HONG KONG JOURNAL of OPHTHALMOLOGY

December 2020 Vol. 24 No. 2 ISSN 1027-8230

香港眼科醫學院

香港眼科學刊

The Official Publication of
The College of Ophthalmologists of Hong Kong

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References: 1. Cavet ME, DeCory HH. The Role of Nitric Oxide in the Intraocular Pressure Lowering Efficacy of Latanoprostene Bunod: Review of Nonclinical Studies. J Ocul Pharmacol Ther 2018; 34(1-2): 52-60. **2.** Braunger BM, Fuchshofer R, Tamm ER. The aqueous humor outflow pathways in glaucoma: A unifying concept of disease mechanisms and causative treatment. Eur J Pharm Biopharm 2015; 95(Pt B): 173-81. **3.** Cavet ME, Vollmer TR, Harrington KL, et al. Regulation of Endothelin-1-Induced Trabecular Meshwork Cell Contractility by Latanoprostene Bunod. Invest Ophthalmol Vis Sci 2015; 56(6): 4108-16. **4.** Wiederholt M, Sturm A, Lepple-Wienhues A. Relaxation of trabecular meshwork and ciliary muscle by release of nitric oxide. Invest Ophthalmol Vis Sci 1994; 35(5): 2515-20. **5.** VYZULTA® Hong Kong prescribing information [version: 06/2018]. **6.** Weinreb RN, Liebmann JM, Martin KR, et al. Latanoprostene Bunod 0.024% in Subjects With Open-angle Glaucoma or Ocular Hypertension: Pooled Phase 3 Study Findings. J Glaucoma 2018; 27(1): 7-15. **7.** Weinreb RN, Ong T, Scassellati Sforzolini B, et al. A randomised, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open angle glaucoma: the VOYAGER study. Br J Ophthalmol 2015; 99(6): 738-45.

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The Official Publication of
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of Hong Kong

December 2020

Volume 24 Number 2

ISSN 1027-8230

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- The *Hong Kong Journal of Ophthalmology* (HKJO) is the official publication of the College of Ophthalmologists of Hong Kong. The Journal aims to promote academic developments in ophthalmology, and to maintain continuing ophthalmological education of doctors of this specialty and other related disciplines. It is hoped that through achieving these aims, the quality of eyecare we offer to our patients can be lifted to new heights. The Journal will consider any submissions that fulfill these aims for publication.
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香 港 眼 科 醫 學 院

THE HONG KONG JOURNAL OF OPHTHALMOLOGY
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To encourage submissions to the *Hong Kong Journal of Ophthalmology* (HKJO) by trainees and fellows of the College of Ophthalmologists of Hong Kong (COHK).

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Two awards will be given out every year. Each awardee will be given a $1000 cash prize (HK dollars), which is supported generously by the Timothy KC Liu Fund.

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- Trainees refer to those who have not been conferred the title 'FCOphthHK' at the time of submission.
- Only the first author of the article will be eligible for the prize. If the first author is not eligible for the award, i.e. not a member or fellow of COHK, then the order of consideration of awardee will be from the second author onwards to the last author.
- Original articles (including, but not limited to, prospective or retrospective clinical studies, observational studies, epidemiological studies, basic science studies, meta-analysis, etc) published in the HKJO during the year will automatically enter the selection process.
- Case reports (with case number <3), review articles and letters to the editor will not be eligible for this award.
- Submissions pending acceptance will not be eligible for the award.
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- 1 representative from the Chinese University of Hong Kong and
- President of the College

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- Originality
- Scientific merit
- Methodology
- Presentation style

Award Presentation Ceremony

The awards will be given out at the following year's conferment ceremony.

EDITORIAL

Hyperbaric oxygen therapy for central retinal artery occlusion; combined triple technique for upper lid cicatricial entropion

In this issue, Yip et al[1] share with us the outcome of hyperbaric oxygen therapy for central retinal artery occlusion. Among the 25 patients with central retinal artery occlusion aged 44 to 89 years, hyperbaric oxygen therapy was provided after a mean onset-to-therapy time of 13.3±7.4 (range, 4.4-32.2) hours. The visual result was encouraging, in particular among the four younger patients aged ≤50 years whose final vision was hand movement (F/45), 0.7 (F/48), 0.8 (F/50), and 0.7 (F/44). It seems that younger patients with central retinal artery occlusion have a more favorable prognosis after hyperbaric oxygen therapy. Readers look forward to data of longer follow-up in a larger patient group in the future.

Another original article in this issue is about the surgical management of upper lid cicatricial entropion. Although trachoma is rarely seen in Hong Kong, upper lid cicatricial entropion still occurs in older patients. This debilitating disease can be challenging to treat as recurrence is common after surgery. Chan et al[2] describe their combined triple technique of upper eyelid blepharoplasty, tarsal margin rotation, and posterior lamellar super-advancement for cicatricial entropion correction. Dissection through scarred tissue planes in cicatricial eyelids can be difficult and bloody, but the authors take on the challenge to tackle pathologies at both the anterior and posterior lamellae once and for all. One would expect a prolonged surgery with such intricacy, yet the mean operation time was <1 hour. Despite being a pilot study, the long-term results were encouraging. It would be interesting to further explore the learning curve of the surgery and the outcome in a larger sample.

Multiple-choice questions related to the above two articles are designed to provide CME credits for Fellows of the Hong Kong Academy of Medicine. Fellows can only complete the CME questions online at https://www.icmecpd.hk/ for immediate credit of the points, as the old hard copy method would not be provided starting from this issue.

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ORIGINAL ARTICLE

Upper eyelid blepharoplasty, tarsal margin rotation, and posterior lamellar super-advancement for correction of severe upper eyelid cicatricial entropion and dermatochalasis

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Abstract

Objective: To report the long-term efficacy and safety of simultaneous correction of upper eyelid cicatricial entropion and dermatochalasis.

Method: A retrospective non-comparative chart review of consecutive patients with severe upper eyelid cicatricial entropion and dermatochalasis who underwent surgical correction from July 2012 to July 2014 at a tertiary referral center by a single surgeon.

Results: Twelve eyes of 10 patients aged 80±7 (range, 65-92) years old received upper eyelid blepharoplasty, tarsal margin rotation, and graded posterior lamellar super-advancement. All eyes resumed normal upper eyelid margin position with no recurrence over a mean follow-up of 48.3±18 (range, 9-70) months. Complications including suture granuloma (n=1), lagophthalmos (n=1), mild lid notching (n=2) and residual peripheral asymptomatic trichiasis or distichiasis (n=3) were managed conservatively successfully. No patients developed exposure keratopathy after surgery, and the number of lubricants required was statistically significantly reduced (p=0.005).

Conclusion: Our pilot study showed that combining upper lid blepharoplasty, tarsal margin rotation and graded posterior lamellar super-advancement is safe and effective in achieving long-term correction of severe upper eyelid cicatricial entropion and dermatochalasis.

Key words: *Blepharoplasty; Entropion*

Introduction

Upper eyelid cicatricial entropion is a surgical challenge. It is characterized by posterior lamellar scarring, in-turning or posterior migration of mucocutaneous junction, and aberrant and misdirected lash growth causing corneal irritation and damage. Trachomatous conjunctival scarring leading to cicatricial entropion and trichiasis is the leading infectious cause of blindness worldwide.[1] Other common secondary causes of cicatricial entropion include progressive scarring of upper lid tarsus and greyline owing to chronic blepharoconjunctivitis related to herpes and vernal keratoconjunctivitis, ocular cicatricial pemphigoid, Stevens-Johnson syndrome, longstanding use of topical glaucoma eyedrops, and previous eyelid surgeries.[2]

Management of cicatricial entropion is graded according to its severity (**Table**).[3] Minimal or moderate entropion can be managed with lubricants, regular epilation, electrolysis with intrafollicular mitomycin C, cautious use of cryotherapy, margin rotation techniques, and/or everting sutures. Severe or recurrent cicatricial entropion can be surgically managed with tarsectomy, lamella repositioning, tarsal margin rotation, tarsal advancement, or posterior lamellar grafting. The reported rates of recurrence or postoperative lash misdirection (including distichiasis and/or trichiasis) ranged from 7% to 62%.[4] For posterior lamella disorder, tarsus- and lid margin-based procedures are preferred to electro-epilation. Of note, use of cryotherapy alone typically worsens the cicatricial process and is generally not recommended.

Tarsal advancement and rotation as a modification of the Trabut procedure is one of the most widely performed operations for severe upper eyelid cicatricial entropion.[3,5] This method involves advancement of the posterior lamella to a position even with the inferior edge of the rotated tarsal margin.[3] Later, tarsal margin rotation with modified posterior lamellar super-advancement is described, in which interlamellar dissection is carried out to the superior fornix, orbital septum is opened, and levator aponeurosis is recessed, after which the posterior lamella is advanced and fixated beyond the inferior edge of the rotated margin for 2 to 3 mm.[6] This modification is useful for severe or recurrent cases that have failed previous surgical correction. The tarsal margin is rotated outwards for 180° and a new upper eyelid margin, the 'neo-greyline', is formed in good position. However, in our experience, eyelash ptosis secondary to relative redundancy of anterior lamella may occur, especially in older patients with mild degree of dermatochalasis (**Figure 1**). This leads to recurrent lash-globe contact and keratopathy, requiring further surgeries including upper eyelid blepharoplasty with or without buried everting sutures and/or electrolysis.

Techniques to prevent downsliding of anterior lamella include anterior lamellar fixation sutures,[3,7] skin grafting,[8] buccal mucosal membrane grafting,[9] and combination of blepharoplasty to anterior lamellar repositioning with complete lid split or bilamellar tarsal rotation.[10,11] We propose a one-stage surgery combining an established cicatricial entropion correction procedure using tarsal margin rotation and graded posterior lamellar super-advancement, with the addition of skin-muscle removing blepharoplasty, for older patients with severe upper eyelid cicatricial entropion and established or early dermatochalasis. We aim to report on the long-term efficacy and safety of this one-stage surgical technique that combines three established surgical procedures in a graded fashion.

Table. Grading of cicatricial entropion[3]

Degree of entropion	Clinical signs
Minimal	Apparent migration of meibomian glands Conjunctivalization of lid margin Lash-globe contact on up-gaze
Moderate	Apparent migration of meibomian glands Conjunctivalization of lid margin Lash-globe contact in primary position Thickening of tarsal plate Lid retraction
Severe	Gross lid distortion Inwards rotation of greyline Metaplastic lashes Decrease or absence of upper lid margin between lashes and cornea on upgaze Tarsoconjunctival scarring Lid retraction causing incomplete closure

Methods

The study adhered to the tenets of the Declaration of Helsinki.

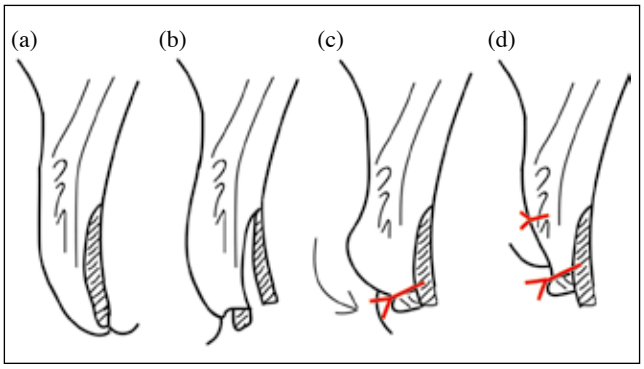

Figure 1. Schematic diagram showing (a) preoperative appearance of cicatricial entropion with internal rotation of eyelash (tarsus represented by shaded area). (b) Intraoperative posterior tarsotomy and interlamellar dissection distally into lash roots and proximally until superior border of tarsus with levator aponeurosis disinsertion, with 180° rotation of the inferior tarsal segment. (c) Traditional tarsal advancement and rotation alone may lead to postoperative anterior lamellar redundancy and secondary lash ptosis. (d) Blepharoplasty combined with tarsal margin rotation, anterior lamellar recession and posterior lamellar super-advancement creates a new eyelid margin and provides a platform to prevent anterior lamellar internal rotation and metaplastic lashes from contacting with the globe

The study was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (CREC 2017.151). Medical records of consecutive patients with upper eyelid cicatricial entropion and dermatochalasis who underwent triple surgical procedures at a tertiary referral center from July 2012 to July 2014 were retrospectively reviewed. Indications for surgery included severe upper eyelid cicatricial entropion defined by lash-globe contact in primary gaze, decrease or absence of upper lid margin between the lashes and cornea on upgaze,[12] associated tarsoconjunctival scarring, and inward rotation of the mucocutaneous junction of greyline, with or without metaplastic lashes.[3]

Digital photographs of the eyelids in primary gaze and side view were taken before and after surgery for each patient. Visual acuity, slit-lamp examinations, surgery-related complications, and use of lubricants before and after surgery were compared to assess outcomes.

Primary outcome was surgical success, defined as correction of upper eyelid entropion with no lash-globe contact in primary gaze, without the need for postoperative epilation or further lash procedures. Surgery-related complications, if any, were recorded.

Statistical analyses were performed using SPSS (version 24.0; IBM, Armonk [NY], USA). Continuous variables were reported as mean ± standard deviation, and unpaired t-test was used to test for their group differences. Categorical data were expressed in frequencies and percentages. P values of <0.05 were considered statistically significant.

Surgical Technique

An upper eyelid blepharoplasty with removal of skin and orbicularis muscle was performed first. Preoperative skin markings were made with the patient sitting upright looking in primary gaze. The lower skin marking was set 4-5 mm above the cilia margin for bilateral operations or at the level of the upper lid crease of the fellow eye for unilateral cases. The upper marking should be at least 15 mm inferior to the lower border of the eyebrow. A skin pinch test was used to adjust preoperative markings and to minimize lagophthalmos. Surgery started with standard aseptic prepping and draping after infiltration of 3 ml of local anaesthetic solution, 2% xylocaine with 1:200,000 adrenaline (Aspen Pharma, Ireland), into the greyline, subcutaneous and submuscular planes. Skin was then incised using a No.15 Park blade. Skin and a thin strip of orbicularis was removed using monopolar or hand-held hot-tip cautery keeping the orbital septum intact. Upper eyelid was then everted over a Desmarres eyelid retractor (**Figure 2b**). An incision was made through the subtarsal sulcus or where the Arlt's line was present with a No.11 blade (**Figure 2c**). A full-thickness tarsotomy was completed across the entire eyelid horizontal length 1 mm short of the upper eyelid punctum to the lateral canthal angle (**Figure 2d**). The lower tarsal segment was dissected off the pretarsal orbicularis until the lash roots can be seen (**Figure 2e**). Importantly, relaxing vertical cuts were made at both ends so that the lower tarsal segment was rotated 180° along with the original greyline (**Figure 2f**). At this point, all lashes should be pointing up and away from the ocular surface. Dissection between the anterior and posterior lamellae proceeded upwards from the tarsotomy incision to the superior border of the upper tarsus (**Figure 1b**). The levator aponeurosis was then recessed in a graded manner, titrated to the amount of lagophthalmos or upper lid retraction during surgery. The Muller's muscle was not disturbed. The anterior lamella including the pretarsal skin and rotated inferior tarsal segment was recessed upwards, while the posterior lamella was recessed downwards and super-advanced 2 mm beyond the edge of the rotated tarsal margin to form the "neo-greyline" (**Figure 2g-2i**). On-table adjustments were made by asking patients to open their eyes and look straight ahead towards the ceiling. Any difficulty in posterior lamellar super-advancement and contour deformity of each lamella or segment was then released in a graded fashion. The repositioned anterior and super-advanced posterior lamellae were then fixed with 3 pairs of double-arm 4/0 silk sutures placed horizontally (**Figure 2j**), entering the pretarsal skin of the rotated lash line full-thickness, then across the superior tarsus in a lamellar fashion, and finally exiting and tied over the recessed anterior lamella (**Figure 2k** and **1d**). Each everting suture should be pre-placed and left long before tying, with the tension adjusted to avoid buckling of the tarsus. The posterior lamella was super-advanced 2 mm showing bare tarsus, and this raw mucosal surface was left to granulate in 4-6 weeks. Finally, the blepharoplasty wound was closed with interrupted 6/0 vicryl or dermalon sutures (**Figure 2l**).

Eyes were dressed with ointment Maxitrol (Novartis, United Kingdom) and double-padded for 1 day. Follow-up examination was scheduled at 1 week, 1 month, 3 months, and 6 months, with annual follow-up thereafter. Non-absorbable blepharoplasty sutures were removed after 1 week. Silk sutures fixating the anterior and posterior lamellae were removed at 4 weeks.

Results

Medical records of 12 eyes (6 left and 6 right) from five male and five female consecutive patients aged 65 to 92 (mean ± SD, 80.1 ± 7) years who underwent the combined triple techniques for severe upper eyelid cicatricial entropion and dermatochalasis by a single oculoplastic surgeon were reviewed.

All 12 upper eyelids had trichiasis or metaplastic lashes involving over half of the upper eyelid, and concomitant dermatochalasis. Four (33.3%) eyes had a history of cryosurgical epilation, and two (16.7%) eyes had a history of folliculectomy for trichiasis. One (8.3%) patient had undergone the Weis procedure elsewhere.[13] Definite Arlt's line was noted during surgery in 4 (33.3%) eyes. No patient had documented history of herpetic infection, ocular cicatricial pemphigoid, Stevens-Johnson syndrome, or was on topical anti-glaucomatous. There was no preoperative lid retraction

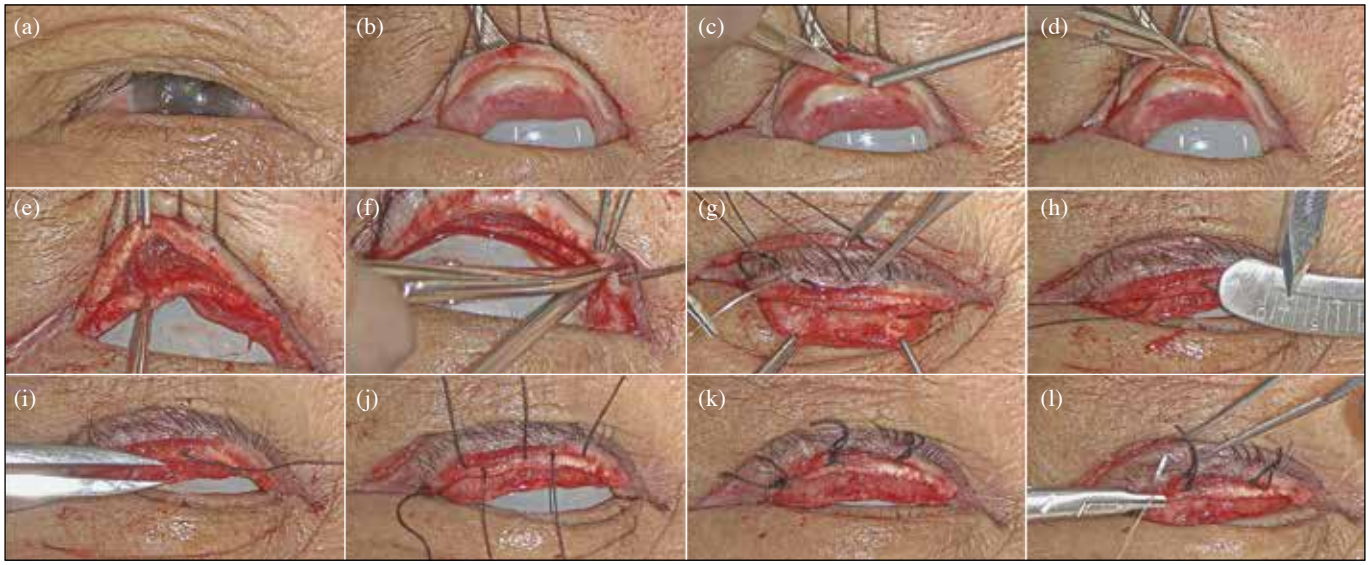

Figure 2. Intraoperative photographs demonstrating the triple surgical technique: (a) Preoperative appearance with severe upper lid entropion and dermatochalasis. (b) After an upper lid blepharoplasty, the upper eyelid was everted over a Desmarres eyelid retractor after placement of Frost sutures and corneal protector. (c) An incision was made at the subtarsal sulcus or Arlt's line (if present) with a No.11 blade. (d) A full thickness tarsotomy was completed across the entire eyelid horizontal length with sharp Westcott scissors. (e) The lower tarsal segment was dissected off the pretarsal orbicularis until the lash roots can be seen. (f) Relaxing vertical cuts were made at both ends. (g) Dissection was further proceeded upwards from the tarsotomy incision to the superior border of the upper tarsus to disinsert the levator aponeurosis. The anterior lamella including the pretarsal skin and 180-degrees rotated inferior tarsal segment was then recessed upwards, while the posterior lamella was pulled downwards. (h, i) The posterior lamella was super-advanced 2 mm (measured with a calliper) beyond the edge of the rotated tarsal margin to form the "neo-greyline". (j, k) The repositioned anterior and posterior lamellae were fixed with 3 pairs of horizontally placed 4/0 silk sutures. (l) Finally, the blepharoplasty wound was closed with interrupted 6/0 vicryl sutures

or lagophthalmos. Five (41.7%) eyes had pre-existing dense corneal scars.

The mean surgery duration was 50±14 (range, 35-84) minutes per eye. After a mean follow-up duration of 48.3±18 (range, 9-70) months, all patients maintained normal upper lid position and improvement of symptoms. Three (25%) patients had residual non-central, asymptomatic trichiasis or distichiasis that was managed on self-epilation, and did not require further surgery. One (8.3%) patient developed suture granuloma that was removed at 2 months after surgery. One (8.3%) patient had lagophthalmos that resolved conservatively after 4 months. Two (16.7%) eyes had mild lid notching that did not require revisional surgery. No eyes developed lid necrosis, worsening of keratopathy, or exposure keratopathy. None of the patients with unilateral treatment received blepharoplasty in the fellow eye, as these patients mostly sought for functional correction rather than eyelid symmetry cosmetically. Following surgery, visual acuity was similar (p=0.58), but the number of lubricants required reduced significantly (p=0.005).

Discussion

Severe upper eyelid cicatricial entropion is difficult to treat. Recurrence is common, and postoperative adjunctive lash destruction procedures are frequently needed. Bilamellar tarsal rotation or posterior lamellar tarsal rotation procedures with various modifications are the most commonly used methods,[14,15] whereas tarsal advancement or posterior lamellar lengthening procedures are used to treat severe cicatricial entropion with posterior lamellar lid shortening.[3]

Although technically challenging, we found that tarsal margin rotation combined with posterior lamellar advancement is effective in severe upper eyelid cicatricial entropion with or without pre-existing upper eyelid retraction. Posterior tarsotomy and marginal rotation divert metaplastic cilia at the entropic upper eyelid margin 180° away from the corneal surface.[3] Any subsequent metaplastic lash or distichiasis can then be easily treated by lash ablation. In addition, super-advancement of the posterior lamellar 2 mm beyond the anterior lamella provides an additional mucosal platform to mechanically shield the upper lid margin and lashes from the cornea.[6] This method can also avoid posterior lamella grafting and associated problems of donor site morbidities, harvesting, and unpredictable graft survival.[6] In eyes with significant tarsal shortening, additional posterior lamellar grafting using buccal mucosa or allogenic material is needed to maintain upper lid stability.

Long-term failure of tarsal margin rotation combined with posterior lamellar advancement has been reported.[3,12] The underlying mechanism of late recurrence is not well

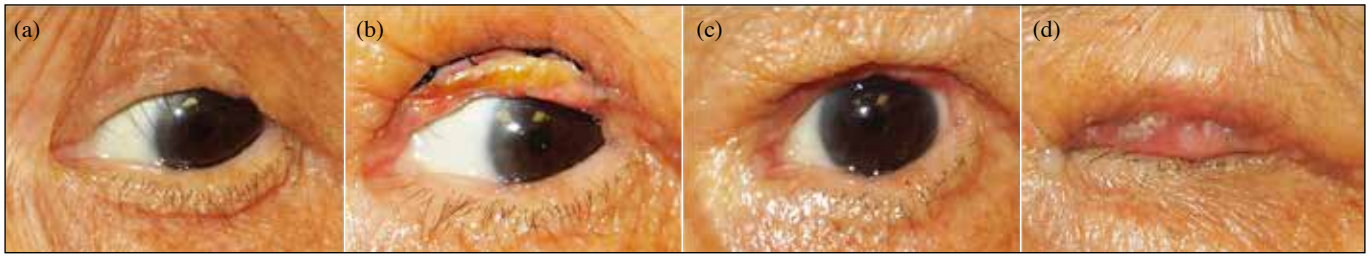

Figure 3. Pre- and postoperative appearance of a patient who received triple surgical technique. (a) Preoperative assessment with severe upper eyelid entropion and dermatochalasis. (b) One-week postoperative appearance. Her "neo-greyline" was left to granulate, and silk sutures holding the anterior and posterior lamellae were left in-situ for 4 weeks. (c) Two-months postoperative photograph showing formation of new eyelid margin with no recurrence. (d) Two-months postoperative appearance on eyelid closure with absence of lagophthalmos

defined and likely related to ongoing cicatricial process. Our experience with tarsal margin rotation and posterior lamellar super-advancement was favourable although ocular irritation may develop over time due to lash ptosis or metaplasia, which required further eyelash everting sutures or simple electrolysis. We believe this is related to relative anterior lamella redundancy after lengthening by the rotated distal tarsal segment. Skin redundancy after tarsal margin rotation together with inadequate posterior lamellar advancement lead to lash ptosis and corneal irritation (**Figure 1c**). In our cohort, additional upper lid blepharoplasty allowed anterior lamella to be shortened and repositioned upwards more effectively. Postoperative anterior lamellar redundancy and secondary eyelash ptosis was minimised (**Figure 1d**). Addition of preaponeurotic fat debulking may be considered in Asian lids, which have a lower insertion of the levator aponeurosis to the orbital septum with consequent lower descent of preaponeurotic fat.[16] Further studies are warranted to evaluate this surgical adjunct.

Marginal tarsal rotation induces upper eyelid retraction due to posterior lamellar shortening. Treatment of upper eyelid cicatricial entropion associated with lid retraction without posterior lamellar grafting depend on adequate posterior lamellar super-advancement which in turn is related to interlamellar dissection and levator aponeurosis disinsertion or recession. Our follow-up results showed that patients usually exhibited very mild postoperative lid retraction after graded recession or disinsertion of levator aponeurosis from the tarsal plate for posterior lamella advancement. This is compatible to findings in a study of terminal tarsal rotation with posterior lamellar advancement that leads to a significant increase in mean palpebral aperture from 10.1 mm to 11.5 mm,[17] suggesting surgically induced upper lid retraction. In our series, lagophthalmos developed in one (8.3%) eye and resolved in 4 months. No patient developed exposure keratopathy despite mild postoperative lid retraction (**Figures 3c**). From our results, interlamellar dissection upwards towards the superior fornix may not be necessary.[6] Rather, dissection up to the superior tarsal border with graded disinsertion of the levator aponeurosis is adequate as verified during surgery.

The neo-greyline with exposed tarsus appears inflamed immediately after surgery and can be alarming to patients (**Figure 3b**). However, it heals with granulation and epidermalization around 2 months after surgery with excellent cosmetic outcomes (**Figure 3c**).[6] Therefore, it is good practice to counsel patients on these expected surgical outcomes before surgery for better preparation and acceptance of initial cosmetic results.

Conclusion

The one-stage combined skin-muscle removing blepharoplasty, tarsal margin rotation, and posterior lamellar super-advancement in a graded fashion can achieve sustained correction in patients with severe upper eyelid cicatricial entropion and dermatochalasis, minimizing recurrence or need of postoperative adjunctive eyelash destruction procedures.

Author contributions

Concept or design: CLL, KKLC
Acquisition of data: KKWC, CLL
Analysis or interpretation of data: KKWC, CLL
Drafting of the article: KKWC, CLL, KKLC
Critical revision for important intellectual content: All authors

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As editors of the Journal, KKL Chong and A Young were not involved in the peer review process for this article. Other authors have disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

This study was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (Ref CREC 2017.151). The need for patient consent was waived. All patients provided informed consent for all treatments and procedures. Patients photographed in figures 2 and 3 provided written consent for publication.

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ORIGINAL ARTICLE

Hyperbaric oxygen therapy for central retinal artery occlusion: experience in Hong Kong

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Abstract

Objective: To review medical records of patients who underwent hyperbaric oxygen therapy (HBOT) for central retinal artery occlusion (CRAO).

Methods: Medical records of patients who underwent HBOT for CRAO between November 2018 and December 2019 were reviewed. The first emergency HBOT was at 2.8 atmosphere absolute for 90 minutes with staged decompression. Subsequent sessions were at 2.4 atmosphere absolute twice daily or daily. Patients were followed up daily at the eye clinic. HBOT lasted for 5 days or 10 treatment sessions if there was visual improvement on day 3. Treatments were discontinued if patients had no visual improvement or were unable to tolerate the treatment or experienced major adverse effects, or when the patient was confirmed to not have CRAO.

Results: Of 31 patients who underwent HBOT, 25 with CRAO (17 men, 8 women; aged 44 to 89 years) were included. Mean onset-to-door time was 3.3±4.2 hours, and mean onset-to-HBOT time was 13.3±7.4 hours. Mean number of HBOT sessions was 7.9±2.7. Mean change in visual acuity (VA) was -0.43 LogMAR (p=0.003). At the end of treatment, 84% had VA of 0.1 (1.0 logMAR) or worse and 64% had VA of finger counting (1.7 logMAR) or worse. No factors were associated with VA improvement including age, onset-to-door time, onset-to-HBOT time, number of HBOT sessions, or pre-HBOT VA.

Conclusion: HBOT for CRAO shows promising visual outcomes. It is important to be aware of the systemic complication of CRAO and provide timely systemic cardiovascular examination for CRAO patients.

Key words: Hyperbaric oxygenation; Retinal artery occlusion

Introduction

Central retinal artery occlusion (CRAO) is an uncommon but disabling ocular emergency.[1] The incidence of CRAO has been reported as <2 per 100000 population in a study in the United States[2] and 1.72 per 100000 population in a study in South Korea.[3] In a large series of 244 patients,[4] natural outcomes of CRAO were poor: 81% of patients had final visual acuity (VA) of 0.1 or worse and 61.5% had final VA of finger counting or worse. With conventional management or without treatment, 38% had VA improvement, whereas 19% had improvement in both VA and visual field. In a subgroup of 171 patients with non-arteritic CRAO with no cilioretinal artery sparing, the outcome was worse: 98.4% had final VA of 0.1 or worse and 78.5% had final VA of finger counting or worse; only 6% had improvement in both VA and visual field.

Conventional management modalities of CRAO include ocular massage, intraocular pressure–lowering drugs or techniques (such as glaucoma eyedrops, intravenous or oral Diamox, intravenous mannitol, and anterior chamber paracentesis, and rebreathing into a bag to increase carbon dioxide concentration that causes vasodilatation). Newer treatment modalities include intravenous thrombolysis with tissue plasminogen activator[5-7] and intra-retinal arterial

cannulation.[8] Nonetheless, there is no consensus on the optimal therapy for CRAO.[4,9-12]

In 2008, the Undersea and Hyperbaric Medical Society approved the use of hyperbaric oxygen therapy (HBOT) for CRAO.[13] The rationale is to supply oxygen to the retina through choroidal circulation by diffusion. Under normal conditions, blood supply to the inner two-third of retina is from the central retinal artery, whereas the outer one-third is from the choroidal circulation by diffusion. Under normoxic conditions, about 60% of retinal oxygen supply comes from choroidal circulation. Under hyperoxic conditions, choroid is capable of supplying 100% oxygen needed by the retina.[14] Other proposed rationales for the use of HBOT in CRAO are related to hyperbaric oxygen effect on edema reduction and its ability to blunt ischemia-reperfusion injury after recanalization occurs.[15]

In September 2018, the Pamela Youde Nethersole Eastern Hospital set up the first hospital-based HBOT center in Hong Kong. HBOT was first used for life-threatening cases including decompression sickness, carbon monoxide poisoning, and necrotizing fasciitis. In November 2018, HBOT was used to treat patients with other indications such as CRAO, osteomyelitis, delayed radiation injuries, and idiopathic sudden sensorineural hearing loss. The HBOT chamber (Haux-Starmed-Quadro 3300-2300) is divided into 3 sub-chambers with individual pressure control. Patients wear oxygen hoods with 100% oxygen, and the entire sub-chamber is pressurized to a desired pressure level.

Methods

Medical records of patients who underwent HBOT for CRAO between November 2018 and December 2019 were reviewed. The diagnosis of CRAO was made by an ophthalmologist, and patients with the symptom onset–to-door time of <6 hours were referred to our center for HBOT (**Figure 1**). Patients with the symptom onset–to-door time of >6 hours were treated with HBOT depending on individual case conditions (such as those with only eye) and manpower availability. Those with CRAO of iatrogenic causes such as filler-related CRAO, branch retinal arterial occlusion, cilioretinal artery occlusion, or any absolute contraindication to HBOT such as untreated pneumothorax were excluded. Emergency treatments such as ocular massage, anterior chamber paracentesis, rebreathing bag, and Diamox were given by the referring ophthalmologists before transfer.

Baseline ophthalmological assessments included VA, intraocular pressure, pupillary reaction, anterior segment and dilated fundal examination. VA measured in Snellen decimals was converted to logarithm of minimal angle of resolution (LogMAR): finger counting = 1.7 logMAR, hand movement = 2.0 logMAR, light perception = 2.3 logMAR, and no light perception = 3.0 logMAR.[16] Fundal fluorescein angiography as a gold standard for diagnosis was performed on the next available working day. Patients were followed up at eye clinic daily for VA, intraocular pressure, dilated fundal examination.

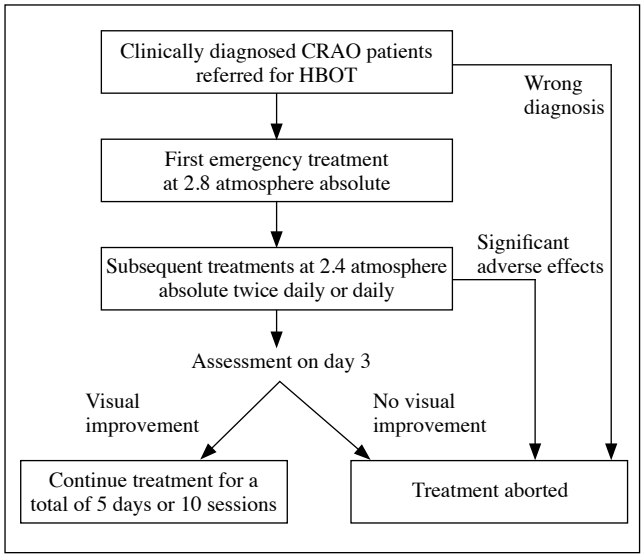

Figure 1. Protocol of hyperbaric oxygen therapy (HBOT) for central retinal artery occlusion (CRAO)

Blood tests for cardiovascular risk factors and chest radiography were performed at the emergency department before HBOT to rule out any contraindication for treatment including pneumothorax. The first emergency HBOT was at 2.8 atmosphere absolute for 90 minutes with staged decompression. Subsequent sessions were at 2.4 atmosphere absolute twice daily or daily based on the US Navy Treatment Table 9. Patients were followed up daily at the eye clinic. HBOT would last for a total of 5 days or 10 treatment sessions if there was visual improvement on day 3. Treatments were discontinued if patients had no visual improvement or were unable to tolerate the treatment or experienced major adverse effects, or when the patient was confirmed to not have CRAO. Patients were subsequently referred to the medical department for detailed assessment to determine whether further investigation such as neuroimaging was necessary.

Statistical analysis was performed using SPSS (version 25, IBM, USA). To determine factors associated with VA improvement, Fisher's exact test was used for categorical variables and t-test was used for continuous variables.

Results

Of 31 patients who underwent HBOT, six were non-CRAO cases including branch retinal arterial occlusion (n=3), central serous choroioretinopathy (n=1), orbital apex tumour (n=1), and retrobulbar optic neuritis (n=1), and HBOT was terminated. The remaining 17 male and 8 female patients with CRAO were aged 44 to 89 years, with the mean onset-to-door time of 3.3±4.2 (range, 0-16) hours, and the mean onset-to-HBOT time of 13.3±7.4 (range, 4.4-32.2) hours. 68% (17/25) were treated within 12 hours of symptom onset. The mean number of HBOT sessions was 7.9±2.7 (range, 3-14) [**Table**].

Table. Patient characteristics and treatment outcomes of hyperbaric oxygen therapy (HBOT) for central retinal artery occlusion (CRAO)

Patient	Sex/ age, y	Comorbidity	Affected eye	Treatment before HBOT	Relative afferent pupillary defect	Cherry red spot	Onset-to-door time, hours	Onset-to-HBOT time, hours	No. of HBOT sessions	Visual acuity	
										Before treatment	After 1 week
1	M/64	Diabetes mellitus, hypertension, hyperlipidemia	Right	Normobaric oxygen	Yes	Yes	16	19.7	10	Hand movement	Hand movement
2	F/80	Diabetes mellitus, hypertension, ischemic heart disease, old cerebrovascular accident	Left	Rebreathing bag, ocular massage	No (fellow eye branch retinal arterial occlusion)	Yes	2	8	14	Hand movement	0.222
3	M/59	Hypertension, hyperlipidemia, atrial fibrillation	Left	Rebreathing bag, ocular massage, diamox 250 mg po, alphagan P	Yes	Yes	2	10	10	Light perception	Finger counting
4	M/74	Hypertension, hyplipidemia, atrial fibrillation, ischemic heart disease	Left	Rebreathing bag, ocular massage, diamox 250 mg po, alphagan P	Yes	Yes	1.5	10	10	Hand movement	Finger counting
5	M/51	Newly diagnosed hypertension, hyperlipidemia	Right	Rebreathing bag, ocular massage, diamox 500 mg IV	Yes	No	0.5	4.4	10	Hand movement	Finger counting
6	F/48	Good	Left	Rebreathing bag, ocular massage	Yes	Yes	3	8.4	10	Hand movement	0.7
7	M/82	Diabetes mellitus, hypertension, hyperlipidemia	Left	Nil	Yes	Yes	5	16	9	Light perception	Hand movement
8	M/68	Impaired fasting glucose, hyperlipidemia, old cerebrovascular accident	Right	Rebreathing bag, ocular massage, diamox 500 mg po, timolol	Yes	Yes	0.5	8	9	Light perception	Finger counting
9	F/74	Diabetes mellitus, hypertension, hyperlipidemia	Left	Ocular massage, diamox 250 mg po	Yes	Yes	5	9	9	Hand movement	Finger counting
10	M/45	Newly diagnosed hypertension and hyperlipidemia	Right	Diamox 500 mg IV, timolol	Yes	Yes	0.75	8.6	3	Hand movement	Hand movement
11	F/64	Good	Left	Diamox 500 mg IV, timolol	Yes	Yes	0	26.9	8	3/60	0.3
12	F/76	Diabetes mellitus, hypertension, hyperlipidemia	Right	ocular massage, timolol	Yes	Yes	1.5	8	3	1/60	0.017
13	M/70	Diabetes mellitus, hypertension, hyperlipidemia, ischemic heart disease	Left	Nil	Yes	Yes	16	18.6	5	Hand movement	0.008
14	M/70	Newly diagnosed hypertension, hyperlipidemia	Right	Nil	Yes	Yes	0.5	8.2	8	Light perception	0.017
15	M/61	hypertension, hyperlipidemia, old cerebrovascular accident	Left	Diamox 500 mg IV, xalacom	Yes	Yes	1.3	18.2	10	Finger counting	Finger counting
16	M/82	Diabetes mellitus, hypertension, hyperlipidemia	Right	Ocular massage, diamox 500 mg IV, timolol	Yes	Yes	0.5	7	7	Hand movement	Finger counting
17	M/75	Diabetes mellitus, hypertension, hyperlipidemia, old cerebrovascular accident	Right	Rebreathing bag, ocular massage, timolol	Yes	Yes	2	8.8	7	Hand movement	Finger counting
18	M/74	Good	Left	Rebreathing bag, ocular massage, diamox 500 mg IV, timolol	Yes	Yes	5.5	19.7	8	Light perception	Hand movement
19	F/50	Impaired fasting glucose, newly diagnosed hypertension	Left	Rebreathing bag, ocular massage, diamox 500 mg IV, timolol	No	No	4	28.8	10	Finger count	0.8
20	M/56	Diabetes mellitus, hypertension	Right	Ocular massage, diamox 500 mg IV, timolol	No (fellow eye no light perception)	Yes	2.3	9.5	10	No light perception	No light perception
21	M/70	Hyperlipidemia, old cerebrovascular accident	Left	Rebreathing bag, ocular massage	Yes	Yes	1.25	8.6	7	Hand movement	Hand movement
22	M/73	Hypertension, carotid stenosis	Left	Rebreathing bag, ocular massage	Yes	Yes	2	10.9	5	Finger counting	Finger counting
23	F/44	Good	Left	Rebreathing bag, diamox 500 mg IV	Yes	Yes	4.8	12	5	Hand movement	0.7
24	F/89	Hypertension	Right	Nil	Yes	Yes	0.7	32.2	4	Hand movement	Finger counting
25	M/69	Good	Left	Nil	Yes	Yes	5	12	6	No light perception	No light perception

At presentation, 92% (23/25) had VA of finger counting or worse. The mean LogMAR was 2.02 (range, 1.3-3.0) and the median was 2.0 (equivalent to hand movement). 88% (22/25) had relative afferent pupillary defect on the diseased eye, and 92% (23/25) had cherry red spot on fundal examination (**Figure 2**).

84% (21/25) had known cardiovascular risk factors including diabetes, hypertension, or hyperlipidemia. 20% (5/25) were not prescribed with long-term aspirin after having CRAO.

Seven patients required additional procedures such as myringotomy (n=4) or otovent (n=3) for pressure equalization. Two patients had early termination of treatment owing to difficulty in pressure equalization and refusal of myringotomy. The first one developed mild tinnitus during the eighth session. The second patient developed otalgia with suspected hemotypanum after four sessions.

The mean VA change was -0.43 LogMAR (p=0.003). 68% (17/25) had a measurable VA improvement (**Figure 3**). At the end of treatment, 84% (21/25) had VA of 0.1 (1.0 logMAR) or worse and 64% (16/25) had VA of finger counting (1.7 logMAR) or worse. Among nine patients who remained to be followed up in our center, the same VA was maintained after 1 week to 20 months.

44% (11/25) received neuroimaging to exclude stroke within 1 week of CRAO and 56% (14/25) within 2 months. 68% (17/25) were treated for cardiovascular risk factor within 2 weeks. 96% (24/25) had regular medical assessment after CRAO; one patient was lost to follow-up. One patient developed acute stroke with an acute infarct over the right middle cerebellar peduncle after 3 sessions of HBOT. The patient was admitted to the acute stroke unit for management, and HBOT was terminated. One patient had a fall and subdural hemorrhage 11 months after CRAO; the subdural

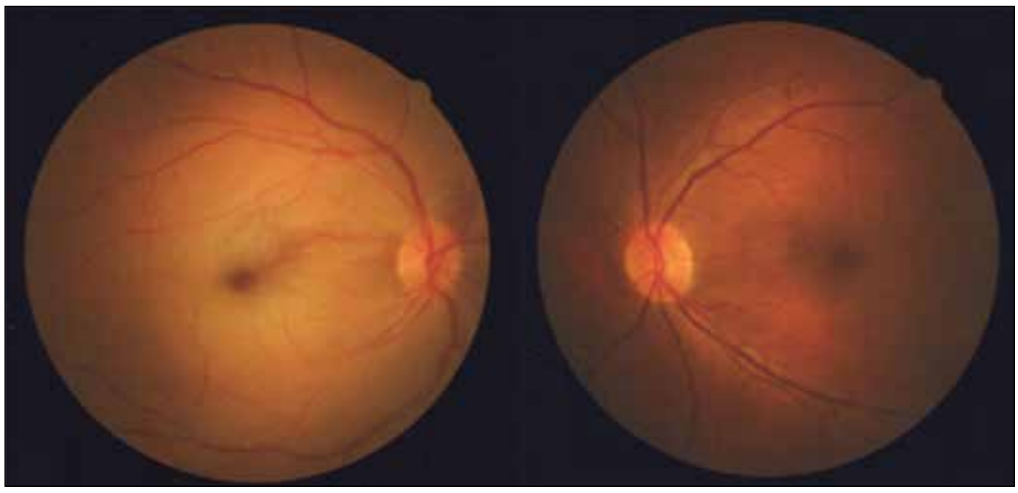

Figure 2. Fundus photos of patient 1 showing a cherry red spot of the right eye.

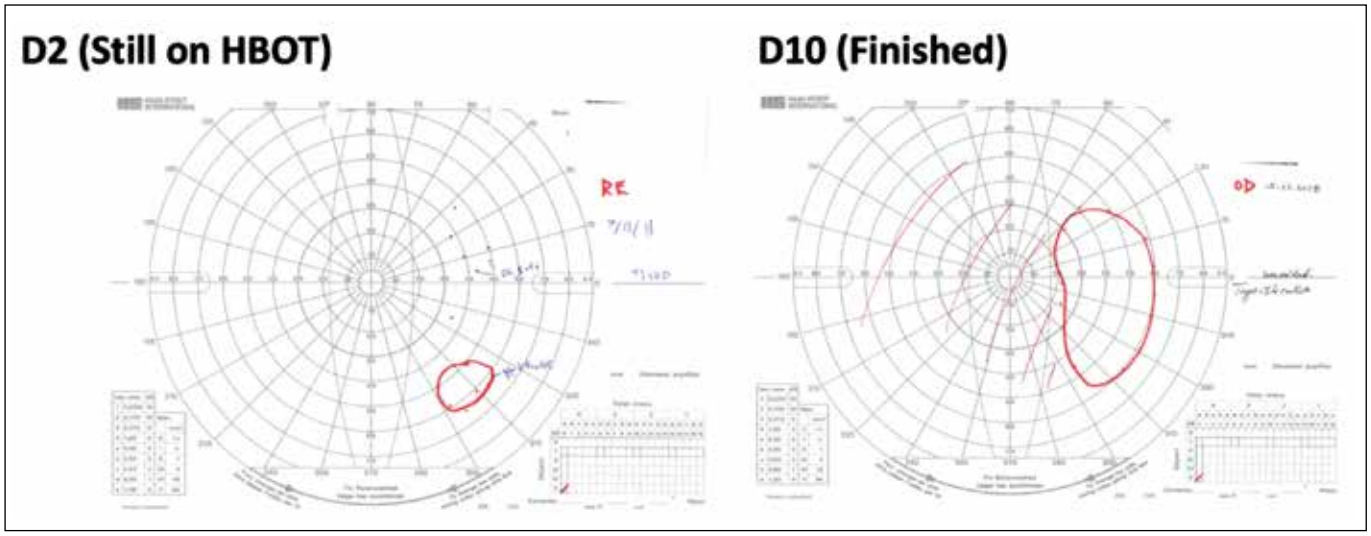

Figure 3. Goldmann visual field of patient 1 on days 2 and 10 of hyperbaric oxygen therapy (HBOT) showing vision improvement

hemorrhage may have been related to the use of aspirin and dipyridamole. 92% (23/25) did not have any cerebrovascular events after CRAO.

No factors were associated with VA improvement including age (p=0.46), onset-to-door time (p=0.77), onset-to-HBOT time (p=0.46), number of HBOT sessions (p=0.20), or pre-HBOT VA (p=0.95). Nor these factors associated with VA improvement of >1 line, with p values of 0.15, 0.59, 0.40, 0.28, 0.14, respectively.

Discussion

Favorable outcomes of HBOT for CRAO have been reported. In 476 patients with HBOT, 306 (65%) patients experienced vision improvement.[17] In our case series, 68% had appreciable VA improvement, compared to 38% based on the natural history of CRAO. 84% had final VA of 0.1 or worse and 64% had final VA of finger counting or worse, compared with 98.4% and 78.5%, respectively, based on the natural history of CRAO.[4]

Central scotoma is the most common visual defect in CRAO,[4] because the macula region is the thickest part of the retina. When circulation in the central retinal artery restores, the retinal capillaries in the central, thickest part of the macula region do not refill because of compression by the surrounding swollen superficial retinal tissue. This results in the 'no re-flow phenomenon' and consequently permanent ganglion cell death in the non-perfused retina.[18-20] In addition, oxygen supply and nutrition from the choroidal vascular bed to the thinner peripheral retina enable longer survival time and maintenance of the peripheral visual field. Therefore, VA measurement alone may not be able to capture all the visual improvements in patients with CRAO. Visual field may improve without a measurable improvement in VA owing to the central scotoma. However, manpower constraints forbid performance of formal visual field tests on all patients before and after treatment.

The rationale for HBOT in CRAO is to support retina's oxygen demand while natural recanalization of the central retinal artery occurs, which is usually present within 72 hours.[21] In our case series, if patients had no visual improvement after 3 days, it was assumed that the chance of natural recanalization was low and treatment was discontinued. If there was visual improvement, HBOT was extended to after recanalization. In patient 2, treatment was extended to 14 sessions until VA stabilized when there was deterioration of vision after 10 sessions. We hypothesized that recanalization was not established or was partial after 10 sessions and thus VA dropped when there was no oxygen support to the retina by the HBOT. Similar treatment protocol to resume HBOT when patients experience vision drop is also advocated.[17]

There is no consensus on the optimal treatment protocol of HBOT for CRAO. One study suggests titration of oxygen pressure and treatment duration based on vision improvements.[17] The Henneipin County Medical Center uses standard treatment pressure for all patients with CRAO,[22] as does our center. Protocols involving titrating treatment pressure for individual patients may be difficult to follow when there are only three individual chambers in our center and patients with different indications are treated at the same time. Manpower and chamber availability should also be considered.

Unlike one study that reported significant correlation between onset-to-HBOT time and visual outcome,[22] no such correlation was identified in our case series. This was likely due to the inclusion of patients with shorter onset-to-HBOT time only and the small sample size. Blood flow is usually re-established via recanalization. However, if ischemia and hypoxia result in cell death and necrosis in the inner layers of the retina, vision may not return when blood flow is re-established.[23] There is a threshold of time beyond which ischemic tissue can no longer recover from a hypoxic event, even if reperfusion occurs.[14] The retina can only survive 90 to 100 minutes of ischemia prior to permanent damage.[24,25] Visual recovery beyond this timeframe has been reported, potentially owing to incomplete occlusion, an intact cilioretinal artery, or collateral flow. In CRAO, some residual retinal blood flow has been detected by fundal fluorescein angiography.[26,27] The shorter the treatment delay, the higher the likelihood of recovering the ischemic retina.[14,27,28] It is important to start the treatment early enough before permanent damage occurs and continue HBOT long enough until natural recanalization occurs. Patients treated within 12 hours of symptom onset achieve greatest improvement in VA.[22] We aimed to perform HBOT within 12 hours for those with the onset-to-door time of <6 hours.

HBOT is generally safe and well tolerated. Most of its adverse effects are mild and reversible. Middle ear trauma is the most common adverse effect, with an incidence of around 2%.[29] It can be prevented by teaching the patients autoinflation techniques or by placement of tympanostomy tubes. In our case series, only one patient developed suspected hemotypanum. Other reported complications of HBOT include sinus barotrauma,[29] seizure secondary to toxicity to the central nervous system,[30,31] pulmonary barotrauma, pulmonary oxygen toxicity,[32] claustrophobia, and chamber fire.[33] Reported ocular adverse effects include visual field narrowing and eyelid twitching. Alteration in refraction secondary to HBOT remains controversial.[29,34-36] Therefore, it is advisable to postpone all keratorefractive surgeries until after HBOT. Increased nuclear cataract formation secondary to oxidative stress in lens protein has been reported,[36] as has a case of early onset of neovascularization.[37] It was hypothesized that ischemic phase was prolonged by the improvement in the retinal oxygen saturation, thus enhancing vascular endothelial growth factor release and potentially worsening choroidal neovascularization.

CRAO has significant systemic implications. It increases the risk of stroke and acute myocardial infarction, with an incidence of 44.51% within 7 days and 14% within 30 days.[3]

CRAO also reduces life expectancy; the life expectancy was 15.4 years in patients with no CRAO and 5.5 years in patients with CRAO. In a Korean study, only one-third of ophthalmologists transferred patients with CRAO to the emergency department for immediate evaluation. Despite being a thromboembolic vascular event in most cases, CRAO is usually not handled in the same manner as a thromboembolic stroke. In a study, 32% of patients with CRAO showed acute or subacute brain infarct on magnetic resonance imaging.[38] One of the 58 patients with CRAO had an acute thromboembolic stroke 8 days after CRAO. In our case series, a 45-year-old man (patient 10) with right CRAO experienced vertigo and dizziness after 3 treatment sessions. He was newly diagnosed with hypertension and hyperlipidemia. Urgent neuroimaging revealed acute infarct over the right middle cerebellar peduncle and the patient was admitted to the acute stroke unit, and treatment was terminated. Fortunately, the patient was able to recover from the stroke and to walk unaided. This case highlights the importance of awareness of the increased stroke risk in patients with CRAO. Timely workup and control of cardiovascular risk factors are essential for all CRAO patients.

Limitations of our case series are the small sample size and relatively short follow-up. Studies with a larger sample size and longer follow-up are warranted to determine the efficacy and safety of HBOT for CRAO.

Conclusion

HBOT for CRAO shows promising visual outcomes. It is important to be aware of the systemic complication of CRAO and provide timely systemic cardiovascular examination for CRAO patients.

Author contributions

Concept or design: LTY, CKLK
Acquisition of data: LTY
Analysis or interpretation of data: LTY, SCLA
Drafting of the article: LTY, SCLA
Critical revision for important intellectual content: LTY, CKLK

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the Journal, CKL Ko was not involved in the peer review process for this article. Other authors have disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

This study was approved by the Hong Kong East Cluster Research Ethics Committee (reference: HKECREC-2020-11). The patients provided written informed consent for all treatments and procedures.

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REVIEW ARTICLE

Laser-induced ocular injury: a narrative review

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Abstract

There is an increasing trend of reported laser-induced ocular injury. We aimed to review the literature on the basic principles of laser, clinical management and safety precaution of laser-induced ocular injury. A literature search on the PubMed database was conducted to include articles dated up to April 2020. One example case of laser-induced ocular injury is provided. Clinical presentation of laser-induced ocular injury is variable. The clinical features can be transient and subtle. Appropriate investigations are useful to establish a diagnosis and to evaluate the severity of the injury. Laser-induced ocular injury most commonly involves the macula, which can be complicated by intraocular haemorrhage, macular hole, epiretinal membrane, and choroidal neovascularization. There are currently no evidence-based or well-recognized treatments for laser-induced retinopathy. Surgical intervention might be considered if there is significant intraocular hemorrhage or macular hole. Laser-induced ocular injury may cause permanent visual sequelae and functional disability. Diagnosis of an eye injury should be supported by objective clinical findings and/or appropriate investigations. As medical and surgical treatment options are currently limited, the key to combat laser ocular injuries lies in prevention and awareness of the general public should be reinforced.

Key words: Eye injuries; Lasers; Safety

Introduction

Laser has been widely used for occupational, military, medical, and cosmetic purposes.[1] There is an increasing trend of laser-related ocular injuries secondary to high-powered handheld laser devices.[2] Lack of awareness regarding the sight-threatening hazards of these devices may lead to inadvertent or deliberate laser use.[3] Laser-induced ocular injury in children is a major public health issue.[4] Aircraft risks attributable to laser strikes have been reported.[5] Public awareness regarding the hazardous effect of laser should be reinforced.[6] The aim of this study is to review the literature on the investigation and management of laser-induced ocular injury, as well as safety precautions that can be taken.

Example case

In January 2020, a 14-year-old boy presented to an eye clinic 4 days after having a sudden drop of left eye vision while playing with a laser pointer at home. At presentation, visual acuity of the right eye and left eye was 20/25 and 20/60, respectively. Fundal examination of his left eye revealed cystoid changes at the fovea, but there was no anterior segment injury or retinal or vitreous hemorrhage. The involved laser pointer was not available for verification of its power and specification. Optical coherence tomography (OCT) of the left eye macula showed subfoveal cystoid change with disruption of inner segment–outer segment junction (**Figure 1a**). The retinal pigment epithelium (RPE) layer was intact. The patient was treated with topical 1% prednisolone acetate four times per day and 0.1% nepafenac three times per day for one week. The visual acuity of his left eye gradually improved to 20/30 at 3 weeks. The cystoid changes at the macula was subsequently resolved. OCT of the left eye macula showed resolution of cystoid changes, re-establishment of inner segment–outer segment junction continuity and foveal depression (**Figure 1b**). There was no discernible anatomical

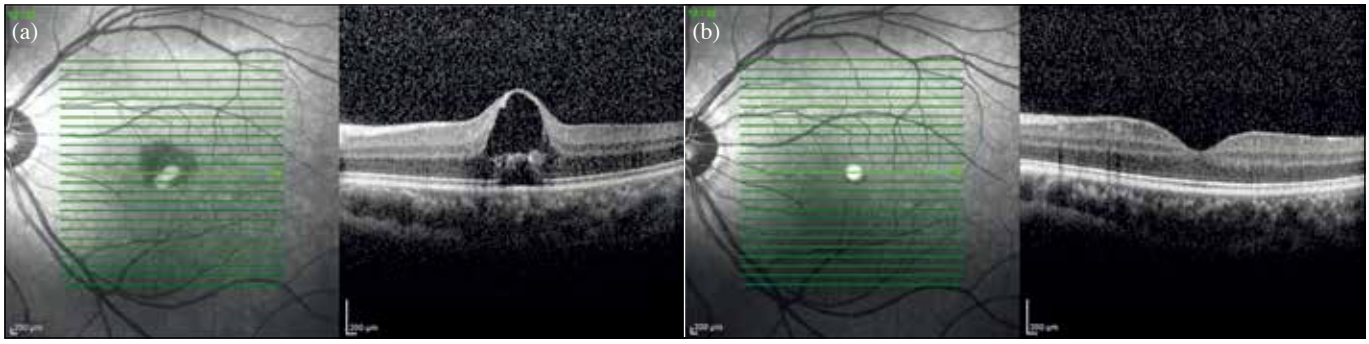

Figure 1. Optical coherence tomography of the left eye fovea (a) at 4 days after the laser-induced injury showing cystoid change at fovea with disruption of inner segment–outer segment junction, an intact retinal pigment epithelium, and a central macular thickness of 518 µm. (b) at 3 weeks after injury showing resolution of cystoid changes, re-establishment of inner segment–outer segment junction continuity and foveal depression.

Table 1. Classification of laser according to the output power[8,9]

Class of laser	Output power, mW	Risk	Precaution	Example
1/1M	<0.4	Considered not hazardous during normal operation unless viewed through specific optical instrument	Exempt from control measures or surveillance other than to prevent potentially hazardous optically aided viewing	Laser printers, CD and DVD players
2/2M	<1	Low risk: safe for brief momentary exposure; may be harmful with prolonged direct viewing or viewed with optical aids	Eye protection afforded by the aversion response; prevent viewing through hazardous optical instruments	Barcode scanners
3R	<5	Moderate risk: potentially hazardous under direct and specular reflection viewing if eye is focused and stable	Avoid direct beam viewing; wear laser protective eyewear; prevent unintentional specular reflections	Laser pointers for presentation and recreational use
3B	<500	Moderate risk: potentially hazardous under direct and specular reflection viewing	As class 3R; designated laser controlled area and laser safety officer required under Hospital Authority regulations	Majority of industrial, military and medical lasers
4	>500	High risk: Hazardous to the eye or skin from direct beam; diffuse reflection or fire hazard; laser generated air contaminants; plasma radiation	As class 3R; protective clothing required if maximum permissible exposure for the skin is exceeded	

abnormality detected. Although outer retinal damages are common in laser-related injury, intraretinal fluid with cystoid change is an uncommon presentation.[7]

Literature search

The PubMed, EMBASE, and Web of Science databases were searched for articles published between 1998 and May 2020 using keywords: 'laser' and 'eye injury' and 'ocular injury' or 'laser eye injury' or 'laser ocular injury' or 'laser retinal injury' or laser macular injury' or 'laser induced maculopathy or 'laser induced retinopathy' or 'laser pointer'. Of 4969 articles yielded, 4637 duplicated or irrelevant articles were excluded and 332 articles were included. References in the included articles were reviewed to identify additional relevant studies. Of the 332 articles, those written in languages other than English were excluded, as were statements, editorials, and letters to the editor. Eventually, 157 articles were reviewed. Internationally adopted guidelines and safety manuals regarding laser use were referenced.

Classification and application of laser

A laser is a monochromatic, coherent, and collimated light beam that is polarized, minimally divergent, and has a single frequency. Lasers are classified by the maximum output power into four classes (**Table 1**): class 1 is safe under all conditions of normal use, whereas class 4 is hazardous to the eye or skin and may pose a diffuse reflection or fire hazard.[8,9] Classes 3 and 4 laser are commonly applied in ophthalmological equipment for the treatment of various ocular conditions such as glaucoma and retinal diseases.

Laser pointers are widely used in educational and business presentations, amateur astronomy, construction work, and entertainment purpose. They are available in various colors on the visible light spectrum, with the most common being green (532 nm) or red (650-670 nm) diode laser.[10,11] Most consumer laser pointers are categorized as class 3R with output power of <5 mW, which is relatively safe to human eyes upon accidental viewing due to limitation of exposure

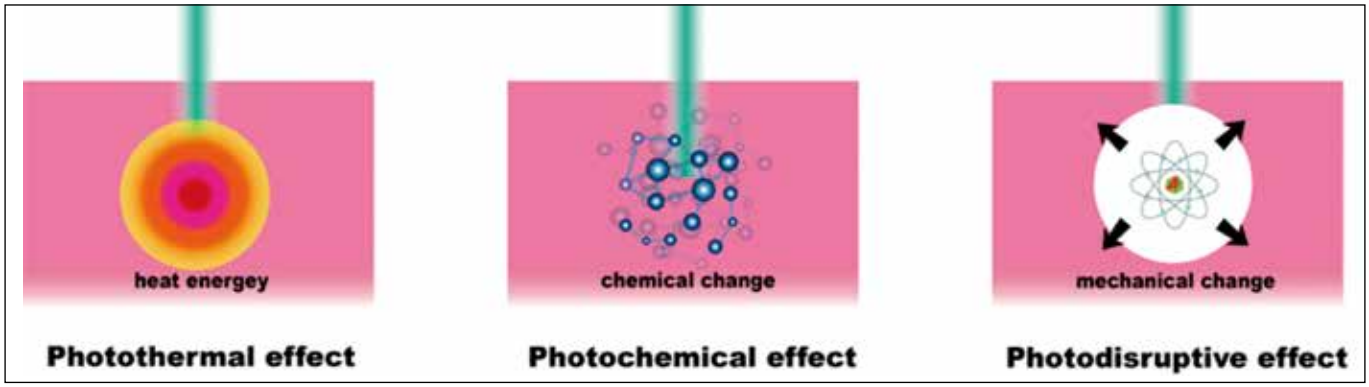

Figure 2. Photothermal effect involves a local temperature rise owing to absorption of laser energy, leading to protein denaturation and tissue damage. Photochemical effect occurs when laser energy induces chemical reactions in the absorbing molecules without significant build-up of heat. Photodisruptive effect happens when rapidly absorbed laser energy causes disintegration of tissue into plasma, eventually leading to mechanical disruption of surrounding tissues.

time by the blink reflex and aversion response. However, mislabeling of output power may impose hidden danger. In a test of 122 commercial laser pointers, 89.7% of green pointers and 44.4% of red pointers labeled as class 3R devices had a power output of >5 mW,[10] and 52.4% of the tested devices exceeded the legal limit by at least a factor of 2 at one or more wavelengths. In Hong Kong, there are no regulations on the usage or purchase of laser pointers. As for sellers, it is an offence to supply or manufacture goods unless it complies with the safety requirements under the Consumer Goods Safety Ordinance.[12] In many other jurisdictions, the power of laser pointer available to the general public is restricted to <5 mW.[13]

Mechanisms of laser-induced eye injury

Laser-tissue interaction in the eye involves three mechanisms: photothermal, photochemical, and photodisruptive (**Figure 2**). Photothermal interaction occurs when laser energy is absorbed by a chromophore, such that the rate of heat energy production is greater than the rate of energy dissipation, leading to local temperature rise.[1,14,15] An increase in temperature causes protein denaturation and coagulation, resulting in cell death followed by tissue necrosis and scarring.[15] Photochemical interaction occurs when laser energy is delivered at relatively low power and long pulses and induces chemical reactions in the absorbing molecules without significant build-up of heat.[1,16] Photodisruptive interaction occurs when energy is absorbed rapidly at a pulse duration of picoseconds to nanoseconds. A rapid increase in temperature causes stripping of electrons from atoms and disintegration of tissue into plasma.[14] In combination with the ensuing vaporization of water molecules, a compressive pressure pulse is generated, mechanically disrupting the surrounding tissues.[1,14]

Effects of laser to ocular tissue

The tissue involved in laser-induced ocular injury depends on the optical property of ocular structures and the wavelength of the laser. Laser-induced injury to ocular structures other than the retina is uncommon, as they are optically transparent in the visible and near-infrared spectrum. Lasers in these wavelengths are transmitted by the optical media of the eye and focused onto the retina by its refractive components (cornea, aqueous humor, lens, vitreous humor).[17] The refractive power of the cornea and lens can produce retinal irradiance of up to 10^5 times greater than corneal irradiance.[18] With the use of binoculars or other magnifying optics, the increase in irradiance may be more than a million fold.[1] This makes the retina highly susceptible to laser injury. Melanin pigment, which is abundant in the retinal pigment epithelium, absorbs laser energy and leads to a localized temperature elevation or even a plasma formation.[18] Continuous-wave lasers such as argon laser and lasers from commercial laser pointers can cause retinal injury mainly by photothermal mechanism, whereas Q-switched lasers such as Nd:YAG laser can cause retinal injury by photodisruptive effect. Q-switched laser injury tends to be more dangerous because they can produce very high power concentration at a localized site.[1,14] In contrast, laser in the ultraviolet spectrum is rapidly absorbed by the cornea, causing corneal injury by the photochemical mechanism.[1,19] One such example is the excimer laser (with wavelength of 193 nm) in keratorefractive surgeries. Laser with longer wavelength, such as the mid-infrared CO_2 laser, is readily absorbed by water molecules in any tissue. It does not penetrate deeper than 100 μm into the cornea but may result in corneal and scleral injury or injury of the external adnexa by the photothermal mechanism.[1,20]

Clinical presentation of laser-induced ocular injury

Clinical presentations of ocular laser injury vary, depending on the type of laser, duration of exposure, and the method of administration (**Table 2**).[4] The retina (the macula in particular) is most susceptible to laser injuries.[2,21,22] The wide availability of handheld laser devices is associated with an increased incidence of pediatric laser-induced ocular injury,[2,22,23] accounting for 70% to 80% of reported cases.[4,22] Handheld laser devices have been reported to be associated with playing with laser,[21] accidental injury inflicted by others,[21] self-inflicted injury,[24] intentional self-harm,[25] and assault.[26] Other mechanisms of injury include occupational,[27] recreational,[28] medical,[29-36] military,[37,38] and air flight exposure to laser.[39]

Table 2. Summary of laser-induced ocular injury in the literature

Types of injury	Clinical signs	Investigation	Treatment	Mechanisms of injury
Eyelid injury[42]	Lid retraction, lagophthalmos	Photography of external adnexa	Topical lubricant, punctal plug	Handheld laser devices: playing with laser,[21] accidental injury inflicted by other,[21] self-inflicted injury,[24] intentional self-harm,[25] assault[26] Medical laser devices: cosmetic laser procedure,[43] laser removal of skin lesion,[32] laser epilation of eyelid[30] / eyebrow,[29,51] ophthalmic laser application[49,50] Occupational exposure to laser[27] Air flight exposure to laser[39] Recreational exposure to laser[28] Military laser accident[37,38]
Corneal injury[43,63]	Bullous keratopathy, intrastromal bleeding, corneal burn with scar, corneal ulcer, corneal perforation, exposure keratopathy	Slit-lamp photography, corneal sensation, tear break-up time, basal secretion test	Topical antibiotics, topical prednisolone, ocular patching, contact lens, corneal transplant	
Iris / uveal tissue injury[32,35,51,87]	Iris atrophy, corectopia, posterior synechiae, atonic pupil, uveitis	Slit-lamp photography	Topical and oral prednisolone, cycloplegic eyedrop, pilocarpine (for atonic pupil), subtenon triamcinolone	
Lens injury[30,51,52]	Cataract	Slit-lamp photography	Cataract surgery	
Elevated intraocular pressure[36]	Corneal edema	Goldmann applanation tonometry	Pressure-lowering agents	
Visual field defect[62]	Scotoma, peripheral visual field loss	Automated perimetry, microperimetry	-	
Retinal injury[28,48,88]	Hypo- or hyper-pigmentation, yellow submacular lesion, vitreous/preretinal/subretinal hemorrhage, retinal pigment epithelium changes, chorioretinal scar, epiretinal membrane, full-thickness macular hole, choroidal neovascularization	Fundus photography (color, infrared or autofluorescence), Amsler grid, fluorescein angiography, optical coherence tomography, optical coherence tomography angiography, electroretinography	Topical or oral prednisolone, intravenous methylprednisolone, anti-vascular endothelial growth factors, Nd:YAG laser hyaloidotomy, pars plana vitrectomy +/- internal limiting membrane peeling +/- intraocular gas tamponade	

Laser is commonly used in aesthetic and dermatological medicine, including treatment of pigmented or vascular lesions, hair removal, and facial rejuvenation.[40,41] The eyelid skin is thin and lacks subcutaneous fat, leaving the globe vulnerable to both anterior or posterior segment injury from laser energy absorption.[35,41] Laser skin resurfacing has been reported to cause thermal injury of the eyelid and corneal damage.[42,43] Anterior segment injury from laser-assisted eyebrow epilation is commonly reported.[44,45]

Occupational laser-induced injuries are primarily associated with pulsed lasers such as Nd:YAG laser in industrial or laboratory settings.[1] Recreational exposure to laser in laser light show has been reported to cause retinal injury,[28,46] as has accidental laser exposure in military exercises, actual combat,[38] and civilian airflight.[1,5]

Patients can usually recall a history of exposure to laser devices. However, elusive exposure history and delayed clinical presentation are not uncommon among pediatric patients.[4,22] Sudden onset of unilaterally decreased vision is the typical presentation of visually significant retinal laser injury.[47] The severity of visual loss depends on the proximity of the laser impact site to the fovea, the extent of chorioretinal disruption, and the amount of intraocular bleeding.[4,21,47,48] Apart from the posterior segment, laser may cause injury of the external adnexa and the anterior segment (**Table 2**). Common symptoms include eye pain, temporary loss of vision, and conjunctival erythema.[41] Mechanisms of injury involving external adnexa and anterior segments tend to differ from those of retinal injury and are often associated with dermatological laser procedure[43] and ophthalmic laser application.[49,50] Anterior segment injuries are more commonly induced by lasers of longer wavelength such as Alexandrite laser (755 nm) and diode laser (810 nm) used in epilation of eyebrow[30-36] and carbon dioxide laser used in skin resurfacing.[42,43] Alexandrite laser and diode laser are readily absorbed by the heavily pigmented iris, causing iris atrophy and corectopia.[30-32,34-36,51] They can result in normotensive or hypertensive anterior uveitis, leading to posterior synechiae formation.[31-36] Carbon dioxide laser may lead to exposure keratopathy secondary to lower lid retraction.[42] Cataract formation[30,51] and cataract in infants treated with argon laser photocoagulation for threshold retinopathy of prematurity have been reported.[52] Although the extent of corneal injury associated with laser procedures is often mild,[53] severe corneal damage with bullous keratopathy or corneal perforation[54] necessitating penetrating keratoplasty[43] has been reported.

In a systematic review on retinal injury secondary to laser pointer exposure,[7] 55% of patients have visual acuity of less than 20/40 at presentation, around 9% of patients have 20/20 or better, and 5% of patient had visual acuity of finger counting. The most common fundoscopic finding was pigmentary changes with hypo- or hyperpigmentation (53%), followed by yellow foveal lesions (33%), macular hole (23%), and hemorrhage (14%). Although a large proportion of laser-induced ocular injury improves spontaneously, medical and/or surgical intervention may be required for complications such as subretinal, intraretinal, subhyaloid, and preretinal

hemorrhage, full-thickness macular hole, and epiretinal membrane and choroidal neovascularization.[7,21,22,28,48,55-57] One case report described rod and cone cells dysfunction leading to diffuse peripheral visual field defect following a diode laser injury.[34]

Differential diagnoses of laser-induced retinal injury include retinal dystrophies (eg, Best disease and Stargardt disease) and inflammatory and ischemic retinopathies.[4,7] Laser-induced injuries rarely progress following acute damage, but inherited retinal diseases are characterized by bilateral involvement and gradual progression. Multimodal investigations including sequential OCT and electrophysiology tests are occasionally indicated.[4,58] Some cases of laser-induced retinal injury in pediatric patients have been mistakenly referred to the genetic service for possible inherited retinal disease.[58] Behavioral or psychiatric conditions have been reported to be associated with self-inflicted laser insults.[23,59] Attention deficit hyperactivity disorder and autism spectrum disorders are proposed to increase the risk of such injuries.[23] Psychiatric conditions should be recognized and collaboration with mental health experts may be necessary.[23]

Investigation

Laser-induced ocular injury may have considerable legal, financial, and medical consequences.[60] Accurate diagnosis requires detailed history taking and prompt ophthalmic assessment, as clinical signs are often transient and subtle.[61] If the mechanism of laser exposure and clinical examination findings are ambiguous, further investigations may be used to confirm ocular insult secondary to the alleged accident. Documentation of best-corrected visual acuity is essential. Photographic documentation of external adnexa, anterior segment, or fundus is invaluable to record clinically apparent pathologies following laser-induced injury. Slit-lamp examination, Goldmann applanation tonometry, corneal sensation, tear break-up time, and basal secretion test can be performed if the anterior segment is involved. Infrared photography and fundus autofluorescence may help to characterize the retinal lesion.[61] Amsler grid testing shows subjective functional deficits including metamorphopsia and scotoma.[7]

Fluorescein angiography of acute photocoagulation laser-induced injuries typically produces a hyperfluorescent ring with a hypofluorescent center.[60] In cases with secondary vitreous or chorioretinal hemorrhages, a hypofluorescent area secondary to overlying blockage may be observed.[28] As the hemorrhage resolves and RPE atrophy ensues, a hyperfluorescent window defect may develop. Late retinal fibrosis or chorioretinal scarring give rise to hyperfluorescence owing to staining. Choroidal neovascularization can also be demonstrated with active leakage.[48] Incidental findings of minor angiographic abnormalities are not uncommon in normal individuals and should be interpreted with caution before attributing it to a laser-induced injury.[62]

OCT of the macula may demonstrate a spectrum of features including RPE change, focal inner segment–outer segment junction disruption, retinal edema and cystoid changes, hemorrhages, and macular hole.[4] The outer retina often demonstrates localized hyperreflectivity, accompanied by persistent disruption of the outer retinal layers.[7] OCT angiography is useful to detect choroidal ischemia or choroidal neovascularization.[48] Based on OCT features, a classification of laser-induced retinal injuries has been proposed to quantify retinal laser energy absorption and RPE damage.[22] However, it is difficult to correlate the severity of injury based on OCT features with the degree of visual impairment or prognosis.[4,22] Electroretinography can be used to assess possible rod and cone cells dysfunction following laser-induced injury.[34]

Functionally, automated perimetry and microperimetry may be used to document visual field defects or reduced macular sensitivity.[7] Follow-up examinations may be arranged to monitor visual field deficits, which may spontaneously improve or remain static.[61]

Treatment

There is no evidence-based consensus on treatment for laser-induced ocular injury. In general, visual symptoms and anatomical changes tend to improve with time, although permanent vision loss and scotoma may persist in some patients.[4] Watchful waiting may be a reasonable option for relatively mild cases, especially for injuries of the extrafoveal or peripheral retina.[4,7]

Treatment is largely determined by the extent of injury and includes medical and/or surgical management. Superficial lesions to the corneal epithelium can be treated with topical antibiotics, patching, or contact lenses.[63] Lid retraction and lagophthalmos are managed with topical lubricants or punctal plug.[42] Cycloplegic eyedrops, topical or oral steroids at varying treatment lengths are helpful to reduce the damaging inflammatory response to injury.[35] Subtenon triamcinolone has been used to manage severe anterior uveitis.[35] Pressure-lowering agents can be used for increased intraocular pressure, and pilocarpine can be used to manage pupil distortion after laser-induced injury.[51]

Topical or systemic corticosteroids have been used to treat laser-induced retinopathy in the belief that they reduce production of inflammatory cytokines, limit neutrophil infiltration, and reduce retinal photoreceptor damage and glial scar formation.[1,47,64-66] Systemic methylprednisolone and indomethacin in animal study improve photoreceptor survival after laser-induced injury.[4,48,67,68] However, negative effects of methylprednisolone in animal model with laser-induced retinal injury have also been reported.[69] The clinical efficacy of corticosteroids in humans is based on case reports only.[1,11,22,28,70-72] The therapeutic effect of medications is often confounded by the natural course of ocular injury.[22,27,73,74] Overall, the role of systemic corticosteroid and non-steroidal anti-inflammatory agents in laser-induced retinopathy remains inconclusive.

Various medications including oral lutein, deferoxamine, and human recombinant fibroblast growth factors have been

used in the treatment of laser-induced retinal injury.[4,75,76] However, results vary widely and are largely experimental. Anti-vascular endothelial growth factors may be of value if secondary choroidal neovascularization develops.[48] There is limited evidence on the indication, dosage, and therapeutic window of medical therapy for laser-induced retinopathy, and the usage of various medical therapies remains controversial.

Severe corneal injury leading to bullous keratopathy or corneal opacity with vision loss may require surgical intervention such as corneal transplantation.[43,63] Mild cataracts can be managed conservatively, whereas surgery is considered for visually significant cataracts.[51,52] Surgical intervention may be considered if there is significant intraocular hemorrhage. It is particularly beneficial in cases that require prompt restoration of vision.[1] As pre-retinal blood may induce fibrosis with formation of chorioretinal scar, epiretinal membrane or secondary macular hole,[21,77] pars plana vitrectomy may be used for vitreous or pre-retinal hemorrhage that do not clear spontaneously within a short period.[57] Nd:YAG laser hyaloidotomy may be an option for cases of subhyaloid or sub-internal limiting membrane hemorrhages.[21,78,79] Laser-induced macular hole can occur immediately or several days after injury.[21,80,81] Spontaneous closure of macular hole has been reported for smaller macular holes (<250 μm),[82] and observation can be considered.[83,84] Macular holes of >250 μm are indicated for surgical intervention to prevent further anatomical and functional deterioration.[84,85] Pars plana vitrectomy with internal limiting membrane peeling and intraocular gas tamponade is used to treat eyes with full-thickness macular hole secondary to laser injury.[21,84,85]

Prognosis

The prognosis for laser-induced retinal injuries is generally favorable. Laser-induced injury involving external adnexa and anterior segment generally have good outcome with visual acuity of 20/40 or better.[32] In a review of laser-induced retinal injury, 55% of eyes recovered to visual acuity of 20/25 or better within a few months and 36% recovered to visual acuity of 20/100 to 20/30.[1] Nevertheless, a large proportion of patients have visual acuity worse than 20/200, especially those in younger age-groups.[4,23] In general, the further away the lesion is from the fovea, the better the recovery. However, development of late complications may adversely affect the outcome. Chorioretinal scarring is the most common complication.[4,48] Other sequelae including macular hole, macular cyst, epiretinal membrane formation, and choroidal neovascularization can lead to unfavorable visual outcome.[4,7,48,84]

Preventive measures

In Hong Kong, there is no statutory regulation on the purchase or usage of laser-incorporated products even for high-energy output classes 3 or 4 lasers.[62] Hand-held laser pointers are commonly used for educational and recreational purposes, giving rise to an increasing incidence of laser-induced ocular injury.[28,56] Public education on the potential harmful effects of lasers should be reinforced in order to prevent accidental or deliberate laser injuries.[2] Furthermore, manufacturers and sellers of laser devices should affix proper explanatory and warning labels to laser products.[86]

In the occupational setting, it is important to ensure that the environment is optimal for the safe operation of laser machines, and all staff are compliant to laser safety protocols. Covering all reflective surfaces and ensuring the room door is locked while a laser is in use are simple but effective measures to minimize inadvertent injuries. Because lasers are monochromatic in nature, wavelength-specific filters are effective in blocking specific laser beams while allowing sufficient light of other wavelengths to be transmitted.[1] These filters are used in safety goggles and operative microscopes to protect operators from laser exposure. Safety goggles with correct corresponding wavelength should be used when operating or switching between laser machines. For patients receiving therapeutic laser treatments, protective eye wear should be used when appropriate.[87,88]

Conclusion

Laser-induced ocular injury may cause permanent visual sequelae and functional disability. Making an accurate diagnosis may have potential medicolegal consequences, and thus it should be supported by clinical findings and/or appropriate investigations. Timely assessment is important, as clinical signs may be temporary and subtle. Prevention and protection of laser-induced ocular injuries is more important than treatment. Awareness of the potential hazardous effects of laser use should be reinforced among healthcare providers and the general public.

Author contributions

Concept or design: EW, FL
Acquisition of data: EW, AL
Analysis or interpretation of data: EW, AL, FL
Drafting of the article: EW, AL, FL
Critical revision for important intellectual content: RL, FL

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have no conflicts of interest to disclose.

Funding/Support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. The patient provided written informed consent for treatments and procedures.

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CASE REPORT

Spontaneous intercalated corneal epithelial folds in thyroid eye disease: a case report

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Abstract

We observed an under-recognized, ethnic-related sign in thyroid eye disease in a 41-year-old Chinese woman. Spontaneous corneal epithelial folds form after fluorescein staining as a result of tear film disruption related to orbital tension and upper lid pressure on the cornea. They occur in anatomically predisposed eyes similar to acquired lower lid epiblepharon. Like their chorioretinal counterparts, presence of corneal epithelial folds prompt for further workup, even in East Asian patients whose thyroid eye changes may appear less impressive.

Key words: Asian continental ancestry group; Epithelium, corneal; Graves ophthalmopathy

Case presentation

In June 2018, a non-smoking 41-year-old Chinese woman presented with a 3-month history of worsening periocular swelling and tightness. She had a 4-year history of stable Graves disease after radioactive iodide treatment, and she was taking 50 mg thyroxine supplement. On examination, visual acuity of each eye was 20/30, with normal Ishihara and pupillary responses and visual field on confrontation. Intraocular pressure was 13 mm Hg and 11 mm Hg at primary gaze and 17 mm Hg and 19 mm Hg on upgaze for right and left eye, respectively. Spontaneous, intercalated corneal epithelial (CE) folds were evident only after fluorescein eyedrop staining and under cobalt-blue lights (Figure 1) before applanation tonometry. She had bilateral upper lid puffiness, retraction, and increased resistance to retropulsion. Despite having mild exophthalmos of 18 mm bilaterally on Hertel exophthalmometry, normal eye movement, and a low clinical activity score of 1 on eyelid swelling, she was referred for further oculoplastic evaluation that showed no chorioretinal fold or optic disc swelling. The patient's anterior chamber depth, intraocular pressures, anterior segment optical coherence tomography, and corneal topographies (Figure 3) were all normal.

Magnetic resonance imaging demonstrated minimally enlarged or inflamed extraocular muscles with predominant fat expansion (Figure 2). Combined intravenous pulse methylprednisolone with orbital radiotherapy was proposed as compassionate treatment for progressive and symptomatic thyroid eye disease despite a low clinical activity score, which was well tolerated.

At the 3-month follow-up, periocular swelling and exophthalmos improved, but CE folds persisted. Patient was offered options of staged rehabilitative orbital decompression, upper lid recession, and blepharoplasty for residual deformities. At the 21-month follow-up, CE folds were static.

Discussion

To the best of our knowledge, there has been only one case report describing corneal stromal (deep) striae (folds) persisting after endoscopic decompression for optic neuropathies in an Asian woman with thyroid eye disease.[1] These corneal stromal striae were evidence of raised orbital

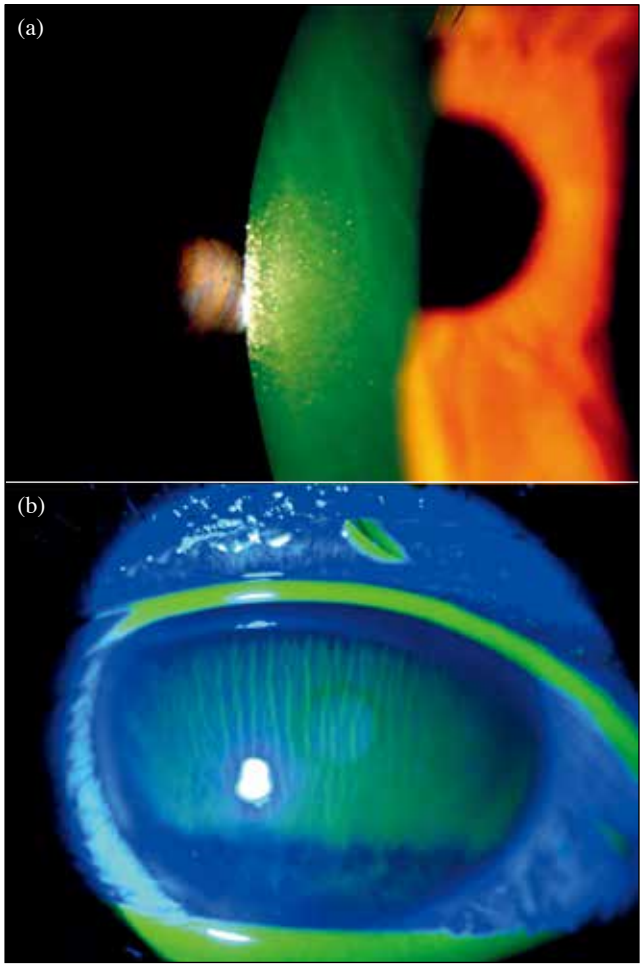

Figure 1. Corneal epithelial folds in an eye with formed anterior chamber and clear cornea visible under (a) fluorescein staining and (b) cobalt-blue lights

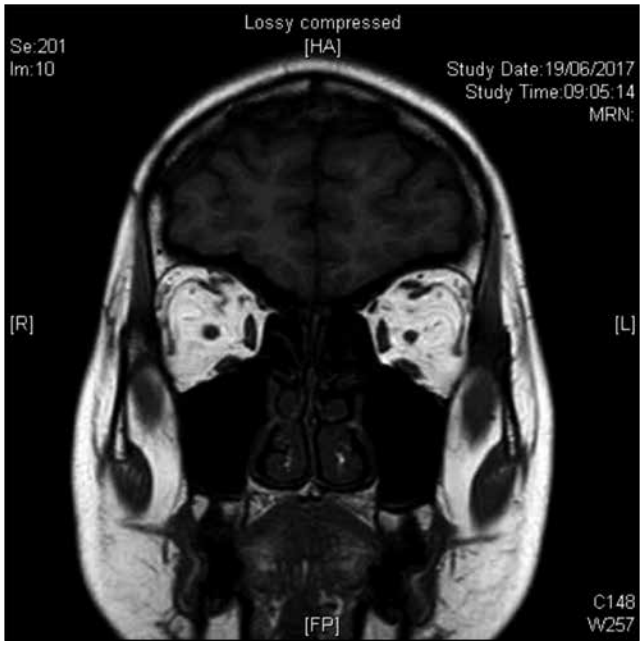

Figure 2. Magnetic resonance imaging showing normal-sized extraocular muscles with fat expansion

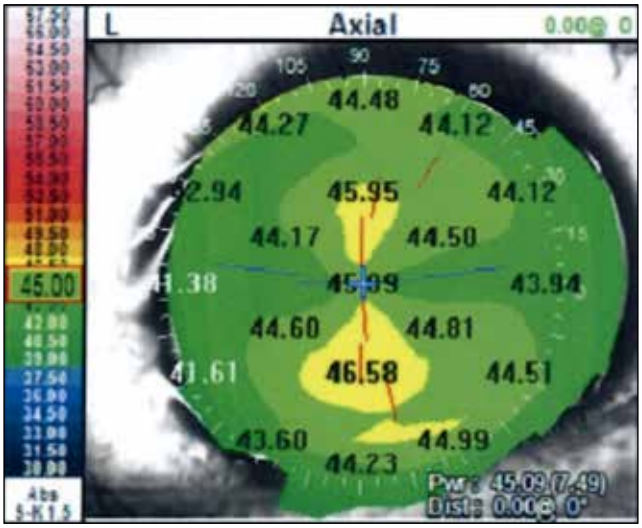

Figure 3. Unremarkable corneal topography

pressure and were resolved upon further three-wall orbital decompression and radiotherapy.[1] In our patient, the CE folds were superficially located as alternating bands of negative staining. They were present only after fluorescein staining and indicated tear film disruption over the elevated, optically disruptive epithelial microfolds. The patient's anterior chamber depth, intraocular pressures, anterior segment optical coherence tomography, and corneal topographies were all normal.

Folds form at the front (cornea) or back (chorioretina) of the eye when tissue layers buckle back as vertical lines. Chorioretinal folds are another sign indicating raised orbital pressure in thyroid eye disease.[2] We propose that CE folds or stromal striae are more prevalent among the anatomically predisposed eyes, similar to acquired lower lid epiblepharon in thyroid eye disease.[3-5] In East Asians whose upper lid creases are low or absent, progressive fat expansion beneath a tight orbital septum exerts pressure on the most superficial (ie epithelial) layer of the cornea leading to formation of CE folds.

In our patient, CE folds did not interfere with visual acuity, analogous to microstriae after LASIK, although contrast sensitivity, higher order aberration or Maddox rod effect was not evaluated.[6] Similar to chorioretinal folds, there is no treatment guideline for CE folds per se in thyroid eye disease. Soft tissue signs improved although CE folds persisted after combined pulse methylprednisolone and radiotherapy. For patients with no demonstratable visual consequence, continuing management of any associated ocular surface problem (eg dry eye) is an acceptable option. In patients with symptomatic periocular deformities (including upper lid swelling, retraction, and exophthalmos), structural changes after orbital decompression, upper lid recession, and blepharoplasties may lead to resolution of CE folds. Persistent chorioretinal folds, attributed to scleral remodeling, was reported despite complete removal of retrobulbar tumor.[7]

Conclusion

The presence of CE or chorioretinal folds in patients with thyroid eye disease may prompt further oculoplastic evaluation or radiological workup, especially in East Asian patients whose periorbital deformities or disease activities are often minimal or subtle.

Author contributions

Concept or design: All authors
Acquisition of data: All authors
Analysis or interpretation of data: All authors
Drafting of the article: All authors
Critical revision for important intellectual content: All authors

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the Journal, KKL Chong was not involved in the peer review process for this article. Other authors have disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. The patient provided written informed consent for treatments and procedures and for publication.

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CASE REPORT

Osteolytic orbital lesion: a case report

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Abstract

A 62-year-old woman presented with optic neuropathy, proptosis, and ocular dysmotility secondary to an osteolytic orbital tumor. Subsequent tests confirmed the diagnosis of multiple myeloma. Differential diagnoses of osteolytic orbital lesions were discussed.

Key words: Multiple myeloma; Orbital neoplasms

Case Presentation

In April 2019, a 62-year-old Chinese woman presented with a 2-month history of progressive proptosis and reduced vision of the left eye. On examination, her visual acuity was vague light perception in the left eye and 6/6 in the right eye. The left eye had optic neuropathy with 5 mm of proptosis and impaired ocular motility in all directions. Fundal examination revealed relative afferent pupillary defect and gross disc swelling with choroidal folds in the left eye. Left facial sensation was reduced over the dermatomes V1 and V2.

Magnetic resonance imaging (MRI) of the brain and orbit demonstrated a 4.8-cm T1- and T2-weighted isointense lesion centered at the left lesser and greater wings of sphenoid bone with involvement of the left posterior orbit (**Figure 1**). It abutted the lateral rectus muscle and extended posteriorly to the anterior part of the left middle cranial fossa causing compression of the left temporal lobe. There was homogenous contrast enhancement after gadolinium contrast injection. Multiple enhancing skull vault lesions were also identified.

Systemic test results showed normochromic normocytic anemia and increased serum immunoglobulin G and Bence-

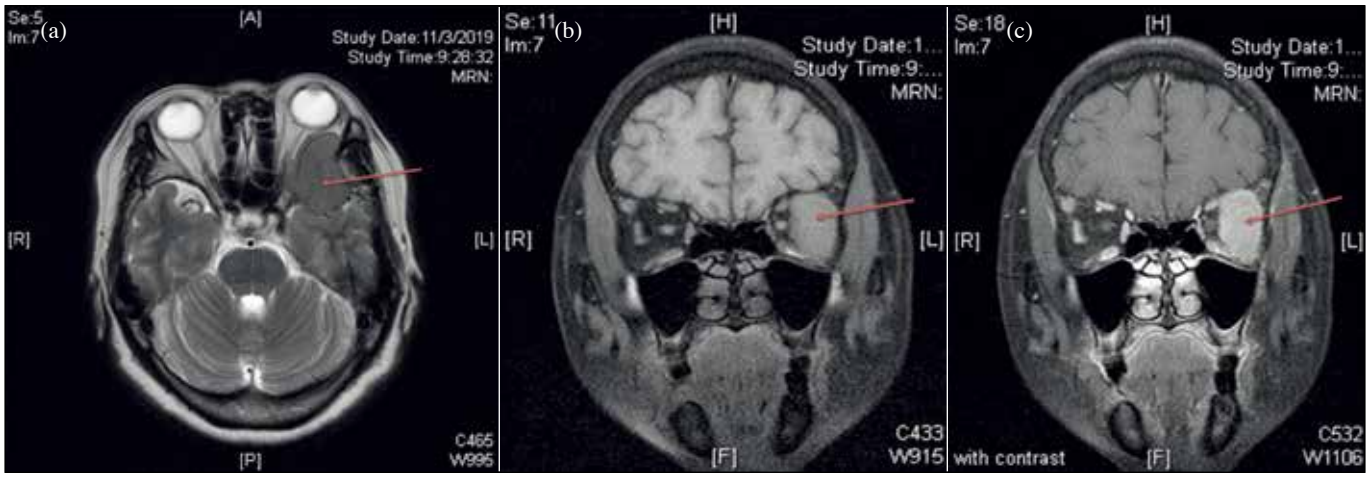

Figure 1. Magnetic resonance imaging showing a left orbital mass in (a) T2-weighted axial view, (b) T1-weighted coronal view, (c) and T1-weighted coronal view with homogeneous contrast enhancement

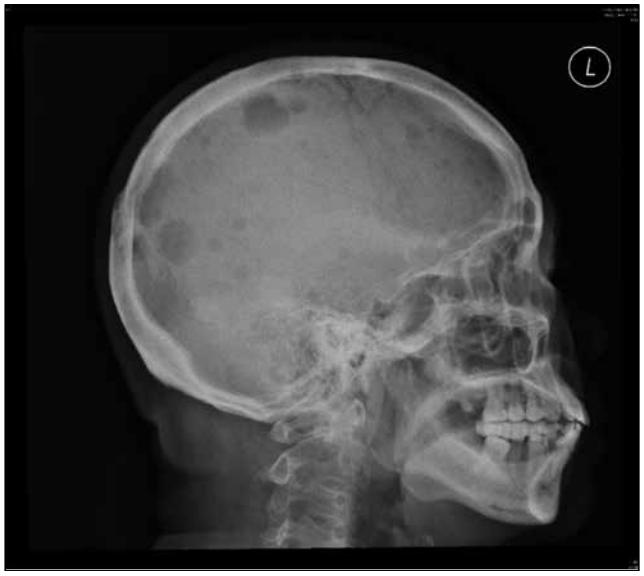

Figure 2. Skull radiograph showing multiple osteolytic lesions

Jones proteinuria. Skeletal examination revealed lytic lesions in multiple ribs, left humerus, and bilateral femurs. Lateral radiographs of the skull showed multiple osteolytic cranial lesions (**Figure 2**). Bone marrow biopsy revealed markedly hypercellular marrow with abnormal plasma cell infiltrate, and a diagnosis of multiple myeloma was made. Left anterior orbitotomy was performed with skin-crease incision, followed by incision of orbicularis muscle and orbital septum. Posterior soft tissue dissection enabled identification of the orbital mass. Biopsy of the lesion confirmed the involvement by myeloma. The abnormal plasma cells comprised eccentric nuclei, prominent Golgi zone, fine chromatin, and distinct nucleoli. The neoplastic plasma cells were positive for kappa light chain but negative for lambda light chain, indicative of clonal proliferation (**Figure 3**).

Chemotherapy was started and the left orbital mass and left eye proptosis reduced considerably. At the 17-month follow-up, the patient visual acuity was finger count in the left eye, with a pale optic disc.

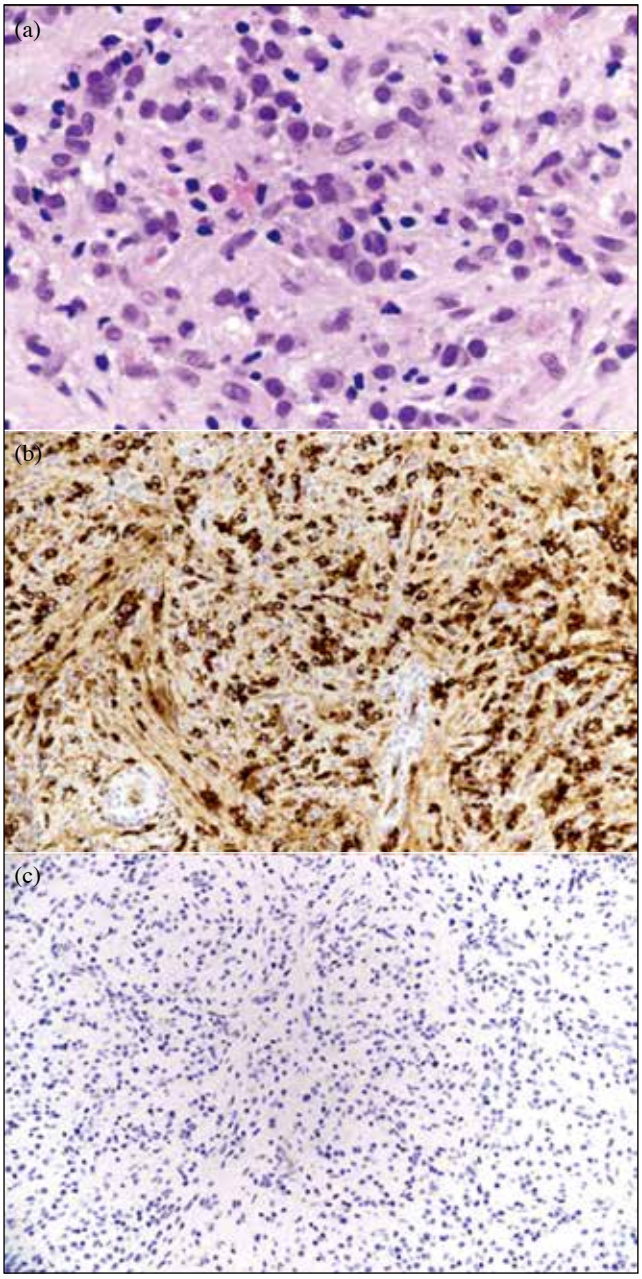

Figure 3. (a) The abnormal plasma cells comprise eccentric nuclei, prominent Golgi zone, fine chromatin, and distinct nucleoli. The neoplastic plasma cells are (b) positive for kappa light chain but (c) negative for lambda light chain, indicative of clonal proliferation.

Discussion

Multiple myeloma and orbital bone metastases are the most common differential diagnoses of osteolytic lesions of the orbit, especially when multiple lesions are detected systemically or when there is a known background of malignancy. Less common differential diagnoses include hyperparathyroidism, adenoid cystic carcinoma of the lacrimal gland, osteosarcoma, Ewing sarcoma, aneurysmal bone cyst, orbital sarcoidosis, and, rarely, intraosseous meningioma with osteolytic activity. Langerhans cell histiocytosis should also be borne in mind in the pediatric age group.

Orbital myeloma is uncommon and accounts for 3% of all orbital tumors.[1] It is likely part of systemic multiple myeloma rather than an isolated lesion. 60% of cases have known myeloma at the time of diagnosis, but the orbital lesion can precede multiple myeloma in more than one-third of patients.[2] A solitary orbital lesion of clonal plasma cells is known as plasmacytoma; there is no end-organ damage or marrow involvement, in contrast to multiple myeloma.

Orbital myeloma most commonly occurs in the supratemporal quadrant of the orbit. It may be mistaken as a lacrimal gland tumor, especially in the absence of background systemic myeloma. Clinical features include proptosis, chemosis,

ocular dysmotility, optic neuropathy, and choroidal folds. Occasionally, patients may have orbital cellulitis and hyperviscosity retinopathy, which are caused by the underlying hematological condition.

Treatment of orbital myeloma is chiefly chemotherapy followed by autologous stem cell transplantation.[2] The role of surgery lies mainly in obtaining tissue for histological diagnosis. Radiotherapy may be useful for local disease control in selected cases. Multidisciplinary management is of utmost importance to arrive at an individualized treatment plan.

Author contributions

CWL was responsible for writing the draft manuscript and conducting the literature review. HKLY was involved in the management and performing biopsy of the patient. WC provided the pathology slides and figure captions. WLP selected the radiology images. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the Journal, HKL Yuen was not involved in the peer review process for this article.
Other authors have disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. The patient provided written informed consent for treatments and procedures.

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Erratum

In the article "Wong E, Chan A, Lam C, Lau W, Yam J, Yu C. Retinoblastoma in Hong Kong from 2008 to 2019: looking back and moving forward. Hong Kong J Ophthalmol 2020;24:6-10. https://doi.org/10.12809/hkjo-v24n1-270", a sentence in the results section of the abstract should have read "The enucleation rate was 0% in groups A to C, 70% in group D, and 93.3% in group E." In addition, a sentence in the results section should have read "The rate of enucleation was proportionally related to the presenting stage (0% in groups A to C, 70% in group D, and 93.3% in group E)."

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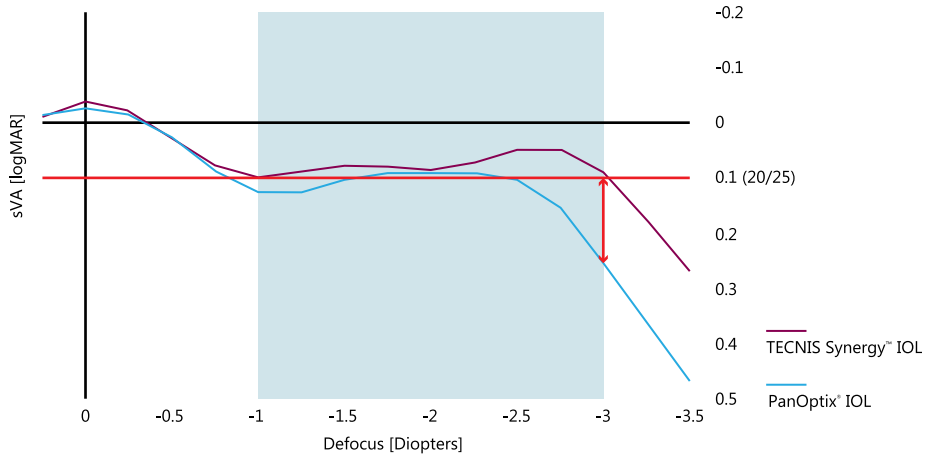

TECNIS Synergy™ vs. AT LISA® IOL
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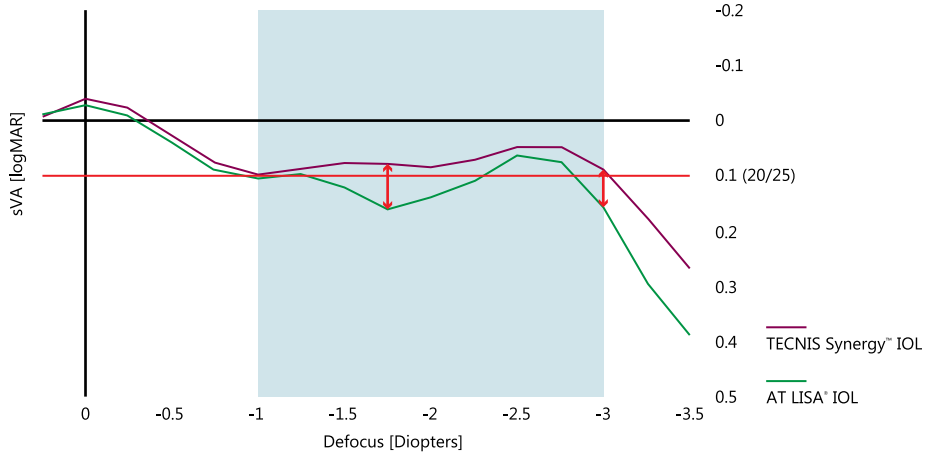

TECNIS Synergy™ vs. FineVision® IOL
Better near and intermediate vision[3]

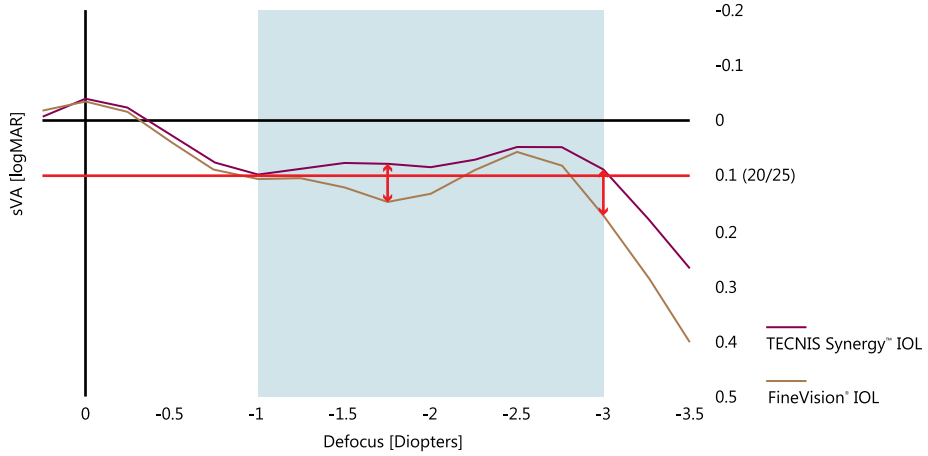

Figure 1. Defocus curves of TECNIS Synergy™ IOL and common trifocal IOLs, calculated from the area under the MTF measured in white light for a 3 mm pupil in the ACE model.[1-3]

* These defocus curves are theoretical/simulated, and are not actual clinical measurements.

ACE = average cornea eye
MTF = modulation transfer function
sVA = simulated visual acuity

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Reference

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- **Sustained long term vision[2,3]**

* PDR=Proliferative Diabetic Retinopathy † DME=Diabetic Macular Oedema

References: 1. Lucentis® Prescribing Information HK, Jun 2020. **2.** Gross JG, *et al.* Panretinal Photocoagulation vs Intravitreous Ranibizumab for Proliferative Diabetic Retinopathy: A Randomized Clinical Trial. JAMA. 2015; 314(20): 2137–46. **3.** Gross JG, *et al.* Five-Year Outcomes of Panretinal Photocoagulation vs Intravitreous Ranibizumab for Proliferative Diabetic Retinopathy. *JAMA Ophthalmol*. 2018; 136(10): 1138–48.

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The interval between two doses injected into the same eye should be at least four weeks. • Treatment is initiated with one injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity. • Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity as assessed by visual acuity and/or anatomic parameters. • Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography). In patients with wet AMD, DME, PDR and RVO, initially, three or more consecutive, monthly injections may be needed. The treatment of visual impairment due to CNV should be determined individually per patient based on disease activity. Some patients may only need one injection during the first 12 months; others may need more frequent treatment, including a monthly injection. For CNV secondary to pathologic myopia (PM), many patients may only need one or two injections during the first year. • treat-and-extend regimen :While applying the treat-and-extend regimen, the treatment interval should be extended by no more than two weeks at a time for wet AMD and extended by up to one month at a time for DME. For PDR and RVO, treatment intervals may also be gradually extended, however there are insufficient data to conclude on the length of these intervals. If disease activity recurs, the treatment interval should be shortened accordingly. **• Lucentis and laser photocoagulation in DME or in branch RVO:** Lucentis has been used concomitantly with laser photocoagulation in clinical studies. When given on the same day, Lucentis should be administered at least 30 minutes after laser photocoagulation. 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Patients should be monitored during the week following the injection to permit early treatment if an infection occurs. • Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of injection of Lucentis. Sustained IOP increases have also been reported. Intraocular pressure and the perfusion of the optic nerve head must be monitored and managed appropriately. Patients should be informed of the symptoms of these potential adverse reactions and instructed to inform their physician if they develop signs such as eye pain or increased discomfort, worsening eye redness, blurred or decreased vision, an increased number of small particles in their vision, or increased sensitivity to light. • There is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors. A low incidence rate of arterial thromboembolic events was observed in the Lucentis clinical trials in patients with AMD, DME, RVO and CNV and there were no major differences between the groups treated with ranibizumab compared to control. Patients with known risk factors for stroke, including history of prior stroke or transient ischemic attack should be carefully evaluated by their physicians as to whether Lucentis treatment is appropriate and the benefit outweighs the potential risk. • Available data do not suggest an increased risk of systemic adverse events with bilateral treatment. • As with all therapeutic proteins, there is a potential for immunogenicity with Lucentis. • Lucentis has not been studied in patients with active systemic infections or in patients with concurrent eye conditions such as retinal detachment or macular hole. • There are insufficient data to conclude on the effect of Lucentis in patients with RVO presenting irreversible ischaemic visual function loss. • Should not be used during pregnancy unless the expected benefit outweighs the potential risk to the fetus. For women who wish to become pregnant and have been treated with ranibizumab, it is recommended to wait at least 3 months after the last dose of ranibizumab before conceiving a child; use of effective contraception is recommended for women of child-bearing potential; breast-feeding is not recommended. • Following treatment patients may develop transient visual disturbances that may interfere with their ability to drive or use machines. Patients should not drive or use machines as long as these symptoms persist. • Risk factors associated with the development of a retinal pigment epithelial tear after anti-VEGF therapy for wet AMD and potentially also other forms of CNV, include a large and/or high pigment epithelial retinal detachment. When initiating ranibizumab therapy, caution should be used in patients with these risk factors for retinal pigment epithelial tears. Interactions: No formal interaction studies have been performed. **Adverse drug reactions: • Very common (≥10%):** vitritis, vitreous detachment, retinal hemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival hemorrhage, eye irritation, foreign body sensation in eyes, lacrimation increased, blepharitis, dry eye, ocular hyperemia, eye pruritus, intraocular pressure increased, nasopharyngitis, headache, arthralgia. **• Common (1 to 10%):** hypersensitivity, retinal degeneration, retinal disorder, retinal detachment, retinal tear, detachment of the retinal pigment epithelium, retinal pigment epithelium tear, visual acuity reduced, vitreous hemorrhage, vitreous disorder, uveitis, iritis, iridocyclitis, cataract, cataract subcapsular, posterior capsule opacification, punctuate keratitis, corneal abrasion, anterior chamber flare, vision blurred, injection site hemorrhage, eye hemorrhage, conjunctivitis, conjunctivitis allergic, eye discharge, photopsia, photophobia, ocular discomfort, eyelid edema, eyelid pain, conjunctival hyperemia, urinary tract infection*, anemia, anxiety, cough, nausea, allergic reactions (rash, pruritus, urticaria, erythema). **• Uncommon (0.1 to 1%)**: blindness, endophthalmitis, hypopyon, hyphema, keratopathy, iris adhesions, corneal deposits, corneal edema, corneal striae, injection site pain, injection site irritation, abnormal sensation in eye, eyelid irritation. **• Serious adverse events** related to intravitreal injections include endophthalmitis, blindness, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. * *observed only in the DME population* A meta-analysis of pooled safety data from completed, randomized, double masked global studies showed a higher incidence rate of non-serious, non-ocular wound infection/inflammation in DME patients treated with ranibizumab 0.5 mg (1.85/100 patient years) compared to control (0.27/100 patient years). 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