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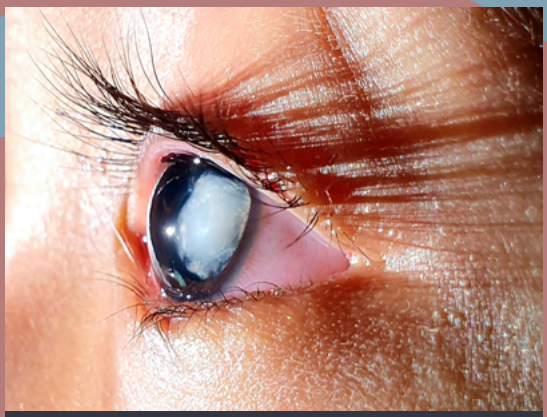

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Malaysian Journal of Ophthalmology

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Table of contents

Malaysian Journal of Ophthalmology

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Editorial

Micropulse trans-scleral cyclophotocoagulation: a light before the end of the tunnel

Liza-Sharmini Ahmad Tajudin

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*This article contains an erratum to the original.

Refractory glaucoma is defined as uncontrolled glaucoma with evidence of progression of the disease structurally and functionally despite maximum tolerable medical therapy, surgical therapy, or combination of medical and surgical therapy and high risk of trabeculectomy failure.[1] Based on the definition, management of refractory glaucoma is challenging, even more so in those with end-stage glaucoma; there is desperation in both patients and ophthalmologists.

Surgical management, and especially glaucoma drainage device (GDD) implantation, may provide better intraocular pressure (IOP) control with presumed better chances of preventing further progression in refractory glaucoma.[2] However, the outcome of GDD implantation is not as expected, with a rate of failure of 10% per year.[2] Trans-scleral cyclophotocoagulation (TSCPC) laser therapy with continuous wave (CW) to reduce aqueous production through destruction of ciliary body has regained popularity.[3] Unfortunately, the higher undesirable ocular complications and pain during the procedure have diminished its popularity.

Recent technological advances have brought micropulse wave TSCPC, known as micropulse cyclophotocoagulation (MPCPC), to expand the surgical options for refractry glaucoma.[4] In this issue of the Malaysian Journal of Ophthalmology, Chung *et. al* illustrate the potential effectiveness of MPCPC as adjunctive therapy in the Malaysian population.[5] Based on their findings, MPCPC has shown good IOP reduction (IOP < 21 mmHg or 20% reduction from baseline) in patients with refractory glaucoma who were not keen or suitable for surgical intervention. This retrospective review was conducted on a small group of patients (34 eyes of 24 patients) for a short period of time (6 months).

Similar findings have been observed in other populations.[3,4,6-8] Most of the studies were retrospective in nature, and therefore subject to bias, especially due to inadequate documentation.[3,4,6,7] Comparison is not possible due to a lack of standardized definition of success (IOP reduction) for this laser procedure. The short

follow-up period is another limitation in the majority of MPCPC reports, the longest follow-up being 18 months. The only consistent finding is that the procedure is less painful compared to TSCPC. However, no standardized scores for pain were used in the previous literature. Chung *et al.* applied a numerical rating scale to score the pain during MPCPC.[5] In the future, a prospective, multicentre, randomized controlled trial with at least a 5-year follow-up period is recommended to evaluate this novel procedure.

With a single-use probe, MPCPC is quite costly, which is a major drawback. The tip of the probe (Micropulse P3™, Iridex Corp., Mountain View, CA, USA) is quite large for small eyes such as Asian eyes. It may be a challenge in eyes with primary angle closure and small interpalpebral fissure. Subliminal TSCPC (SubCyclo®, Quantel Medical, Cournon-d'Auvergne, France), uses the same principle of micropulse wave but with a smaller and reusable probe.[9] Asians have highly pigmented eyes that may require less power delivery of MPCPC compared to less pigmented individuals. The power settings for patients with good central vision may differ from painful, blind eyes. Thus, individualised power settings are recommended. Despite the limitations and lack of strong evidence, MPCPC has the potential of shining a light before the end of the tunnel: a gleaming hope for patients at the end-stage of glaucoma.

*Erratum

The author of this article wishes to amend the following sentence in the original editorial: "Subliminal TSCPC (SubCyclo®, Quantel Medical, Cournon-d'Auvergne, France), uses the same principle of micropulse wave but with a smaller and reusable probe.[9]" The sentence should read: "Subliminal TSCPC (SubCyclo®, Quantel Medical, Cournob-d'Auvergne, France), uses the same principle of micropulse wave with smaller probe, but reusability of the probe is still not recommended by the manufacturer.[9]" Dr. Liza-Sharmini regrets the error.

References

1. Kitazawa Y, Yamamoto T, Sawada A, Hagiwara Y. Surgery for refractory glaucoma. Aust N Z J Ophthalmol. 1996; 24(4):327-332.
2. Patel S, Pasquale RL. Glaucoma Drainage Devices: A Review of the Past, Present, and Future. Semin Ophthalmol. 2010;25(5-6):265–270. doi: 10.3109/08820538.2010.518840
3. Aquino CM, Barton K, Tan AM, Sng C, Li X, Loon SC, Chew PT. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study. Clin Exp Ophthal. 2015;43(1):40-46. doi: 10.1111/ceo.12360

4. Tan AM, Chockalingam M, Aquino MC, Lim ZIL, See JLS, Chew PTK. Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. Clin Exp Ophthalmol. 2010;38:266–272. doi: 10.1111/j.1442-9071.2010.02238.x
5. Liu CC, Pappanayakan G, Ch'ng TW, et al. Micropulse trans-scleral cyclophotocoagulation: treatment outcomes of refractory glaucoma in Malaysia. Malaysian Journal of Opthalmology. 2020;2(4):258–268.
6. Preda MA, Karancsi LO, Munteanu M, Stanca TH. Clinical outcomes of micropulse transscleral cyclophotocoagulation in refractory glaucoma: 18 months follow up. Lasers Med Sci. 2020;35:1487-1491.
7. Varikuti V, Shah P, Rai O, et al. Outcomes of Micropulse Transscleral Cyclophotocoagulation in Eyes With Good Central Vision. J Glaucoma. 2019;28(10):901-905. doi: 10.1097/IJG.0000000000001339
8. Zaarour K, Abdelmassih Y, Arej N, Cherfan G, Tomey K, Khoueir Z. Outcomes of Micropulse Transscleral Cyclophotocoagulation in Uncontrolled Glaucoma Patients. J Glaucoma. 2019;28(3):270-275. doi: 10.1097/IJG.0000000000001174
9. Lutic I, Dragne C, Filip M, et al. Subcyclo laser procedure results in patients with glaucoma. Romanian J Ophthalmol. 2018:62(4):296-299. doi:10.22336/rjo.2018.45

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Original article

Micropulse trans-scleral cyclophotocoagulation: treatment outcomes of refractory glaucoma in Malaysia

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Abstract

Introduction: A more novel form of cycloablation, micropulse cyclophotocoagulation (MPCPC), has gained popularity in recent years due to its proven efficacy in lowering intraocular pressure (IOP) as well as higher safety profile compared to conventional trans-scleral cyclophotocoagulation.
Purpose: The aim of this study was to investigate the treatment outcome of MPCPC as an adjunctive treatment for refractory glaucoma.
Study design: Retrospective interventional case series.
Materials and methods: Subjects were patients with refractory glaucoma and glaucoma progression; with or without prior glaucoma surgery, who were not keen or not suitable for glaucoma surgery. Outcomes were IOP-lowering effect and reduction of glaucoma medications at 6 months follow-up. Treatment success was defined as either achieving IOP < 21 mmHg or IOP reduction of 20% from baseline IOP.
Results: The median age of patients was 57.5 years. A total of 34 eyes of 24 patients were treated with MPCPC with a mean follow-up period of 6 months. The majority of our patients (79%) experienced mild to moderate pain during the procedure. The median IOP prior to MPCPC was 30 mmHg and was significantly reduced at 1 week (17.5 mmHg), 1 month (17.5 mmHg), 3 months (21.0 mmHg), and 6 months (21.0 mmHg), with a 19.2% IOP reduction at the last follow-up. There were no

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cases of hypotony. The reduction in the number of glaucoma medications was not statistically significant. Our treatment success rate after a mean of 1.1 treatment sessions was 53% (16 out of 34 eyes).
Conclusions: Our study showed that MPCPC offers good IOP-lowering efficacy and patient tolerability in the treatment of refractory glaucoma. Larger, prospective, comparative studies are needed to determine a standardized MPCPC treatment protocol with high success and low complication rates.

Keywords: cyclophotocoagulation, glaucoma, intraocular pressure, laser, micropulse

Sitokoagulasi transkleral mikropal: hasil rawatan glaukoma refraktori di Malaysia

Abstrak

Pendahuluan: Satu bentuk sikloablasi yang baru, siklofotokoagulasi mikropal (MPCPC), telah mendapat populariti dalam beberapa tahun kebelakangan ini kerana keberkesanannya yang terbukti dalam menurunkan tekanan intraokular (IOP) serta profil keselamatan yang lebih tinggi berbanding dengan siklofotokoagulasi trans-scleral konvensional.
Tujuan: Tujuan kajian ini adalah untuk menyiasat hasil rawatan MPCPC sebagai rawatan tambahan untuk glaukoma refraktori.
Reka bentuk kajian: Rangkaian kes intervensi retrospektif.
Bahan dan kaedah: Subjek adalah pesakit dengan glaukoma refraktori dan glaucoma melarat; samada dengan atau tanpa pembedahan glaukoma sebelumnya, yang mana mereka tidak berminat atau tidak sesuai untuk pembedahan glaukoma. Dapatannya adalah kesan penurunan IOP dan pengurangan ubat glaukoma pada tarikh susulan 6 bulan. Kejayaan rawatan ditakrifkan sebagai mencapai IOP < 21 mmHg atau penurunan IOP sebanyak 20% dari IOP awal.
Dapatan: Umur median pesakit adalah 57.5 tahun. Sebanyak 34 mata daripada 24 pesakit dirawat dengan MPCPC dengan min rawatan susulan selama 6 bulan. Sebilangan besar pesakit kami (79%) mengalami kesakitan ringan hingga sederhana semasa prosedur. IOP median sebelum MPCPC adalah 30 mmHg dan dikurangkan dengan ketara pada 1 minggu (17.5 mmHg), 1 bulan (17.5 mmHg), 3 bulan (21.0 mmHg), dan 6 bulan (21.0 mmHg), dengan pengurangan IOP 19.2% pada susulan terakhir. Tidak ada kes hipotoni. Pengurangan jumlah ubat glaukoma tidak signifikan secara statistik. Tahap kejayaan rawatan kami selepas min 1.1 sesi rawatan adalah 53% (16 dari 34 mata).

Kesimpulan: Kajian kami menunjukkan bahawa MPCPC menawarkan keberkesanan penuruanan IOP yang baik dan toleransi pesakit dalam rawatan glaukoma refraktori. Kajian perbandingan yang lebih besar, prospektif, diperlukan untuk menentukan protokol rawatan MPCPC standard supaya mencapai tahap kejayaan yang tinggi dan tahap komplikasi yang rendah.

Kata kunci: glaukoma, laser, mikropal, siklofotokoagulasi, tekanan intraokular

Introduction

Glaucoma remains the leading cause of irreversible blindness in the world.[1] Conventionally, it is managed in a stepwise algorithm, beginning with medications, laser, and lastly, surgery. Intraocular pressure (IOP) is the only current modifiable risk factor in glaucoma and lowering IOP remains the primary aim for all treatment modalities. Recently, laser in glaucoma management has undergone numerous advancements with modern techniques and alternative applications developed. Refined laser modalities have led to an expansion in the role of laser in glaucoma treatments with a trend towards utilizing them in the earlier course of the disease.

Trans-scleral cyclophotocoagulation (TSCPC) with continuous wave (CW) diode laser has been conventionally used in treating refractory glaucoma. It delivers CW of high-intensity energy to the pars plicata, causing destruction of the ciliary body, thus reducing the aqueous production and lowering IOP.[2] However, complications such as hypotony, visual deterioration, phthisis bulbi, and unpredictable effects frequently occur.[3] A more novel form of cycloablation, micropulse cyclophotocoagulation (MPCPC), has gained popularity in recent years due to its proven efficacy in lowering IOP with a higher safety profile compared to conventional TSCPC.[4,5] MPCPC divides continuous-wave laser beam into periodic short pulses ("on" pulses), followed by "off" intervals. Each laser pulse heats up the pars plana of the ciliary body. The "off" intervals between each pulse allow thermal relaxation, thus reducing thermal buildup in tissues. The above mechanism results in targeted tissue damage and minimal collateral thermal burn to adjacent tissues, consequently reducing adverse effects.[6]

Our study describes the use of MPCPC in our center as an adjunctive treatment modality for refractory glaucoma. The primary treatment outcome was IOP reduction. Secondary outcomes were the pain score as reported by the subjects and the reduction in the number of glaucoma eye drops after the treatment.

Materials and methods

This is a retrospective, non-comparative, interventional case series of patients with uncontrolled glaucoma seen in the glaucoma clinic of Hospital Kuala Lumpur, Malaysia. All subjects were treated with MPCPC and recruited between January 1 to June 30, 2017. The study was conducted in accordance with the principles of the Declaration of Helsinki. Given this was a retrospective study, no ethics approval was required from the institutional review board.

The inclusion criteria were patients with refractory glaucoma (not achieving target IOP on maximally tolerated medications) and those with glaucoma progression; with or without prior glaucoma surgery and who were not keen or not suitable for glaucoma surgery.

The exclusion criteria were patients with significant scleral thinning and those who had undergone intraocular surgery within 2 months of enrolment.

MPCPC was performed by two surgeons. Sub-Tenon local anesthesia of 1.5 ml lignocaine 2% and 1.5 ml bupivacaine 0.5% were administered. A Cyclo G6™ Glaucoma Laser System (Iridex Corp., Mountain View, CA, USA) was used in this study. The diode laser contact probe (Micropulse P3™, Iridex) was held perpendicular to the limbal surface. The probe is designed such that the laser tip is positioned 3 mm posterior to the limbus. The laser was applied in continuous painting fashion: in an arc motion, to and fro over 360˚ for 100 seconds (50 seconds for each semicircle). The 3- and 9-o'clock meridians of limbus, thinned sclera area, area of previous trabeculectomy, or drainage device site were avoided during the laser application. The settings used were 2000 mW of energy, 0.5 milliseconds "on"/1.1 milliseconds "off" (31.3% duty cycle), with a maximum total energy level of 62.6 J. The amount of energy in Joules (J) = power in Watts (W) x total treatment duration in seconds (s) x "on" cycle (31.3%).

Data collected prior to treatment were age, gender, race, laterality of eyes, glaucoma type, previous ocular surgery history, glaucoma medications, and IOP (measured using Goldman applanation tonometer).

During the treatment procedure, pain experienced by patients was documented using the Numerical Rating Scale (NRS). Pain score was categorized into no pain (0), mild (1–3), moderate (4–6), and severe (7–10).[7] After the procedure, all patients were given paracetamol for analgesia and gutt dexamethasone 0.5% every 4 hours for 1 week and tapered off over a month. All pre-procedure glaucoma eye drops were continued. Follow-up reviews were done at 1 week, 1 month, 3 months, and 6 months after the procedure. At each review, visual acuity, anterior segment examination, optic nerve examination and IOP were recorded. All IOPs were measured using the Goldmann applanation tonometer (GAT, Haag-Streit Diagnostics, Koeniz, Switzerland) by trained medical officers or specialists. The IOP-lowering medications were adjusted according to IOP response at follow-up. If the IOP was less than 21 mmHg post-MPCPC, medications were reduced in a

stepwise method. If it remained high (> 21 mmHg), a second MPCPC treatment or glaucoma surgery was offered. Outcome measures were IOP-lowering effect and reduction in the number of glaucoma medications. Treatment success was defined as either achieving IOP < 21 mmHg or IOP reduction of 20% from baseline IOP at 6 months.

Continuous variables were checked for normality using numerical and graphical methods. Non-parametric data (age in years and IOP in mmHg) were described using median (25^{th} percentile, 75^{th} percentile), while normally distributed data (number of glaucoma eye drops) was described using mean ± SD. Categorical data were described in frequency and percentage. Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS)® Statistics Version 25. IOP was compared relative to preoperative baseline at four postoperative time points (1 week, 1 month, 3 months, and 6 months) using the Wilcoxon signed-rank test. The reduction in number of glaucoma eye drops was analyzed using the paired t-test. A *P* value of < 0.01 was considered statistically significant.

Results

A total of 34 eyes of 24 patients were included in this study. The mean follow-up period was 6 months. Table 1 summarizes the demographics, types of glaucoma, previous surgeries, and pain score. The majority of our patients (79%) experienced mild to moderate pain during the laser procedure. Five eyes (14.7%) underwent a second MPCPC treatment with an overall mean of 1.1 treatment sessions per eye. At the end of 6 months, three patients were lost to follow-up, leaving 21 patients (30 eyes) for the overall success rate. Figure 1 shows the flow chart for patient recruitment and follow-up.

We were able to achieve significant reduction in median IOP at all follow-up periods up to 6 months ($p < 0.01$). There were no cases of hypotony (IOP < 6 mmHg). Table 2 summarizes the IOP after MPCPC.

Glaucoma medications were reduced from a mean of 3.3 ± 0.9 (range 1–5) to 2.6 ± 1.0 (range 0–4) at 6 months (t (26) = 2.401, $p = 0.024$). The reduction in number of medications was not statistically significant. Figure 2 shows the cluster graph for the number of glaucoma medications used pre- and post-procedure.

The success rate of our study was 53%. Fourteen out of 30 eyes did not fulfil the criteria of a successful treatment at 6 months. The IOP remained uncontrolled within 6 months in neovascular glaucoma (3), steroid-induced glaucoma (4), primary angle-closure glaucoma (5) and primary open-angle glaucoma (4).

Table 1. Demographics, types of glaucoma, previous surgeries, pain score

Patients demographics	**Number (*n* = 24)**	**Percentage (%)**
Age group, years (median)	(57.5)	
10 to 19	1	4
20 to 29	4	17
30 to 39	0	0
40 to 49	4	17
50 to 59	5	21
60 to 69	1	4
70 to 79	8	33
80 to 89	1	4
Gender		
Male	16	67
Female	8	33
Eye parameters	**Number (*n* = 34)**	
Laterality		
Right	19	56
Left	5	15
Bilateral	10	29
Types of glaucoma		
Neovascular glaucoma	7	20.5
Primary angle-closure glaucoma	8	23.5
Primary open-angle glaucoma	11	32.4
Axenfeld-Rieger syndrome	2	5.9
Steroid-Induced glaucoma	4	11.8
Uveitic glaucoma	1	2.9
Pseudoexfoliative glaucoma	1	2.9
Previous surgeries†		
Cataract extraction, lens implant	20	59
Trabeculectomy	13	38
Glaucoma drainage device	2	6
Nil	11	32
Pain score during procedure		
1–3 (mild)	11	32
4–6 (moderate)	16	47
7–10 (severe)	7	21

†Twelve patients underwent a combination of two previous surgeries.

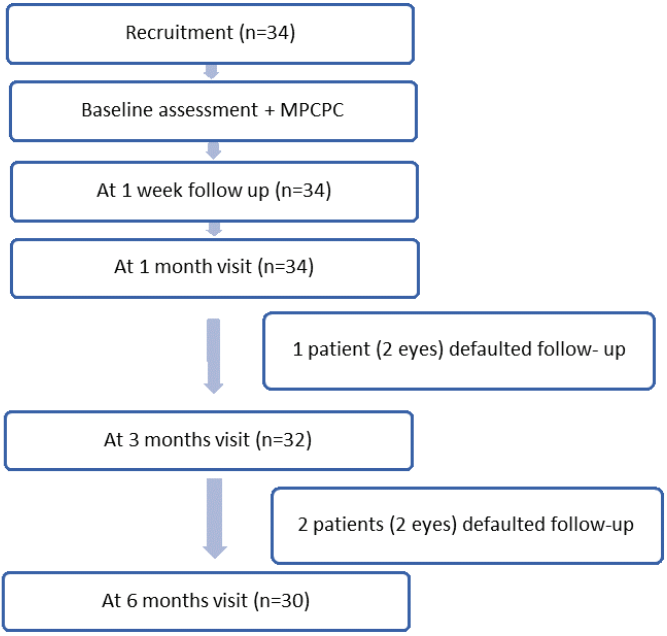

Fig. 1. Flow chart of patient recruitment and follow-up.

Table 2. IOP (mmHg) after micropulse cyclophotocoagulation

	Baseline (*n* = 34)	**1 week (*n* = 34)**	**1 month (*n* = 34)**	**3 months (*n* = 32)**	**6 months (*n* = 30)**
Median IOP (25th percentile, 75th percentile), mmHg	30.0 (24.0, 36.0)	17.5 (12.0, 22.5)	17.5 (15.75, 24.5)	21.0 (18.0, 32.75)	21.0 (17.0, 33.0)
IOP reduction in %		42.7	32.8	21.5	19.2
Z statistic [a]		-4.683 [b]	-4.618 [b]	-3.036 [b]	-2.605 [b]
p-value [a]		< 0.001	< 0.001	0.002	0.009

[a]Wilcoxon Signed Ranks Test; [b]Based on positive ranks

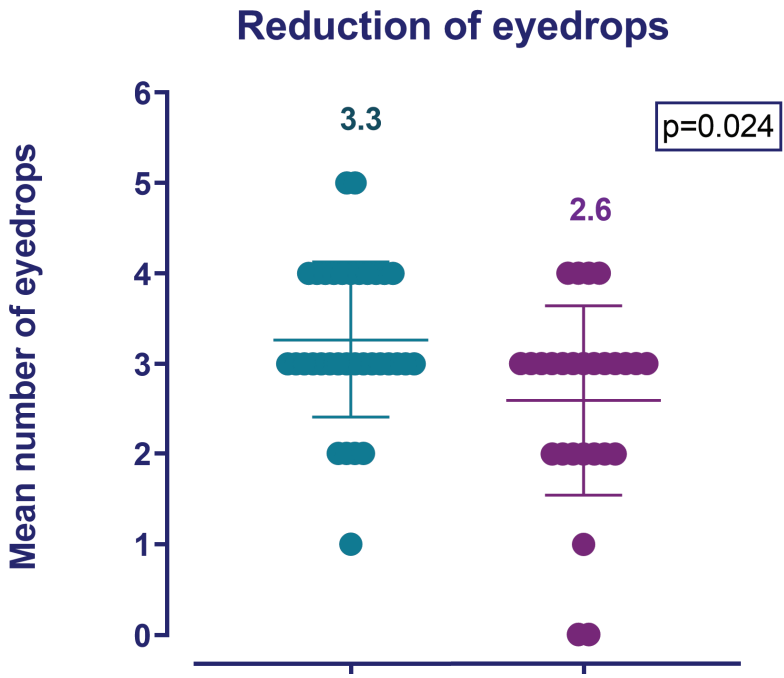

Fig. 2. Reduction in the number of glaucoma medications.

Discussion

In our study, the median IOP was significantly reduced from 30 to 21 mmHg within 6 months ($p < 0.01$). There were no cases of hypotony. The extent of IOP-lowering effect was well sustained (42.7% within 1 week to 19.2% within 6 months). Our treatment success rate was 53% (16 out of 30 eyes) at 6 months. It is hypothesized that each laser pulse on the pars plana generates heat that causes ciliary body inflammation, which in turn reduces aqueous formation and enhances uveoscleral outflow.[8]

Most of the eyes (9 out of 14) that failed MPCPC treatment had previous failed filtration surgery (eight underwent trabeculectomy and one underwent tube surgery). The mean number of glaucoma medications was not significantly reduced in the final follow-up. The pain score showed that the MPCPC procedure is tolerable, as most patients complained of mild to moderate pain only.

To date, knowledge on the effectiveness and risks of MPCPC is limited due to the small number of studies, most of which are retrospective and non-comparative, with relatively limited sample sizes.[9] Currently, there are no standardized parameters on micropulse technique. In our study, we utilized a relatively low

energy level (maximum of 62.6 J) with a mean of 1.1 treatment sessions per eye. We adopted our laser settings from an earlier study by Tan *et al.*, where a 72.7% success rate was achieved at an average follow-up of 16.3 months after a mean of 1.3 treatment sessions.[4] Another similar study by Williams *et al.* achieved a better success rate (66.1%) within 6 months using a mean energy level of 187 J on 79 eyes, with only 12.6% of the eyes undergoing additional MPCPC treatment.[10] Meanwhile, Sanchez *et al.* achieved a lower success rate (27.3%) in their study within 6 months, utilizing energy levels within a range of 62–112 J on 22 eyes with only one session per eye.[11] The total amount of energy (J) applied appears to be among the key factors affecting the treatment outcome. Sanchez *et al.* carried out a literature review on nine studies to approximate the ideal MPCPC parameters for a single session treatment by comparing the efficacy and complication rates of different energy levels in J. They hypothesized that the ideal energy was around 150 J. This energy setting gives good efficacy with few or no complications.[12]

Conventional TSCPC is not widely used as a primary treatment in eyes with good vision due to its complications. MPCPC, on the other hand, provides a more exquisite control of the photothermal effect by "chopping" the CW into multiple shorter laser pulses, avoiding the ciliary body tissue disruption which is routinely seen in conventional TSCPC. This explains the absence of complications like hypotony in our study.[4,5,13] However, a recent cohort study on 84 eyes by Emanuel *et al.* showed that persistent hypotony had occurred at 3 and 6 months (8 and 3 eyes, respectively) after MPCPC treatment. This might be due to their longer treatment time of 319 seconds over the 360° area with a mean power of 1939 mW, which converts to a total energy of 193 J.[14]

MPCPC has been proven to be better tolerated by patients intra- and postoperatively.[15,16] This is presumably due to the fact that the micropulse laser deliver less total energy and limits the thermal damage to adjacent structures compared to TSCPC. Its favorable tolerability for patients indicates the possibility of performing this procedure in an outpatient clinic setting rather than in the operating room, thus reducing surgical burden, time, and cost.

Nevertheless, MPCPC has its own downsides. This novel laser contact probe is costly due to its strict single-use policy, which is not a cost-effective treatment modality in our setting. In addition, this procedure has no clinical evident endpoint (for example, the "pop" sound in TSCPC), making it difficult to ascertain the adequacy of treatment in each eye.[4] Lastly, the laser contact probe is bulkier than the G-probe used in TSCPC, which can present a problem in treating small eye sizes. This probe is designed to aim more posterior from the limbus, which is 3 mm compared to the 2 mm of TSCPC, aiming at the pars plana of the ciliary body.

The limitations of this study reside in its design — non-comparative, retrospective case series —, small sample size, and short duration. Since MPCPC is a new treatment modality, there was no clear protocol on deciding the treatment parameters and timing of re-treatment. A clear treatment protocol is needed to

assess the reproducibility of the results. One major confounding factor was the heterogenicity of glaucoma types in our study. Different types of glaucoma carry inconsistent response to treatment and complication rates. The study endpoint can be improved by proper stratification according to types of glaucoma. Another confounding factor may be the different ethnicities in our multiracial Malaysian population; this may need to be stratified in future studies. In our study, the primary treatment outcome was IOP, and treatment success was defined similarly to other studies.[4,5,10,13,16] Even though IOP remains the only modifiable factor in glaucoma, we wish to clarify that our definition of successful treatment does not equate to success in the treatment of the disease or control of disease progression, because IOP reduction may not reach the patient's specific target IOP; their glaucoma may still progress and require additional management.

In conclusion, our study showed a significant IOP-lowering effect with MPCPC and favorable patient tolerability in the treatment of refractory glaucoma. MPCPC has a promising role in the management of refractory glaucoma as a viable alternative to conventional TSCPC and surgery. Nonetheless, larger, prospective, stratified, and comparative studies are needed to determine a standardized MPCPC treatment protocol with high success and low complication rates.

Acknowledgments

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References

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. 2006;90(3):262-267.
2. Feldman RM, el-Harazi SM, LoRusso FJ, et al. Histopathologic findings following contact transscleral semiconductor diode laser cyclophotocoagulation in a human eye. J Glaucoma. 1997;6(2):139-140.
3. Mistlberger A, Liebmann JM, Tschiderer H, et al. Diode laser transscleral cyclophotocoagulation for refractory glaucoma. J Glaucoma. 2001;10(4):288-293.
4. Tan AM, Chockalingam M, Aquino MC, et al. Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. Clin Exp Ophthalmol. 2010;38(3):266-272.
5. Aquino MC, Barton K, Tan AM, et al. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study. Clin Exp Ophthalmol. 2015;43(1):40-46.
6. Aquino MC, Lim D, Chew PT. Micropulse P3 (MP3) Laser for Glaucoma: An Innovative Therapy. J Curr Glaucoma Pract. 2018;12(2):51-52.

7. Boonstra AM, Stewart RE, Koke AJ, et al. Cut-Off Points for Mild, Moderate, and Severe Pain on the Numeric Rating Scale for Pain in Patients with Chronic Musculoskeletal Pain: Variability and Influence of Sex and Catastrophizing. Front Psychol. 2016;7:1466.
8. Liu GJ, Mizukawa A, Okisaka S. Mechanism of intraocular pressure decrease after contact transscleral continuous-wave Nd:YAG laser cyclophotocoagulation. Ophthalmic Res. 1994;26(2):65-79.
9. Ma A, Yu SWY, Wong JKW. Micropulse laser for the treatment of glaucoma: A literature review. Surv Ophthalmol. 2019;64(4):486-497.
10. Williams AL, Moster MR, Rahmatnejad K, et al. Clinical Efficacy and Safety Profile of Micropulse Transscleral Cyclophotocoagulation in Refractory Glaucoma. J Glaucoma. 2018;27(5):445-449.
11. Sanchez FG, Lerner F, Sampaolesi J, et al. Efficacy and Safety of Micropulse(R) Transscleral Cyclophotocoagulation in Glaucoma. Arch Soc Esp Oftalmol. 2018;93(12):573-579.
12. Sanchez FG, Peirano-Bonomi JC, Grippo TM. Micropulse Transscleral Cyclophotocoagulation: A Hypothesis for the Ideal Parameters. Med Hypothesis Discov Innov Ophthalmol. 2018;7(3):94-100.
13. Kuchar S, Moster MR, Reamer CB, et al. Treatment outcomes of micropulse transscleral cyclophotocoagulation in advanced glaucoma. Lasers Med Sci. 2016;31(2):393-396.
14. Emanuel ME, Grover DS, Fellman RL, et al. Micropulse Cyclophotocoagulation: Initial Results in Refractory Glaucoma. J Glaucoma. 2017;26(8):726-729.
15. Friberg TR, Venkatesh S. Alteration of pulse configuration affects the pain response during diode laser photocoagulation. Lasers Surg Med. 1995;16(4):380-383.
16. Yelenskiy A, Gillette TB, Arosemena A, et al. Patient Outcomes Following Micropulse Transscleral Cyclophotocoagulation: Intermediate-term Results. J Glaucoma. 2018;27(10):920-925.

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Original article

Repeatability and comparability of simulated K values between a grid projection-based device and a Placido/dual Scheimpflug device

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Abstract

Purpose: To evaluate the repeatability and comparability of simulated K values obtained by the Galilei G4 Corneal Tomographer and the iDesign Wavefront Abberometer.
Methods: The right eyes of 100 consecutive pre-laser-assisted *in situ* keratomileusis (LASIK) patients were included in this study. Patients with a history or signs of previous corneal or ocular trauma and infection were excluded. Paired corneal measurements for flat (K1) and steep (K2) meridians were obtained with both the Galilei and the iDesign. Repeatability was evaluated by calculating the coefficient of variation (CV) of the paired measurements. The comparability between platforms was evaluated by calculation of the mean differences followed by the construction of Bland-Altman plots and calculation of limits of agreement (LOA).
Results: While the mean CV for both devices was low (0.17% *versus* 0.57% for the Galilei and iDesign, respectively), a large proportion of eyes measured by the iDesign (22%) showed an absolute difference of > 0.5 D between paired readings, compared to 1% as measured by the Galilei. The Galilei consistently measured higher than the iDesign. Although the mean difference did not exceed 0.17 D, the LOAs were unacceptably wide at -0.52 D to 0.85 D and -0.69 D to 0.89 D for K1 and K2, respectively.
Conclusion: As regards keratometry, the iDesign demonstrated clinically unacceptable repeatability. Both platforms demonstrated sufficiently wide LOA that we could not recommend that they are used interchangeably.

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Keywords: comparability, Galilei, iDesign, keratometry, LASIK, repeatability

Kebolehulangan dan perbandingan nilai K seleppas simulasi antara peranti berasaskan unjuran grid dan peranti Placido/dual Scheimpflug

Abstrak

Tujuan: Untuk menilai kebolehulangan dan perbandingan nilai K simulasi yang diperoleh oleh Galilei G4 Corneal Tomographer dan iDesign Wavefront Abberometer.
Kaedah: Mata kanan 100 pesakit pra-laser in-keratomileusis in situ (LASIK) disertakan dalam kajian ini. Pesakit dengan riwayat atau tanda-tanda trauma dan jangkitan kornea atau okular sebelumnya disisihkan. Pengukuran kornea berpasangan untuk meridian rata (K1) dan curam (K2) diperolehi dengan Galilei dan iDesign. Kebolehulangan dinilai dengan mengira pekali variasi (CV) pengukuran berpasangan. Perbandingan antara platform dinilai dengan pengiraan perbezaan min diikuti dengan pembinaan plot Bland-Altman dan pengiraan had perjanjian (LOA).
Dapatan: Walaupun CV rata-rata untuk kedua-dua peranti rendah (masing-masing 0,17% berbanding 0,57% untuk Galilei dan iDesign), sebilangan besar mata yang diukur oleh iDesign (22%) menunjukkan perbezaan mutlak > 0,5 D antara bacaan berpasangan , dibandingkan dengan 1% yang diukur oleh Galilei. Galilei secara konsisten diukur lebih tinggi daripada iDesign. Walaupun perbezaan min tidak melebihi 0.17 D, LOAs lebarnya tidak dapat diterima pada -0,52 D hingga 0,85 D dan -0,69 D hingga 0,89 D untuk K1 dan K2, masing-masing.
Kesimpulan: Mengenai keratometri, iDesign menunjukkan kebolehulangan yang tidak dapat diterima secara klinikal. Kedua-dua platform menunjukkan LOA yang cukup luas sehingga kami tidak dapat mengesyorkan agar platform tersebut digunakan secara bergantian.

Kata kunci: Galilei, iDesign, kebolehulangan, keratometry, LASIK, perbandingan

Introduction

Precise corneal measurements are critical to the success of laser and lens refractive surgery. When planning for laser refractive surgery, precise keratometry is required to screen for ectatic corneal disorders,[1-3] detection of postoperative complications, and to allow planning for repeat treatments. Precise keratometry is also critical for the success of refractive cataract surgery,[4,5] with keratometric errors accounting for as many as 23% of refractive surprises after cataract surgery.[6]

Available corneal topographers can generally be classified into Placido disc systems and Scheimpflug-based systems. Placido disc systems project the image of a Placido disc off the anterior corneal surface. A video camera then analyses the distance between the reflected mires to calculate corneal power by direct determination of corneal slope. However, the ability of Placido disc systems to measure central corneal power is limited due to the central placement of the video camera. In contrast, Scheimpflug platforms employ a rotating Scheimpflug camera that indirectly calculates corneal power by measuring corneal elevation. Single and dual camera platforms like the Pentacam (Oculus, Germany) and Galilei G4 (Ziemer, Switzerland), respectively, have demonstrated good comparability with manual keratometry.[7,8]

The Galilei G4 combines a dual Scheimpflug camera system with a Placido disc that allows calculation of anterior corneal power and axes, as well as posterior and total corneal powers and axes, amongst other parameters. The Galilei G4 measures approximately 100,000 data points[9] and obtains data (weighted in favour of Placido disc) from the central 4 mm to calculate anterior corneal power.

Unlike Placido or Scheimpflug systems, the iDesign Wavefront Aberrometer (Johnson & Johnson, NJ, USA) measures anterior corneal power by utilising a grid projection based on raster photogrammetry. Instead of a Placido disc, the iDesign projects a 37 x 37 spot grid onto the anterior corneal surface, capturing approximately 1400 data points. The system then uses non-coaxial cameras to analyse the reflected grid pattern. In contrast to Placido disc systems, this method measures gradient of surface elevation to calculate the corneal power. In contrast to the Galilei, the iDesign takes into account the central 3 mm to determine corneal power.

This study evaluated the repeatability and comparability of corneal power values measured by the Galilei and the iDesign to determine if they may be used interchangeably in clinical practice.

Materials and methods

The study protocol was prospectively approved by the Borneo Medical Centre Institutional Review Board (IRB) and adhered to the tenets of the Declaration of Helsinki. One hundred consecutive healthy pre-laser-assisted in situ keratomileusis

(LASIK) patients at the Eye and LASIK Clinic, Borneo Medical Centre, Malaysia were enrolled in the study. The objective of the study, the process of data collection, and the potential side effects of the examination were explained to patients, after which written consent was obtained. Patients who had a history or signs of ocular trauma or surface disease were excluded from our study. A single experienced technician (CC) performed a set of measurements on the iDesign followed by measurements on the Galilei. All measurements were conducted in a darkened room before any slit-lamp examination or refraction was performed. No pre-test lubrication was utilised. On each platform, each person had their head comfortably secured with a soft elastic headband. They were instructed to blink immediately before, then to hold their eyes open wide during the measurement. They did not lift their head off the chin rest until the set of measurements was complete. All sets of measurements were completed within 10 minutes. The right eyes of selected patients were included in this study.

The iDesign software evaluates the validity of scans by evaluating the quality of the following three components: the amount of iris detail available, total ocular wavefront, and corneal topography. Poor quality scans are flagged and deemed non-valid.

Three valid scans are required before the machine selects, via proprietary algorithms, the scan on which it deems best to base a laser refractive treatment. For this study, the first two valid scans were selected.

For the Galilei, the 'Standard' resolution option was selected. Upon image capture, an algorithm is employed to determine the overall quality of the image. The quality of the following components determines overall image quality: camera compensation for eye motion, Placido image quality, Scheimpflug image quality, and the amount of motion in the Z-axis.

Each of the components is then graded with either a 'tick', indicating that it passes an internally set standard for quality, or a 'question mark', indicating that it has failed the set standard. Poor quality scans were flagged and discarded. We selected the first two valid scans.

Statistical Analysis

Statistical analysis was performed with Microsoft Excel 2011. The mean and absolute differences, standard deviation (SD), and coefficient of variation (CV) were calculated for each pair of K1 and K2 measurements to determine the repeatability of each platform. Finally, the mean CV (%) ± SD for each platform was calculated and compared.

We evaluated comparability by calculating the mean of each pair of readings as measured by both platforms, followed by the paired t-test. Bland-Altman plots demonstrating 95% limits of agreement (LOA) were constructed for the differences between the mean readings of both platforms.

Results

Demographics

The right eyes of 100 consecutive pre-LASIK patients were included in this study. Thirty-three patients were men and 67 were women. Sixty patients were Chinese, 19 were Malay, 9 were Dayak, and 12 were Indonesian. The mean age was 30.88 ± 6.7 years. The mean refractive sphere was -4.78 ± 2.21 D and the mean refractive cylinder was -1.07 ± 0.89 D.

Repeatability

The range of absolute differences between paired measurements was low with the Galilei (only 1% of eyes (1/*n* = 100), having a difference of > 0.50 D in at least one of paired K1 or K2 measurements. In contrast, the range of absolute differences for the iDesign was more extensive, with 22% of eyes (22/*n* = 100) having a measured difference of > 0.50 D in at least one of paired K1 or K2 measurements. The Galilei demonstrated superior repeatability for both K1 and K2 with CV of 0.16% and 0.17%, compared to 0.55% and 0.56% by the iDesign. The results are shown in Table 1.

Table 1. Results for two consecutive measurements from the Galilei and iDesign by mean difference, absolute range of differences, and coefficient of variation (*n* = 100)

	Galilei		**iDesign**	
	K1	**K2**	**K1**	**K2**
Mean difference of 2 readings (D) ± SD	0.1 ± 0.08	0.11 ± 0.1	0.34 ± 0.36	0.36 ± 0.36
Range of absolute difference between 2 readings (D)	0.00–0.44	0.00–0.55	0.00–2.46	0.00–2.35
Mean CV (%) ± SD	0.16 ± 0.13	0.17 ± 0.15	0.55 ± 0.57	0.56 ± 0.56

Coefficient of variation (CV) calculated for the mean difference between paired readings of both platforms to calculated dispersion.
CV: coefficient of variation; D: dioptres; K1: flat meridian; K2: steep meridian; SD: standard deviation

Comparability

For K1, the Galilei and iDesign measured a mean ± SD of 43.47 ± 1.37 D and 43.31 ± 1.39 D, respectively. For K2, the Galilei and iDesign measured a mean ± SD of 44.88 ± 1.60 D and 44.74 ± 1.63 D, respectively. The iDesign consistently measured lower compared to the Galilei. The mean values for both devices were compared with the paired t-test. The differences were statistically significant ($p < 0.001$ for both K1 and K2).

Table 2. Results for comparison of 100 paired K1 and K2 measurements between devices

Parameter	Galilei	iDesign	*p*-value
Mean K1 (D) ± SD	43.47 ± 1.37	43.31 ± 1.39	< 0.001
Mean K2 (D) ± SD	44.88 ± 1.60	44.74 ± 1.63	< 0.001
Galilei vs iDesign Mean K1 Difference (D) ± SD	0.16 ± 0.34		-
Galilei vs iDesign Mean K2 Difference (D) ± SD	0.14 ± 0.38		-
LOA K1 (D)	-0.50 to 0.83		-
LOA K2 (D)	-0.60 to 0.88		-

Paired t-test used in statistical analysis to compare mean values of K1 and K2 for both platforms.
D: dioptres; K1: flat meridian; K2: steep meridian; LOA: limits of agreement; SD: standard deviation

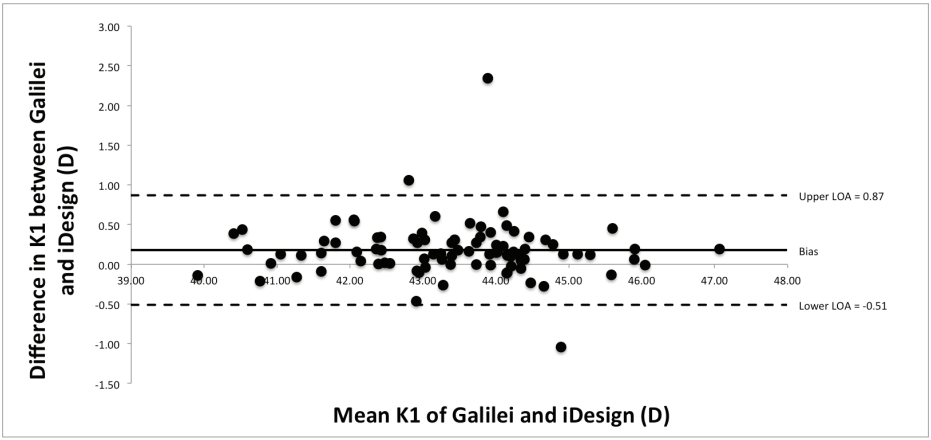

Fig. 1. Bland-Altman plot demonstrating the difference in mean corneal power measurements between the Galilei and iDesign for K1.

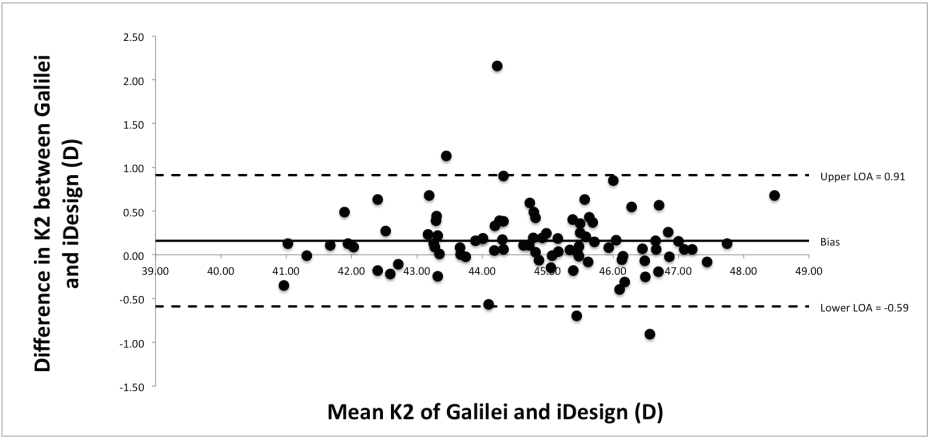

Fig. 2. Bland-Altman plot demonstrating the difference in mean corneal power measurements between the Galilei and iDesign for K2.

For K1 and K2, the mean difference ± SD between measurements for the Galilei and iDesign was 0.16 ± 0.34 D and 0.14 ± 0.38 D, respectively. The LOA were wide, ranging from -0.50 to 0.83 D for K1 and -0.60 to 0.88 D for K2. The results are shown in Table 2 and Figures 1 and 2.

Discussion

The success of cataract and corneal refractive surgery hinges upon the precision of corneal power measurements. This study examined the repeatability and comparability of the Galilei and iDesign in measuring anterior corneal power. We found that, while both devices demonstrated low CV, the poorer recorded repeatability of the iDesign was more likely to be clinically significant. Our findings loosely mirror reports regarding the repeatability of the Galilei, alternately reported to be as low as 0.12% by Shirayama[8] and as high as 0.29% by Crawford.[10] These discrepancies between studies may be due to various factors, including variation in examination order, ocular laterality, and the number of measurement sets performed. In the two cited studies as well as in our own, a single observer recorded all the measurements. In our study, in order to avoid the potential for bias, we ceased measurements once there were two acceptable scans. In comparison, three measurements were recorded per patient in the above-mentioned studies, but it was not clear whether these were the first three that were acceptable, or whether they were selected from a pool of acceptable scans. It is apt to consider any inter-study agreement with caution due to differing methodologies in data collection.

We are unaware of similar studies that assess the repeatability of the iDesign. However, data regarding the Accugrid platform (PAR Vision Systems, NY, USA) is

available. The Accugrid is similar in that it directly determines the curvature of a surface by analysing a projected grid pattern.

Belin and associates reported the measured variability of the Accugrid to be as low as 0.06 D when examining diameter calibrated test spheres over an 8 mm test area.[11] However, the accuracy and variability were reported to be worse with smaller test areas.

While the Accugrid has not been examined *in vivo*, Jindal and associates reported an average of 0.28 D difference between readings when examining cadaveric eyes over various area sizes that ranged from 3–6 mm in diameter.[12] Differences between methodologies notwithstanding, we report similar average differences between paired iDesign readings (0.34 D and 0.36 D) for K1 and K2 in our study. Given the dearth of *in vivo* studies regarding the iDesign, we would be prudent to hesitate in drawing firm conclusions regarding the repeatability of the iDesign.

Our study findings, however, suggest that the repeatability of the Galilei is superior, measuring > 0.5D between paired readings in only 1% of eyes as opposed to 22% by the iDesign. During the calculation of intraocular lens powers, for example, this difference in repeatability is likely to be clinically significant.

We also evaluated comparability between platforms. While the mean difference between platforms did not exceed 0.16 D, which is of minimal clinical significance, there was a clinically significant measured difference of > 0.5 D between platforms in 18% of evaluated eyes (18 eyes). The iDesign also consistently measured lower than the Galilei. Because the iDesign measures the central 3 mm, it would be expected to measure higher than the Galilei, which measures the central 4 mm. This discrepancy may be due to Galilei's camera placement excluding measurement of the central 1 mm.

To date, comparability between the iDesign and other platforms has not been examined. Available studies involving the Galilei suggest good comparability with the Placido disc-based Zeiss Atlas (Carl Zeiss AG, Oberkochen, Germany). Shirayama and associates found a mean difference ± SD of 0.08 ± 0.14 D with an LOA of 0.54 D.[8] This similarity could be due to Galilei depending primarily on Placido disc data for anterior corneal power values.

In contrast, the comparability between the Galilei and the Orbscan II (Bausch and Lomb, Rochester, NY, USA) has been reported to be poorer. The Orbscan II combines slit scanning with a Placido disc. Menassa and associates compared the Galilei to the Orbscan II and found a mean difference (D) ± SD of 0.04 ± 0.37 and 0.09 ± 0.44 for K1 and K2, respectively.[13] It is unclear if data collected by the Orbscan II is weighted in favour of data collected by the slit scan, upon which the earlier iteration of the platform was wholly dependent. This difference in measurement method could be the reason for the larger standard deviation.

When comparing the Galilei and the Orbscan II, Crawford and associates reported LOA of 1.7 D and 1.5 D for Mean K and K1.[10] When comparing the Mean K

Table 3. Summary of comparison between devices in the current study and other automated devices

Study	Devices	Mean difference (D) ± SD	Range of 95% LOA (D)
Crawford[10]	Galilei *vs* Pentacam (K1)	-0.1 ± 0.2	0.9
	Galilei *vs* Pentacam (K2)	0.0 ± 0.3	N/A
	Galilei *vs* Orbscan II (K1)	± 0.4	1.5
	Galilei *vs* Orbscan II (K2)	0.2 ± 0.5	N/A
Menassa[13]	Orbscan II *vs* Galilei (K1)	0.04 ± 0.37	N/A
	Orbscan II *vs* Galilei (K2)	0.09 ± 0.44	N/A
Shirayama[8]	Galilei *vs* IOLMaster (Mean K)	-0.12 ± 0.07	0.27
	Galilei *vs* Atlas (Mean K)	-0.08 ± 0.14	0.54
	Galilei *vs* Manual Keratometer (Mean K)	0.05 ± 0.13	0.51
Current study	Galilei *vs* iDesign (K1)	0.16 ± 0.34	1.33
	Galilei *vs* iDesign (K2)	0.14 ± 0.38	1.48

D: dioptres; K1: flat meridian; K2: steep meridian; LOA: limits of agreement; N/A: not available; SD: standard deviation

and K1 of the Galilei and the Scheimpflug-based Pentacam, they recorded slightly lower but still unacceptable LOA of 1.1 D and 0.9 D.[10]

The above studies demonstrate that the Galilei is capable of producing near-identical mean K values when compared to the Orbscan II and Pentacam (Table 3). However, variability between platforms as reflected by standard deviation and LOA were beyond clinically acceptable limits.

Conclusion

In summary, we studied the repeatability and comparability of the Galilei and iDesign platforms in measuring anterior corneal power. The repeatability of the Galilei was suggested to be superior compared to the iDesign. Whilst the iDesign was found to be less repeatable, there were obvious limitations in our study design. These shortcomings included the use of a single observer and non-randomisation of selected eyes. These may have inadvertently affected outcomes. We look forward to further studies that address these limitations.

When examining comparability between platforms, LOA between platforms was sufficiently wide as to be clinically unacceptable. Other studies examining

concordance between the Galilei and other platforms offer conflicting reports.[7,8,10,13]

As the true 'gold standard' of corneal power measurement is unknown, and there are no prior studies comparing the iDesign to other platforms, we are currently unable to offer a conclusion as to whether the Galilei or iDesign is closest to actual corneal power. They appear to be sufficiently disparate that we cannot recommend that they be used interchangeably in clinical practice.

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References

1. N Maeda, S D Klyce, M K Smolek, H W Thompson. Automated keratoconus screening with corneal topography analysis. Invest Ophthalmol Vis Sci. 1994;35(6):2749-2757.
2. Rabinowitz, Y.S. Keratoconus. Surv Ophthalmol.1998;42(4):297-319.
3. Ömür Ö. Uçakhan, Volkan Çetinkor, Muhip Özkan, Ayfer Kanpolat. Evaluation of Scheimpflug imaging parameters in subclinical keratoconus, keratoconus, and normal eyes. J Cataract Refract Surg. 2011;37(6):1116-1124.
4. Norrby S. Sources of error in intraocular lens power calculation. J Cataract Refract Surg. 2008;34:368–376.
5. Olsen T. Sources of error in intraocular lens power calculation. J Cataract Refract Surg. 1992;18:125–129.
6. Jin GJC, Crandall AS, Jones JJ. Intraocular Lens Exchange due to Incorrect Lens Power. Ophthalmology 2007;114:417–424.
7. Whang WJ, Byun YS, Joo Ck. Comparison of refractive outcomes using five devices for the assessment of preoperative corneal power. Clin Exp Ophthalmol. 2012;40(5):425-432.
8. Shirayama M, Wang L, Weikert MP, Kock DD. Comparison of corneal powers obtained from 4 different devices. Am J Ophthalmol. 2009;148(4):528-535
9. Galilei. [Internet] Switzerland: Ziemer Ophthalmic Systems.; 2020. Available from https://www.ziemergroup.com/en/products/galilei/
10. Crawford AZ, Patel DV, McGhee CN. Comparison and repeatability of keratometric and corneal power measurements obtained by Orbscan II, Pentacam, and Galilei corneal tomography systems. Am J Ophthalmol. 2013;156(1):53-60.
11. Belin MW, Litoff D, Strods SJ, Winn SS, Smith RS. The PAR Technology Corneal Topography System. Refract Corneal Surg. 1992;8(1):88-96.

12. Jindal P, Cheung S, Pirouzian A, Keates RH, Ren Q. Evaluation of the PAR corneal topography system. Ophthalmic Technologies V. Photonic West; 1995; San Jose, CA, United States. SPIE. 1995;2393:10.
13. Menassa N, Kaufmann C, Goggin M, Job OM, Bachmann LM, Thiel MA. Comparison and reproducibility of corneal thickness and curvature readings obtained by the Galilei and the Orbscan II analysis systems. J Cataract Refract Surg. 2008;34:1742–1747.

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Case report/Case series

Leber's hereditary optic neuropathy

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Abstract

Leber's hereditary optic neuropathy (LHON) is a maternally inherited mitochondrial disease caused by several point mutations in mitochondrial DNA. We present the case of a healthy 12-year-old Chinese boy who presented with bilateral, painless, subacute loss of central vision (more severe in the left eye the than right eye) for one week. No abnormalities were detected on magnetic resonance imaging of the brain and orbit. Serial Humphrey visual field tests initially showed a centrocaecal scotoma that worsened progressively. Cerebrospinal fluid samples and blood investigations showed normal results. A trial of steroid therapy was commenced with not much improvement in the patient's vision. A blood sample was then sent for LHON genetic testing and a mitochondrial DNA (mtDNA) G11778A pathogenic mutation was detected. The same mutation was also present in the patient's mother.

Keywords: genetic testing, Leber's hereditary optic neuropathy, mitochondrial disease

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Neuropati optik keturunan Leber

Abstrak

Neuropati optik warisan Leber (LHON) adalah penyakit mitokondrial yang diwarisi secara maternal yang disebabkan beberapa titik mutasi pada DNA mitokondria. Di sini kami melaporkan satu kes yang melibatkan seorang kanak-kanak lelaki berbangsa Cina yang mengalami kehilangan penglihatan pusat pada kedua-dua mata secara subakut (mata kiri lebih teruk berbanding dengan mata kanan) tetapi tidak menyakitkan selama seminggu. Penyiasatan lanjut mendapati tiada sebarang perubahan pada bahagian otak dan orbit melalui imej resonan magnetik (MRI). Sementara itu pemeriksaan medan penglihatan bersiri mengunakan mesin Humphrey menunjukkan scotoma centrocecal pada awalnya dan kemudian menjadi semakin teruk secara progresif. Manakala pemeriksaan darah dan cecair cerebrospinal tiada menunjukkan sebarang perubahan. Percubaan rawatan steroid gagal membantu dalam pemulihan penglihatan pesakit ini. Sampel darah juga diambil bagi ujian genetik LHON dan menunjukkan mutasi patogenik pada DNA mitokondria (mtDNA) G11778A. Mutasi yang sama juga dikesan pada ibu pesakit ini.

Kata kunci: neuropati optik keturunan Leber (LHON), penyakit mitokondrial, ujian genetik

Introduction

Leber's hereditary optic neuropathy (LHON) was first described in 1871 by German ophthalmologist Theodore Leber, and was subsequently named after him.[1] LHON is a maternally inherited mitochondrial disease caused by three primary mutations (*i.e.* m.3460G>A in *MT-ND1*, m.11778G>A in *MT-ND4,* and m.14484 T>C *MT-ND6*) in the mitochondrial DNA (mtDNA) genes.[2] For unknown reasons, males are more commonly affected than females. Patients are usually young adults who present with bilateral, painless, subacute visual loss. Blurring of vision may begin unilaterally or bilaterally; if vision loss starts in one eye, the fellow eye is usually affected within several weeks or months. Visual acuity and colour vision in both eyes progressively worsens over time. This condition mainly affects central vision, which is vital for tasks such as facial recognition, writing, reading and driving. Optic atrophy usually results by 6 months after onset with stabilization of visual loss.[3]

Case report

A healthy 12-year-old Chinese boy presented with bilateral, painless, subacute loss of central vision (more severe in the left eye the than right eye) for one week. Initially, right eye vision was refracted at 6/24 and left eye at 6/36. Bilateral pupillary reflexes were brisk with no relative afferent pupillary defect. Anterior segments were unremarkable with normal intraocular pressure. Bilateral fundi were initially unremarkable. A week later, the patient's vision deteriorated, with fundi showing hyperaemic discs with blurred margins and a single peripapillary blot haemorrhage in the left eye (Fig. 1). Figure 2 shows fundi photographs at 3 months after presentation. The patient also exhibited impaired colour perception. No abnormalities were detected on magnetic resonance imaging of the brain and orbit. Serial Humphrey visual field tests initially showed a centrocaecal scotoma that worsened progressively (Figs. 3 and 4). Figure 5 shows results from the Esterman Binocular Visual Field test done 3 months after presentation.

A lumbar puncture was performed and cerebrospinal fluid (CSF) samples were sent for routine stains and cultures, in addition to a polymerase chain reaction test to rule out herpes and cytomegalovirus infections. All CSF samples and blood investigations showed normal results.

The patient underwent a visual evoked potential (VEP) test that showed no consistent P100 in the left eye (Fig. 6). There was reduced amplitude and more prolonged implicit time for P100 in the left eye compared to the right eye. This was

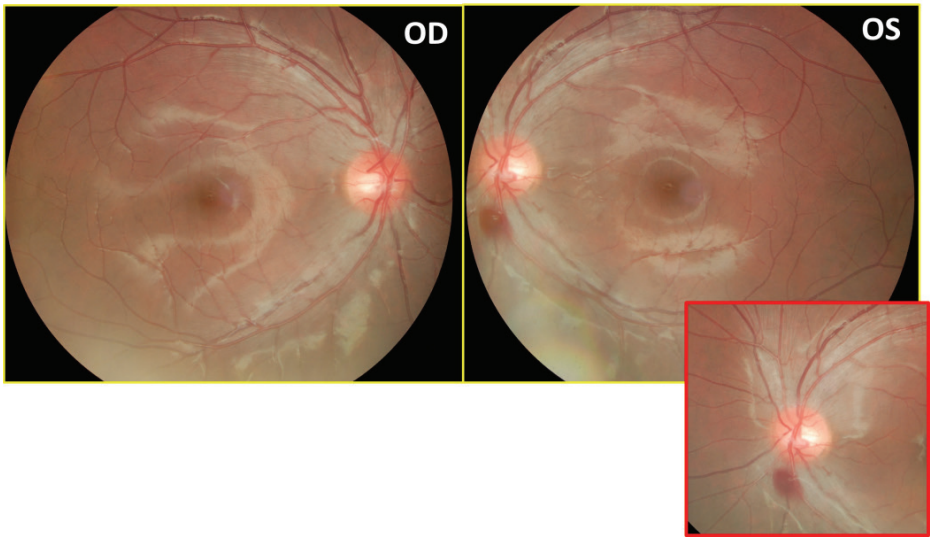

Fig. 1. Fundus photographs taken 1 week after presentation showing hyperaemic discs with blurred margins and a single peripapillary blot haemorrhage in the left eye.

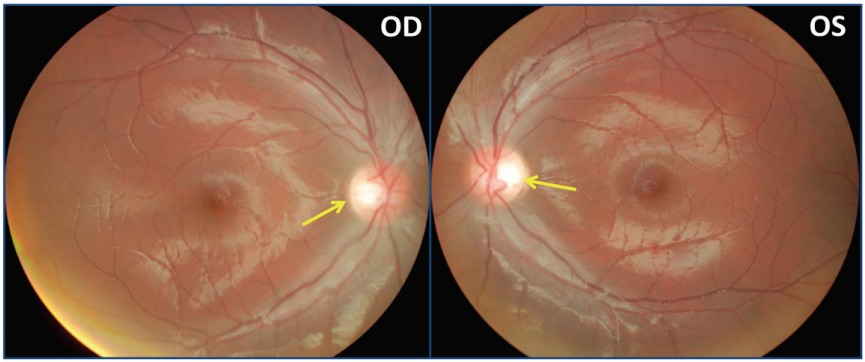

Fig. 2. Fundus photographs taken 3 months after presentation showing bilateral temporal disc pallor (*yellow arrows*).

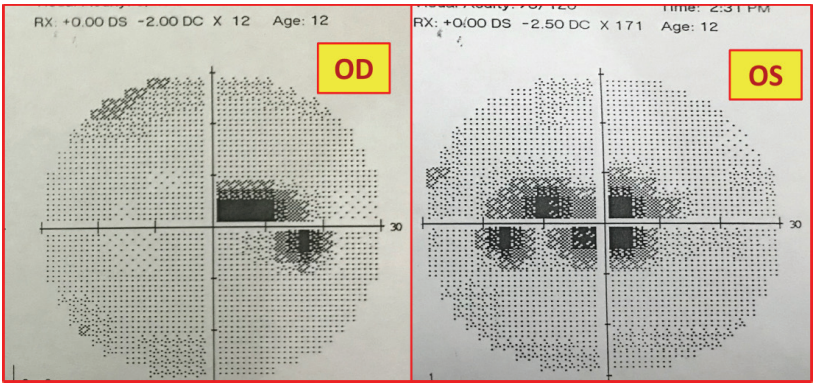

Fig. 3. Humphrey Visual Field test done at initial presentation showing a centrocaecal scotoma.

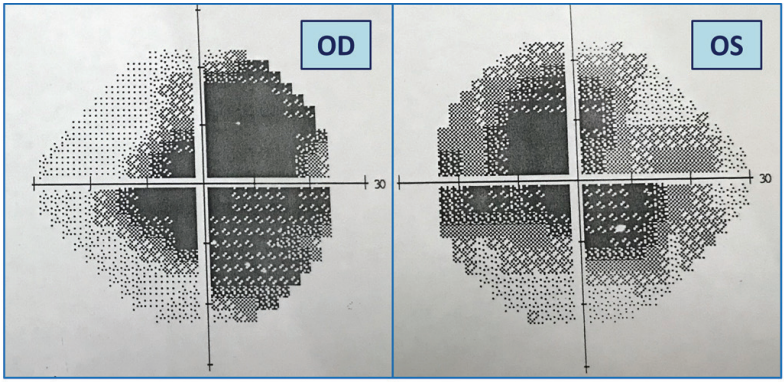

Fig. 4. Humphrey Visual Field test at 3 months after presentation showing significant deterioration.

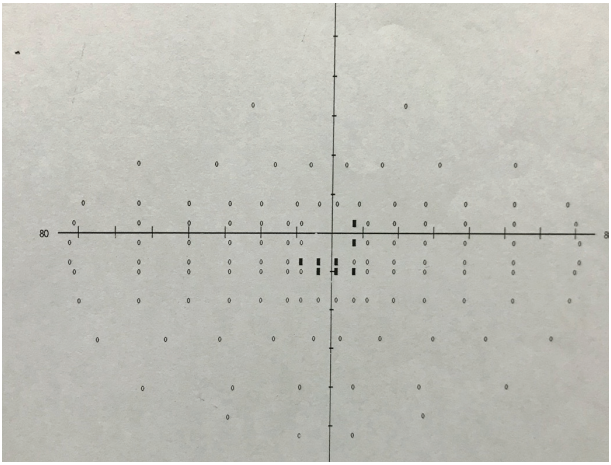

Fig. 5. Esterman Binocular Visual Field test at 3 months after presentation.

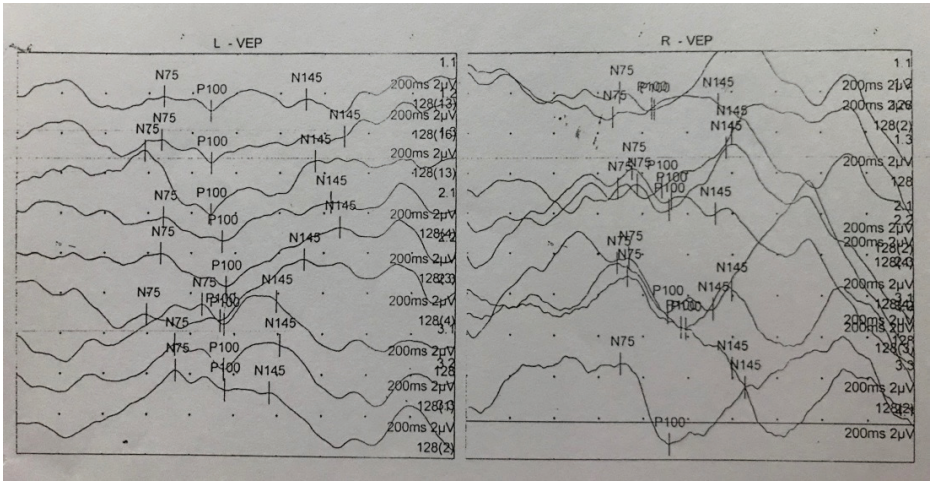

Fig. 6. VEP showed inconsistent P100 for the left eye (L-VEP), suggestive of very poor vision. The right eye (R-VEP) exhibited a small VEP amplitude with P100 still within normal range.

suggestive of very poor vision. The right eye exhibited a small VEP amplitude with P100 still within normal range; this was reported by the neurologist to be suggestive of axonal degeneration of the anterior visual pathway.

A trial of steroid therapy was commenced without much improvement in the patient's vision. A blood sample was then sent for LHON genetic testing and a mitochondrial DNA (mtDNA) G11778A pathogenic mutation was detected. The same mutation was also present in the patient's mother. The child is currently legally blind with best-corrected visual acuity of 3/60 in the right eye and 1/60 in the left eye. At the time of writing, he is registered in special education school.

Discussion

LHON has a mean age of onset between 18 and 35 years old.[4] This case had a rare presentation of symptoms in childhood with rapid progression. This is consistent with the study done by Barboni *et al.* in Italy, which reported that childhood onset (< 10 years) of LHON accounted for only 11.5% of cases among paediatric patients with hereditary optic neuropathy.[5]

Among the Asian population, a study done in Chinese children aged ≤ 14 years with suspected hereditary optic neuropathy showed that 29.3% patients carried one of the three primary mtDNA mutations (LHON group). Mutations at m.11778, m.14484, and m.3460 were observed in 85.4%, 10.1%, and 4.5% of the cases, respectively.[6]

Patients with the m.14484 T>C mutation have been observed to have a better visual prognosis than those carrying either the m.11778 G>A or the m.3460 G>A mutation. The latter two mutations manifest a more severe clinical presentation and the chance of spontaneous recovery from vision loss is lower.[7] Interestingly, a person may carry a mitochondrial DNA (mtDNA) mutation that causes LHON without experiencing any signs or symptoms of vision loss.

The classic clinical signs of optic neuropathy are visual field defect, dyschromatopsia, and abnormal pupillary response. Eyecare providers should suspect hereditary optic neuropathy in children who exhibit discrepancies between pupillary reflex and other optic nerve functions.[1] All it takes is a simple mtDNA blood test to determine if an individual has one of the primary mutations if LHON is suspected.

Sadly, there is currently no established medical treatment for LHON. Gene therapy using an adeno-associated viral vector carrying ND4 genetic material injected intravitreally is still under investigation.[8] In the absence of any clinically effective treatment, supportive services such as low vision aids remain the mainstay of management and should be provided early.

Conclusion

Due to its rarity, a diagnosis of LHON may be missed if the ophthalmologist does not have a high index of suspicion. This case was initially treated as bilateral optic neuritis with commencement of steroid therapy to no avail. A string of blood and CSF investigations initially yielded negative results. Neuroimaging results were also unremarkable. After ruling out infectious, inflammatory, space-occupying lesion, trauma, and autoimmune causes, we subsequently suspected LHON as a possible aetiology. Hereditary optic neuropathies must always be in an ophthalmologist's differential diagnosis list. A detailed family history is also imperative in diagnosing hereditary optic neuropathies.

References

1. Iorga RE, Mihailovici R, Ozturk MR, Costin D. Leber's hereditary optic neuropathy: Case report. Rom J Ophthalmol. 2018;62(1):64-71.
2. Man PYW, Turnbull DM, Chinnery PF. Leber hereditary optic neuropathy. J Med Genet. 2002;39:162-169.
3. Carelli V. Leber's hereditary optic neuropathy. In: Schapira AHV, DiMauro S. Mitochondrial Disorders in Neurology. Blue Books of Practical Neurology. Vol. 26. 2nd ed. Boston: Butterworth-Heinemann; 2002. p. 115-142.
4. Orssaud C. Leber's hereditary optic neuropathy. Orphanet Encyclopedia. November 2003. Available at: http://www.orpha.net/data/patho/GB/uk-LHON.pdf
5. Barboni P, Savini G, Valentino ML, et al. Leber's hereditary optic neuropathy with childhood onset. Invest Ophthalmol Vis Sci. 2006;47(12):5303-5309.
6. Li Y, Li J, Jia X, et al. Genetic and Clinical Analyses of DOA and LHON in 304 Chinese Patients with Suspected Childhood-Onset Hereditary Optic Neuropathy. PLoS One. 2017;12(1):e0170090
7. Mascialino B, Leinonen M, Meier T. Meta-analysis of the prevalence of Leber hereditary optic neuropathy mtDNA mutations in Europe. Eur J Ophthalmol. 2012;22(3):461-465
8. Peragallo JH, Newman NJ. Is there treatment for Leber hereditary optic neuropathy? Curr Opin Ophthalmol. 2015;26(6):450-457

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Case report/Case series

Treatment of conjunctival squamous cell carcinoma: balancing disease eradication with minimising treatment-induced morbidity

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Abstract

A 41-year-old male presented with a large non-pigmented lesion on the ocular surface involving 8 clock hours of limbus, bulbar conjunctiva, and palpebral conjunctiva. Incisional biopsy confirmed poorly differentiated conjunctival squamous cell carcinoma (SCC). It was staged as a T3, N0, M0 lesion. Treatment was with surgical excision, amniotic membrane transplant, and buccal mucosa graft. Three weekly cycles of 0.04% mitomycin C were administered postoperatively. Six months following excision, although there was no evidence of residual conjunctival SCC, the patient suffered from poor vision, significant pain, and diplopia due to severe dry eye, limbal stem cell deficiency, and symblepharon.

This case illustrates the difficult clinical decisions which confront the clinician when treating conjunctival SCC, particularly with balancing the need to eradicate the disease to prevent local invasion and metastatic spread on the one hand and minimising ocular morbidity on the other.

Keywords: conjunctival intraepithelial neoplasia, conjunctival squamous cell carcinoma

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Rawatan bagi karsinoma sel skuamos pada konjunktiva: mengimbangi antara eradikasi penyakit dan mengurangi morbiditi akibat kesan rawatan

Seorang lelaki berusia 41 tahun dengan satu ketumbuhan tanpa pigmentasi yang besar pada permukaan okular yang melibatkan bahagian limbus pada kedudukan pukul 8, bulbar dan palberal konjunktiva. Biopsi insisional mengesahkan diagnosa karsinoma sel skuamos (SCC) jenis yang kurang perbezaan. Pemeriksaan lanjut mengesahkan peringkat karsinoma sebagai T3, N0 dan M0. Pembedahan eksisi beserta transplantasi membran amniotic dan graf mukosa mulut bukal telah dibuat. Dituruti oleh tiga kali kitaran rawatan dengan mitomycin C 0.04% pada setiap tiga minggu selepas pembedahan.

Pembedahan tersebut berhasil tanpa sebarang residual SCC enam bulan selepas pembedahan. Namun pesakit mengalami masalah penglihatan yang berkurangan, kesakitan yang signifikan dan diplopia disebabkan oleh kekeringan mata yang teruk, defisiensi sel stem limbal dan pembentukan simbleparon.

Kes ini mengilustrasikan kesukaran membuat keputusan klinikal yang dihadapi oleh doktor perawat, terutama dari segi mengimbangi keperluan eradikasi penyakit dan menghalang rebakan setempat dan metastasis pada satu aspek dengan mengurangkan mobiditi okular dari aspek yang lain.

Kata kunci: karsinoma sel skuamosa konjunktiva, neoplasia intraepithelial konjunktiva

Case report

A 41-year-old male was referred with a large lesion on the right globe that had been slowly growing for the previous 10 years. There was no significant past medical history and specifically no history of prior malignancy or immunosuppression. There was no past ophthalmic history.

Examination revealed a corrected distance visual acuity (CDVA) of 20/50 in the right eye and 20/20 in the left eye. There was a non-pigmented, gelatinous lesion involving 8 clock hours of the limbus, the entire temporal and inferior bulbar conjunctiva, the entire lateral and inferior forniceal conjunctiva, and most of the inferior tarsal conjunctiva (see figure 1). Gonioscopy showed no involvement of the angles. Fundus examination was normal. Examination of the left eye was unremarkable. There was no lymphadenopathy.

Anterior segment optical coherence tomography (OCT) (Casia 2, Tomey, Aichi, Japan) showed there was no invasion of the globe. An incisional biopsy was

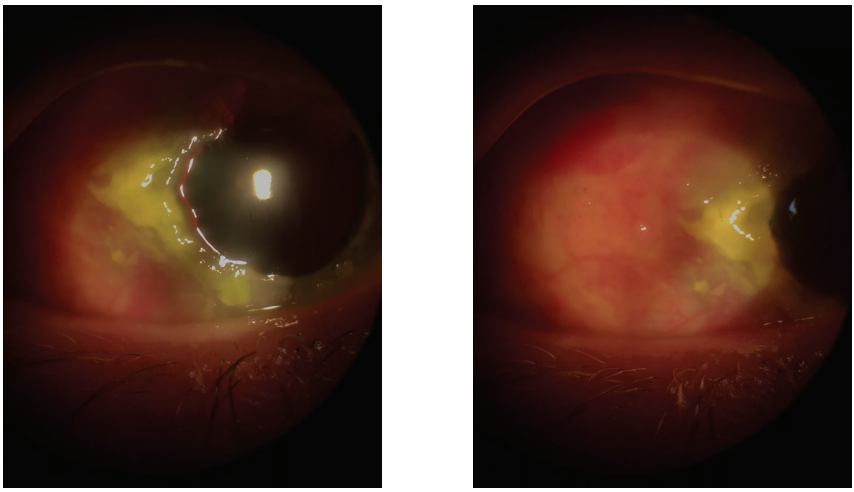

Fig. 1. Anterior segment photos of the right eye showing (*left*) conjunctival SCC involving the limbus and (*right*) conjunctival SCC involving a large section of the bulbar conjunctiva.

performed, and the biopsied section showed a poorly differentiated conjunctival squamous cell carcinoma (SCC). A magnetic resonance imaging (MRI) scan of the orbits, brain, and neck was performed which showed no evidence of orbital invasion, lymph node involvement or cerebral metastasis. This lesion was classified as T3, N0, M0 according to the American Joint Committee on cancer classification of ocular surface squamous neoplasia.

Given the concern for possible metastasis if not treated aggressively, a decision was made to treat the lesion with primary excision rather than with topical and/or sub-conjunctival chemotherapeutic agents. Due to the absence of orbital extension, exenteration was considered unnecessary. The corneal team performed excision of the lesion from globe with 4 mm margins. Double freeze-thaw cryotherapy was applied to the limbus and conjunctival edge. An amniotic membrane transplant was applied to the area of excision and fixed with fibrin glue. The oculoplastics team performed excision of the lesion from the forniceal and palpebral conjunctiva. A buccal mucosa graft was harvested and sutured to the area of excision. Postoperatively, topical mitomycin C 0.04% four times a day for three weekly cycles, with 1 week without drops in between cycles was prescribed. The patient reported good adherence to treatment.

Two months postoperatively, the patient was troubled by severe eye discomfort, poor vision, and diplopia. Examination of the affected eye showed that CDVA was count fingers at 50 cm. No evidence of residual disease was present although there was significant limbal stem cell deficiency as evidenced by pannus, which extended to involve the central cornea. There was severe dry eye with grade 4 Oxford ocular surface staining. Extraocular motility was severely impaired (-3 adduction, -2

abduction, -1 elevation, -1 depression) due to symblepharon which extended from 3 o'clock to 12 o'clock, resulting in significant forniceal shortening. These symptoms and signs have persisted until the last review 6 months following excision of the lesion. Plans for future ocular surface reconstruction include: upper and lower forniceal reconstruction with buccal mucosa graft, *ex vivo* limbal stem cell transplantation, and possible corneal transplantation depending on the extent of corneal scarring and irregularity following the limbal stem cell transplant.

Discussion

Conjunctival SCC is a conjunctival tumour arising from the epithelial layer that breaches the epithelial basement membrane and invades the underlying stroma.[1] This tumour has the ability to invade the lamella of the cornea and sclera to invade the anterior chamber of the eye. Furthermore, conjunctival SCC can also penetrate the orbital septum to invade the orbit, sinuses, and brain.[2] In rare cases, conjunctival SCC can gain access to blood vessels and lymphatics, resulting in local and distant metastasis, and even death.[3]

Several treatment modalities for conjunctival SCC are described in the literature. The most commonly reported treatment is wide-margin excision with or without cryotherapy.[4] Other treatments include topical or perilesional chemotherapy,[5] external beam radiotherapy,[6] plaque radiotherapy,[7] and orbital exenteration.[8]

An important challenge facing the clinician treating extensive conjunctival SCC is achieving disease eradication whilst minimising treatment-induced morbidity. In this case, priority was given to treating the disease to ensure no further local and metastatic spread. An alternative treatment course considered was to treat with topical interferon α-2b in the hope of reducing the size of the lesion (chemo-reduction), thus allowing a smaller and less invasive excision. However, the treating team was concerned regarding the possibility of local invasion and metastasis occurring during the period of chemo-reduction.

Ultimately, the treatment resulted in significant ocular morbidity, including limbal stem cell deficiency, severe dry eye, ophthalmoplegia, and diplopia. Given the significant iatrogenic morbidity, the question arises whether the treatment undertaken was justified to minimise the risk of metastasis. Published data of conjunctival SCC shows that rates of metastatic disease following treatment for conjunctival SCC ranges from 0 to 18%, depending on the series, with rates of death ranging from 1% to 12%.[2,9,10] The average follow-up period in these studies ranges from 24 to 56 months. Sites of metastatic disease include regional lymph nodes, lungs, and brain.

The authors considered the option of treating with topical or perilesional chemotherapeutic agents. However, this was decided against as the evidence regarding the longer-term outcomes of local chemotherapy for conjunctival SCC is limited.

Arguably, the best evidence comes from a case series of 18 eyes published by Kim *et al.,* which showed excellent outcomes in eyes treated with topical and/or injected interferon α-2b, with no cases of metastasis or death.[5] However, this case series' median follow-up period was only 11 months and metastatic disease may not manifest until several years later.

In conclusion, this case illustrates the difficult issues that arise when treating conjunctival SCC as the clinician attempts to balance disease eradication and treatment-induced morbidity. There is no clear consensus regarding the appropriate treatment of such cases and certainly more research is needed to clarify the most effective treatment modalities for conjunctival SCC.

References

1. Lee GA, Hirst LW. Ocular surface squamous neoplasia. Surv Ophthalmol. 1995;39(6):429-450.
2. Miller CV, Wolf A, Klingenstein A, et al. Clinical outcome of advanced squamous cell carcinoma of the conjunctiva. Eye (Lond). 2014;28(8):962-967.
3. Shields CL, Shields JA. Tumors of the conjunctiva and cornea. Surv Ophthalmol. 2004;49(1):3-24.
4. Shields JA, Shields CL, De Potter P. Surgical management of conjunctival tumors. The 1994 Lynn B. McMahan Lecture. Arch Ophthalmol. 1997;115(6):808-815.
5. Kim HJ, Shields CL, Shah SU, Kaliki S, Lally SE. Giant ocular surface squamous neoplasia managed with interferon alpha-2b as immunotherapy or immunoreduction. Ophthalmology. 2012;119(5):938-944.
6. Lommatzsch P. Beta-ray treatment of malignant epithelial tumors of the conjunctiva. Am J Ophthalmol. 1976;81(2):198-206.
7. Arepalli S, Kaliki S, Shields CL, Emrich J, Komarnicky L, Shields JA. Plaque radiotherapy in the management of scleral-invasive conjunctival squamous cell carcinoma: an analysis of 15 eyes. JAMA Ophthalmol. 2014;132(6):691-696.
8. McKelvie PA, Daniell M, McNab A, Loughnan M, Santamaria JD. Squamous cell carcinoma of the conjunctiva: a series of 26 cases. Br J Ophthalmol. 2002;86(2):168-173.
9. Chauhan S, Sen S, Sharma A, et al. American Joint Committee on Cancer Staging and clinicopathological high-risk predictors of ocular surface squamous neoplasia: a study from a tertiary eye center in India. Arch Pathol Lab Med. 2014;138(11):1488-1494.
10. Tunc M, Char DH, Crawford B, Miller T. Intraepithelial and invasive squamous cell carcinoma of the conjunctiva: analysis of 60 cases. Br J Ophthalmol. 1999;83(1):98-103.

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Case report/Case series

Lamellar hole-associated epiretinal membrane in retinitis pigmentosa: a surgical correlation

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Abstract

Retinitis pigmentosa (RP) is a rare hereditary disease, yet it is the commonest cause of retinal dystrophy. Although lamellar hole-associated epiretinal membrane (LHEP) is commonly associated with macular holes, the development of macular holes in RP itself is rare. In this article, we report a rare case of bilateral LHEP in RP, and the surgical outcome of LHEP embedding and internal limiting membrane (ILM) flap in repairing a lamellar macular hole (LMH).

A 57-year-old woman who had RP with bilateral LHEP underwent a combination of cataract and vitrectomy surgery in her left eye. We preserved LHEP tissue and performed an ILM flap to avoid a iatrogenic full-thickness macular hole (FTMH) and facilitate LMH closure. Her right eye was monitored conservatively. At 2 weeks postoperative, the LMH in her left eye was anatomically repaired. There was limited improvement of visual acuity, which could be justified by disruption of the junction between the photoreceptors' inner and outer segments (IS/OS junction) as evidenced by spectral-domain optical coherence tomography (SD-OCT).

The presence of LHEP in LMH is highly associated with disruption of the IS/OS junction and therefore patients should be counselled regarding guarded visual improvement post-vitrectomy. LHEP, which is derived from a Müller cell-driven process, is closely associated with LMH in RP, likely due to the progressive retinal tissue loss as a result from the disease nature of RP. Therefore, we suggest preserving LHEP tissue and performing an ILM flap as an improvised technique to avoid iatrogenic FTMH and facilitate LMH closure.

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Keywords: epiretinal membrane, internal limiting membrane flap, lamellar hole, retinitis pigmentosa

Membran epiretinal yang berkaitan dengan lubang lamela pada retinitis pigmentosa: korelasi pembedahan

Abstrak

Retinitis pigmentosa (RP) adalah penyakit keturunan yang jarang berlaku, namun ia adalah penyebab distrofi retina yang paling kerap berlaku. Walaupun membran epiretinal yang berkaitan dengan lubang lamela (LHEP) biasanya dikaitkan dengan lubang makula, pembentukan lubang makula pada RP itu sendiri jarang berlaku. Dalam artikel ini, kami melaporkan kes LHEP kedua belah mata yang jarang terjadi dalam RP, dan hasil pembedahan penyisipan LHEP dan membrane pemisah dalaman (ILM) dalam memperbaiki lubang makula lamela (LMH).

Seorang wanita berusia 57 tahun yang menjalani RP dengan LHEP pada kedua belah mata menjalani kombinasi pembedahan katarak dan vitrectomy di mata kirinya. Kami memelihara tisu LHEP dan melakukan flap ILM untuk mengelakkan berlakunya lubang makular ketebalan penuh iatrogenik (FTMH) dan memudahkan penutupan LMH. Mata kanannya dipantau secara konservatif. Pada 2 minggu selepas pembedahan LMH di mata kirinya dibaiki secara anatomi. Peningkatan ketajaman penglihatan adalah terhad, yang disebabkan oleh gangguan persimpangan antara segmen dalaman dan luar fotoreseptor (persimpangan IS / OS) seperti yang dibuktikan oleh tomografi koheren optik-domain spektrum (SD-OCT).

Kehadiran LHEP di LMH sangat berkaitan dengan gangguan pada persimpangan IS / OS dan oleh itu pesakit harus diberi khidmat nasihat mengenai ketidakpastian pada peningkatan visual akuiti selepas jagaan vitrektomi. LHEP, yang berasal dari proses yang didorong oleh sel Müller, berkait rapat dengan LMH dalam RP, mungkin disebabkan oleh kehilangan tisu retina progresif akibat dari sifat penyakit RP. Oleh itu, kami mencadangkan pemeliharaan tisu LHEP dan melakukan flap ILM sebagai teknik improvisasi untuk mengelakkan FTMH iatrogenik dan memudahkan penutupan LMH.

Kata kunci: kepak membran dalaman, lubang lamela, membran epiretin, retinitis pigmentosa

Introduction

Retinitis pigmentosa (RP) is a rare hereditary disease, yet it is the commonest cause of retinal dystrophy. It is characterized by dystrophy of rod and cone photoreceptors, causing decreased night vision and progressive peripheral vision loss, which affect 0.025% of the population worldwide.[1] Fundus examination typically reveals pale optic discs, bony spicule pigmentary changes involving the equatorial retina, arteriolar narrowing, retinal pigment epithelium, atrophy, and cystoid macular oedema.[1]

Although lamellar hole-associated epiretinal membrane (LHEP) is commonly associated with macular holes, the development of macular holes in RP itself is rare.[2] LHEP is defined as an homogenous material with medium reflectivity evidenced on spectral-domain optical coherence tomography (SD-OCT), and its presence signifies more severe macular defects and outer retinal disruptions.[2,3] While some studies reported anatomical and functional improvement following vitrectomy surgery for lamellar macular hole (LMH) repair,[4] others suggested conservative management as spontaneous closure is frequently observed and warranted the risk of developing full-thickness macular hole (FTMH) post-vitrectomy.[5,6]

We report a rare case of bilateral LHEP in RP, and the surgical outcome of this patient. The presence of LHEP in LMH is highly associated with disruption of the IS/OS junction and therefore the patient should be counselled regarding guarded visual improvement post-vitrectomy. As a safety measure to prevent iatrogenic FTMH, we propose using LHEP and internal limiting membrane (ILM) flap for LMH repair instead of the conventional LHEP and ILM peeling.

Case report

A 57-year-old woman who was diagnosed with RP at the age of 20 presented with gradual worsening of vision in both eyes over the past 3 years. On examination, her Snellen best-corrected visual acuity (BCVA) was 6/24 in the right eye and 3/60 in the left eye. Slit-lamp examination of the anterior segment revealed nuclear sclerotic cataract 3+ in both eyes, and posterior segment revealed LMH with LHEP present in both eyes. Narrowing of retinal arterioles and bony spicule pigmentary changes were observed in both eyes. Figure 1 depicts the retinal pathology observed and Figure 2 depicts the serial SD-OCT findings of her left eye.

The patient was counselled regarding guarded visual prognosis and risk of developing FTMH, but she decided on going ahead with surgery. She underwent left eye phacoemulsification and implantation of intraocular lens, combined with 23-gauge pars plana vitrectomy. The optic disc gliosis was removed, followed by peeling of the LHEP centripetally using intraocular forceps. The LHEP was left attached to the edge of the LMH, forming a perifoveal crown phenomenon, and

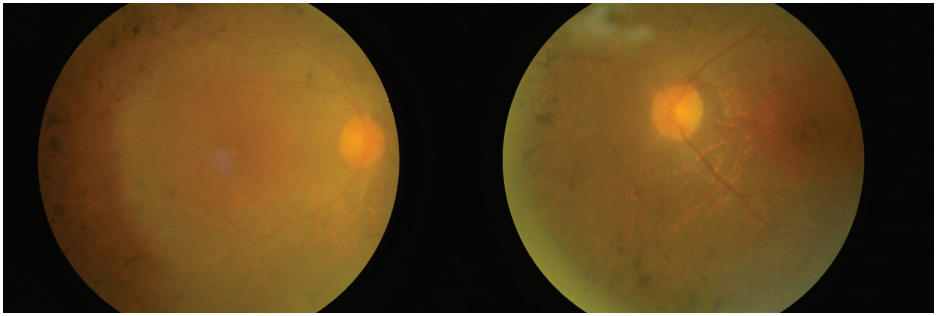


Fig. 1. Narrowing of retinal arterioles, bony spicule pigmentary changes and macular hole on the right (*left*) and left (*right*) eye

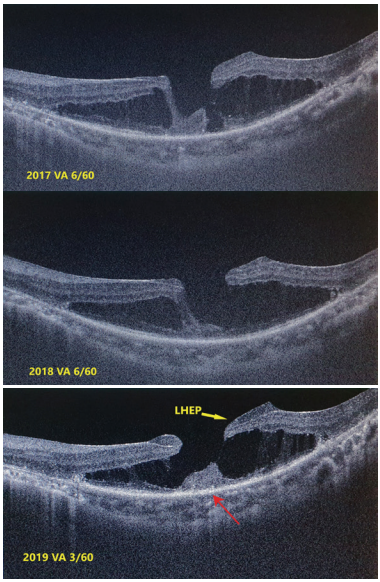
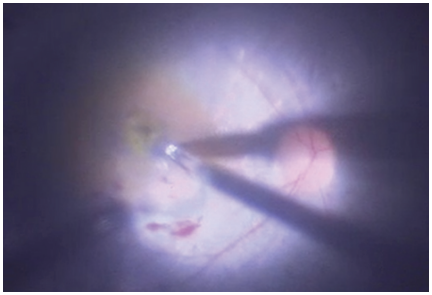


Fig. 2. The serial preoperative SD-OCT images reveal the lamellar hole with LHEP (*yellow arrow*) in the left eye, with evidence of disruption of the IS/OS junction (*red arrow*).



Video 1. Steps of lamellar macular hole repair with internal limiting membrane (ILM) flap, starting with optic disc gliosis removal, followed by lamellar hole-associated epiretinal membrane peeling, forming a perifoveal crown phenomenon. Brilliant blue-assisted ILM flap was performed, and the surgery was completed by 20% sulphur hexafluoride gas exchange.

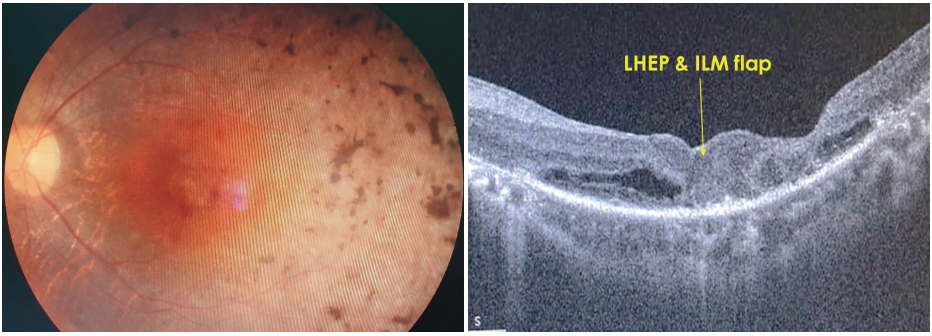


Fig. 3. Fundus photograph (*A*) and SD-OCT image (*B*) of the left eye showing repaired lamellar hole using LHEP and ILM flap (*yellow arrow*) at the 2-week postoperative follow-up.

then gently embedded into the retinal cleavage. We were cautious to minimize unnecessary traction on the fovea. Viscoelastic was injected as protection to the ocular structures, and brilliant blue-assisted ILM flap was performed. The ILM was peeled from the periphery towards the LMH, and then inverted to completely cover the LMH with the embedded LHEP. The surgery was completed by 20% sulphur hexafluoride gas exchange. Video 1 illustrates the steps of the vitrectomy surgery.

At 2 weeks postoperative, the LMH in her left eye was anatomically repaired, but with limited improvement in visual acuity to 6/60. At 2 months postoperative, her BCVA remained stable at 6/60 in the left eye and 6/24 in the right eye. No FTMH development nor macular scarring was observed. Figure 3 describes the anatomically repaired LMH using LHEP and ILM flap in the left eye.

Discussion

This case report exhibits a rare case of bilateral LHEP in RP, and demonstrates a new technique using LHEP and ILM flap in repairing LMH. Due to the scarcity of LMH formation in RP patients, the mechanism of formation remains unknown.[1] To date, the literature suggests two main mechanisms of LMH formation: tractional LMH due to posterior vitreous detachment with conventional epiretinal membrane (ERM) and intact ellipsoid layer on the one hand, and degenerative LMH due to contraction of LHEP and disrupted ellipsoid layer on the other.[4,5] The latter mechanism is more likely to explain LMH formation in our patient.

Recent studies[3,7] have established that the presence of LHEP is associated with deeper tissue defects, thinner hole bases, and IS/OS junction defects. An immunohistochemical study by Pang *et al.*[7] revealed that LHEP is derived from a Müller cell-driven process originating in the inner retinal layers of the macular defect, which act as a central plug to stabilize the structurally compromised macula.[7] Therefore, progressive retinal tissue loss as a result from the disease nature of RP

may be accountable for the high prevalence of LHEP in RP patients, as observed in our patient.

Vitrectomy for LMH repair in RP remains controversial due to its limited visual improvement postoperatively and the stable nature of LMHs. Pang *et al.*[7] observed that 80% of the LMHs remain functional and morphologically stable without surgical intervention, and spontaneous closure of LMH has been frequently observed in other studies.[2,5] It is not surprising to learn that 20% of the patients with LHEP who underwent vitrectomy developed FTMH,[8] as LHEP is postulated to originate from of Müller cell proliferation onto the inner retina.[7] However, there are a growing number of studies demonstrating favourable outcomes in terms of anatomical and functional aspects.[4]

Instead of the conventional vitrectomy, LHEP and ILM peeling, we performed 23-gauge pars plana vitrectomy, LHEP embedding with ILM flap and gas tamponade in our patient. Intraoperatively, LHEP was peeled carefully from the outside to the edge of the LMH, forming a perifoveal crown phenomenon, described by Son *et al.* as a floating, crown-like yellowish tissue with its base attached to the edge of the margin on the macula.[9] We then embedded the LHEP tissue into the LMH to prevent a iatrogenic FTMH, and performed ILM flap to repair the LMH. Shiode *et al.*[10] suggested that performing an ILM flap after LHEP embedding can retain the LHEP in the retinal cleavage during fluid-gas exchange, and that the ILM flap acts as a scaffold to promote the proliferation and migration of glial cells into the LHEP, thus expediting LMH closure[10] and preventing progressive retinal tissue loss.[2]

At 2 weeks postoperative, our patient showed anatomical recovery in the left eye with limited visual acuity improvement, which could be attributed to the pre-operative disruption of the IS/OS junction. This outcome is consistent with a study by Ko *et al.*[6] which demonstrated limited postoperative visual acuity improvement for eyes with LHEP despite anatomical improvement given the preoperative disrupted IS/OS line integrity was not restored postoperatively. Furthermore, our patient's right eye, which also had LHEP, remained stable on conservative monitoring. This affirms that LHEP is a stable clinical entity, as established by multiple studies.[6,8]

In this case report we described a rare occurrence of bilateral LHEP in RP, and reported successful anatomical closure of LMH by LHEP embedding and ILM flap technique. However, we were unable to exclude the possibility of recurrence of LHEP, development of secondary ERM, or macular scar formation during long-term follow up, but these were absent at our 2-month post-operative follow up. We hope that this case report could prompt further prospective studies to determine the efficacy and monitor the long-term outcomes of this technique.

Acknowledgements

The case patient consented to the publication of this case report, including the usage of her fundus photograph, OCT scans, and video of the surgery. The authors received no financial support for the research, authorship, and/or publication of this article, and disclose no conflict of interest.

References

1. Hartong DT, Berson EL, Dryja TP. Retinitis pigmentosa. The Lancet. 2006;368:1795-1809.
2. Liu J, Lyu J, Zhang X, Zhao P. Lamellar hole-associated epiretinal membrane is a common feature of macular holes in retinitis pigmentosa. Eye. 2020;34:643–649.
3. Lai T-T, Chen S-N, Yang C-M. Epiretinal proliferation in lamellar macular holes and full-thickness macular holes: clinical and surgical findings. Graefe's Arch Clin Exp Ophthalmol. 2016;254:629-638.
4. Guber J, Scholl HP, Valmaggia C. Surgical Outcome after Lamellar Macular Hole Associated with Epiretinal Membrane. Ophthalmologica. 2019;241:56-60.
5. Coassin M, Mastrofilippo V, Stewart JM, et al. Lamellar macular holes: surgical outcome of 106 patients with long-term follow-up. Graefe's Arch Clin Exp Ophthalmol. 2018;256:1265-1273.
6. Ko J, Kim GA, Lee SC, et al. Surgical outcomes of lamellar macular holes with and without lamellar hole-associated epiretinal proliferation. Acta Ophthalmol. 2017;95:e221-e6.
7. Pang CE, Spaide RF, Freund KB. Epiretinal proliferation seen in association with lamellar macular holes: a distinct clinical entity. Retina. 2014;34:1513-1523.
8. Coassin M, Mori T, Di Zazzo A, Sgrulletta R, Varacalli G, Bonini S. Lamellar macular holes: monitoring and management strategies. Clin Ophthalmol. 2019;13:1173.
9. Son G, Lee JS, Lee S, Sohn J. Epiretinal proliferation associated with macular hole and intraoperative perifoveal crown phenomenon. Kor J Ophthalmol. 2016;30:399-409.
10. Shiode Y, Morizane Y, Takahashi K, et al. Embedding of lamellar hole-associated epiretinal proliferation combined with internal limiting membrane inversion for the treatment of lamellar macular hole: a case report. BMC Ophthalmol. 2018;18:257.

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Case report/Case series

Spontaneous retinal pigment epithelial rip

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Abstract

This is a case report of a spontaneous retinal pigment epithelial (RPE) rip in a 64-year-old woman who presented with progressive, painless, blurring of vision in her right eye for 2 weeks. Her vision was 6/60 in the right eye and 6/6 in the left eye. On fundoscopy, there was a large depigmented area over the right posterior pole. A large area of RPE rip involving the fovea was revealed via optical coherence tomography and angiogram. Spontaneous RPE rip is a rare manifestation. However, when the fovea is involved the visual prognosis is poor. This article aims to highlight the vital role of multimodal imaging in aiding the diagnosis of RPE rips or tears.

Keywords: retinal pigment epithelium, retinal pigment epithelium rip, retinal pigment epithelium tear

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Pemisahan epitel pigmen retina secara spontan

Abstrak

Ini adalah laporan kes pemisahan epitel pigmen retina secara spontan (RPE) pada wanita berusia 64 tahun yang mengalami pengaburan penglihatan mata kanan selama 2 minggu. Penglihatannya 6/60 di mata kanan dan 6/6 di mata kiri. Dalam funduskopi terdapat kawasan pemisahan RPE yang besar. Sebilangan besar koyakan RPE yang melibatkan fovea didedahkan melalui tomografi koheren optik dan angiogram.Koyakan RPE spontan adalah manifestasi yang jarang berlaku. Walau bagaimanapun, apabila fovea terlibat, prognosis visual adalah kurang baik. Artikel ini bertujuan untuk menonjolkan peranan penting pengimejan multimodal dalam membantu diagnosis koyakan RPE.

Kata kunci: epitel pigmen retina, koyakan epitelium pigmen retina, rip epitel pigmen retina

Introduction

Spontaneous large retinal pigment epithelial (RPE) rip is an uncommon sight-threatening complication usually associated with wet age-related macular degeneration.[1] Recently, due to the vast use of anti-vascular endothelial growth factor (anti-VEGF), there has been a rise in the occurrence of RPE rips.[2] RPE tears or rips are graded based on the most significant linear diameter of the tear, measured by fluorescein angiography.[3] This case highlights a spontaneous large RPE rip diagnosed with multimodal imaging.

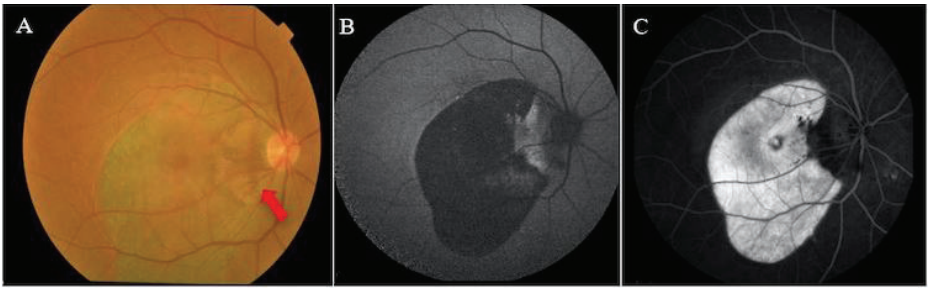

Fig. 1. (*A*) Right eye fundus showing large depigmented area at the posterior pole extending to the inferior retina and pigmented area nasally (*arrow*). (*B*) Autofluorescence of the right eye showing hypofluorescence over bare area devoid of RPE. (*C*) FFA of the right eye with a large area of window defect.

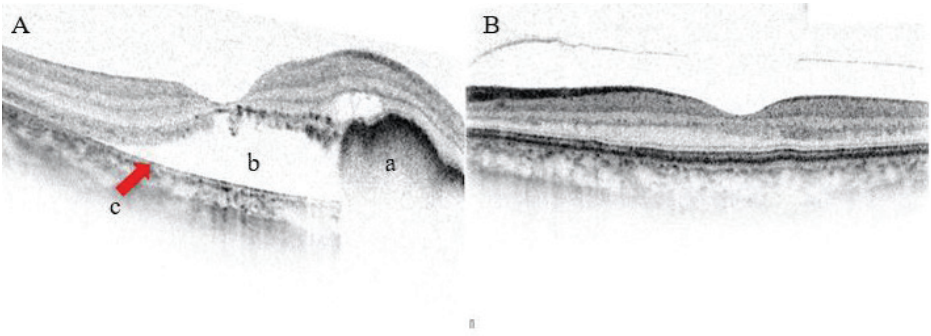

Fig. 2. (*A*) Right eye OCT showing disruption of the RPE layer, hyper-reflectivity on the nasal side due to the rolled RPE. (*a*) Presence of empty subretinal space. (*b*) RPE is missing with a visible Bruch's membrane (*c with red arrow*). (*B*) Left eye OCT showing normal contour.

Case report

A 64-year-old woman with underlying hypertension presented with painless blurring of vision and metamorphopsia of the right eye for 2 weeks. She denied history of ocular trauma or taking medication containing steroids. Her best-corrected visual acuity (BCVA) was 6/60 in the right eye and 6/6 in the left eye. Her anterior segment examination was otherwise unremarkable.

On fundus biomicroscopy, there was a large depigmented area over the right posterior pole extending to the inferior retina (Fig. 1A). The area was crescent-shaped, with a well-demarcated margin. There was an adjacent hyperpigmented area nasally. Clinically, the depigmented area resembled an area of absent RPE with bare choroid, whereas the adjacent hyperpigmented lesion represented redundant retracted RPE. However, there was no retinal haemorrhage, drusen, orange nodule, pigment epithelial detachment, or other chorioretinal lesions. The left eye revealed normal findings.

On autofluorescence, there was hypoautofluorescence in the area where RPE was void and hyperautofluorescence coinciding with the area of retracted RPE (Fig. 1B). The fundus fluorescein angiogram (FFA) revealed the reverse, with a well-demarcated window defect of hyperfluorescence corresponding to the RPE rip, surrounded by a rim of hypofluorescence nasally caused by retracted RPE (Fig. 1C).

Optical coherence tomography (OCT) revealed a large area devoid of RPE (Fig. 2A). Nasal to the lesion, there was an area of rolled RPE with an irregular contour that was responsible for the dense hyper-reflectivity. This is likely due to the duplication of RPE in that area. The hyper-reflectivity gives rise to an intense posterior shadowing, completely masking the choroid beneath it.

Discussion

Vascularized retinal pigment epithelial detachment (PED) in patients with exudative macular degeneration is the most usual cause for RPE tear.[2] Other reasons that account for this rare manifestation are RPE thinning, choroidal swelling, vitreoretinal traction, blunt trauma, and iatrogenic causes such as laser photocoagulation and photodynamic therapy.[2]

Our patient presented with a spontaneous rip. There was absence of drusen and chorioretinal lesions. Fryczkowsi *et al.* described a patient with high myopia (refractive error 10.0 D) complicated with RPE tear. Physical forces secondary to ocular movement are passing through the thin sclera and Bruch's membrane to the RPE, predisposing myopes to have RPE rip at the margin of posterior staphyloma.[4] This was unlikely the case for our patient, as there was no evidence of posterior staphyloma clinically or on OCT. There was also an absence of subretinal haemorrhage.

The most likely cause of RPE rip in this patient is secondary to PED due to the accumulation of hydrostatic pressure within the PED and wearing out of the intercellular connection between RPE cells.[5] Besides that, the tangential traction on the RPE itself accounts for rips or tears.[1] Rips occur commonly at the margin of PED, which is the area of significant strain.[6] There is a retraction of the edge of RPE, exposing the underlying Bruch's membrane and choroidal vessels.[3]

On OCT, the trademark of an RPE rip is the discontinuity in the RPE layer.[2] Rips tend to occur at the base of PED close to the junction between the attached and detached RPE.[2] In this patient, the irregular contour of rolled RPE gives rise to increase reflectivity with strong back-shadowing completely masking the choroid. Studies by Doguizi and Ozdex[6] measured > 580 um height of PED and < 4.5 months duration of PED as an important risk factor for RPE rip occurrence after anti-VEGF therapy.

Autofluorescence aids better in detecting small tears compared to fundoscopy.[2] FFA provides a distinctive appearance of RPE rips where there is an area of hyperfluorescent window defect, which lies parallel to an area of blocked hypofluorescence.[1] The hyperfluorescence indicates the bare choroid, while the hypofluorescence indicates an area of retracted redundant RPE.[1]

RPE rips may cause a sudden and drastic loss in vision.[1] The most crucial prognostic factors for recovery are involvement of the fovea and size of RPE rip.[3] This case study reflects a poor visual prognosis, as the rip involved the fovea. Although photoreceptors can survive up to 325 days post-RPE rip, the surgical outcome for macular translocation, autologous pigment epithelium, and choroidal transplantation does not provide promising benefits.[7]

Spontaneous RPE rips are rare occurrences. Multimodal imaging plays an essential role in the diagnosis of this disease, even though there is no specific treatment for RPE tears. It helps to find the underlying cause of the disease.

References

1. Tsujikawa A, Hirami Y, Nakanishi H, et al. Retinal pigment epithelial tear in polypoidal choroidal vasculopathy. Retina. 2007;27(7):832-838. doi: 10.1097/IAE.0b013e318150d864.
2. Gupta A, Chhabra M, Mehta P, Ghosh B. Tears of The Retinal Pigment Epithelium–A Review. The Official Scientific Journal of Delhi Ophthalmological Society. 2017;27(4):243-249. doi: 10.7869/djo.258.
3. Ersoz MG, Karacorlu M, Arf S, Muslubas IS, Hocaoglu M. Retinal pigment epithelium tears: classification, pathogenesis, predictors, and management. Surv Ophthalmol. 2017;62(4):493-505. doi: 10.1016/j.survophthal.2017.03.004.
4. Fryczkowski P, Jedruch A, Kmera-Muszyńska M. Spontaneous RPE tear in high myopia. Klinikaoczna. 2006;108(7-9):327-331. Available from: https://europepmc.org/article/med/17290835
5. Lim Z, Wong D. Retinal pigment epithelial rip associated with idiopathic central serous chorioretinopathy. Eye. 2008;22(3):471. doi: 10.1038/sj.eye.6703020.
6. Doguizi S, Ozdek S. Pigment epithelial tears associated with anti-VEGF therapy: incidence, long-term visual outcome, and relationship with pigment epithelial detachment in age-related macular degeneration. Retina. 2014;34(6):1156-62. doi: 10.1097/IAE.0000000000000056
7. Sinawat S, Bhoomibunchoo C, Yospaiboon Y, Sinawat S. Spontaneous bilateral retinal pigment epithelium rips with good visual acuity. J Med Assoc Thai. 2014;97(Suppl 10): S115-119.

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Case report/Case series

Corneal foreign body self-removal using polymer banknotes

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Abstract

Since the introduction of polymer banknotes, they have become a new tool for corneal foreign body (CFB) self-removal. Being easily available, lightweight, and sturdy, polymer papers have become a popular and innovative method to dislodge CFB. Although ophthalmology services are easily accessible in Malaysia, ignorance, lack of health awareness, and the desire to avoid medical costs are among the reasons why patients remove CFB themselves. The sequalae span from only a faint scar with relatively good vision to total blindness. Our case series highlights three cases of CFB self-removal using polymer banknotes and their sequalae. To echo what has been known previously, self-awareness and occupational hazard education remain the most important and effective way to prevent vision loss.

Keywords: corneal foreign body self-removal, polymer bank notes

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Pembuangan bendasing pada kornea menggunakan wang kertas polimer

Abstrak

Sejak pengenalan kepada wang kertas polimer, ianya telah menjadi alat baru untuk mengeluarkan bendasing pada kornea (CFB). Kertas polimer yang mudah didapati, ringan, dan kukuh, telah menjadi kaedah yang popular dan inovatif untuk membuang CFB. Walaupun perkhidmatan oftalmologi mudah diakses di Malaysia, kejahilan, kekurangan kesedaran kesihatan, dan keinginan untuk mengelakkan kos perubatan adalah antara sebab mengapa pesakit membuang sendiri CFB. Sorotan komplikasi selepas itu berlaku dari hanya sekadar parut samar dengan penglihatan yang agak baik hingga kebutaan secara total dan kekal. Siri kes kami menyoroti tiga kes pengeluaran CFB menggunakan wang kertas polimer dan sekuelnya. Untuk mengetahui apa yang telah diketahui sebelumnya, kesedaran diri dan pendidikan bahaya pekerjaan tetap merupakan cara yang paling penting dan berkesan untuk mencegah kehilangan penglihatan.

Kata kunci: penyingkiran bendasing kornea, wang kertas polimer

Introduction

Corneal foreign body (CFB) is a common preventable ocular-related occupational injury.[1,2] It comprises up to 58% of all ocular traumas.[3] Although the majority of patients were wearing protective glasses when the accidents occurred, CFB was still reported at 43%.[4] Most CFB can be removed using a hypodermic needle under guidance with a slit lamp. It is a simple, quick, and safe procedure. Our case series highlights three cases of CFB self-removal (CFB-SR) using polymer banknotes and their sequalae.

Case series

The following three cases of CFB presented to the emergency eye clinic of Hospital Raja Permaisuri Bainun (HRPB) Ipoh, in Perak, Malaysia from 2016 to 2019. They were males aged 19 to 38 years. Only one of the patients was wearing goggles while grinding metal, while the other two did not wear any protective glasses when the accidents occurred. All three performed CFB-SR with a polymer banknote themselves prior to presenting to the eye clinic. The polymer banknote was folded several times (Fig. 1a) and the sharp edge was used to dislodge the CFB with an aid

Fig. 1a. A polymer banknote was folded several times.

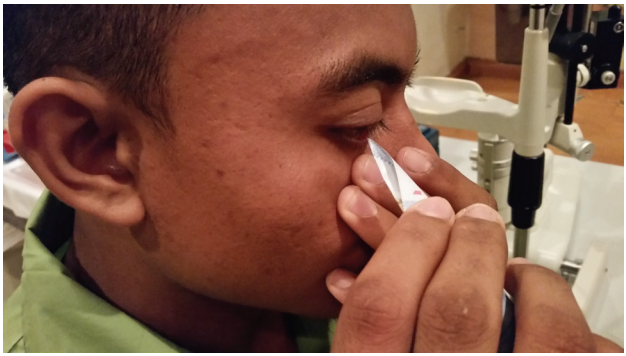

Fig. 1b. The sharp edge was used to dislodge the corneal foreign body.

of mirror or the help of an assistant (Fig. 1b). They only sought medical attention when they developed pain and redness associated with poor vision.

At presentation, all of them had central corneal ulcers with vision worse than 6/60. Corneal scraping for culture and sensitivity grew *Pseudomonas aeruginosa* from one of the ulcers, while no organism was identified in the other two eyes.

The ulcers responded well to intensive topical antibiotics. However, the long term sequalae differed between patients, with outcomes ranging from only a faint corneal scar to evisceration of the eye.

Case 1

A 35-year-old man presented with pain and redness in the left eye for 2 days after a foreign body entered the eye while welding. CFB-SR was done at home. On presentation, vision was hand movement with a large central corneal ulcer measuring 8 x 8.5 mm and corneal thinning (Fig. 2). Corneal scraping revealed *Pseudomonas aeruginosa*. The ulcer responded well to antibiotics. It healed with a dense central corneal scar and a final visual acuity of hand movement.

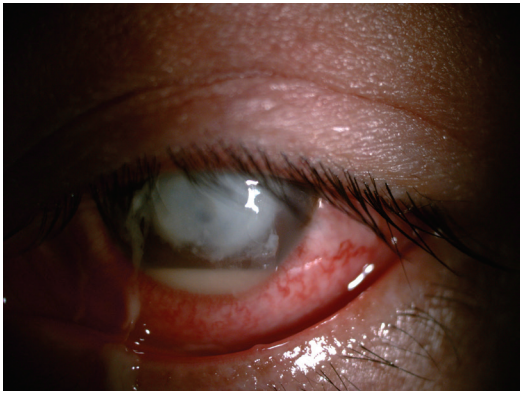

Fig. 2. Large and thin central corneal ulcer in the first case.

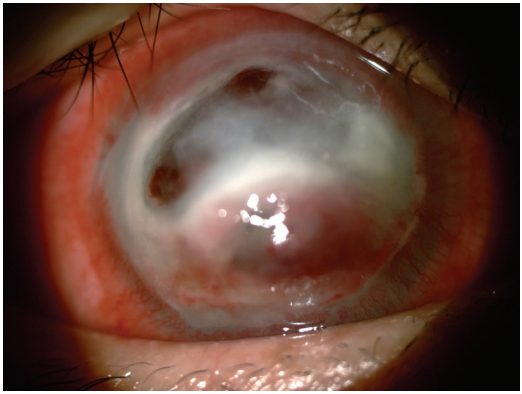

Fig. 3. Perforated corneal ulcer in the second case.

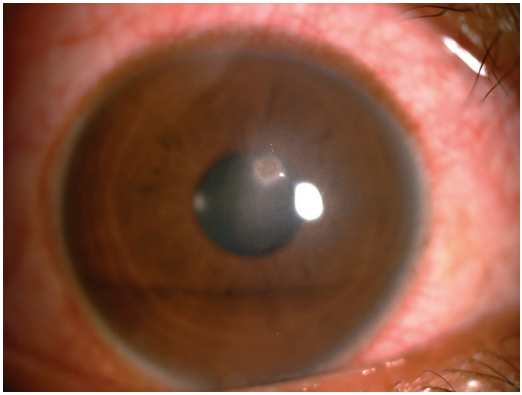

Fig. 4. Faint corneal scar in the third case.

Case 2
A 38-year-old welder presented with pain and redness in the right eye with blurring of vision 1 week after a foreign body lodged in the eye while welding. CFB-SR was done by the patient. Vision was light perception at presentation. There was a large right corneal ulcer with peripheral corneal thinning (Fig. 3). Unfortunately, the ulcer perforated despite intensive antibiotics. The eye was eventually eviscerated.

Case 3
A 19-year-old man presented on day 2 of CFB-SR after foreign body entry into the right eye while grinding metal. He did not use protective eyewear. At presentation, visual acuity was 6/60 with pinhole 6/36. Upon examination, a central corneal ulcer of 2.4 x 4 mm in size was noted. After 1 week of inpatient treatment, the corneal ulcer healed with faint scarring (Fig 4). His vision improved to 6/9.

Discussion

Direct visualisation with a slit lamp in a medical setting remains the safest method for CFB removal with a good visual outcome. Undeniably, some CFB are still removed in primary care settings without a microscope. Even though ophthalmology services are easily accessible in Malaysia, we are surprised that some patients still choose to remove CFB themselves. From the clinical history taking, we found that these patients removed the CFB themselves due to a lack of occupational hazard awareness and a desire to avoid medical costs.

There are several methods used for CFB-SR, including needles, toothpicks, paper cards, threads, and magnets.[5] Needles and toothpicks are sharp and hard. In contrast, napkins and cloth are too soft, while paper cards become soft when in contact with tears. Recently, polymer banknotes have become a popular material utilized by individuals to remove CFB themselves. Being a polymer material, banknotes are lightweight and sturdy. They are also readily available.

Given they are designed for durability, actively circulating polymer banknotes harbour microorganisms, and specifically human pathogens, with the enteropathogen *Escherichia coli* being the most common.[6] Hazem *et al.* found that the lower denominations were more contaminated than higher ones,[6] as lower currency notes are exposed to more microorganisms due to high frequency of circulation.

CFB removal using a sharp object with no direct microscope visualisation may cause inadvertent injury to the adjacent healthy tissue. On top of that, incomplete CFB removal, such as retained residual rust rings, incites inflammation. Without proper topical antibiotic cover, CFB removal may predispose to ocular infection.

Conclusion

In addition to what has been previously known, patients these days are becoming more creative in finding alternative ways to remove CFB themselves. This predisposes the delicate eye to risk of blindness. Therefore, self-awareness and occupational hazard education remain the most importance and effective ways to avoid blindness in these instances.

References

1. Islam SS, Doyle EJ, Velilla A, Martin CJ, Ducatman AM. Epidemiology of compensable work related ocular injuries and illnesses: Incidence and risk factors. J Occup Environ Med 2000;42:575-581.
2. Qayum S, Anjum R, Garg P. Epidemiological pattern of ocular trauma in a tertiary hospital of Northern India. Int J Med Clin Res 2016;7:420-422.
3. Voon LW, See J, Wong TY. The epidemiology of ocular trauma in Singapore: perspective from the emergency service. Eye (Lond). 2001;15:75-81
4. Zeynep et al. Metallic corneal foreign bodies: an occupational health hazard. Arq Bras Oftalmol. 2014;77(2):81-83
5. Arif Hussain et al. Metallic Corneal Foreign Body; A Preventable Work Related Cause of Ocular Morbidity. The Professional Medical Journal. 2019;26(4):688-691.
6. Hazem S, Mahmoud AM. Bacterial Contamination of Paper Banknotes in Circulation; a Case Study in the Jenin District, Palestine. Journal of Science. 2012;1(2):36-39

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Case report/ Case series

A case report of recurrent corneal erosion post-blepharoplasty

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Abstract

Our purpose is to report a case of recurrent corneal erosion post Asian blepharoplasty or double-eyelid surgery. The patient was initially treated with bandage contact lens, lubricants, and mild steroids with temporary improvement. Complete resolution of symptoms was achieved only following suture removal. Upper eyelid eversion with proper exploration of the fornix is key to identify hidden sutures.

Keywords: recurrent corneal erosion, post-blepharoplasty

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Laporan kes hakisan kornea berulang selepas blepharoplasty

Abstrak

Tujuan kami adalah untuk melaporkan kes hakisan kornea berulang selepas pembedahan blepharoplasti Asia atau kelopak mata berganda. Pesakit pada awalnya dirawat dengan kanta lekap, pelincir, dan steroid ringan melalui penyembuhan yang sementara sahaja. Kesembuhanlengkap semua gejala hanya dicapai setelah benang jahitan dibuang. Eversi kelopak mata dengan sempurna pada bahagian atas dengan pemeriksaan fornik yang betul adalah kunci untuk mengenal pasti wujudnya jahitan tersembunyi.

Kata kunci: hakisan kornea berulang, pos-blepharoplasti

Introduction

Recurrent corneal erosion (RCE) syndrome is a common disorder worldwide. The main presenting complaint is sudden onset of mild to severe eye pain (especially on awakening), redness, photophobia, and tearing. Episodes may last from seconds to days.[1] Ocular trauma, corneal dystrophies such as epithelial basement membrane dystrophy, Meesmann dystrophy, Reis-Bücklers' corneal dystrophy, lattice degeneration, and granular dystrophy, as well as contact lens wear can result in RCE syndrome.[2,3] Less common causes include non-inherited corneal conditions such as Salzmann's nodular degeneration, band keratopathy, herpes infections, ocular rosacea, lagophthalmos, keratoconjunctivitis sicca, bullous keratopathy, and systemic diseases such as diabetes mellitus and epidermolysis bullosa.[4]

A retrospective review by Reidy *et al.*[5] of 104 patients with RCE identified trauma (45%) as the most common cause, followed by epithelial basement membrane dystrophy (29%). Of these patients, 17% had both trauma and epithelial basement membrane dystrophy. More than 87% of all RCE occurred on the inferior third of the cornea.

RCE has also been seen postoperatively in patients treated for refractive errors, cataracts or corneal pathologies needing keratoplasty. However, RCE induced by late suture exposure from prior blepharoplasty has been rarely reported. Here, we describe a case of RCE syndrome in a female patient, 2 years after double-eyelid surgery. She presented with corneal erosion in the upper nasal quadrant that recurred soon after treatment with topical lubricants, mild steroids, and bandage contact lens.

Case report

A 26-year-old woman presented with redness in her right eye for 1 month. She complained of decreased visual acuity and eye pain. She had previously seen three other ophthalmologists for the same condition and was treated as a case of idiopathic RCE and herpetic keratitis. However, her condition did not improve. She had worn contact lens for several years. Her past medical history was not significant, with no diabetes or known allergies. The patient denied any recent ocular trauma preceding her symptoms.

At presentation, her best-corrected visual acuity (BCVA) was counting fingers (CF) in the right eye and 6/6 in the left eye. The right eye showed a 2.8 x 4.5 mm corneal epithelial defect with rough edges and surrounding sloughy corneal epithelium. There was associated mild subepithelial haze but no stromal infiltrate. The epithelial defect was located at the superior nasal region of the corneal surface. It was slightly off-centre, involving the visual axis (Fig. 1). On staining with fluorescein, the epithelial defect was clearly evident (Fig. 2). The anterior chamber was deep and quiet. There was no evidence of corneal dystrophy in either eye. Examination of the left eye was completely normal. Having a high index of suspicion for a retained upper lid foreign body given the unusual location of the epithelial defect and its recurrent nature, eyelid eversion was performed. However, no foreign body was evident at this stage.

The patient was treated with bandage contact lens and commenced on topical antibiotic eye drops three times per day as well as preservative-free topical lubricants every 2 hours. On review 2 days later, the patient was symptomatically better. The epithelial defect was healing, and was less than half the size at presentation, with well-defined edges. Treatment was continued and low-potency topical steroid eye drops twice daily were added. On follow-up 6

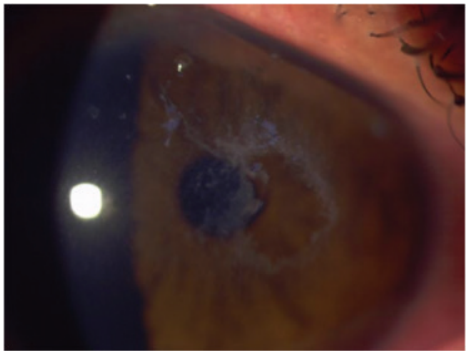


Fig. 1. Corneal epithelial defect as seen at initial presentation prior to fluorescein staining.

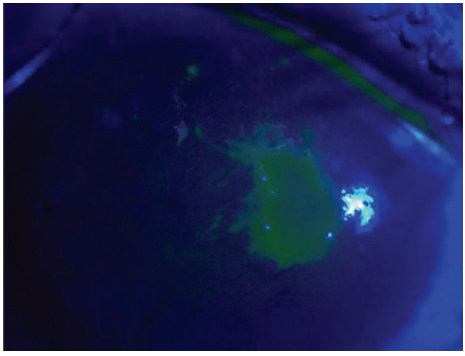


Fig. 2. Corneal epithelial defect as seen at initial presentation with fluorescein staining.

days after initial presentation, her BCVA had improved to 6/9 in the right eye. On slit-lamp examination, the epithelial defect had healed (Fig. 3) with the presence of negative staining and some superficial punctate keratopathy (Fig. 4). The bandage contact lens was removed. The patient continued treatment with similar topical eye drops and a topical lubricant eye gel was added at night. She was then discharged from further follow-up but was advised to return if symptoms recurred.

The patient presented again 9 days later with similar symptoms of pain, tearing and photophobia in her right eye for 3 days. Her BCVA was counting fingers, pinhole 6/18 in the right eye. On examination, she was found to have an epithelial defect over the same region as her previous corneal abrasion, which stained with fluorescein. A bandage contact lens was reapplied. The patient was commenced on topical antibiotic eye drops three times a day, topical steroid eye drops daily, and topical preservative-free artificial tears every 2 hours in the right eye.

Having suspected a retained upper lid foreign body, we further questioned the patient specifically about double-eyelid surgery. Only then she divulged her history of previous Asian blepharoplasty two years prior. The patient had not voluntarily informed us about undergoing eyelid surgery in the past visits. This new information led us to strongly suspect the presence of a buried upper eyelid suture. Hence, on follow-up, once her pain had subsided, we repeated upper eyelid eversion at the slit lamp. This time, the patient was made to look in extreme downgaze and the superior conjunctival fornix was explored with a suture-tying forceps. At this point, a tiny portion of the tip of the retained nylon suture was visualized over the superior fornix (Fig. 5). Thorough exploration of the superior conjunctival fornix enabled us to identify the whole hidden suture. The nylon suture was then exposed fully with the forceps, cut with scissors, and removed (Figs. 6 and 7).

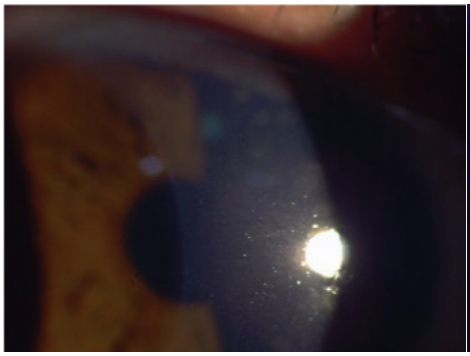


Fig. 3. Slit-lamp examination of the corneal epithelial defect 2 days after initial review

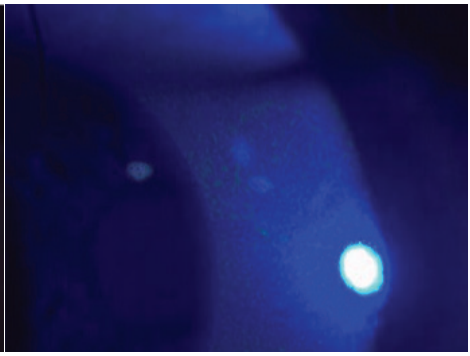


Fig. 4. Slit-lamp examination of corneal epithelial defect 2 days after initial review, with fluorescein staining.

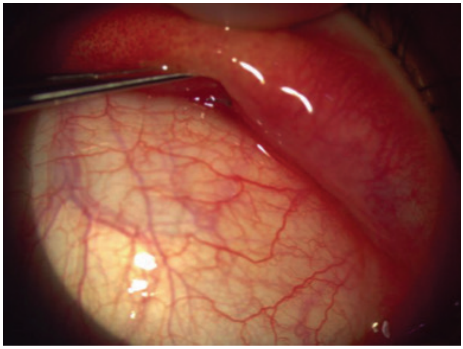


Fig. 5. Examination of the upper fornix with double eyelid eversion revealing hidden nylon suture

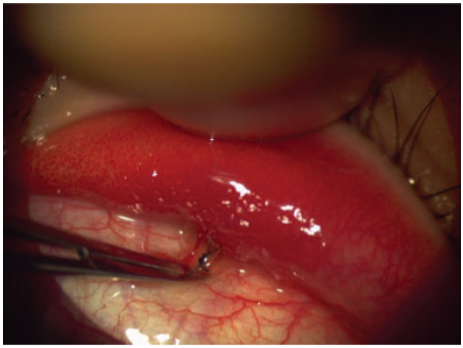


Fig. 6. Hidden nylon suture exposed at slit lamp with forceps.

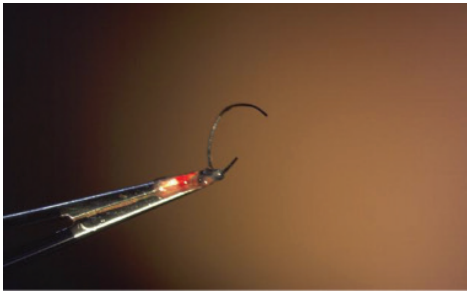


Fig. 7. Removed nylon suture.

Post-suture removal, the epithelial defect recovered fully and her BCVA returned to 6/6 in both eyes. She no longer had symptoms of RCE 2 years after the removal of the suture. The patient was very happy with the outcome.

Discussion

RCE typically occurs in eyes following abrading injuries, eyes with corneal dystrophies such as epithelial basement membrane dystrophy and lattice dystrophy, or in eyes with previous ocular surgery such as refractive surgery, cataract surgery, or corneal transplantation.[6] The majority of cases will respond to simple conservative medical management with topical lubricants, topical antibiotics, and soft bandage contact lenses. This is a case report of an unusual cause of RCE that occurred post-double-eyelid blepharoplasty and remained persistent with conservative medical treatment.

The majority of acute corneal erosions in a prospective randomized controlled trial by Hykin *et al.* occurred wholly within the lower half of the cornea, irrespective of aetiology. This can be attributed to upper eyelid movement across this region of the ocular surface and local tear film drying, which most likely disrupts the corneal surface at this site.[7] Patients with tarsal conjunctival foreign bodies can present with linear vertical epithelial defects from the movement of the foreign body during blinking. The site and nature of corneal erosions provide clues to diagnosis. In our patient, the corneal erosion was noted to be off-centre, in the superior half of the cornea, which was unusual. This led to the suspicion of an upper eyelid foreign body and was followed up with eyelid eversion. However, lid eversion alone was not sufficient to identify the hidden suture. Thorough exploration of the superior conjunctival fornix revealed the hidden offending suture.

Normal adhesion of the corneal epithelium is maintained by structures known as adhesion complexes, which are composed of hemidesmosomes, the lamina densa and lamina lucida of the basement membrane, anchoring fibrils, laminin, fibronectin, and type IV as well as VII collagen.[8] In RCE, reattachment of the corneal epithelium appears to be faulty following an initial abrasion. A variety of adhesion complex defects have been observed in RCE including reduplication of basement membrane, loculation of connective tissues, and absence of basement membrane and hemidesmosomes.[9] Apart from pain relief, the aim of RCE management is to promote re-epithelialisation and re-establishment of a competent basement membrane complex. The healed epithelium needs to remain intact for a sufficient length of time to enable the re-formation of adhesion complexes.[10] In our patient, the nylon suture from the prior blepharoplasty prevented the establishment of a healthy basement membrane for long-term healing. The bandage contact lens acted as a mechanical barrier in protecting the corneal epithelium from the offending suture. However, definitive treatment involved the discovery and removal of the offending upper eyelid nylon suture.

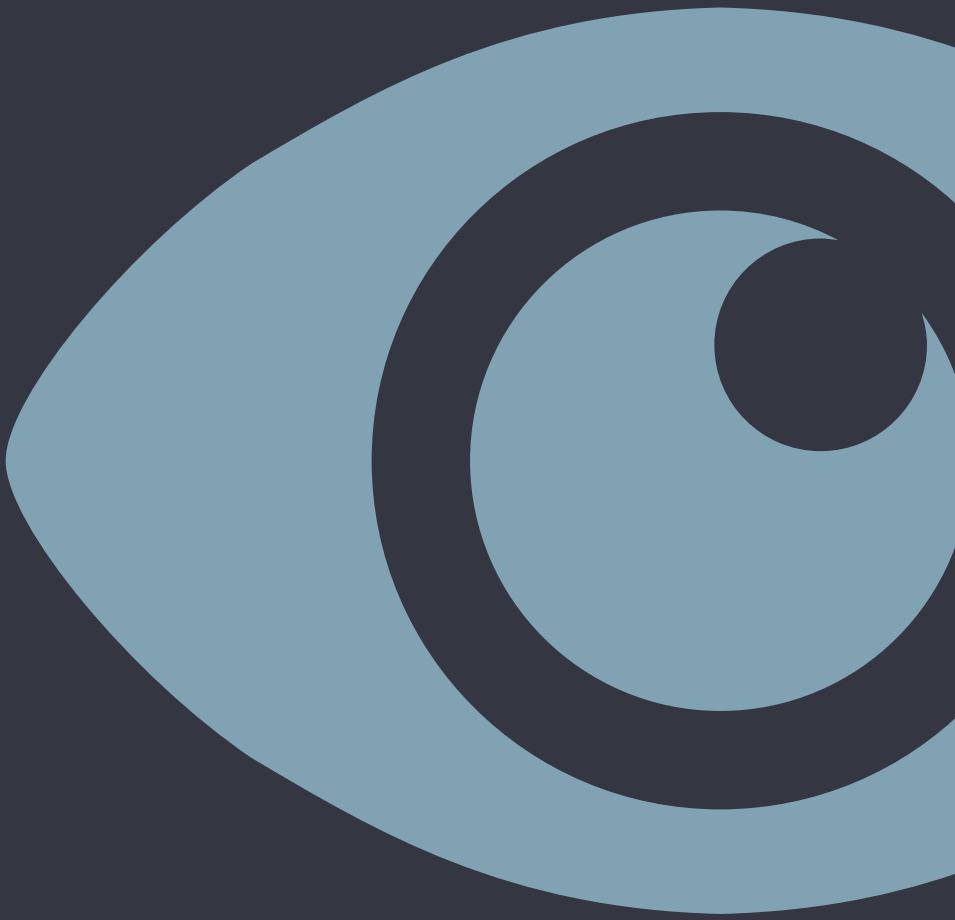
Double-eyelid blepharoplasty is commonly performed in Asian countries. The buried suture technique is done to avoid visible surgical scars.[11] The incision technique, on the other hand, is performed through the external incision and does not involve the palpebral conjunctiva. The buried suture technique is preferred to the incision method as the patient can avoid visible surgical scars and can be more easily revised.[12] However, there are substantial risks involved with this technique, such as chronic inflammation of the conjunctival plate and risks associated with a retained foreign body including suture granuloma, ocular discomfort, and pulling sensation. Here we have illustrated another complication of blepharoplasty using the buried suture technique, namely late suture exposure and RCE.

Conclusion

Blepharoplasty-induced RCE due to exposure of buried upper eyelid sutures is rarely reported. Late suture exposure needs to be considered in patients with a history of blepharoplasty with RCE. A good history and a high index of suspicion of upper eyelid foreign body, together with proper eyelid eversion and thorough exploration of the fornices is imperative to identify these hidden sutures.

References

1. Xu Kunyong, Kam Ka Wai, Young Alvin L, Jhanji Vishal. The Asia-Pacific Journal of Ophthalmology. 2012;1(56):349-354.
2. Nanba H, Mimura T, Mizuno Y, et al A. Clinical course and risk factors of recurrent corneal erosion. Medicine. 2019;98(16)
3. Bron AJ, Burgess SE. Inherited recurrent corneal erosion. Trans Ophthalmol Soc UK. 1981;101:239–243.
4. Brown N, Bron AJ. (Recurrent erosion of the cornea. Br J Ophthalmol 1976,60:84–96.
5. Reidy JJ, Paulus MP, Gona S. Recurrent erosions of the cornea: epidemiology and treatment. Cornea. 2000;19:767–771.
6. Darby DM, Syed AH, Nathaniel LS, Michael WS. Recurrent corneal erosion: A comprehensive review. Clin Ophthalmol. 2019; 13: 325–335.
7. Hykin PG, Foss AE, Pavesio C, Dart JK. The natural history and management of recurrent corneal erosion: a prospective randomised trial. Eye (Lond). 1994;8(Pt 1):35–40. doi:10.1038/eye.1994.6.
8. Gipson IK. Adhesive mechanisms of the corneal epithelium. Acta Ophthalmol. 1992;202(Suppl):13–17.
9. Rodrigues MM, Fine BS, Laibson PR, Zimmerman LE. Disorders of the corneal epithelium. A clinico-pathologic study of dot, geographic, and fingerprint patterns. Arch Ophthalmol. 1974;92:475–482.
10. Ramamurthi S, Rahman M, Dutton, G, et al. Pathogenesis, clinical features and management of recurrent corneal erosions. Eye 2006;20:635–644. doi:10.1038/sj.eye.6702005.
11. Chen WPD. Suture ligation methods. In: Chen WPD, editor. Asian Blepharoplasty and the Eyelid Crease. 3rd ed. Philadelphia: Elsevier; 2016. pp. 51–66.
12. Mizuno T. Treatment of Suture-related Complications of Buried-suture Double eyelid Blepharoplasty in Asians. J Plast Reconstr Aesthet Surg. 2016;4(8):e839.
13. Lelli GJ Jr, Lisman RD. Blepharoplasty complications. Plast Reconstr Surg. 2010;125(3):1007-1017



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