acrylic intraocular lens (IOL) in the bag or within the ciliary sulcus when possible, followed by the administration of intracameral antibiotics. Direct supervisor intervention was required in surgeries in which complications could not be managed by the resident surgeon.

Analysed data included age, sex, ocular comorbidities, preoperative and postoperative best corrected visual acuity (BCVA), date of operation, operative complications, attending cataract and resident surgeon, number of cases performed by the resident, and number of operations which necessitated direct supervisor intervention. Operative complications included anterior capsule tears, posterior capsule rupture, wound burns, dropped nucleus or nuclear fragments, vitreous loss, Descemet's membrane detachments and corneal edema lasting for more than 10 days postoperatively. Operative complications were divided into two categories with respect to their anatomical position: complications anterior to the iris plane included wound burns, Descemet's membrane detachments, and corneal edema lasting for more than 10 days; complications posterior to the iris plane included anterior capsule tears, posterior capsule rupture (with/without vitreous loss), zonular dialysis and dehiscence, and dropped nucleus or nuclear fragments. Each complication for each surgery was separately recorded and grouped according to its anatomic position. All data of the 180 eyes were grouped into three categories according to the number of operations previously performed by the resident. Chi-square test for independence was used to compare the rates of different types of complications observed in the groups. Statistical Package for the Social Sciences 16.0 for Windows was used for statistical calculations.

Results

A total of 180 eyes of 140 patients (73 male, 67 female) underwent phacoemulsification surgery by 2 residents under the supervision of a qualified cataract surgeon. The data of the 180 eyes were grouped into 3 categories with 60 operated cases in each group. Groups A, B and C consisted of the data from surgeries 1-60, 61-120, and 121-180, respectively, performed by the residents.

Mean (standard deviation) patient age at the time of surgery was 67.3 (6.9) years (range, 52-81 years). Direct supervisor intervention was recorded in 45 (75%) surgeries in group A, 35 (58.3%) surgeries in group B and 19 (16.6%) surgeries in group C.

Of the 180 operations performed, complications were observed in 42 (23.3%) (Table 1). The total numbers of complications in groups A, B and C were 9, 18, and 15, respectively. There was no statistically significant difference in total complication rates among the groups (p=0.141).

Posterior capsule rupture with or without vitreous loss was observed in 15 (8.8%) eyes, 9 of which were in group B. The IOL could be implanted into the sulcus in 14 eyes where there was sufficient capsular support, and 1 eye underwent scleral-fixated IOL implantation surgery.

Table 1. Distribution of complications among groups

Complications	Group A	Group B	Group C
Anterior to the iris plane			
Wound burns	0	1	3
Descemet's membrane detachment	0	1	6
Corneal edema lasting for more than 10 days	3	2	3
Total	3	4	12
Posterior to the iris plane			
Anterior capsule tear	2	2	0
Posterior capsule rupture (with/without vitreous loss)	4	9	3
Zonular dialysis/dehiscence	0	1	0
Dropped nucleus/nuclear fragments	0	2	0
Total	6	14	3

Dropped nucleus or nuclear fragments occurred in 2 cases, both in group B. Synchronous pars plana vitrectomy was performed for these cases; the IOL could be implanted into the sulcus in 1 patient, while the other patient required scleral-fixated IOL implantation surgery.

The number of complications anterior to the iris plane was 3, 4 and 12 in groups A, B and C respectively. The difference in the rate of complications between group B and C was statistically significant (p=0.029). The number of complications posterior to the iris plane was 6, 14 and 3 in groups A, B and C respectively. The difference in the rate of complications between the groups was statistically significant (p=0.042, p=0.004).

Discussion

The incidence of complications in resident phacoemulsification surgeries ranges from 1.8% to 27.4% in different studies.[9] The overall rate of complications in this study was 23.3% and is consistent with other studies. There were no cases of endophthalmitis in our study. The rate of major complications such as posterior capsule rupture and vitreous loss may affect surgical and visual outcomes. Posterior capsule rupture with or without vitreous loss occured in 15 cases (8.8%). This rate is comparable to rates reported in the literature (2.5-14.7%).[3,9,10,11,12,13,14,15]

Sixty percent of the posterior capsule ruptures occured in group B. The reason for the low complication rates in group A could be the high intervention rates (75% of surgeries) by the supervising cataract surgeon. The complication rates increase as the intervention rates of the supervising cataract surgeon decrease. Although intervention rates decreased in group C, vitreous loss occurred in only 3 cases. This finding may suggest that the resident phacoemulsification learning curve was assessed with regard to total number of cases, with a break point of 60 cases identified in our study. This finding is similar to a previous study by Randleman et al.,[6] who reported a break point of 80 cases. The Residency Review Committee of the Accreditation Council for Graduate Medical Education[16] has recently increased the minimum number of cataract procedures performed by the resident as primary surgeon from 45 to 86. Thus, individual variations are common not only in surgical skill but also in surgical volume among residents of the same level.

Several previous studies reported that residency year was not a risk factor for intraoperative complications.[1,7] Therefore, in our study all data of the 180 eyes were grouped into 3 categories according to the number of operations performed by the resident rather than residency year.

Complications during phaco surgery primarily occur due to mechanical trauma by the phaco probe or the application of excessive ultrasound energy to the ocular tissues. The rise of complications posterior to the iris plane in group B could be explained by the learning curve for nuclear emulsification. The occurrence of dropped nucleus or nuclear fragments in group B can also be interpreted as a consequence of this learning curve. Woodfield et al.[7] supports this idea as posterior capsule ruptures were more frequently observed in second-year residents in their study.

The current study also found a low rate of dislocated lens fragments in the vitreous: 2 eyes (1.11%). The reported risk of requiring pars plana vitrectomy to remove lens fragments dislocated during cataract surgery ranges from 0.2% to 1.68% in the literature.[12,17,18]

While the rates of complications posterior to the iris dropped significantly between group B and C, complications anterior to the iris plane peaked in group C. This could be explained by the rise in posterior capsule ruptures in group B, which might have influenced the resident to utilize phacoemulsification more anteriorly in order to avoid posterior capsule related complications. Consequently, wound burn, Descemet's membrane detachment and corneal edema lasting longer than 10 days were observed more frequently in group C. This data is also consistent with previous studies. Woodfield et al.[7] found capsule tears more frequently in second-year resident surgeries and wound burns more frequently in third-year resident surgeries.

The rate of supervisor intervention is also a measure in the learning curve of resident phaco surgery.[1,3] Direct supervisor intervention was required in 90 of the cases, and the rest were completed exclusively by the residents in this study. The rate of direct supersivor requirement (50%) is similar to previous studies. Lee et al.[1] reported a completion rate of 47% and Dooley and O'Brien[3] reported a completion rate of 42% in their studies.

In an article published in Turkey by Erdoğan et al.[19] related to the phacoemulsification learning period, the rates of posterior capsule rupture and dropped nucleus were 10.6% and 2.7%, respectively. These rates are similar to those in our study.

Limitations of this study include the retrospective nature of the study and the relatively small numbers of surgeons and surgical cases analyzed. Prospective validation of our findings will be necessary.

Conclusion

Phacoemulsification is a challenging technique to learn and to teach due to its small error margins. Residents face nearly all complications of phaco surgery in the learning curve period. These complications show a rise when the resident starts to take more action during the surgery. This is one of the few studies which report the trend in the rates of different complications of resident phaco surgery according to number of operations performed, and it provides some insight into which types of complications might arise in the phaco training period. Trends in the rates of different complication types in clinics may be analyzed, and this analysis may be used to improve and modify phaco training programmes according to the needs of residents.

Ethics

Ethics Committee Approval: It was taken, Informed Consent: It was taken.

Peer-review: External and Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Mehmet Serhat Mangan, Eray Atalay, Concept: Mehmet Serhat Mangan, Eray Atalay, Design: Mehmet Serhat Mangan, Eray Atalay, Ceyhun Arıcı, Data

Collection or Processing: Mehmet Serhat Mangan, Eray Atalay, Analysis or Interpretation: Mehmet Serhat Mangan, Eray Atalay, İbrahim Tuncer, Literature Search: Mehmet Serhat Mangan, Eray Atalay, Mustafa Değer Bilgeç, Writing: Mehmet Serhat Mangan, Eray Atalay.

Conflict of Interest

No conflict of interest was declared by the authors.

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Original Article

Active Silicone Oil Removal with a Transconjunctival Sutureless System: Is the 23-Gauge System Safe and Effective?

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Summary

Objectives: To evaluate the safety and efficacy of active silicone oil removal with a 23-gauge (G) transconjunctival sutureless system.

Materials and Methods: One hundred sixteen eyes of 113 patients who had previous retinal detachment surgery with pars plana vitrectomy and silicone oil injection surgery, and underwent silicone oil removal surgery with 23-G transconjonctival sutureless technique in our clinic between January 2009 and April 2014 were reviewed retrospectively. The patients were evaluated with regard to postoperative changes in best corrected visual acuity and intraocular pressure (IOP), and complications that occurred during and after surgery.

Results: Of the 113 patients with mean age of 61.1±9.7 years (29-88 years), 62 (54.8%) were males and 51 (45.2%) were females. Silicone oil removal was performed 8.43±5.24 months after the initial surgery. Mean follow-up was 13.38±4.35 months. Visual acuity improved in 69 eyes (59.48%). Anatomic success was achieved in 113 eyes (97.41%). Mean IOP was 16.2±7.2 mmHg at baseline and 14.4±2.6 mmHg at postoperative day 1 (p=0.643). Eight eyes needed suturation of at least one sclerotomy. Retinal redetachment occurred in 3 eyes (2.5%) resulting in a decrease in vision. There were no cases of choroidal detachment, endophthalmitis, clinically significant corneal endothelial decompensation, or macular edema.

Conclusion: Active removal of 1,300-centistoke silicone oil with a 23-G transconjunctival sutureless system is a simple, sutureless technique causing minor surgical trauma. Active removal of silicone oil with the 23-G transconjunctival sutureless technique was found to be effective and safe in both phakic and pseudophakic eyes.

Keywords: 23-gauge transconjunctival sutureless technique, silicone oil removal

Introduction

Silicone oil is currently used as a replacement for the vitreous during vitreoretinal surgeries, especially in complicated conditions such as retinal detachment (RD) with giant tears, proliferative vitreoretinopathy, trauma, and endophthalmitis.[1] Because the long-term presence of silicone oil in the eye leads to complications such as cataract, glaucoma, late corneal decompensation, and band keratopathy, it is recommended that silicone oil be removed as soon as possible after it has fulfilled its purpose as a tamponade.[1,2,3]

Silicone oil removal (SOR) is an important procedure in vitreoretinal surgery. Although there are various methods and techniques for SOR,[4,5,6,7] the procedure can basically be performed through either the anterior or the posterior segment.[8] SOR via the anterior segment is preferred in aphakic patients or with cataract surgery, whereas removal via the pars plana is preferred in phakic and pseudophakic patients.[8] SOR through the pars plana also allows adequate examination of the retina during procedures like epiretinal membrane peeling, endolaser application, membranectomy and posterior capsulotomy.

SOR can be performed with 20-gauge (G), 23-G or 25-G extraction cannulae.[9,10,11] In recent years, smaller gauge sclerotomies have become a preferred technique in SOR.[9,10,11] The main advantages of small-gauge sclerotomies are their self-sealing properties, early incision healing, low ocular surface irritation and more cosmetically satisfying results.[10,11,12] The major benefit of using 23-G

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instruments versus 25-G instruments during surgical procedures is that they are more powerful and self-sealing (valve system).

The purpose of this study was to evaluate the effectiveness and safety of the 23-G transconjunctival sutureless system in SOR.

Materials and Methods

The study included 116 eyes of 113 patients who were diagnosed with RD (rhegmatogenous RD associated with multiple or giant tears, diabetic tractional RD, traumatic RD, etc.), underwent pars plana vitrectomy (PPV) with silicone oil injection, and later underwent SOR by 23-G transconjunctival sutureless technique in the retina unit of our clinic between January 2009 and April 2014. All patients received 1,300-centistoke (cSt) silicone oil tamponade. Data from the patient's medical records were reviewed retrospectively. Patients' predisposing factors for RD prior to PPV, type of RD, presence or absence of macular involvement, RD duration, best corrected visual acuity (BCVA) and lens status were recorded. We included patients over 18 years of age and excluded patients with retinal redetachment, hypotonic eyes [intraocular pressure (IOP) <8 mmHg], or scleral thinning in the sclerotomy area prior to SOR. Data regarding patients' BCVA (ETDRS chart), slit-lamp examination, IOP measured by Goldmann applanation tonometry, macular status on spectral domain optic coherence tomography (SD-OCT), and dilated fundus examination after SOR were recorded for all patients. There were no complications related to silicone oil such as glaucoma or keratopathy in these eyes. Complete retinal reattachment at 6 month follow-up was considered anatomic success; a BCVA improvement of ≥1 LogMAR row was considered functional success.

Surgical Technique

Before surgery, retrobulbar anesthesia (2 ml lidocaine+2 ml bupivacaine) was administered to all patients using a standard 4 ml Atkinson needle. A pars plana entry was performed with the Constellation vitrectomy system (Alcon laboratories, USA) using 23-G vitrectomy system and valved trocars in the inferotemporal area and superior quadrant at 4 mm from the limbus in phakic patients and 3.5 mm in pseudophakic patients. An infusion port was inserted in the temporal area and the fluid pressure was set to 25 mmHg, after which the silicone oil was removed as a whole from the superior quadrant with 480-650 mmHg vacuum. After the bulk of the silicone oil was removed, the remaining emulsified particles were cleared. For patients with emulsified silicone particles in the anterior chamber, an incision into the anterior chamber was made with a 20-G Stiletto blade and the emulsified particles were removed by passive aspiration. Because complete retinal reattachment was observed on preoperative dilated fundus examination and additional laser treatment was deemed unnecessary, there was no further entry into the eye after SOR. Following SOR, the trocars were removed and leakage was tested. In case of leakage, the sclerotomy was sutured with 8/0 vicryl suture.

Statistical Package for the Social Sciences version 17.0 software was used for statistical analyses. The mean and standard deviation were calculated for all data. Statistical analysis was done with a parametric t-test. Dependent samples t-test was used to evaluate changes in BCVA and IOP before and after SOR. Level of significance was accepted as α=0.05.

Results

One hundred sixteen eyes of 113 patients were included in the study. The mean age of the patients was 61.1±9.7 years (range, 29-88 years); 62 (54.8%) were male, 51 (45.2%) were female. Sixty-one (52.5%) of the eyes were left eyes. Fifty-six (48.2%) of the eyes were pseudophakic. In pseudophakic patients, the mean time between cataract surgery and RD was 3.6±2.5 years (median, 4 years; range, 8 months-9 years). The mean duration of follow-up after SOR was 13.38±4.35 months (range, 6-26 months). The etiologies of the patients' RD are shown in Table 1.

The clinical characteristics of the patients are summarized in Table 2. The mean time between silicone oil injection during vitrectomy surgery and SOR using the 23-G transconjunctival sutureless technique was 8.43±5.24 months (range, 3-16 months). The mean BCVA at the last examination before SOR was 1.31±0.85 logMAR (range, 0.5-3.0 logMAR). At 3 months after SOR, the mean BCVA was 0.84±0.74 logMAR (range, 0.05-3.0

Table 1. Causes of retinal detachment

Etiology	n=116 (100%)
Pseudophakic	49 (42.3%)
High myopia (≥5.0 D)	26 (22.4%)
Spontaneous Emmetropia (±0.75 D) Myopia (≤4.99 D) Hypermetropia (≤3.0 D)	18 (15.5%) 5 (4.3%) 10 (8.6%) 3 (2.6%)
Tractional (DM)	16 (13.8%)
Trauma Blunt Perforating	7 (6%) 2 (1.7%) 5 (4.3%)

DM: Diabetes mellitus, D: Diopter

Table 2. Clinical characteristics of the patients	
Lens status (n, pseudophakic/phakic)	**56/60**
Silicone removal time (months)	8.43±5.24 (3-16)
Follow-up duration (months)	13.38±4.35 (6-26)
Intraocular pressure (mmHg) Before silicone oil removal After silicone oil removal (day 1)	 18.2±7.1 (12-34) 16.4±2.6 (12-26)
Visual acuity (logMAR) Before silicone oil removal After silicone oil removal (3 months)	 1.31±0.85 (0.5-3.0) 0.84±0.74 (0.05-3.0)
Complication (n) Retinal redetachment	 3

logMAR). The improvement in BCVA after SOR was statistically significant ($p<0.001$). Of the 40 phakic eyes, 18 (45%) developed cataract associated with silicone oil. The mean IOP was 18.2±7.1 mmHg (range, 12-34 mmHg) before SOR and 16.4±2.6 mmHg (range, 12-26 mmHg) after SOR ($p=0.643$). Prior to SOR, an elevated IOP of 28-34 mmHg was detected in 16 (13.8%) of the 116 eyes, and was controlled in all cases with a single fixed combination (10 mg/ml brinzolamide+5 mg/ml timolol or 20 mg/ml dorzolamide HCL+5 mg/ml timolol maleate) anti-glaucoma therapy. None of the patients exhibited elevated IOP requiring medical treatment after SOR. Silicone oil was found in the anterior chambers of 13 of the pseudophakic eyes. In these patients, the silicone oil in the anterior chamber was successfully removed in the same surgical session as the SOR from the posterior segment. Retinal redetachment occurred in 3/116 (2.5%) eyes within 3 months of SOR. The first of these cases had giant tear RD, and SOR was performed in the 8th postoperative month; the second and third cases had RD due to multiple tears and tractional RD, respectively, and both underwent SOR in the 6th postoperative month. All three of the eyes had successful retinal attachment with vitrectomy surgery (using silicone oil tamponade).

In our study, anatomic success was achieved in 113/116 (97.41%) eyes in the first vitrectomy surgery using silicone oil tamponade. Functional success was achieved in 88/116 (75.86%) eyes after phacoemulsification of the eyes that developed cataract. Eight (6.89%) eyes exhibited leakage after trocar removal and required suturing. None of the patients developed persistent hypotony following the 23-G transconjunctival sutureless technique.

Discussion

In recent years, sutureless small-gauge incisions have been preferred for the majority of intraocular surgeries in order to provide better anatomic outcome and functional improvement. The development of small-gauge (23-G and 25-G) vitrectomy, or minimally invasive vitreous surgery, without compromising outcomes is one of the most important goals of surgeons.[13] With this aim, Fujii et al.[6] began to use the 25-G transconjunctival sutureless vitrectomy technique in the surgical treatment of uncomplicated vitreoretinal patients. In later years, Eckardt[7] introduced the 23-G transconjunctival sutureless vitrectomy technique. Surgeons familiar with 20-G preferred 23-G transconjunctival sutureless vitrectomy over the 25-G technique due to the greater durability of 23-G instruments. In current conditions, however, 25-G vitrectomy is preferred when possible. These developments in vitrectomy surgery have led to innovations in other surgeries related to the posterior segment. The main benefits of small incisions are that they generally do not require suturing, they prevent adhesions from repeated operations, and they provide a short operating time, minimal trauma, less irritation, comfortable surgery and speedy recovery.[9,10,11,12]

There are currently several different methods (20-G, 23-G and 25-G) by which silicone oil can be removed.[10,11,12] SOR by 25-G microcannula was first described by Kapran and Acar.[10] Later, it was observed that the eye was more stable and the procedure was more comfortable when silicone oil was removed using a 23-G transconjunctival system compared to the 20-G system.[12,14] In 20-G systems, a tendency to collapse was observed due to incision with a 20-G MVR blade. Although 23-G vitrectomy systems are considered simple and reliable, there have also been reports of possible disadvantages such as intraoperative subconjunctival hemorrhage, incision leakage, trocar displacement, and leakage of infusion fluid under the conjunctiva; in fact, in some cases it was necessary to continue the surgery with a 20-G system.[11,15]

The most common problem encountered in sutureless systems is hypotony.[16,17] In our study, IOP was compared before and 1 day after SOR. Although a drop in IOP was observed, the difference was not statistically significant. Similarly, Kapran and Acar[10] investigated IOP changes after SOR with a 25-G system; although they observed a significant drop in IOP 2 hours after SOR, no significant differences were found at postoperative 1 day, 1 week or 1 month. Reports vary regarding the need for postoperative sutures in small-gauge transconjunctival vitrectomy systems. In the current study, 6.8% of the eyes had positive leakage tests after SOR and required suturation of at least one of the sclerotomy sites. Doğanay et al.[11] used a 23-G vitrectomy system for SOR in 34 patients and sutured at

least one of the sclerotomy sites in 15 (44%) cases. In a study by Patwardhan et al.[9] after SOR from 20 eyes with a 23-G system, suturation was required in 3 (15%) eyes. Romano et al.[16] sutured at least one sclerotomy site of 5 (50%) of 10 eyes after SOR with a 23-G transconjunctival system. In contrast, Kapran and Acar[10] reported that none of the 13 eyes in their study required suturation after SOR with a 25-G transconjunctival sutureless system.

The most significant risk in sutureless surgeries is development of endophthalmitis.[18,19,20] In the current study, endophthalmitis did not occur in any of the 116 eyes of 113 patients that underwent SOR via 23-G transconjunctival sutureless system. In all of our patients, 5% povidone-iodine drops were instilled and the eyelids and face were cleaned with 10% povidone-iodine preoperatively. During surgery, the conjunctiva was held away from the trocar entry point and the trocars were inserted gradually into the sclera. At the end of the procedure, the edges of the scleral incisions were patted down over the entry point and closed with the removed intact conjunctiva and Tenon's capsule.

Retinal redetachment after SOR has been reported at rates of 6-33%.[21,22,23] Kapran and Acar[10] observed it in 2 cases (15.3%); Doğanay et al.[11] in 2 cases (5.8%). In our study, retinal redetachment was found in 3 eyes (2.5%). In all 3 eyes, reattachment was successfully achieved with a second surgery. Romano et al.[16] reported that none of their patients developed retinal redetachment.

In the current study, all patients with the exception of the three with retinal redetachment had improved or stable visual acuity. There was a statistically significant increase in mean BCVA following SOR. We achieved anatomic and functional success rates of 97.4% and 75.8%, respectively. Of the phakic eyes, 45% developed cataract at different times. Cataract surgery was not performed in the same surgical session as the SOR.

Conclusion

Our study demonstrates that the 23-G transconjunctival sutureless technique for SOR has no negative impact on anatomic or functional success, and considering the benefits provided, it was concluded to be a reliable and effective system. Using transconjunctival small-gauge sclerotomy technique in SOR provides the advantages of a closed system as well as benefits such as protection of the conjunctiva, shortened surgery time and fewer suture-related complications. We believe that with the development of new techniques and methods, the 23-G transconjunctival sutureless system will be safe to use in SOR regardless of phakic, pseudophakic or aphakic lens status.

Ethics

Ethics Committee Approval: None (retrospective study), Informed Consent: Patients were informed of the details of the study and all signed an informed consent form prior to their participation.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Nilüfer Koçak, Süleyman Kaynak, Concept: Mahmut Kaya, Nilüfer Koçak, Süleyman Kaynak, Design: Mahmut Kaya, Arif Taylan Öztürk, Nilüfer Koçak, Süleyman Kaynak, Data Collection or Processing: Ayhan Özyurt, Duygu Er, Mahmut Kaya, Analysis or Interpretation: Mahmut Kaya, Arif Taylan Öztürk, Nilüfer Koçak, Literature Search: Ayhan Özyurt, Duygu Er, Mahmut Kaya, Writing: Ayhan Özyurt, Mahmut Kaya, Arif Taylan Öztürk, Nilüfer Koçak, Süleyman Kaynak.

Conflict of Interest

No conflict of interest was declared by the authors.

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Original Article

Treatment Outcomes in Patients with Polypoidal Choroidal Vasculopathy

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Summary

Objectives: To report outcomes of photodynamic therapy (PDT) and combined therapy with PDT and intravitreal bevacizumab (IVB) in patients with polypoidal choroidal vasculopathy (PCV).

Materials and Methods: Thirty-four eyes of 31 patients with subfoveal PCV were evaluated. Nine eyes were treated with PDT and 25 eyes treated with combined therapy of PDT and IVB. All eyes had a follow-up period of at least 12 months. In this retrospective study the demographic features, best corrected visual acuity, fundus color photography, optical coherence tomography, fluorescein angiography and indocyanine green angiography of the 34 eyes were evaluated.

Results: Visual acuity improved but did not change significantly in the patients treated with PDT and combined PDT+IVB therapy (p=0.149; p=0.087). Although the mean central foveal thickness decreased in both groups, there was no statistically significant difference between groups (p=0.98). The polypoidal lesions regressed in 6 (66.7%) of 9 eyes in the PDT monotherapy group and 16 (64%) of 25 eyes in the PDT+IVB combined therapy group.

Conclusion: Both PDT and a combined therapy of PDT and IVB yielded successful outcomes in patients with PCV.

Keywords: Polypoidal choroidal vasculopathy, photodynamic therapy, intravitreal bevacizumab

Introduction

Polypoidal choroidal vasculopathy (PCV) is a retinal disorder characterized by aneurysmal polypoidal lesions in the choroidal vasculature. It has been considered a subgroup of age-related macular degeneration (AMD), but the presence of polypoidal lesions beyond the macula and differing responses to treatment suggest it is a separate pathology.[1] Polypoidal lesions may be visible as red-orange lesions on fundus examination, though the definitive diagnosis is made by indocyanine green angiography (ICGA).[2] Many studies have reported successful results with subfoveal PCV treatment by photodynamic therapy (PDT), anti-vascular endothelial growth factor (anti-VEGF) therapy, and combination therapy with both PDT and anti-VEGF.[3]

The purpose of this study was to present the treatment outcomes of subfoveal PCV patients who underwent PDT or combined PDT and anti-VEGF therapy.

Materials and Methods

Nine eyes of 9 patients treated with FDT and 25 eyes of 22 patients treated with FDT and intravitreal bevacizumab (IVB) due to subfoveal PCV between 2004 and 2014 were evaluated retrospectively. Patients with previous ocular surgery, cataract development that would affect visual acuity, glaucoma, or other retinal pathologies were excluded from the study.

Initial and follow-up examinations included visual acuity (VA) assessment by ETDRS chart, intraocular pressure (IOP) measurement and examinations of the anterior segment and fundus, followed by fluorescein angiography (FA), ICGA and optical coherence tomography (OCT). Standard PDT was performed as described in our previous study,[4] after which all patients were followed-up by examinations at 1 month, 3 months, and at 3 month intervals thereafter for at least 12 months. In the combined therapy group, patients underwent standard PDT followed

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by IVB injections each month for the first 3 months and as needed thereafter as described in our previous study,[5] and were followed for at least 12 months. The earliest leakage from neovascular structures was observed after 6 months; these patients underwent repeated PDT.

In accordance with the principles of the Declaration of Helsinki, patients were informed about their current status, natural course, treatment success rates and risks, and consent was obtained for all PDT and anti-VEGF treatments.

Patients' age, gender, number of PDT sessions and anti-VEGF injections and duration of treatment, pre- and post-treatment VA and foveal thickness were evaluated. Recurrences, regression of polypoidal lesions and complications were also reported.

Wilcoxon significance test, Mann-Whitney U test and Pearson's chi-square test were used in the statistical analyses. The level of significance was accepted as α=0.05.

Results

Nine patients with subfoveal PCV underwent FDT alone and were followed for a mean of 23.6±13.9 months (range 12-48 months); 2 were women and the average age of the group was 64±7.6 years. Although an increase in mean VA was observed between pre-treatment (0.40±0.27 logMAR) and both 1 year post-treatment (0.25±0.36 logMAR) and at the end of follow-up (0.25±0.36 logMAR), a significant difference in VA could not be detected between the time points, possibly due to the small patient number (p=0.149, p=0.149, respectively). At the end of the mean 24 month follow-up period, VA had increased in 6 (66.7%) patients and remained stable in 2 (22.2%). The VA of one patient declined by two rows according to the ETDRS chart. A decrease in mean foveal thickness was observed by OCT at 1 year post-treatment (256.22±86.73 µm) and after a mean of 24 months follow-up (276.78±142.98 µm) compared to pre-treatment (312.56±61.74 µm); however, the differences were not statistically significant (p=0.236 and p=0.441, respectively). Recurrence was observed in 3 (33.3%) of the patients during the first 12 months of follow-up, in 1 (25%) of the 4 patients followed for 13-24 months, and in 1 (50%) of the 2 patients followed for 25-36 months; no recurrence was observed during months 37-48 of follow-up. Recurrence was observed in 3 eyes (33.3%) and regression of polypoidal lesions was detected by ICGA in 6 eyes (66.7%) during the follow-up of mean 24 months. Cases with recurrence underwent a mean of 3.3±1.4 sessions of PDT in total.

Twenty-two patients (9 women, 13 men) underwent combined treatment with PDT and IVB and were followed for a mean of 24.6±15.4 months (range, 12-48 months); the mean age of the group was 64.8±8.2 years. Patients received an average of 8.3±5.8 IVB injections. A significant difference in VA was found between pre-treatment (0.33±0.32 logMAR) and 1 year post-treatment (0.22±0.29 logMAR) (p=0.025). Although there was also VA improvement between pre-treatment and during follow-up with a mean duration of 24 months (0.23±0.31 logMAR), the difference was not statistically significant (p=0.087). At the end of follow-up, VA had improved in 16 (64%) eyes, remained the same in 6 (24%) eyes and declined by 2 rows on the ETDRS chart in 3 (12%) eyes. There was a significant difference in mean foveal thickness determined by OCT between pre-treatment (349.76±122.09 µm) and both 1 year post-treatment (248.96±87.63 µm) and during the follow-up of mean 24 months (249.8±49 µm) (p=0.001 for both). Recurrence was observed in 4 (16%) of the patients during the first 12 months of follow-up, in 5 (45.4%) of the 11 patients followed for 13-24 months, in 4 (50%) of the 8 patients followed for 25-36 months, and in 2 (50%) of the 4 patients followed for 37-48 months. During the follow-up period lasting a mean 24 months, recurrence was found in 11 eyes (44%) and regression of polypoidal lesions detected by ICGA was found in 16 eyes (64%). Cases with recurrence underwent an average of 2.7±1.1 sessions of PDT.

There were no differences between the two groups in age, gender, and VA or foveal thickness before treatment or after an average follow-up of 24 months (p=0.80, p=0.67, p=0.41, p=0.95, p=0.57, and p=0.98, respectively). None of the patients developed complications related to treatment.

The patients' demographic and treatment characteristics are shown in Table 1. Pre- and post-treatment visual and anatomical outcomes of the PDT and combined PDT+IVB treatment groups are shown in Table 2. Figures 1, 2, 3, 4, 5, 6, 7 show the pre-treatment appearance and post-treatment results at 1, 2, 3, 6, and 12 months of an eye with subfoveal PCV that underwent PDT and received 3 consecutive doses of IVB.

Discussion

PCV presents with polypoidal vascular dilations in the choroidal vasculature and a branching choroidal vascular network. Definitive diagnosis can be made using ICGA, in which polypoidal structures appear as vascular aneurysmal dilations originating from the choroidal vessels and hyperfluorescence from the branching vascular network is visible.[2,6,7] Retinal pigment epithelial detachment (PED) typical of PCV can be detected with OCT. The visualization of subretinal fluid accumulation, a branching vascular network in the form of shallow fibrovascular PED, and the

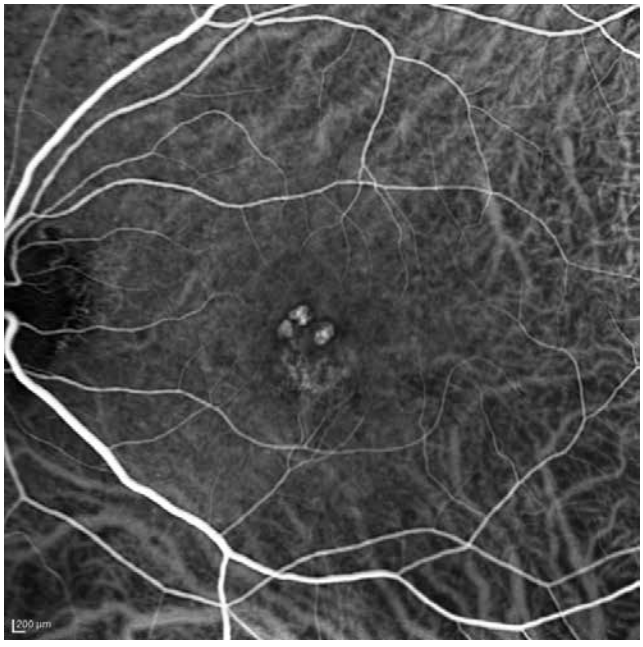

Figure 1. Indocyanine green angiography of a patient with polypoidal choroidal vasculopathy in the left eye showing three subfoveal polyps and an area of hyperfluorescence from a branching vascular network

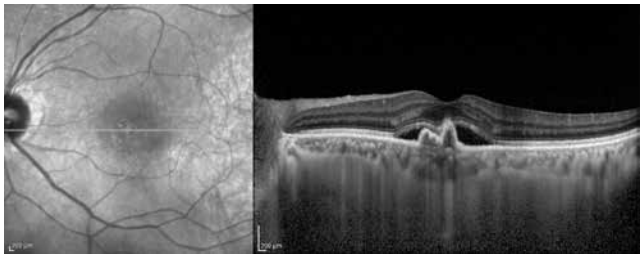

Figure 2. Optical coherence tomography from the same patient showing the polyp from the last section and shallower pigment epithelial detachment due to the brancing choroidal network

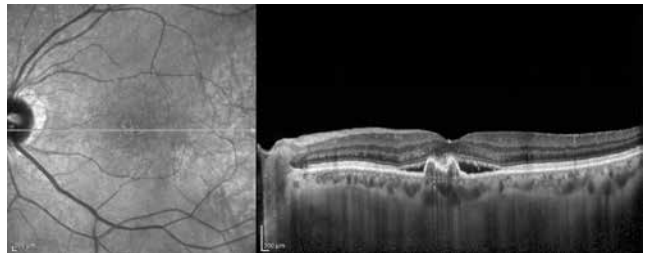

Figure 3. Optical coherence tomography of the same patient at 1 month follow-up, after photodynamic therapy and the first intravitreal bevacizumab injection. Regression of the subretinal fluid in the left eye can be seen, but it is still present in sporadic areas

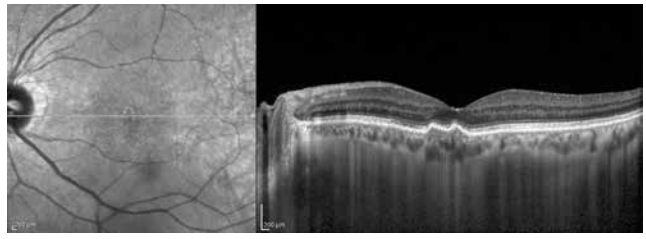

Figure 4. Optical coherence tomography of the same patient at 2 month follow-up, after injection of the second dose of intravitreal bevacizumab. Regression of the subretinal fluid in the left eye can be seen

Table 1. Demographic and treatment characteristics of the patient groups

	FDT	FDT+IVB
Eyes (n)	9	25
Gender (Female/Male)	2/7	9/13
Mean age (years)	64±7.6 (54-73)	64.8±8.2 (45-81)
Mean duration of treatment (months)	23.6±13.9 (12-48)	24.6±15.4 (12-48)
Mean FDT sessions (n)	1.8±1.3 (1-5)	1.7±1.1 (1-5)
Mean IVB injections (n)	-	8.4±5.4 (3-22)

FDT: Photodynamic therapy, IVB: Intravitreal bevacizumab

Table 2. Pre- and post-treatment visual and anatomic outcomes

	FDT	FDT+IBV
Pre-treatment mean VA (logMAR)	0.40±0.27 (0.10-0.70)	0.33±0.32 (0.10-1.00)
Post-treatment mean VA (logMAR)	0.25±0.36 (0-0.70)	0.23±0.31 (0-1.00)
Pre-treatment mean CMT (µm)	312.56±61.74 (221-390)	349.76±122.09 (165-620)
Post-treatment mean CMT (µm)	276.78±142.98 (154-395)	249±80.12 (150-454)
Recurrence (%)		
0-12 months	3 (33.3%)	4 (16%)
13-24 months	1 (25%)	5 (45.4%)
25-36 months	1 (50%)	2 (50%)
37-48 months	-	2 (50%)
Regression (%)***	6 (66.7%)	16 (64%)

VA: Visual acuity, CMT: Central macular thickness, PDT: Photodynamic therapy, IVB: Intravitreal bevacizumab
***Polypoidal lesion regression determined by indocyanine green angiography

presence of polypoidal structures within the raised PED on OCT facilitates the diagnosis of PCV, and OCT is also beneficial in monitoring treatment response (Figure 8).[6,7]

Thermal laser coagulation is used to treat extrafoveal polypoidal lesions, but it is not currently recommended for the treatment of subfoveal and juxtafoveal PCV.[6,8]

Many studies have demonstrated that PDT alone has short- and medium-term success rates of 80% and 95% in the treatment of subfoveal PCV.[3] Gomi et al.[9] reported that of 36 patients who underwent PDT, VA was increased in 67% and stable in 17%, and polyp regression was achieved in 86% at 1 year follow-up. Şentürk et al.[4] found VA had increased in 60% and stabilized in 40% of their patients at 1 year after PDT. Otani et al.[10] also found that after PDT, 82.2% of their 45 patients exhibited polypoidal lesion regression at 1 year follow-up. Similarly, in the current study we found that VA increased in 67% of our patients and stabilized in 22% over a mean follow-up duration of 24 months, and polypoidal lesion regression was detected in 67% of the cases.

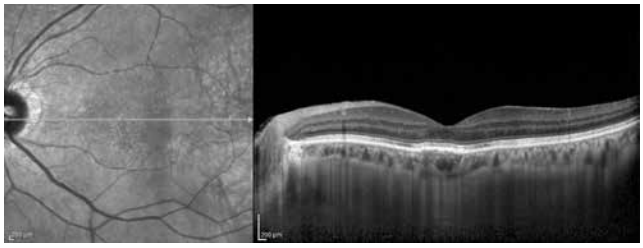

Figure 5. Optical coherence tomography of the same patient at 3 month follow-up, after injection of the third dose of intravitreal bevacizumab. Further regression of the subretinal fluid in the left eye can be seen

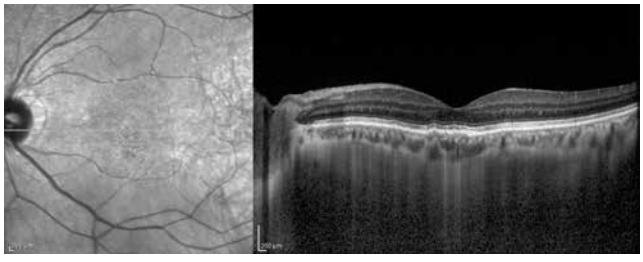

Figure 6. Optical coherence tomography of the same patient at 6 month follow-up; no intraretinal or subretinal fluid is visible in the left eye

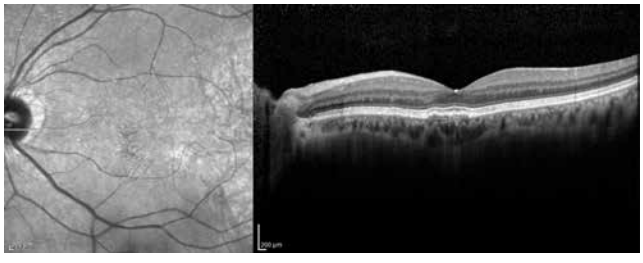

Figure 7. Optical coherence tomography of the same patient at 1 year follow-up. No intraretinal or subretinal fluid is visible in the left eye

Intravitreal anti-VEGF agents have been shown in many studies to be effective in the treatment of choroidal neovascularization associated with AMD, but their efficacy in the treatment of PCV is limited.[5,11,12] Several studies have shown that anti-VEGF therapy resulted in decreased retinal thickening on OCT and visual and anatomic success; however, polypoidal lesion regression has been achieved through its combined use with PDT or thermal laser coagulation.[11,13] Although there is evidence of the short-term efficacy of aflibercept (another anti-VEGF agent derived from VEGF receptor) in the treatment of PCV, long-term randomized clinical studies are needed.[14]

There are reports of improved VA and decreased foveal thickness 1 year after combined PDT and IVB injection therapy for PCV.[15] Similarly, Ruambiboonsuk et al.[16] found improved VA and polypoidal lesion regression in all of their cases after combined therapy. During the mean 24 month follow-up period in our study, VA increased in 64% and remained unchanged in 24% of patients who underwent PDT and IVB injection. There was also a statistically significant decrease in central macular thickness at the end of the mean 24 month follow-up period, and polypoidal lesion regression was achieved in 64% of the cases.

Studies have demonstrated that the combination of PDT and IVB injection is as effective as PDT alone in the treatment of subfoveal PCV.[3] Gomi et al.[17] compared the results of PDT alone and combined PDT and IVB injection and reported that combined therapy yielded significantly better visual outcomes during the 1 year follow-up period. However, in the randomized controlled study EVEREST, no difference was found between PDT and combined PDT and anti-VEGF therapy in terms of VA improvement or polyp regression (71.4% and 77.8%, respectively), and the rate of polyp regression with anti-VEGF therapy alone was low (28.6%).[13] Similarly, when we compared the results from our patients

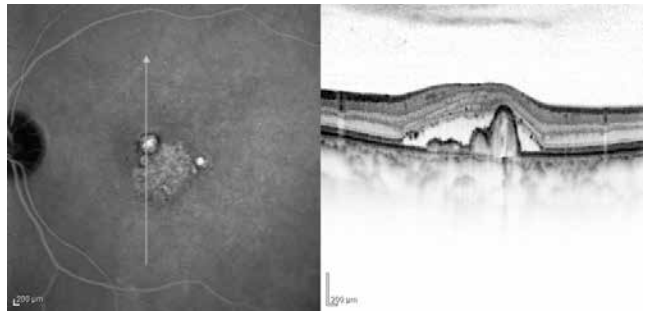

Figure 8. Left: Indocyanine green angiography of polypoidal choroidal vasculopathy patient showing polypoidal formations appearing as vascular aneurysmal dilations of the inner choroidal vessels as well as hyperfluorescence typical of the branching vascular network. Right: Polypoidal choroidal vasculopathy diagnosis is facilitated by optical coherence tomography showing subretinal fluid accumulation, branching vascular network in the form of shallow fibrovascular pigment epithelial detachment, and polypoidal structures within the raised pigment epithelial detachment

treated with PDT or combined PDT and IVB injection during the mean 24 months of follow-up, we found post-treatment anatomic and functional recovery in both groups, and no statistically significant difference emerged in the results.

It has been reported that the visual and anatomic success achieved in the short and medium terms with PDT alone and combined therapy cannot be maintained in the long term.[3] Because of the high post-treatment recurrence rate, long-term follow-up of these patients is recommended. In our study, additional PDT was administered due to recurrence in 33.3% of cases treated with PDT alone and 44% of those treated with combined PDT+IVB injection. While studies with short follow-up times report approximately 80% visual and anatomical success, our rate was approximately 65%, suggesting that our lower success rate was due to our relatively longer follow-up period.

Conclusion

Both PDT monotherapy and PDT combined with IVB injection yielded successful outcomes in this study. Limitations of this study are that it is retrospective, the study groups had very different patient numbers, and the follow-up period was not long enough. Prospective studies with larger patient numbers and longer follow-up will be useful to demonstrate the long-term treatment results.

Ethics

Ethics Committee Approval: It was taken, Informed Consent: In accordance with the principles of the declaration of Helsinki, patients were informed about their current status, natural course, treatment success rates and risks, and consent was obtained for all PDT and anti-VEGF treatments.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Serra Arf, Hakan Özdemir, Murat Karaçorlu, Concept: Işıl Sayman Muslubaş, Serra Arf, Hakan Özdemir, Murat Karaçorlu, Design: Işıl Sayman Muslubaş, Serra Arf, Murat Karaçorlu, Data Collection or Processing: Işıl Sayman Muslubaş, Mümin Hocaoğlu, Analysis or Interpretation: Işıl Sayman Muslubaş, Serra Arf, Murat Karaçorlu, Literature Search: Işıl Sayman Muslubaş, Mümin Hocaoğlu, Writing: Işıl Sayman Muslubaş, Mümin Hocaoğlu, Serra Arf, Hakan Özdemir, Murat Karaçorlu.

Conflict of Interest

No conflict of interest was declared by the authors.

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Original Article

Outcomes of Unilateral Inferior Oblique Myectomy Surgery in Inferior Oblique Overaction Due to Superior Oblique Palsy

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Summary

Objectives: To present the outcomes of unilateral inferior oblique myectomy performed in patients with inferior oblique overaction due to superior oblique palsy.

Materials and Methods: Twenty-seven eyes of 27 patients that underwent inferior oblique myectomy surgery for superior oblique palsy between 2002 and 2008 were included. Inferior oblique overaction scores (between 0-4) at preoperative, early postoperative (within 1 week after surgery) and late postoperative (earliest 6 months) visits were reviewed.

Results: There were 12 male and 15 female patients. Eighteen were operated on the right eye, and 9 were operated on the left eye. The mean age was 15.62±13.31 years, and the mean follow-up was 17±11.28 months (range, 6-60 months). Patients who had horizontal component and V-pattern deviation were excluded. Preoperative and early postoperative inferior oblique overaction scores were 2.55±0.75 and 0.14±0.36, respectively, and the difference was statistically significant ($p<0.01$). This improvement was maintained up to the late postoperative period.

Conclusion: Due to its promising short-term and long-term results, inferior oblique myectomy can be the first choice of surgery for inferior oblique overaction due to superior oblique palsy.

Keywords: Inferior oblique myectomy, inferior oblique overaction, superior oblique palsy

Introduction

Superior oblique palsy (SOP) is the most frequent single extraocular muscle paralysis diagnosed by ophthalmologists.[1] Due to the torsional component and the frequency of incomitance, medical treatment using prisms is generally not tolerated by SOP patients. The condition is commonly treated with surgery.

The first surgical approaches for the inferior oblique (IO) muscle date back to the mid 19th century. In 1841, John Taylor made an incision into the outer edge of the IO and probably performed tenotomy on the IO in order to treat strabismus patients. Duanne was the first to begin safely and deliberately performing IO surgery in 1905.[2] Until 1943, myectomy was the only IO surgery performed. White[3] and Brown[4] later described the recession procedure. The transposition approach for IO surgery was first reported in 1982 by Elliott and Nankin.[5] Prior to that, Parks[6] showed that recession was more effective than myectomy.

Inferior oblique muscle overaction (IOOA) was classified by Parks[6] into two groups: primary and secondary. Secondary IOOA is associated with ipsilateral SOP, whereas in primary IOOA there is no SOP or contralateral superior rectus palsy. Primary IOOA is frequently bilateral and usually asymmetrical, making it difficult to choose a surgical option. In these cases, overaction is generally greater in the non-fixating, amblyopic eye, though a very small, even imperceptible amount may be found in the fixating eye. V-pattern is typical. This type of overaction does not spontaneously resolve. Chamberlain[7] recommended asymmetric bilateral surgery for these cases. He showed that after a unilateral weakening surgery for the eye with more overaction, secondary IOOA is unmasked in the fellow eye in 37% of cases.

In this study, we present the outcomes of unilateral IO myectomy in patients with SOP-associated IOOA.

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Materials and Methods

Twenty-seven eyes of 27 patients who underwent unilateral IO myectomy due to unilateral SOP at the Gülhane Military Medical Academy Department of Ophthalmology between 2002 and 2008 were evaluated retrospectively. Patients with bilateral or masked SOP were excluded from the study. Preoperative, early postoperative (within 1 week of surgery), and late postoperative (at least 6 months after surgery) IOOA scores (on a scale of 0-4) were analyzed.[8] Patients who were followed for at least 6 months after surgery were included in the study.

Forced traction test was conducted preoperatively under topical anesthesia for patients aged 20 years or older. For patients under 20 years old, the test was done under general anesthesia immediately before the surgery.

In the forced traction test, toothed forceps were used to grasp the eye near the limbus at the 6 and 12 o'clock positions and check whether the eye moved left and right freely. If eye movement was limited, the test was considered positive and the patient was excluded from the study.

All surgeries were performed under general anesthesia after the forced traction test. An incision was made in the inferotemporal conjunctiva 6 mm from and parallel to the limbus. Blunt and sharp dissection were used to expose the IO muscle. The IO was suspended with a fine muscle hook and separated from the insertion site. A length of approximately 5 mm was resected, and the muscle ends were released after establishing hemostasis. The conjunctiva was closed with 8/0 silk suture.

Statistical Package for the Social Sciences version 16.0 software was used for statistical analyses. A t-test was used to compare pre- and postoperative IOOA and the initial and final postoperative follow-up results. Level of statistical significance was accepted as α=0.05.

Results

The study included 12 male patients and 15 female patients. The mean age of the patients was 15.62±13.31 years (range, 2-59 years) and the mean follow-up time was 17±11.28 months (range, 6-60 months). Unilateral-ipsilateral myectomy was performed in all cases. The right eye was operated in 18 patients and the left eye in 9 patients. Patients with horizontal component and V-pattern deviation were excluded from the study. Descriptive statistics of the patients includedin the study are shown in Table 1.

The patients' mean preoperative IOOA grade was 2.55±0.75. In the early postoperative period the mean IOOA grade was 0.14±0.36, and this difference was statistically significant (p<0.01). Postoperative IOOA severity remained stable throughout follow-up for most of the patients; however, 2 patients' IOOA grade increased from 0 to 1 in the final follow-up and 2 other patients' IOOA grade decreased from 1 to 0. Cumulatively, there was no statistically significant difference in IOOA severity between the early and late postoperative periods (p>0.05) (Table 2).

Fifteen of the 27 patients (55.5%) had abnormal head position (AHP) preoperatively. After surgery, AHP was corrected in 12 of those 15 patients (80%).

Discussion

IOOA is an incomitant vertical deviation characterized by eye elevation caused by adduction. Its etiology is categorized as primary or secondary. Although mechanical and innervational causes are suspected to act in the etiology of primary IOOA, the cause is not fully understood. It frequently accompanies horizontal deviation, but it can also occur in isolation. It usually does not lead to vertical deviation in primary position. It may be unilateral or bilateral, symmetrical or asymmetrical. Secondary IOOA develops due to weakness of the ipsilateral superior oblique muscle or the contralateral superior rectus muscle. These patients may exhibit vertical or cyclovertical deviation in primary position and AHP.

SOP is the most common isolated extraocular muscle paralysis and is usually treated with surgery. It is most commonly congenital or idiopathic (63%), though head trauma, cerebrovascular disorders, tumors, sinusitis and myasthenia gravis have also been reported as etiologic factors. The most important symptoms of SOP are hypertropia, extorsion, AHP and diplopia.[9,10]

Both primary and secondary IOOA have been successfully treated with myectomy, recession and transposition procedures

Table 1. Demographic and clinical characteristics of the patients (n=27)

Age (years)	**15.62±13.31**
Gender	
Male	12 (44.4%)
Famale	15 (55.6%)
Lateralization	
Right eye	18 (66.6%)
Left eye	9 (33.4%)
Follow-up duration (months)	17±11.28

Table 2. Comparison of pre- and postoperative inferior oblique overaction severity

	Preoperative	**Early postoperative period**	**Late postoperative period**
Mean ± standard deviation	2.55±0.75	0.14±0.36	0.14±0.36
p*	<0.01		
*t-testi			

for many years. Ghazawy et al.[11] evaluated the early and late postoperative outcomes of myectomy and transposition surgeries in 120 eyes of 81 patients irrespective of etiology. The two procedures had very similar outcomes, but they recommended myectomy, which is a shorter and easier procedure. Their myectomy results (mean postoperative IOOA was 0.29) were quite similar to those in our clinic.

Soyugelen et al.[12] evaluated the outcomes of IO myectomies in a total of 28 patients, 18 unilateral and 10 asymmetric. The mean follow-up duration was 15 months; the mean pre-and postoperative IOOA severity was 2.88±0.75 and 0.16±0.38, respectively. The asymmetric cases had pre- and postoperative IOOA severity of 4.40±0.69 and 2.00±0.94, respectively. Patients with a horizontal component were not included in our study, but the results we obtained with isolated myectomy are comparable.

Recession is another surgical procedure used to treat IOOA. In a study by Rajavi et al.[8] including 82 eyes of 50 patients, eyes randomly underwent myectomy (42 eyes) or recession (40 eyes). They were unable to detect a statistically significant difference in the outcomes of the two procedures. Min et al.[13] conducted a prospective study in which 20 children with bilateral +3 IOOA underwent myectomy in one eye and anterior transposition in the fellow eye and were followed for 20 months. They detected recurrence starting in the first month in myectomized eyes, whereas they detected no major changes during the 20 month follow-up period in the eyes that underwent anterior transposition. Because the success criterion accepted for the study was zero IOOA, success rates of 25% for the myectomy group and 85% for the anterior transposition group were achieved after 20 months. In other words, Min et al.[13] stated that at the end of 20 months, the success of the myectomies had progressively decreased, whereas there was no marked change in the anterior transposition group. We did not observe such outcomes with myectomy. However, Min et al.[13] accepted +1 IOOA as failure criteria, although this grade of IOOA has been evaluated in many studies in the literature as subclinical and asymptomatic. Therefore, like many other clinical studies, our results are not consistent with those of Min et al.[13] in terms of change over time or success criteria.[12,14,15,16,17]

AHP is one of the important diagnostic criteria of SOP. Bahl et al.[18] compared IO myectomy and recession surgeries in SOP cases and found no differences between the two surgical procedures in terms of AHP. In their study, 49% of the myectomy patients had AHP preoperatively, and approximately 53% of those patients' ABP improved postoperatively. Elliott and Nankin[5] reported an ABP correction rate of 88% after IO anterotransposition surgery. Of the patients in our study, 55.5% had AHP prior to surgery, and AHP improved after surgery in 80% of those cases. We believe that the varying rates of AHP correction reported in the literature can be attributed to differences in diagnosis, age groups, surgical technique and success criteria.

The most important complications in IO myectomy are adherence syndrome, which results from the free ends adhering to the sclera or one another, and IOOA recurrence.[4] Furthermore, if hemostasis is not achieved, severe bleeding can occur both during and after surgery, which can affect success in the early and late postoperative periods. We did not encounter these types of complications in any of our cases.

Conclusion

In conclusion, in the treatment of IOOA, myectomy is a procedure that can be completed quickly. As scleral sutures are not required, it carries no risk of scleral perforation, and several possible complications can be easily avoided with good hemostasis. Due to its satisfactory results in both the short and long terms, myectomy can be the first choice of surgical method for cases of IOOA due to SOP.

Ethics
Ethics Committee Approval: It was taken, Informed Consent: It was taken, Peer-review: Externally peer-reviewed.
Authorship Contributions
Surgical and Medical Practices: Fatih Mehmet Mutlu, Concept: Fatih Mehmet Mutlu, Design: Erhan Yumuşak, Murat Küçükevcilioğlu, Data Collection or Processing: Oktay Diner, Ümit Yolcu, Analysis or Interpretation: Erhan Yumuşak, Literature Search: Erhan Yumuşak, Writing: Erhan Yumuşak.
Conflict of Interest
No conflict of interest was declared by the authors.
Financial Disclosure
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Original Article

Canaliculitis Awareness

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Summary

Objectives: To evaluate the demographic characteristics, treatment, and results of patients with canaliculitis.

Materials and Methods: Medical records including the demographic characteristics, clinical findings, and treatment outcomes of patients diagnosed and treated for canaliculitis between September 2009 and March 2014 were analyzed retrospectively.

Results: The median age of the 7 canaliculitis patients consisting of 4 women and 3 men was 49 (range 8-58) years. All patients had unilateral canaliculitis (on the right side in 2 and left side in 5 patients) and the inferior canaliculus was involved more frequently (71.4%). Epiphora, chronic conjunctivitis, a palpable and thickened canaliculus, and yellow discharge from the punctum were present in all cases. *Actinomyces* spp. was the most frequently cultured microorganism (75%). Dacryolith was observed in 6 patients. Canaliculotomy and dacryolith removal with canalicular curettage were performed, followed by medical treatment (topical penicillin 100,000 U/ml and oral ampicillin/sulbactam) for 10 days. Patients were followed up for a mean duration of 17.0±15.2 (range 3-46) months. Signs and symptoms resolved completely within a month. Epiphora recurred in the 36th month in a single patient and was treated with daily canalicular irrigation with antibiotics and there were no further symptoms during 10 months of follow-up after the recurrence.

Conclusion: Canaliculitis is often overlooked and can be misdiagnosed. Every patient with chronic conjunctivitis and lacrimal infection should be examined carefully for canaliculitis.

Keywords: Canaliculitis, canaliculotomy, conjunctivitis, curettage

Introduction

Primary canaliculitis is a rare, chronic condition that develops with no underlying cause, usually due to actinomyces or staphylococci infection. It accounts for only 1.2-2% of all lacrimal disease.[1,2,3] The clinical signs are punctal or canalicular edema, redness, and purulent discharge from the punctum when pressure is applied. Despite its clinical signs being very well defined, it can be easily overlooked and misdiagnosed.[4] There are reports in the literature of diagnosis being delayed up to three years.[5] Conservative treatment with topical antibiotic eye drops alone results in a high recurrence rate.[6,7] Canaliculotomy and curettage of the dacryoliths are the gold standard in treatment.[4,8] The aim of this study was to evaluate the demographic characteristics, treatments and outcomes of patients with canaliculitis.

Materials and Methods

Medical records including demographic characteristics, clinical findings, and treatment outcomes of patients diagnosed and treated for canaliculitis in the Oculoplasty Unit of the Ulucanlar Eye Education and Research Hospital between September 2009 and March 2014 were analyzed retrospectively. The study was approved by the institutional review board.

Seven patients referred by various doctors had been previously misdiagnosed and received inappropriate treatment. All cases were evaluated for potential coexisting eyelid diseases. All patients underwent surgical treatment consisting of canaliculotomy and dacryolith removal. Canaliculotomy was performed by making an incision in the affected canaliculus with a number 11 blade attached to a Bowman lacrimal probe. All dacryoliths and sulfur granules were carefully removed by curettage using a chalazion curette.

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The samples were transported to the laboratory for microbiological analysis as soon as possible using anaerobic transport medium. For example, direct Gram staining revealed gram-positive, branching filamentous structures; cultures were made to ascertain the presence of aerobic and anaerobic bacteria and fungi. Columbia blood agar plates were incubated at 37 °C in anaerobic conditions for at least 5 days. Blood agar and MacConkey agar plates were incubated at 37 °C for 24-48 hours. Sabauroud dextrose agar plates were incubated at both 25 °C and 37 °C. Gram staining of the bacteria grown in the anaerobic environment revealed gram-positive branching bacilli, which were identified by biochemical tests. A diagnosis of *Actinomyces* canaliculitis was confirmed.[9]

The canaliculi were irrigated with an antibiotic. All patients were treated with hot compresses, 100,000 U/ml topical penicillin 8 times daily for 10 days, and systemic ampicillin/sulbactam, 750 mg orally twice a day for adults and 1 dose in the morning and 1/2 a dose in the evening of 400/57 mg/5 ml (1 dose) suspension for children. The canaliculi were allowed to heal without silicone intubation or reconstruction.

Results

Seven patients were diagnosed with canaliculitis during the study period. Four of the patients were female, 3 were male, and the median age was 49 (range, 8-58) years. The mean follow-up time was 17.0±15.2 (range, 3-46) months. Four of the patients had been initially misdiagnosed with conjunctivitis, one with nasolacrimal duct obstruction (NLDO), and one with chalazion. One patient was found to have secondary canaliculitis due to an eyelash that entered the canaliculus during routine follow-up for glaucoma. This patient had also been previously treated for conjunctivitis. All cases were unilateral (two right, five left); the inferior canaliculus was affected more often (71.4%) (Table 1). Epiphora, chronic conjunctivitis, a palpable and thickened canaliculus, and yellow discharge from the punctum were present in all cases (Figure 1a). The median duration of symptoms was 9 (range, 1-36) months. Six patients had dacryoliths. Lacrimal lavage through the unaffected canaliculus was patent in all patients. Canaliculotomy was performed as surgical treatment. An incision was made in the inner palpebral area and mushroom-like whitish-yellow dacryoliths were removed (Figure 1b). After removing the dacryoliths from the canaliculi by curettage, all patients underwent medical treatment for 10 days (100,000 U/ml topical penicillin eight times a day and systemic ampicillin/sulbactam, 750 mg orally twice a day for adults or 1 dose in the morning and 1/2 dose in the evening of 400/57 mg oral suspension. Evaluation of the whitish-yellow dacryoliths revealed the presence of actinomycosis (Figure 1c). *Actinomyces* spp. were the most frequently cultured microorganism (75%). One patient was found to have secondary canaliculitis due to an eyelash entering the canaliculus (Figure 2). The patient had presented with eye redness and discharge to a primary care physician, who attempted to treat the condition believing it was conjunctivitis. The patient's symptoms completely resolved with removal of the eyelash and topical antibiotic treatment. The patients were followed for a mean duration of 17.0±15.2 (range, 3-46) months. All patients' signs and symptoms completely resolved within the first month (Figure 1d). For one patient, epiphora recurred in the 36th month; the patient was treated with canalicular irrigation with antibiotics daily for three days and then every other day for one week. The symptoms did not return during the 10 month post-recurrence follow-up period (46 months after surgery).

Discussion

The clinical signs of primary canaliculitis include a 'pouting' punctum, eyelid edema and erythema, mucopurulent discharge from the punctum when pressure is applied, and in some cases yellow dacryoliths called 'sulfur granules' in the punctum. Although these clinical signs are well defined, because the condition is rarely encountered it can easily be missed and misdiagnosed as conjunctivitis, mucocele, dacryocystitis, blepharitis or meibomian gland cyst, resulting in delayed diagnosis.[3,4,7,10]

Primary canaliculitis usually occurs with no underlying cause, although canalicular occlusion or diverticulum may precipitate infection in the canaliculus.[11] It is usually unilateral and affects the inferior canaliculus, though there are reports in the literature of cases in the superior canaliculus.[3,10] In our study the inferior canaliculus was involved in 71.4% of the cases.

Table 1. Demographic, clinical and microbiological characteristics of canaliculitis patients

Case no	Gender	Age	Laterality	Localization	Symptom duration (months)	Microbiological analysis	Follow-up duration (months)
1	Male	49	Left	Inferior canaliculitis	36	*Actinomyces* spp.	46
2	Male	51	Right	Inferior canaliculitis	12	Negative	27
3	Female	43	Right	Inferior canaliculitis	12	*Actinomyces* spp.	8
4	Female	36	Left	Superior canaliculitis	6	Could not be done	12
5	Female	53	Left	Superior canaliculitis	9	Could not be done	5
6	Male	58	Left	Inferior canaliculitis secondary to foreign body	1	Could not be done	18
7	Female	8	Left	Inferior canaliculus	3	*Actinomyces* spp.	3

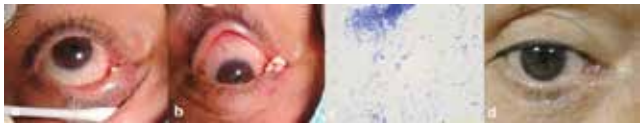

Figure 1. (a) Findings of purulent discharge from the right inferior punctum and hyperemia of the nasal conjunctiva in a patient with right inferior canaliculitis; (b) macroscopic appearance of the sulfur granules after inferior canaliculotomy and curettage; (c) 100x magnification of Gram staining showing infiltration of *Actinomyces* colonies; (d) patient's appearance 6 months after surgery

Figure 2. A patient with canaliculitis due to an eyelash entering the left inferior canaliculus

Canaliculitis is most commonly seen in middle-aged and elderly patients, although 5- and 6-year old patients have also been reported in the literature.[10,12,13] According to age, the annual incidence of canaliculitis per 100,000 population has been reported as 0.04 in the first decade, 0.27 in the second decade, 0.59 for the 40-59 age group, and 1.37 for the 60-79 age group.[14] Similarly, the median age of the patients in our study was 49, and we had one 8-year-old patient. Park et al.[12] reported a 5-year-old patient who underwent surgery after repeated probing and balloon dacryoplasty to treat congenital NLDO did not improve symptoms; canaliculitis was diagnosed during the surgery and curettage was performed. Park et al.[12] believed that the patient's previous surgeries may have created a predisposition to canaliculitis. Yaman et al.[10] reported no history of any diseases or surgical procedures underlying their cases. Many investigators have reported that canaliculitis occurs more frequently in women.[3,4,6,11,13] This is thought to be due to hormonal changes in menopause and reduced tear production disrupting the barriers that prevent infection.[4,6] In our study, 4 of the 7 patients were women, but only one was in menopause. There have also been reports of secondary canaliculitis associated with the use of oral 5-fluorourasil in breast cancer treatment and more recently, due to trauma related to the insertion of punctal plugs.[15,16,17] We found that one of our patients had secondary canaliculitis due to an eyelash entering the canaliculus. The patient's symptoms resolved completely with removal of the eyelash and topical antibiotic treatment. Previously this patient had been unsuccessfully treated for what the physician believed was conjunctivitis.

Canaliculitis is a condition that can easily be diagnosed with a careful clinical examination, without the need for detailed examinations like dacryocystography.[3] However, in cases that are uncertain, feeling the presence of dacryoliths in the canaliculus during nasolacrimal duct lavage can aid diagnosis.[11] Without correct diagnosis and appropriate treatment, the condition recurs frequently. If patients with complaints of recurrent unilateral epiphora and discharge were started on topical antibiotics for conjunctivitis but their signs and symptoms return after a brief period of improvement, as occurred with our patients, a more careful examination of the canaliculi should be done with canaliculitis in mind for the differential diagnosis. Kaliki et al.[13] reported a median diagnostic delay of 6 (range, 1-60) months in their series of 74 primary canaliculitis patients. The median symptom duration in our cases was 9 (range, 1-36) months.

Anand et al.[3] emphasized that repeated forceful nasolacrimal lavage can push canalicular granules into the lacrimal sac and lead to NLDO, which increases the importance of early and accurate diagnosis. At the same time, canaliculitis can be mistaken for dacryocystitis or NLDO, as occurred with one of our patients. Observing patency to nasolacrimal duct lavage through the unaffected canaliculus is important in the differential diagnosis.

Of the agents involved in canaliculitis, actinomyces varieties–gram-positive, anaerobic bacteria that are difficult to isolate and identify–are the most commonly isolated, although other bacteria, fungi and viruses may also appear.[1,5,10,18,19] In contrast, there are some studies in which the most common pathogenic agent was staphylococci, followed by actinomyces.[3,13] Because actinomyces are difficult to culture and occur in complex infections with other, easier to culture pathogens, the actinomyces growth rate reported in the literature ranges from 25 to 54%.[1,5,18,19,20] However, it has been emphasized that actinomyces can be discovered in all cases on histopathological examination.[5,10,18] There are case reports in which *Arcanobacterium (Corynebacterium) haemolyticum* (from the *Actinomyces pyogenes* family) grew in culture.[21] We found actinomyces as the agent in three (75%) of the four cases we were able to analyze microbiologically, but the other three cases were using topical antibiotics when they presented to our clinic. Microbiological culture samples were not taken from these three patients due to the possible effects of the antibiotics used. However, the typical sulfur granules seen during surgery in two of the cases suggested actinomyces. In our one case of secondary canaliculitis due to a foreign body in the canaliculus, typical clinical examination findings facilitated the diagnosis.

Despite initial improvement seen with conservative treatment consisting of topical and systemic antibiotics, recurrences are common. This is thought to be due to the canalicular dacryoliths creating an obstruction that impairs tear drainage and hinders treatment penetration,[11] which further increases the importance of early diagnosis and appropriate treatment. To repair the canaliculus, lacrimal irrigation with aqueous penicillin or povidone-iodine and sulfonamide eye drops 4 times daily, plus

high-dose systemic penicillin for 3-6 months have been reported in the literature as effective against actinomyces.[20,22,23] Briscoe et al.[5] treated 4 *Actinomyces* canaliculitis patients with 20 million units/day intravenous (IV) penicillin for the first 3 weeks, followed by 3-6 months of 2 g/day oral penicillin; another 3 patients who refused IV treatment only received 2 g/day oral penicillin for 3-6 months. They found that long-term systemic penicillin was an effective treatment for *Actinomyces* canaliculitis. Long-term treatment has also been reported to reduce the risk of recurrence.[24]

The widely accepted treatment for canaliculitis is canaliculotomy and curettage of the canaliculus.[1,3,4,10,20] Considering that canaliculotomy may lead to narrowing and scarring of the canalicular lumen, lacrimal pump dysfunction, and canalicular fistulas, some investigators recommend canalicular curettage alone or with the less invasive procedure of canaliculoplasty.[6,11] However, Pavilack and Frueh[11] reported that repeated treatment was necessary in 10 of 11 cases treated with curettage alone. In contrast, Çiftçi et al.[18] observed recurrence in 2 of their 13 patients, and Lee et al.[6] needed to perform repeated curettage in only 2 (6.7%) of their 30 cases, which they believed may have been the result of failure to completely remove the contents of the canaliculus. To reduce the risk of recurrence, postoperative topical and systemic antibiotic treatment is also recommended in addition to surgical treatment.[5,6,21] Vecsei et al.,[4] Yaman et al.[10] and Anand et al.[3] followed their patients for 3, 10, and a mean of 26 months, respectively, and emphasized that curettage performed with canaliculotomy was as a safe and effective treatment for canaliculitis that did not cause disruption to the canalicular or lacrimal pump systems. In order to minimize iatrogenic trauma which can lead to canalicular scarring and/or dysfunction, vertical canaliculotomy and retrograde removal of dacryoliths has been recommended as an alternative method in surgical treatment of canaliculitis.[25] The authors performed this procedure 1 month after treatment with a 2-week course of topical antibiotic/steroid drops and oral antibiotic (doxycycline); a 2 mm vertical canaliculotomy was made, followed by the retrograde removal of the canalicular contents by medial-to-lateral pressure applied to the canaliculus with 2 cotton-tipped applicators.[25] They reported complete clearing of the canalicular contents in their 8 patients, and observed resolution of symptoms and patency to lacrimal lavage during the follow-up period of mean 9 (range, 2-27) months.[25]

As an alternative to these surgical methods, Mohan et al.[26] found that intracanalicular irrigation with a broad-spectrum antibiotic (50 mg/ml fortified cefazolin, 2 ml) and topical antibiotic therapy (50 mg/ml fortified cefazolin + 0.3% ciprofloxacin) were effective in the treatment of chronic suppurative canaliculitis. They reported the complete recovery of 12 patients with chronic suppurative canaliculitis using topical and intracanalicular antibiotic treatment only, without surgical intervention.[26] Physicians sometimes encounter very rare cases of canaliculitis caused by unusual microorganisms as reported by Şen et al.[27] where the facultative anaerobe *Gemella haemolysans* and anaerobe *Porphyromonas asaccarolytica* were determined as the causal agents. However, the patient was treated with the standard method of canaliculotomy with curettage.[27] We used canaliculotomy and curettage in our cases and recommended the use of both oral (ampicillin/sulbactam) and topical antibiotics (100,000 U/ml penicillin) to reduce the risk of recurrence in the postoperative period. Our patients were followed up for an average of 17 (range, 3-46) months. Recurrence occurred in only one patient in the 36th month. This patient was treated with daily intracanalicular antibiotic irrigation to avoid a second surgery. Recurrence in this patient after 36 months makes us believe that a long follow-up period is necessary for canaliculitis patients. The limitations of this study are the small patient number, heterogeneous follow-up duration and its retrospective nature; however, the strength and novel contribution of this study is its emphasis on the importance of canaliculitis awareness.

Conclusion

Canaliculitis should definitely be considered during the differential diagnosis of cases of recurrent, unilateral conjunctivitis in particular. Otherwise, the diagnosis may be delayed considerably, leading to incorrect treatments and even unnecessary surgical procedures such as dacryocystorhinostomy. After an accurate diagnosis, the most effective and reliable treatment is canaliculotomy with curettage. Treatment should be initiated quickly, as most patients have experienced diagnostic delays. Furthermore, culturing of the dacryoliths and discharge may facilitate better outcomes.

Ethics

Ethics Committee Approval: It was taken, Informed Consent: It was taken.

Peer-review: External and Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Emine Şen, Concept: Emine Şen, Design: Emine Şen, Data Collection or Processing: Emine Şen, Ebru Evren, Melike Balıkoğlu Yılmaz, Analysis or Interpretation: Emine Şen, Ebru Evren, Ufuk Elgin, Pelin Yılmazbaş, Literature Search: Emine Şen, Melike Balıkoğlu Yılmaz, Writing: Emine Şen, Melike Balıkoğlu Yılmaz.

Conflict of Interest

No conflict of interest was declared by the authors.

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Review

The Choroid and Optical Coherence Tomography

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Summary

The choroid is the most vascular tissue in the eye and it plays an important role in the pathophysiology of various common chorioretinal diseases such as central serous retinopathy, age-related macular degeneration and degenerative myopia. Quantitative assessment of the choroid has been quite challenging with traditional imaging modalities such as indocyanine green angiography and ultrasonography due to limited resolution and repeatability. With the advent of optical coherence tomography (OCT) technology, detailed visualization of the choroid in vivo is now possible. Measurements of choroidal thickness have also enabled new directions in research to study normal and pathological processes within the choroid. The aim of the present study is to review the current literature on choroidal imaging using OCT.

Keywords: Choroid, optical coherence tomography, age-related macular degeneration, central serous retinopathy, degenerative myopia

Introduction

The choroid is a pigmented vascular tissue that was first histologically examined in the 17th century, and to date has been studied by various imaging methods. It extends from the ora serrata anteriorly to the optic nerve head posteriorly. According to histopathological examination, the choroid has a mean thickness of 0.15 mm anteriorly and 0.22 mm posteriorly; anatomically it forms the posterior portion of the uveal tract, which continues anteriorly with the ciliary body and the iris. From retina to sclera, the choroid comprises Bruch's membrane, the choriocapillaris, the medium diameter choroidal vessels, and the large diameter choroidal vessels.[1]

A structurally and functionally healthy choroid is essential for retinal function. The central retinal artery nourishes the inner two-thirds of the choroid, whereas the choroidal vasculature nourishes the outer third. Abnormal choroidal circulation leads to retinal photoreceptor dysfunction and death.[2] It has been shown that the choroid has a vital role in the pathophysiology of many diseases such as central serous retinopathy (CSR), age-related macular degeneration (AMD), pathological myopia and Vogt-Koyanagi-Harada (VKH) disease.[3,4,5,6] Thus, the clear and accurate identification of choroidal changes will allow the proper assessment of many posterior segment diseases. However, unlike the retina, choroidal structures are not found in distinct, ordered layers and they lack contrasting reflective properties; therefore, for many years it was not possible to examine the choroid in as much detail as the retina.

Choroidal Imaging Methods

Until recently, the choroid was evaluated in vitro by histological analysis or in vivo by indocyanine green angiography (ICGA), laser Doppler flowmetry and ultrasonography.[7,8] As histologic studies were done in conditions that did not preserve the tone of the vascular structures, the analysis was very limited in terms of understanding disease pathophysiology. The choroid of a lifeless eye is deflated, resulting in greatly underestimated thickness measurements. Furthermore, considering that many of the factors influencing vascular tone do not exert their effect in histological sections, it is clear that in vitro evaluation is insufficient.

ICGA allows the visualization of the choroidal vessels and circulation under the retinal pigment epithelium (RPE). It has been shown that ICGA is better than fundus fluorescein angiography (FFA) in showing the details of choroidal neovascularization (CNV) and detecting choroidal polyps. In addition, the longer wavelengths used in ICGA enable better

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visualization of underlying lesions in cases with blood, exudates and pigment epithelial detachment (PED).[9,10]

Laser Doppler flowmetry is a non-invasive diagnostic method that allows the evaluation of hemodynamic parameters of optic nerve head, iris and subfoveal choroidal circulation by determining the average speed and number of erythrocytes moving in a specific volume. Laser Doppler flowmetry has been used to show that choroidal circulation is decreased in diseases like diabetic retinopathy, AMD and retinitis pigmentosa.[11,12]

Ultrasonography has been an important diagnostic tool in situations where the posterior pole cannot be evaluated due to opacities in the anterior of the eye. In particular, it enabled the detection of thickening and tumors in the choroid and retina. However, because of its low image resolution, detecting small changes in the choroid is difficult, and it is not an ideal method for measuring a relatively thin tissue like the choroid.[13]

Although these three techniques were used for many years to detect choroidal vessel abnormalities and circulation changes, none of them provided in vivo cross-sectional images of the anatomy of the retinal pigment epithelium or choroidal layers, and none provided sufficient data regarding true choroidal thickness and morphology.

Optical coherence tomography (OCT) is a relatively new method that has enabled the acquisition cross-sectional images of the retina in a way similar to ultrasound, but at much higher resolution. Technically, OCT is a partial coherence interferometer. Coherent light refers to light of a single wavelength, like laser light. Partially coherent light includes light of different wavelengths within a narrow range. The partially coherent light used in OCT is of a specific wavelength provided by a laser source. The basic principle of OCT is similar to B-scan ultrasound, but by means of light instead of sound.[14]

The first OCT technology was time domain (TD) OCT, in which light from a light source passes through a semitransparent mirror called the beamsplitter. This mirror splits the beam in two and sends half to a reference mirror at a known and adjustable distance from the detector, and the other half into the eye. A tomographic cross-section of the tissue is created based on the temporal difference between the beams reflected from the reference mirror and the ocular structures with various reflective properties. With the most advanced and recently produced TD-OCT device, the Stratus OCT, it is possible to acquire an average of 400 A-scans per second and images at 10 µm resolution.[15]

The OCT technology currently used in routine practice is spectral domain (SD) OCT. Unlike TD-OCT, SD-OCT does not use a reference mirror; instead, light reflected from the various tissue layers is detected simultaneously by a high-speed spectrometer and processed with a Fourier transform. For this reason, SD-OCT is also known as Fourier domain OCT. The use of a spectrometer to detect light reflected from tissue allows SD-OCT instruments to acquire 20,000-52,000 A-scans per second and produce images with 5 µm resolution.[16]

The signal-to-noise ratio is used to express the quality of OCT images. The choroid cannot be visualized by TD-OCT due to its low signal-to-noise ratio. The hyperreflectivity of the RPE layer prevents light from reaching the choroid and therefore a return signal is not received from the deeper choroidal layers. The low resolution of TD-OCT also prevents the detailed visualization of the choroid. Although SD-OCT is better than TD-OCT for choroidal imaging, it is not possible to obtain images extending to the choroidoscleral junction. Imaging of the entire choroid by SD-OCT is also prevented by the posterior position of the choroid, the use of wavelengths too short to penetrate the choroid, and the aforementioned hyperreflectivity of the RPE. OCT devices use light at a wavelength of 800 nm, whereas a wavelength of 1060 is required for choroidal imaging. Increasing the wavelength results in lower image resolution and quality. Because of these limitations, even with SD-OCT instruments it was not possible to visualize the entire choroid at high resolution until the development of enhanced depth imaging (EDI) OCT technology.[17]

Enhanced Depth Imaging-Optical Coherence Tomography

In standard SD-OCT instruments, tissue depths are encoded by different frequencies of the interference spectrum. With increasing tissue depth, the reflected light echoes from the deep tissue layers travel farther to the detector located at the zero delay line. Because these echoes have lower signal strength and higher frequency, the spectrometer cannot differentiate them. Thus, in standard OCT, the proximity of the retinal structures to the zero delay line results in high-sensitivity images of the retina and vitreoretinal junction and decreasing sensitivity toward the choroid. Two ways to overcome this are increasing the sensitivity of the spectrometer for high frequency detection or increasing the pixel number on the camera at the zero delay line. However, the image resolution of standard OCT cannot be increased and desired image quality cannot be achieved with these techniques. Therefore, specific protocols are used for choroid imaging. One of these protocols involves taking multiple images from the same area of the retina, increasing the signal-to-noise ratio, and combining them to produce an averaged image. This technique has been integrated as software into many SD-OCT instruments. Depending on the type of device, 8 to 100 images can be obtained and merged. Eye movement tracking systems have been developed to improve the image quality and signal strength while taking simultaneous images from the same location. However, even with this protocol it has not been possible to acquire choroid images of the desired quality.[14]

Another protocol emerged as the result of a technical characteristic of SD-OCT devices. SD-OCT cannot distinguish between positive and negative echoes; therefore, if a retinal structure is brought closer to the zero delay line, after a certain point positive echoes become negative echoes. When the detector produces an image from these echoes, an inverted mirror image appears reflected across the zero delay line. If the device is

advanced toward the eye, an inverted SD-OCT image of the choroid can be captured on the screen (Figure 1). Because the choroid is closer to the zero delay line, its echoes have high signal strength and low frequency, increasing the resolution of the choroidal image. This technique was first described by Spaide et al.[18] as EDI, and has been integrated as software into SD-OCT devices.

Enhanced Depth Imaging-Optical Coherence Tomography Capture Technique

The EDI-OCT imaging technique does not require any changes to the hardware of SD-OCT devices. As previously described, the technique consists of bringing the choroid closer to the zero delay line to focus the device more posteriorly in the optical system and processing the acquired images via software. Therefore, choosing EDI-OCT mode in the user interface of the original or updated software for choroidal imaging is sufficient. The patient is then asked to look at the reference light and images are acquired as in standard macular imaging. Dilating the pupil before imaging is not necessary.

The most useful application of choroidal imaging with EDI-OCT reflected in clinical practice is the detection of choroidal thickness. Although this measurement is currently performed manually on all devices, the intervisit, interobserver and intersystem agreement is very good, and highly reliable measurements can be obtained. The most common measurement used in daily practice is subfoveal choroidal thickness, which is detected by using the software's caliper tool to draw a line connecting the outer border of the retinal pigment epithelium and the inner border of the sclera. Care should be taken that this line is perpendicular to the line tangential to the foveal contour. The same tool can also be used to take thickness measurements at different points in the choroid.

Enhanced Depth Imaging-Optical Coherence Tomography and the Normal Choroid

Normal choroidal thickness was first described by Margolis and Spaide[19] using the Spectralis (Heidelberg Engineering, Heidelberg, Germany) and Manjunath et al.[20] using the Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA). Choroidal thickness was measured manually as the distance perpendicularly between the hyperreflective outer edge of the RPE to the choroidoscleral junction (Figure 2). It may not be possible to detect the choroidoscleral junction in some eyes. For this reason it is recommended to obtain as clear images as possible, and black-over-white OCT images are preferable to white-over-black or colored OCT images (Figure 3). As a result of their examinations, they found that the choroid was thickest under the fovea and thinner at the nasal retina compared to the temporal. Choroid thickness decreases with distance from the fovea. The reason for the maximum subfoveal choroidal thickness is to meet the high oxygen demand of the retinal cells at the fovea. Subfoveal choroidal thickness was measured as 287±76 µm (54 eyes of 30 patients) with the Spectralis and 272±81 µm (34 eyes of 34 patients) with the Cirrus. Both groups showed a negative correlation between choroidal thickness and age.[20] In other words, the choroid thins with increasing age. However, we predict that larger studies of choroidal thickness and the effect of aging on choroidal thickness in normal eyes will yield more quantitative data about this thinning. Furthermore, choroidal thickness of the same individual can vary between measurements taken at different times.[21]

Reproducibility and reliability are basic prerequisites for the utilization of any technique. In EDI-OCT, choroidal thickness measurements are done manually, not automatically. Ikuno et al.[22] studied the reliability and reproducibility of manual normal choroidal thickness measurements on EDI-OCT. In their study, the choroidal thickness of 10 volunteers was measured by 6 different people twice with an interval of 4 months. Interobserver correlation was found to be 0.970 (95% CI, 0.948-0.985) and intervisit correlation was 0.893 (95% CI, 0.864-0.916). In a study comparing the Cirrus, Spectralis and Optovue (Optovue, Inc, Fremont, CA, USA), choroid thickness at five different locations was measured with each of the three devices, and the measurements were strongly correlated ($p<0.0001$).[23]

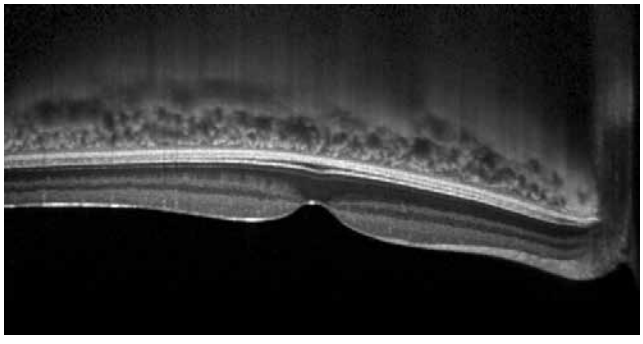

Figure 1. The choroid appears as an inverted image on optical coherence tomography imaging without enhanced depth imaging-optical coherence tomography mode. This image was captured using the Spectralis spectral domain-optical coherence tomography device (Heidelberg Engineering, Heidelberg, Germany)

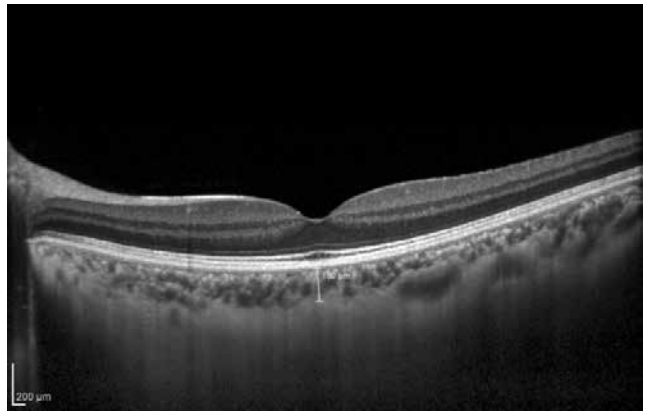

Figure 2. Choroidal thickness measurement at the fovea in a healthy eye. Choroidal thickness is measured manually as the horizontal distance between the outer edge of the hyperreflective retinal pigment epithelium and the inner edge of the choroidoscleral junction

To accurately evaluate choroidal pathologies, normal choroidal morphology on EDI-OCT must be determined in addition to normal choroidal thickness. In a study including 42 subjects, all were shown to have a bowl-shaped choroidoscleral junction, 98.8% of the patients' choroidal vessels were distributed along the nasal-temporal axis, and large choroidal vessels comprised 80% of the subfoveal choroidal thickness.[24]

With current OCT technology, it is not possible to see Bruch's membrane, the first superficial layer of the choroid immediately under the RPE, in normal eyes. The echoes from this tissue cannot be differentiated from the strong signals coming from the RPE. However, in eyes where the RPE has separated from Bruch's membrane (as in PED due to AMD or CSR), Bruch's membrane appears as a thin line of mild hyperreflectivity (Figure 4). Angioid streaks have a known basis in collagen tissue disease, and the histological changes they cause in Bruch's membrane have been known for many years. EDI-OCT of cases with angioid streaks reveals thickening of Bruch's membrane and interruptions in its hyper-reflective line (Figure 5). Folding of Bruch's membrane has been clearly shown on EDI-OCT in hypotony maculopathy (Figure 6).[25]

The choroidal network of capillaries (choriocapillaris) found beneath Bruch's membrane cannot be visualized using current OCT technology. However, the next layer contains mid-sized vessels (choroidal arterioles and venules), which appear as two to four rows of small hyperreflective spots immediately beneath the hyperreflective line of the RPE layer (Figure 7). This layer is referred to as Sattler's layer in some sources, which usually portray it as the first 20-30 microns of choroid under the RPE.[25] The largest vessels, the choroidal arteries and veins, can be distinguished as round or oval shapes deeper in the choroid (Figure 8). This layer is also called Haller's layer.

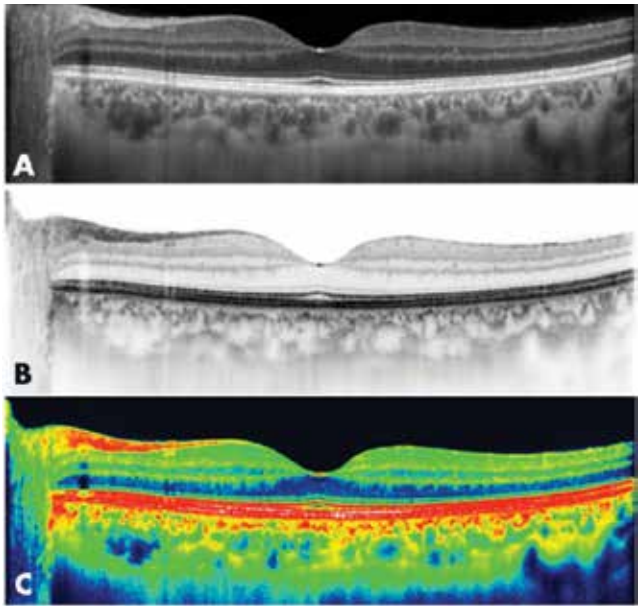

Figure 3. Black-over-white (A) optical coherence tomography images are preferrable to white-over-black (B) or colored (C) optical coherence tomography images for visualization of the choroid

Enhanced Depth Imaging-Optical Coherence Tomography and Chorioretinal Diseases

Central Serous Chorioretinopathy

Central Serous Chorioretinopathy (CSC) is a condition characterized by exudative detachment of the neurosensory retina, and is usually seen in young men. In the acute stage, it appears on OCT as subretinal fluid accumulation and PED. Studies of CSC using ICGA have revealed hyperpermeability of the choroidal vessels that is much greater than expected based on RPE leakage seen on FFA. It is believed that this increased permeability of the choroidal vasculature and RPE barrier dysfunction play an important role in the pathophysiology of the disease.[26]

As the primary pathology in CSC is in the choroid, EDI-OCT is especially important in the diagnosis of the disease (Figure 9).[27] It has also been shown that patients with unilateral CSC have increased choroidal thickness in the unaffected eye,[28] which suggests that there may be bilateral elevated hydrostatic pressure in the choroidal vasculature in CSC. In a comparison of photodynamic therapy and laser photocoagulation in patients with chronic CSC, it was shown with EDI-OCT that photodynamic therapy resulted in a decrease in choroidal thickness, whereas this effect was not observed after laser photocoagulation.[29] Therefore, EDI-OCT can be used in the differential diagnosis of CSC from serous retinal detachment and

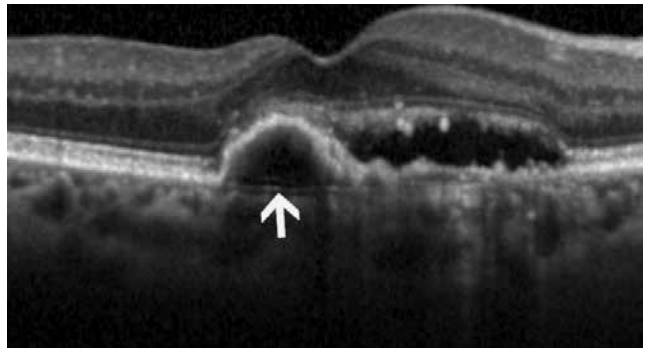

Figure 4. Bruch's membrane (white arrow) in an age-related macular degeneration patient with pigment epithelial detachment

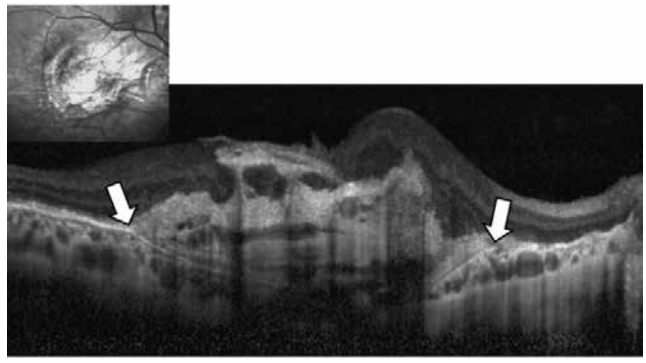

Figure 5. Thickening of Bruch's membrane and breaks in its hyperreflective line (white arrows) in a patient with angioid streaks

in the follow-up of CSC patients. Furthermore, we believe EDI-OCT data are valuable in the identification of patients that may show susceptibility to CSC, which is important in order to warn these patients of factors that may trigger CSC attacks.

Age-Related Macular Degeneration

AMD is one of the leading causes of blindness in individuals over 60 years old, especially in developed countries.[30] OCT is currently the imaging method most frequently utilized in the diagnosis, treatment planning and follow-up of AMD patients. OCT enables detailed detection of changes in the retina and RPE layer of AMD patients and even allows the identification of disease subtypes. As with CSC, it is currently widely accepted that the choroid is the primary tissue responsible for AMD. Therefore, evaluation of the choroid by EDI-OCT is of major importance in AMD patients; there are hundreds of studies in the literature on this topic.

In practical terms, the main application of EDI-OCT in AMD is the recognition of patients with polypoidal choroidal vasculopathy (PCV). Several studies using EDI-OCT have shown greater subfoveal choroidal thickness in PCV compared to other AMD subgroups (Figure 10).[31] This choroidal thickening occurs due to dilation of the mid-sized and large choroidal vessels and an increase in the choroidal vascular permeability seen on ICGA. This OCT finding is crucial because PCV, the frequency of which has not been determined in Turkey, is known to be resistant to anti-VEGF injection, the accepted standard treatment for AMD. PCV cannot be detected by FFA; the polypoidal structures of PCV can be detected with a difficult and expensive procedure like ICGA. Therefore, PCV must be considered upon observation of a thick choroid in AMD patients. Other important OCT findings that support a PCV diagnosis are the presence of RPE elevations similar but sharper than those found in PED with neighboring RPE irregularities.[25]

Another advantage of EDI-OCT in AMD is the opportunity to examine the interior of PED. In a study of 22 eyes, Spaide[32] showed regression of a hyper-reflective structure within the PED after anti-VEGF therapy, suggesting that CNV is present and leads to the formation of PED. EDI-OCT was used in another study to detect choroidal thickness changes in AMD patients after anti-VEGF therapy.[33] These studies may be valuable for guiding anti-VEGF treatment protocols, especially when

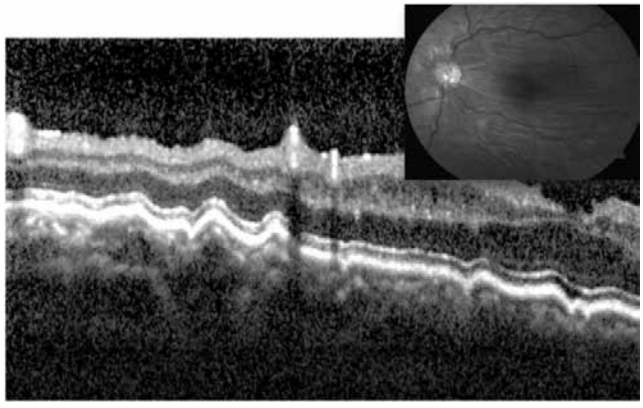

Figure 6. Enhanced depth imaging-optical coherence tomography reveals folding of Bruch's membrane in hypotony maculopathy

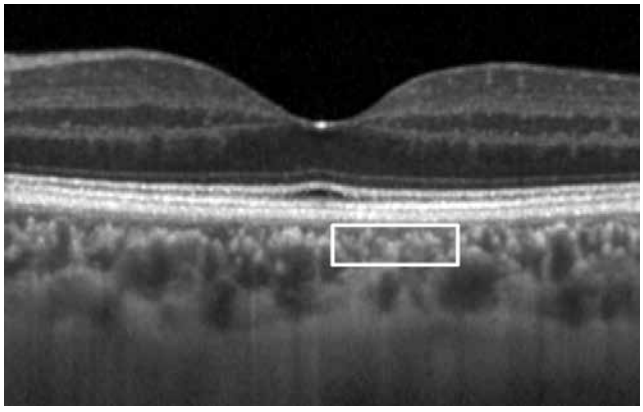

Figure 7. Beneath the hyperreflective retinal pigment epithelium, medium diameter choroidal vascular structures typically appear as two to four rowls of small, hyperreflective spots (white box). This layer is sometimes referred to as Sattler's layer

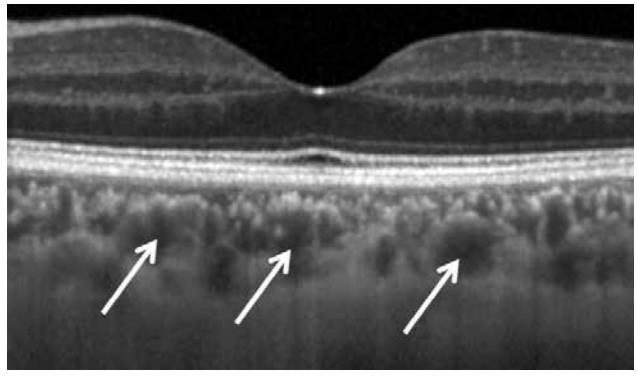

Figure 8. Choroidal arteries and veins are indicated with white arrows. This layer comprises the largest choroidal vessels and is also called Haller's layer

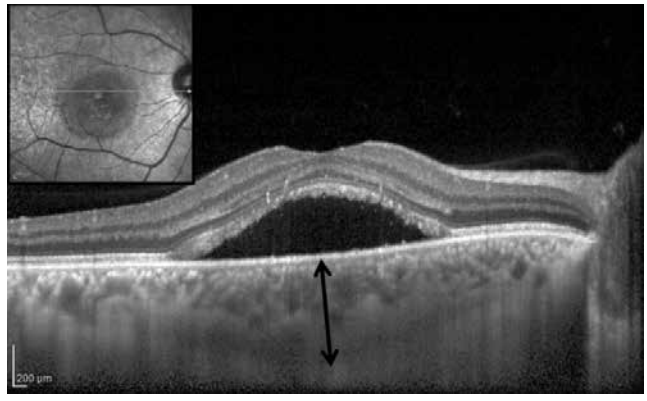

Figure 9. Thickened choroid in an eye with central serous retinopathy. Subfoveal choroidal thickness (black arrow) is 542 microns

discussing a side effect like the development of geographic atrophy.

EDI-OCT also enabled the identification of age-related choroidal atrophy, the basic pathology of which is advanced atrophic choroid. Age-related choroidal atrophy is characterized by an extremely thin choroid (without high myopia), senile sclerotic glaucoma, macular pigmentary changes, and severe impairment of near vision compared to far vision. The condition is generally seen in patients between 70 and 80 years old, and EDI-OCT is the principal diagnostic method.[4]

Degenerative Myopia

Myopia is a refractive error resulting from a discrepancy between the eye's optic power and its length. Degenerative myopia is a pathological condition with progressive lengthening of the eye, thinning of the sclera and choroid, and accompanying degenerative changes in the retina and RPE. Macular CNV and retinal detachment are frequently seen in these eyes and may lead to severe vision loss.[34]

The most important OCT finding in degenerative myopic eyes is an extremely thin choroid (Figure 11). Fujiwara et al.[35] demonstrated with EDI-OCT that choroidal thickness was significantly decreased in patients with high myopia. They also found that choroidal thickness was negatively correlated with age, refractive error, and presence of CNV. Myopic CNV causes less leakage than CNV in AMD and can be treated with less invasive therapies because choroidal vasculature supplying the CNV is not atrophic. Thus, much less subretinal accumulation is seen in myopic CNV compared to cases of AMD, which reduces the ability of OCT to show activity in myopic CNV.[25]

Glaucoma

EDI-OCT is an important diagnostic method for understanding the vascular pathogenesis of glaucoma. Both macular and peripapillary choroidal thinning are used to investigate this pathogenesis. In studies of normal peripapillary macular thickness measurements, the inferior quadrant was significantly thinner than the superior quadrant, and the nasal quadrant was significantly thinner than the temporal quadrant.[36]

Maul et al.[37] used EDI-OCT to evaluate whether choroidal thickness was associated with parameters such as age, axial length and nerve fiber layer, and found no significant difference between the peripapillary and macular choroidal thicknesses of patients with suspected glaucoma and patients with a glaucoma diagnosis. Many other studies have also shown that glaucoma does not affect choroidal thickness.[38,39,40]

The lack of significant changes in the macular choroidal thickness of glaucoma patients with severe visual field and retinal nerve fiber layer loss supports the view that there is no association between glaucoma and the macular choroid. Even in unilateral glaucoma cases there is no difference in macular choroidal thickness between the two eyes, which allows the elimination of systemic factors.

Diabetic Retinopathy

Our clinical experience suggests that choroidal vasculopathy is an important factor in the pathogenesis of diabetic retinopathy. Some histopathologic studies of diabetic eyes have shown various choroid pathologies like choroidal anomalies, choriocapillaris occlusion, CNV and choroidal aneurysm.[41]

Particularly in type 2 diabetes, choroidal thinning has been found in all eyes independent of the severity of retinopathy.[42] This supports the reduced speed of the choroidal circulation previously demonstrated by laser Doppler flowmetry and ICGA.[43] Because the choroid is the principal vascular structure nourishing the outer retinal layers and the RPE, choroidal thinning can result in hypoxia of the retinal tissues.

Vogt-Koyanagi-Harada Syndrome

OCT allows a noninvasive evaluation of uveitis patients, in whom investigation of the posterior segment is particularly challenging; therefore, SD-OCT is gaining popularity in the examination of uveitis patients.[44]

VKH is bilateral granulomatous panuveitis associated with autoimmunity against melanocytes. It is characterized by

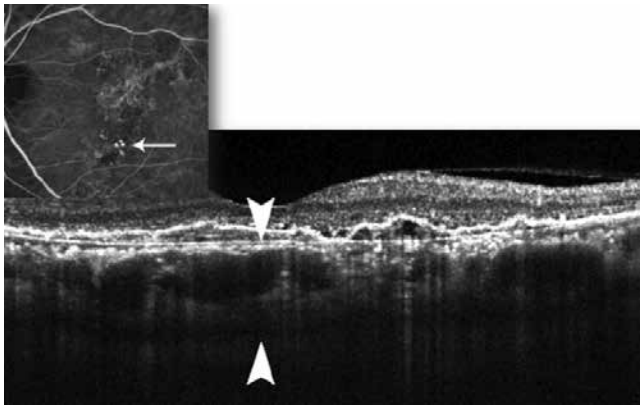

Figure 10. Thickened choroid in polypoidal choroidal vasculopathy

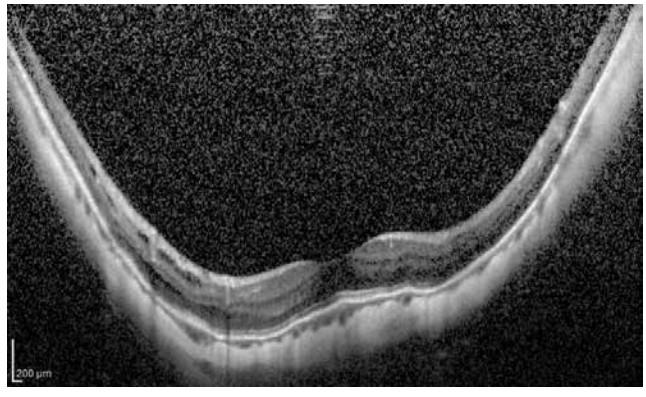

Figure 11. Vertical optical coherence tomography sections reveal extremely thin choroid in an eye with refractive error of -14.00 diopters

bilateral anterior and posterior uveitis with exudative retinal detachment.[45] Increased choroidal thickness is seen in VKH, likely due to the inflammatory process and exudation.[46] A significant reduction in the choroidal thickness of VKH eyes has been shown within two weeks of steroid treatment.[47] Choroidal thickness evaluation is important for the assessment of treatment efficacy and the follow-up of recurrences.

Conclusion

The EDI-OCT technique used with SD-OCT devices enables in vivo cross-sectional visualization of the choroid that is simple, reproducible, high-resolution and noninvasive, and has provided a better understanding of the choroidal changes that occur in many pathologies. However, this technique also has some limitations. One of the major drawbacks of the technique is that software allowing automated measurement of the choroid has not yet been developed. Manual measurement takes time and can result in inaccuracies. Eye tracking systems are necessary on OCT devices to ensure that the simultaneous images are taken at the same position. Another shortcoming of EDI-OCT is that in certain eyes, especially those with media opacities, relatively clear images of the retina can be obtained but the choroidoscleral junction cannot be clearly visualized.

The continuing search for new choroidal imaging technology has led to both software and hardware innovations like swept source OCT, Doppler OCT, long wavelength SD-OCT and en face OCT, and will remain a topic of interest for many years to come.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Taha Sezer, Muhammet Altınışık, İbrahim Arif Koytak, Mehmet Hakan Özdemir, Design: Taha Sezer, Muhammet Altınışık, İbrahim Arif Koytak, Mehmet Hakan Özdemir, Data Collection or Processing: Taha Sezer, Muhammet Altınışık, Analysis or Interpretation: Mehmet Hakan Özdemir, İbrahim Arif Koytak, Literature Search: Taha Sezer, Muhammet Altınışık, Mehmet Hakan Özdemir, Writing: Mehmet Hakan Özdemir, Taha Sezer, Muhammet Altınışık.

Conflict of Interest

No conflict of interest was declared by the authors.

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Case Report

Transpupillary Argon Laser Cyclophotocoagulation in a Refractory Traumatic Glaucoma Patient with Aphakia and Aniridia

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Summary

We present a case of transpupillary argon laser cyclophotocoagulation (TALC) in a patient with traumatic aniridia and aphakia secondary to blunt trauma who had previous bilateral trabeculectomy. Four months after the trauma the patient's intraocular pressure (IOP) rose to 35 mmHg despite topical antiglaucomatous medication. Inferior 180 degrees cyclophotocoagulation was performed with transpupillary argon laser in the first session and his IOP fell to values of 12-17 mmHg. Twelve weeks after TALC, his IOP rose to 22 mmHg and we had to apply TALC to the residual ciliary processes. Seven months later his IOP was 13 mmHg with topical dorzolamide/timolol and latanoprost administration. TALC may be an effective treatment alternative for lowering IOP in patients with visible ciliary processes who do not respond to conventional medical or laser treatment.

Keywords: Transpupillary argon laser cyclophotocoagulation, traumatic aniridia, aphakia, glaucoma

Introduction

Transpupillary argon laser cyclophotocoagulation (TALC) is an alternative cyclodestructive procedure in selected patients with glaucoma.[1,2,3] This procedure includes argon laser photocoagulation of the ciliary processes after visualization with a goniolens. The proportion of visualized ciliary processes depends on the extent of iris defect, which ranges from peripheral iridectomy to aniridia.

Case Report

A 55-year-old man who had been followed up at our glaucoma unit for 5 years with the diagnosis of primary open-angle glaucoma (POAG) presented with sudden loss of vision and pain in his right eye after a blunt trauma sustained from a fist during a physical confrontation. The patient had a history of bilateral trabeculectomy 2 years earlier. On initial examination after the blunt trauma to the right eye, visual acuity was light perception and the eye had a corneoscleral laceration approximately 5 mm long extending from the previous trabeculectomy incision. The iris was totally dialyzed and prolapsed from the wound along with the crystalline lens. After removal of the totally prolapsed iris and extruded crystalline lens, anterior vitrectomy and repair of the corneoscleral laceration with 10-0 nylon suture were performed. The intraocular pressure (IOP) was between 12-18 mmHg with topical anti-glaucomatous medication for a period of 4 months after the trauma. His IOP rose to 35 mmHg despite administration of topical latanoprost, dorzolamide/timolol fixed combination and brimonidine in the 4th month. Uncorrected visual acuity (UCVA) was hand motion, best corrected visual acuity (BCVA) was counting fingers from one meter with aphakic spectacle correction in the right eye and 20/20 in the left eye. IOP in the left eye was 13 mmHg with latanoprost and dorzolamide/timolol fixed combination. Clear cornea, quiet anterior chamber, aphakia and total aniridia were seen on slit-lamp examination of the right eye (Figure 1). Dilated fundus examination of the right eye revealed a normal retina and a glaucomatous optic nerve head with a cup-to-disc ratio of 0.9. Slit-lamp examination was normal and the cup-to-disc ratio was 0.7 in the left eye. The ciliary body was normal except the superior degenerated area of 60 degrees in the right eye (Figure 2). Surgical intervention (trabeculectomy with antimetabolite or tube shunt implantation) was planned to reduce the IOP. Complications of glaucoma surgery were explained to the

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patient, but we had to take into account alternative IOP reducing procedures due to patient's refusal of any surgical intervention. Therefore, we planned TALC for the right eye to lower IOP.

A Goldmann three-mirror lens was placed onto the right eye after instillation of 0.5% proparacaine hydrochloride (Alcaine, Fort Worth, Texas, USA) in the laser therapy room. Methylcellulose was placed on the contact surface of the lens to fill the lens-cornea interface. The argon laser settings were 700 mW power, 100 µm spot size, and 0.1 seconds exposure time (Visulas 532s, Carl Zeiss Meditec AG, Jena, Germany). A total of 145 laser exposures were administered through the Goldmann contact lens to the inferior 180 degrees of the ciliary processes. We avoided performing 360-degree argon laser cyclophotocoagulation of the right eye due to the risk of phthisis bulbi. The patient did not report any remarkable pain or discomfort during laser treatment.

The patient was treated with dorzolamide/timolol fixed combination, latanoprost and topical ketorolac tromethamine after TALC. The anterior chamber was quiet, despite the lack of steroid treatment. The IOP ranged between 12-17 mmHg during the first 12 weeks after TALC. In the 12th week, IOP raised to 22 mmHg, so we performed TALC to the residual healthy ciliary processes of the right eye. A total of 105 exposures were administered using the same settings specified above.

Seven months after the TALC procedure, the patient's UCVA was counting fingers from one meter, BCVA was 20/200 with aphakic contact lens correction, and the diurnal mean IOP was 13 mmHg with topical dorzolamide/timolol and latanoprost administration. The ciliary processes were seen as atrophic on gonioscopy (Figure 3).

Discussion

Refractory glaucoma is a difficult condition to manage. In cases who are unresponsive to medical, laser, and surgical treatments for lowering IOP, drainage procedures, such as trabeculectomy with antimetabolite, are potential solutions but may be associated with a series of complications including hypotony, leaking blebs, and endophthalmitis.[4] Bloom et al.[5] showed that tube surgery, Nd-YAG laser, and diode laser cyclophotocoagulation all effectively lower IOP in the short and medium term in refractory glaucoma. They also reported that tube surgery was associated with a greater incidence of sight-threatening complications, despite its better control of IOP in refractory glaucoma. Kaplowitz et al.[6] reported in their review that the visual outcomes were better with endoscopic cyclophotocoagulation (ECP) when compared with both trabeculectomy and aqueous shunt implantation, but the IOP outcomes were very similar. They concluded that ECP as a very effective and safe option in cases with refractory glaucoma.

When done as an outpatient procedure, TALC of the ciliary processes also shows promise as a convenient, low-risk, and useful alternative procedure in selected aphakic glaucoma cases that are poorly controlled by medical or surgical measures. Kim and Moster[1] reported a case who had a significant decrease in

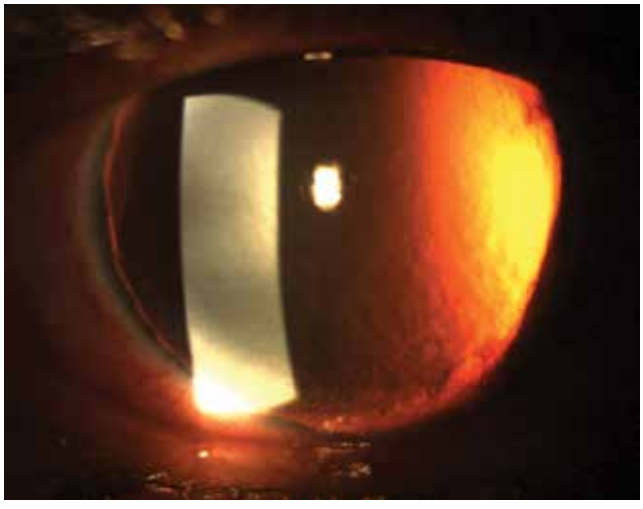

Figure 1. Anterior segment photograph of the right eye showing the aniridia and aphakia

Figure 2. Gonioscopic photograph of the right eye showing the ciliary processes before transpupillary argon laser cyclophotocoagulation

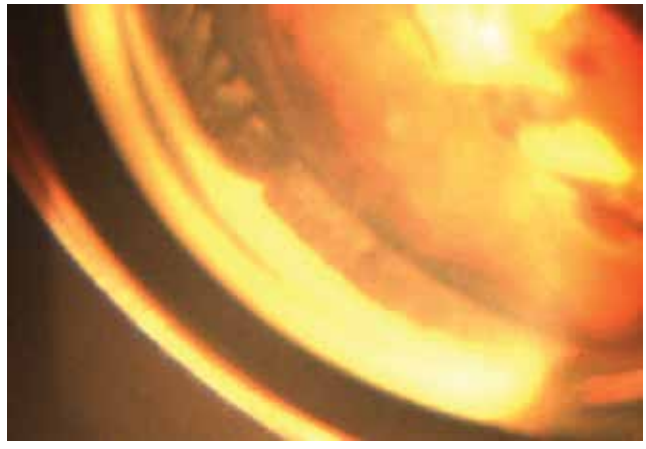

Figure 3. Gonioscopic photograph of same region of showing the ciliary processes 7 months after transpupillary argon laser cyclophotocoagulation

IOP 10 weeks after TALC. Shields et al.[7] reported a successful outcome in 6 of 27 patients. Merritt[8] reported that only one in seven patients had a significant decrease in IOP after TALC and that patient had the largest proportion of their ciliary processes treated in the series. The author concluded that the limiting factor in effective TALC may be the total number of ciliary processes visualized and treated.[8] In our case, the IOP lowering effect was limited when TALC was applied to only 180 degrees of the ciliary processes. The IOP lowering effect was increased when TALC was applied to all healthy ciliary processes. We did not observe any inflammatory reaction, so we believe that TALC is a repeatable procedure without any serious side effects.

Conclusion

Aphakia may negatively affect the success rate of penetrating glaucoma surgery or tube shunt implantation due to blockage of the new drainage route by the vitreous. Thus, treatment alternatives that aim to reduce aqueous humour production may be chosen primarily in aphakic patients. TALC may be an effective treatment alternative for lowering IOP in patients with visible ciliary processes who do not respond to conventional medical or laser treatment. This approach may also be used as an adjunct to the medical and/or surgical management of selected glaucoma cases with aniridia and aphakia. TALC is a treatment which can be done under topical anesthesia and does not cause serious inflammation, so it may help physicians gain time to select the appropriate treatment for the patient. Future studies with large case series may shed more light on the advantages and limitations of this procedure.

Ethics

Informed Consent: It was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Umut Duygu Uzunel, Concept: Umut Duygu Uzunel, Berna Yüce, Tuncay Küsbeci, Halil Ateş, Design: Umut Duygu Uzunel, Berna Yüce, Tuncay Küsbeci, Halil Ateş, Data Collection or Processing: Umut Duygu Uzunel, Analysis or Interpretation: Umut Duygu Uzunel, Berna Yüce, Tuncay Küsbeci, Halil Ateş, Literature Search: Umut Duygu Uzunel, Berna Yüce, Tuncay Küsbeci, Halil Ateş, Writing: Umut Duygu Uzunel, Berna Yüce, Tuncay Küsbeci, Halil Ateş.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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Case Report

Peripheral Vasculitis, Intermediate Uveitis and Interferon Use in Multiple Sclerosis

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Summary
Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system. A 40-year-old female patient with a 12-year history of MS was admitted to our clinic with blurred vision and floaters in her right eye for about 1 month. Here, we share the findings and the management of intermediate uveitis and retinal periphlebitis in an MS case being treated with interferon beta-1a for 7 years.
Keywords: Multiple sclerosis, intermediate uveitis, peripheral vasculitis, interferon

Introduction

The most common ocular sign in multiple sclerosis (MS) patients is optic neuritis, although uveitis may also be present at a rate varying between 0.4 and 26.9%. Uveitis is more common among women between 20 and 50 years of age; although chronic, the long-term visual prognosis is usually good. Intermediate uveitis is the most common form of uveitis seen in MS and is characterized by vitreous condensation and snowball-like structures in the pars plana and peripheral retina. Retinal periphlebitis may occur in 5-36% of cases, presenting with exudation and vascular sheathing due to the accumulation of inflammatory cells.[1] The association between MS and retinal vein sheathing was first described by Rucker[2] in 1944. Rucker[2] reported that retinal vasculitis was mild, temporary and asymptomatic, especially in patients with only periphlebitis, without the presence of choroiditis.

Medications such as interferon beta-1a (IFN-β-1a) (intramuscular and subcutaneous forms), IFN-β-1b, glatiramer acetate, natalizumab and mitoxantrone are currently used in the long-term treatment of MS and have a positive impact on the course of the disease. In clinical studies, IFN-β has been shown to decrease the frequency of attacks and slow disease progression. Interferons also have immune system suppressing, anti-inflammatory effects. IFN-β prevents proinflammatory cytokine production and antigen presentation by inhibiting T cell activation. It also shows an immunomodulatory effect by preventing the migration of lymphocytes into the central nervous system, thus preventing demyelination and decreasing the frequency and severity of MS attacks.[3]

Case Report

A 40-year-old female patient presented to our clinic with complaints of blurred vision and floaters in the right eye for 1 month. She had a 12-year history of MS and had been treated with intramuscular IFN-β-1a (Avonex® 30 μg [6 million IU]) once a week for the previous 7 years. Her visual acuity was measured as 1.0 in both eyes using the Snellen chart. Her pupils were isochoric and a relative afferent pupillary defect was observed in her right eye. In the Farnsworth-Munsell 40 Hue test, her color vision was 18/40 in the right eye and 26/40 in the left eye. Slit-lamp examination of the anterior segment of both eyes was normal and no inflammation was observed. Intraocular pressure was 15 mmHg in the right eye and 16 mmHg in the left as measured by Goldmann applanation tonometry. Ophthalmoscopic examination revealed vitritis (+1), widespread perivenous sheathing in the peripheral retina, and exudation in both eyes, but more pronounced in the right eye (Figure 1). On fundus fluorescein angiography (FFA) of the right eye, staining

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around the major arc and hyperflorescence due to minimal vascular leakage in the perivenous segments were observed; FFA in the left eye revealed staining of the vessel walls of the inferior temporal vein branches (Figure 2).

On pattern visual-evoked potential (pVEP) analysis, the p100 latency and amplitude were 112.20 ms and 12.3 μV in the right eye, 117.60 ms and 12.3 μV in the left eye, respectively (Figure 3). Localized visual field defects were observed in the right eye on automatic static perimetry (Octopus 500), while the left eye was normal. Cranial magnetic resonance imaging revealed multifocal demyelinating plaques in the periventricular area (Figure 4). The patient had perfect visual acuity (1.0) in both eyes, so she was advised to continue systemic IFN-β-1a without additional ophthalmologic treatment. She was followed for two years and was clinically stable; at last examination her vision was perfect (1.0) in both eyes. Slit-lamp examination revealed (+1) cells in the anterior vitreous of both eyes. Perivenous sheathing and snowball-like exudations were observed in the anterior quadrants of both eyes during fundoscopic examination. On follow-up FFA, persistent perivenous staining and minimal vascular leakage were observed. Macula edema was not apparent in either eye on optic coherence tomography (OCT) and the retinal nerve fiber layer at the optic disc appeared normal (Figure 5).

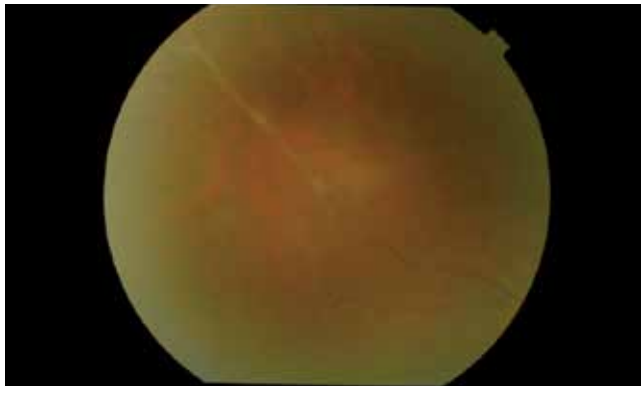

Figure 1. Perivenous sheathing and exudation in the peripheral retina of the right eye

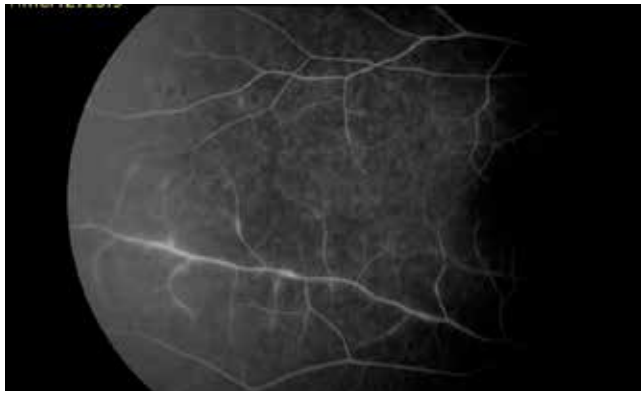

Figure 2. Hyperfluorescence due to with segmental minimal vascular leakage in the right eye

Discussion

MS patients may show signs of ocular inflammation such as uveitis, pars planitis or retinal vasculitis. Periphlebitis is more common in the active phase of MS, and leakage due to perivenous inflammation may be observed on FFA.[4] Yılmaz et

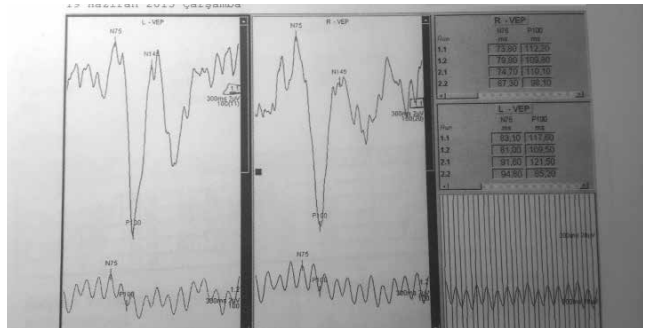

Figure 3. Pattern visual-evoked potential analysis revealed significant p100 latency delays in both eyes

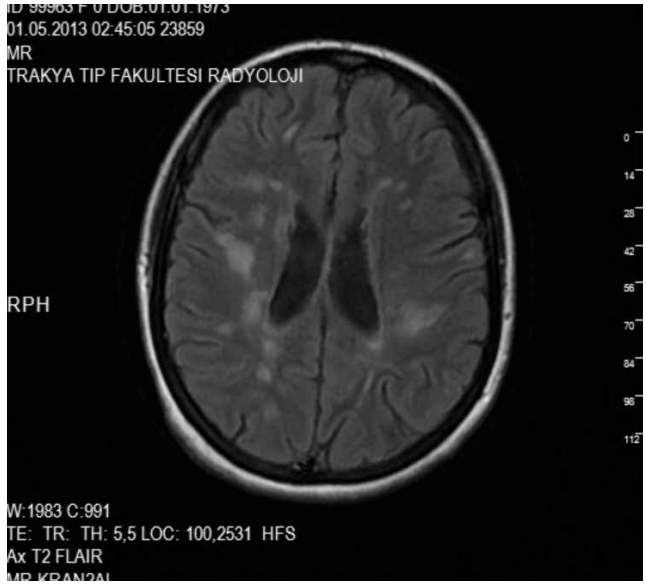

Figure 4. Cranial magnetic resonance imaging showing multifocal demyelinating plaques in the periventricular area

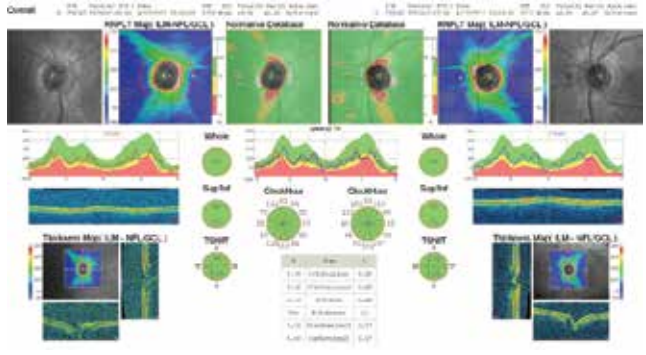

Figure 5. Retinal nerve fiber layer thickness at the optic disc was within normal range in both eyes

al.[5] reported an MS patient with bilateral iridocyclitis and retinal periphlebitis, but they could not show perivenous leakage on FFA. In our case, the appearance of perivenous leakage on FFA suggests that the inflammation was active, although it was not severe.

In our patient, the presence of relative afferent pupillary defect in the right eye, impaired color vision in both eyes, and significantly prolonged p100 latency on pVEP were considered evidence of previous optic neuritis attack and optic nerve demyelination.

IFN decreases ocular inflammation in MS patients. It has been shown to prevent the development of macular edema by decreasing vascular leakage, especially in the posterior segment. Okada et al.[6] demonstrated clinically and histopathologically that IFN treatment was effective in decreasing ocular inflammation in rats with experimentally induced autoimmune uveoretinitis.

There are a limited number of studies investigating treatment approaches in cases with both MS and uveitis. In a case series of 13 patients with MS and uveitis, Becker et al.[7] reported that IFN-β-1a was effective in suppressing intraocular activity and preserving visual acuity. In a study conducted in Turkey including 8 patients with MS-related uveitis being treated with IFN-β-1a, it was reported that visual acuity was largely protected and MS attack frequency and risk of serious complications were reduced.[8] Our case used systemic IFN-β-1a for 7 years, and we also observed that retinal periphlebitis and intermediate uveitis findings were under control, visual acuity had been protected for 2 years, and there were no signs of macular edema.

Wakefield et al.[9] reported uveitis attacks characterized by serious visual acuity decline and cystoid macular edema in a series of 5 MS patients not receiving long-term immunomodulatory therapy. After just 7 days of treatment with high-dose (1 g/day) intravenous pulse methylprednisolone, the patients' visual acuity improved and ocular inflammation was decreased.

It was reported that retinal vasculitis was much more severe in an MS patient using glatiramer acetate, and that it was necessary to perform panretinal photocoagulation for the regression of the retinal neovascularization and preretinal hemorrhage.[10]

IFN therapy seems to be a superior treatment option due to its anti-inflammatory effects before the development of ocular inflammation, which improves the prognosis of uveitis attacks, and also because it is safer than systemic corticosteroids in terms of side effects.

Conclusion

Ocular inflammation such as intermediate uveitis and retinal periphlebitis may occur in MS. In patients using IFN, ocular inflammation may be mild and asymptomatic, and visual acuity can be protected without the need for additional ophthalmologic treatment.

Ethics

Informed Consent: It was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Şeref Kinyas, Concept: Şeref Kinyas, Design: Şeref Kinyas, Haluk Esgin, Data Collection or Processing: Şeref Kinyas, Analysis or Interpretation: Şeref Kinyas, Haluk Esgin, Literature Search: Şeref Kinyas, Writing: Şeref Kinyas.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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Case Report

Secondary Glaucoma Associated with Encircling Scleral Buckle Migration into the Cornea

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Summary
Transmuscular migration of the encircling band through rectus muscles and straddling of the cornea has only been reported in a few cases previously in the literature. This rare condition has never been associated with glaucoma. In this report, we aimed to describe a unique case with transmuscular migration of encircling buckle as a probable cause of glaucoma. A 17-year-old female presented with transmuscular migration of buckle and high intraocular pressure (IOP). Limbal/corneal migration of the silicone band was thought to be the main reason for the IOP rise; therefore, scleral band removal was performed. One month after removal, the patient was free of glaucoma medications and IOP was within normal limits. The retina remained attached during all postoperative visits. Transmuscular migration of the encircling band through rectus muscles and straddling of the cornea may act as a trigger for glaucoma.
Keywords: Scleral buckle, migration, glaucoma

Introduction

Scleral buckling surgery is a commonly used surgical technique in the management of rhegmatogenous retinal detachment (RD). Extrusion, erosion, and intrusion of scleral buckling elements are rare yet significant complications of the scleral buckling procedure. These complications are more common with radial sponge material; however, they also occur as a rare complication with encircling silicone bands.[1] Transmuscular migration of the encircling band through rectus muscles and straddling of the cornea has only been reported in a few cases previously in the literature.[2,3,4,5] In this report, we aimed to describe a unique case with transmuscular migration of encircling buckle, which probably acted as a trigger for glaucoma.

Case Report

A 17-year-old female with vitreous hemorrhage and retinal detachment secondary to penetrating eye injury in the right eye underwent encircling silicone band surgery using 240S 2.4 mm silicone band together with pars plana vitrectomy, lensectomy, endolaser and silicone oil tamponade in October 2007. After surgery, the primary suturation zone of the penetrating injury appeared as a broad radial line extending from central cornea to peripheral infero-temporal zone. Iris loss in the same quadrant and aphakia were also noted. Glaucoma medications were administered for a short time after the surgery to prevent post-operative/traumatic intraocular pressure (IOP) spikes. Three weeks after the surgery, the patient was free of glaucoma medications and her IOP was 16 mmHg in that eye. The silicone oil was removed 3 months later and the retina was attached at all postoperative visits. Her corneal scarring, aphakia and slightly pale optic disc persisted (Figure 1). Her visual acuity was counting fingers from 4 meters with aphakic correction 3 months after silicone oil removal. IOP was 17 mmHg. She was discharged without any ocular medication and continued the follow-up visits in her hometown with her primary ophthalmologist.

Two years after silicone oil removal, the patient was referred again to our clinic because of intractable IOP increase. Her visual acuity was hand motions and IOP was 42 mmHg in the right eye. On slit-lamp examination, the most prominent finding in the anterior segment evaluation was the view of encircling silicone band at the nasal limbal intrastromal cornea and under

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the conjunctiva at the superior and inferior nasal quadrants (Figure 2a, 2b). There was no restriction in ocular movements. Gonioscopically, the band was seen to be positioned within the cornea and projected as a ridge into the anterior chamber with close proximity to the trabecular meshwork. No iris or angle neovascularization were observed. On fundoscopic examination, the retina was attached and the optic nerve was pale.

Limbal/corneal migration of the silicone band was thought to be the main reason for the IOP rise; therefore scleral band removal was planned. Surgery was performed under local anesthesia. Inferotemporal conjunctival incision was used to reach the silicone band and the suture knot was cut to relieve the band. The sclera under the band was very necrotic and the choroid was clearly visible. The silicone band could easily be pulled out without any resistance and the movement of the band could be observed through the nasal limbal-corneal migration area (Figure 3a, 3b). After the removal, a mild leakage of sero-hemorrhagic fluid from the nasal iridocorneal angle filling the intrastromal groove was noticed (Figure 3c). The patient's IOP in the right eye was 20 mmHg on the first postoperative day and fell to 16 mmHg within two weeks with anti-glaucoma topical medication. One month after the surgery the patient was again free of glaucoma medications and her IOP was 15 mmHg. The retina remained attached during all postoperative visits.

Discussion

Only a few cases of anterior transmuscular migration and intracorneal localization of the encircling band have been reported.[1,2,3,4,5] The 'cheesewiring' process, which means spontaneous reattachment of muscle fibers to the sclera after erosion by the band, has been suggested to explain transmuscular migration. Similar to our case, in most of the cases no ocular motility problem has been observed.[1,2,3] Kreis et al.[4] reported the only case causing vertical diplopia. Saatci et al.[2] reported a case of an encircling band causing corneal groove formation where the band was observed under intact corneal epithelium. The corneal groove disappeared following the band removal surgery. In another intracorneal encircling band case by Lopez et al.,[3] the band was reported to be embedded deeper in the corneoscleral junction, and because the patient was asymptomatic, the encircling band was left at that position. In addition, Pearce and Roper-Hall[5] reported a silicone strap case, eroded through the sclera and located intracorneally, which projected into the anterior chamber and caused iritis. None of those cases were determined to cause secondary glaucoma.

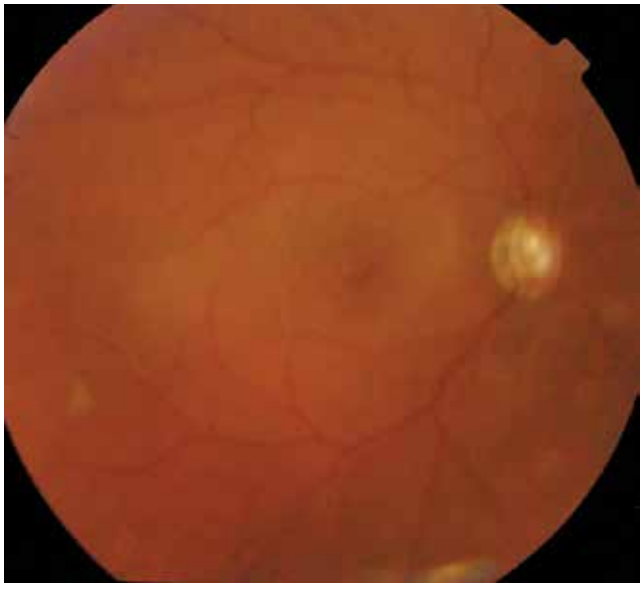

Figure 1. Fundus view of the patient after silicone oil removal. Slightly pale and tilted optic disc and attached retina can be seen. Note the fundus view is a bit cloudy because of the corneal scar

Conclusion

In the presented case, severe IOP rise was observed after migration of the buckle. Due to the co-appearance of glaucoma and the intracorneal silicone band, the former was thought to be secondary to the latter. Therefore, the decision to remove the encircling band was made. The mechanism for IOP rise may be explained with the localization of the band at the deeper corneoscleral junction, which might narrow the iridocorneal angle and partially prevent aqueous humour out-flow. The almost immediate postoperative normalization of the patient's IOP supports this idea. On the other hand, previous ocular

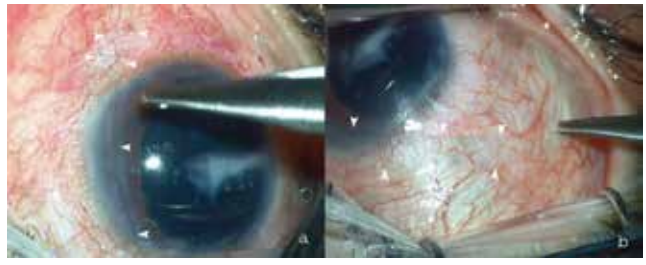

Figure 2. Anterior segment photos prior to silicone encircling band removal. Silicone band can easily be seen in the cornea at the nasal quadrant (a) and under the conjunctiva at the superotemporal quadrant (b) (White arrowheads)

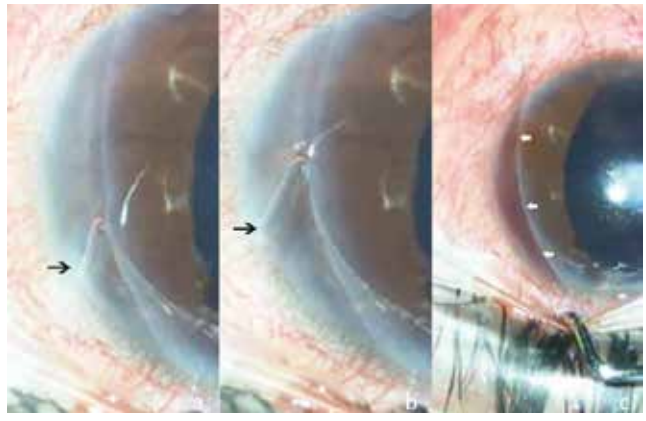

Figure 3. Silicone band leaving an intracorneal groove during removal from the cornea. The free edge of silicone band is marked with black arrows (a,b). Sero-hemorrhagic fluid filling the intrastromal groove after complete removal of silicone band (white arrows) (c)

trauma, presence of aphakia and previous vitrectomy could all be predisposing factors to IOP rise in this patient. Meticulous follow-up is crucial in order to observe any kind of secondary glaucoma and preserve the patient's vision.

To the best of our knowledge, this is the first case of limbal intracorneal migration of encircling buckle as a cause of elevated IOP.

Ethics

Informed Consent: It was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Şengül Özdek, Zeynep Aktaş, Ufuk Adıgüzel, Concept: Şengül Özdek, Murat Hasanreisoğlu, Design: Şengül Özdek, Murat Hasanreisoğlu, Data Collection or Processing: Şengül Özdek, Murat Hasanreisoğlu, Analysis or Interpretation: Şengül Özdek, Murat Hasanreisoğlu, Literature Search: Murat Hasanreisoğlu, Writing: Şengül Özdek, Murat Hasanreisoğlu.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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2016 INTERNATIONAL CONGRESSES

World Ophthalmology Congress (WOC)
5-9 February 2016 - Guadalajara, Mexico
http://www.woc2016.org

European Society of Cataract and Refractive Surgeons (ESCRS) 20th Winter Meeting
26-28 February 2016 - Athens, Greece
http://www.escrs.org/athens2016/

American Association for Pediatric Ophthalmology and Strabismus (AAPOS) 42nd Annual Meeting
6-10 April 2016 - Vancouver, BC Canada
http://www.aapos.org/meeting/2016_annual_meeting/

Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting
1-5 May 2016 - Seattle, USA
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American Society of Cataract and Refractive Surgery (ASCRS) Annual Meeting
6-10 May 2016 - New Orleans, USA
http://www.ascrs.org/

16th European VitreoRetinal Society (EVRS) Meeting
5-7 June 2016 - Monaco
http://www.evrs.eu

12th European Glaucoma Society (EGS) Congress
19-22 June 2016 - Prague, Czech Republic
http://www.egs2016.org

American Society of Retina Specialists (ASRS) Meeting
10-14 August 2016 - San Francisco, USA
http://www.asrs.org/annual-meeting

54th International Society for Clinical Electrophysiology of Vision (ISCEV) Symposium and Courses
13-18 August 2016 - Singapore
http://www.iscev.org/symposia/2016/index.html

9th International Symposium on Uveitis
18-21 August 2016 - Dublin, Ireland
http://uveitis2016.ie/

16th European Society of Retina Specialists (EURETINA) Congress
8-11 September 2016 - Copenhagen, Denmark
http://www.euretina.org/copenhagen2016/default.asp

34th European Society of Cataract and Refractive Surgeons (ESCRS) Congress
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http://www.escrs.org/

American Association for Pediatric Ophthalmology and Strabismus (AAPOS)/Strabismus and Pediatric Ophthalmological Society of India (SPOSI) Joint Conference: An Intercontinental Perspective of Pediatric Ophthalmology & Strabismus
2-4 December 2016 - Jaipur, India
http://www.aapos.org/meeting/2016_joint_meeting_jaipur_india_/

2016 NATIONAL CONGRESSES

Turkish Ophthalmological Society (TOS) Winter Symposium
22-24 January 2016 - Antalya, Turkey
http://todnet.org/KisSempozyumu2016/

TOS Cataract and Refractive Surgery Subsociety Live Surgery Symposium
20-21 February 2016 - İstanbul, Turkey
http://todnet.org/KRC-CanliCerrahi2016/

TOS March Symposium
11-13 March 2016 - Adana, Turkey

X Esat Işık Applied Course in Optical Refraction and Low Vision Rehabilitation
18-20 March 2016 - İzmir, Turkey

Education in Ophthalmology Meeting
31-31 March 2016 - Ankara, Turkey

TOS April Course
1-3 April 2016 - Ankara, Turkey

Medical Retina, Vitreoretinal Surgery and Uvea-Behcet's Subsocieties Active Members' Meeting
23-24 April 2016 - Mudanya, Turkey

Vitreoretinal Surgery Subsociety Live Surgery Meeting
14-15 May 2016 - İzmir, Turkey

Strabismus Subsociety Meeting
14-15 May 2016 - İstanbul, Turkey

Cornea and Ocular Surface Subsociety Active Members' Meeting
14-15 May 2016 - Cappadocia, Turkey

TOS Spring Symposium
27-29 May 2016 - İstanbul, Turkey

TOS Summer Symposium
2-4 September 2016 - Elazığ, Turkey

XI Esat Işık Applied Course in Optical Refraction and Low Vision Rehabilitation
7-9 October 2016 - İzmir, Turkey

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Distance Visual Acuity Measurements Related Equivalency Table								
ETDRS Standard Line Number								***Spatial Frequency***
	Qualitative Measurements	Decimal	Snellen			LogMAR	Angle of Resolution	Cycle per Degree
-3		2.00	20	Ğ	10	-0.30	0.5	60.00
-2		1.60	20	Ğ	12.5	-0.20	0.625	48.00
-1		1.25	20	Ğ	16	-0.10	0.8	37.50
0		1.00	20	Ğ	20	0.00	1	30.00
		0.90				0.05		27.00
1		0.80	20	Ğ	25	0.10	1.25	24.00
		0.70				0.15		21.00
2		0.63	20	Ğ	32	0.20	1.6	18.75
		0.60				0.22		18.00
3		0.50	20	Ğ	40	0.30	2	15.00
4		0.40	20	Ğ	50	0.40	2.5	12.00
		0.30				0.52		9.00
5		0.32	20	Ğ	63	0.50	3.15	9.52
6		0.25	20	Ğ	80	0.60	4	7.50
7		0.20	20	Ğ	100	0.70	5	6.00
8		0.16	20	Ğ	125	0.80	6.25	4.80
9		0.13	20	Ğ	160	0.90	8	3.75
10	CF form 6 m	0.10	20	Ğ	200	1.00	10	3.00
11	CF from 5 m	0.08	20	Ğ	250	1.10	12.5	2.40
12	CF from 4 m	0.06	20	Ğ	320	1.20	16	1.88
13	CF from 3 m	0.05	20	Ğ	400	1.30	20	1.50
14		0.04	20	Ğ	500	1.40	25	1.20
15	CF from 2 m	0.03	20	Ğ	640	1.51	32	0.94
16		0.025	20	Ğ	800	1.60	40	0.75
17		0.020	20	Ğ	1000	1.70	50	0.60
18	CF from 1 m	0.016	20	Ğ	1250	1.80	62.5	0.48
21	CF from 50 cm	0.008	20	Ğ	2500	2.10	125	0.24
31	HM from 50 cm	0.0008	20	Ğ	25000	3.10	1250	0.02

Abbreviations:
CF: Counting fingers, HM: Perception of hand motions, m= meter, cm= centimeter

Equations of conversions for Microsoft Excel:
- Log10 (Decimal Acuity)= LogMAR Equivalent
Power (10; -Logmar Equivalent)= Decimal Acuity (for English version of Microsoft Excel)
Kuvvet (10; -Logmar Equivalent)= Decimal Acutiy (for Turkish version of Microsoft Excel)
Reference
Eğrilmez S, Akkın C, Erakgün T, Yağcı A. Standardization in evaluation of visual acuity and a comprehensive table of equivalent. Turk J Ophtalmol. 2002;32:132-136.