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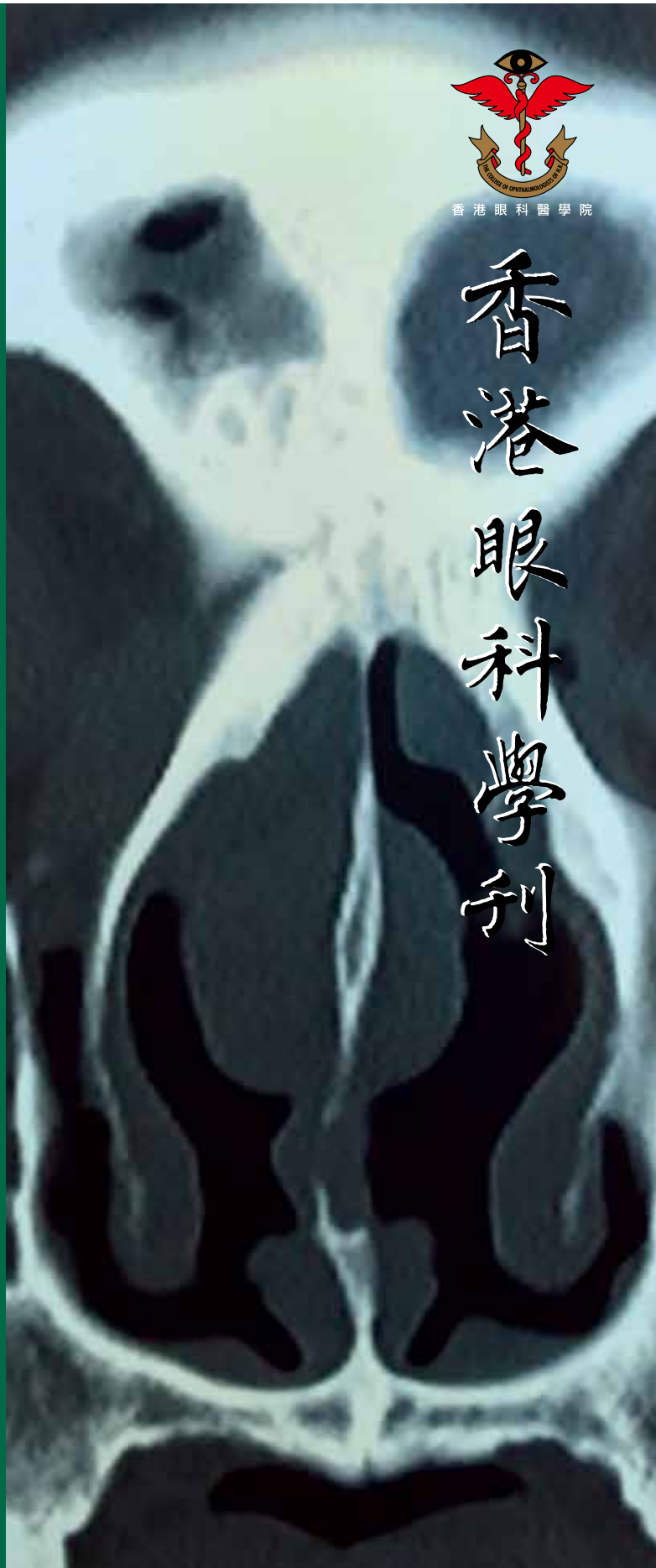

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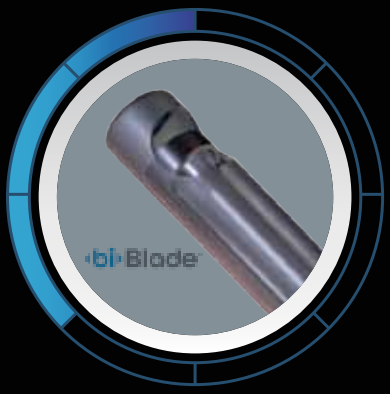

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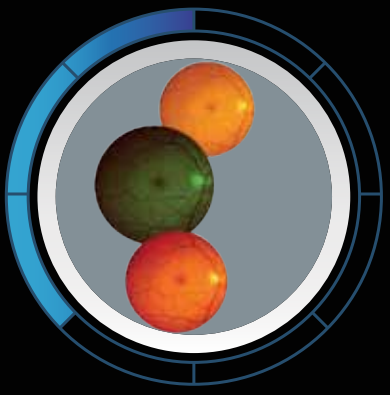

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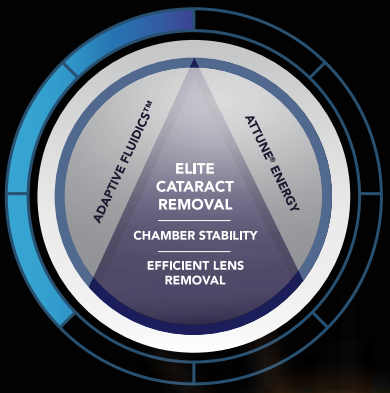

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HONG KONG JOURNAL OF OPHTHALMOLOGY

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Introduction

- The *Hong Kong Journal of Ophthalmology* is the official publication of the College of Ophthalmologists of Hong Kong. The aims of the Journal are 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.
- The *Hong Kong Journal of Ophthalmology* is circulated to all members of the College of Ophthalmologists of Hong Kong and other professional societies and academic institutions in Hong Kong and internationally.

Authorship and Copyright

- Each author of any article submitted to the *Hong Kong Journal of Ophthalmology* is expected to have made significant contributions to the project or the review. Each author must share responsibility for his/her publication. If a manuscript or part of it has been previously published in another journal, this should be disclosed on its submission. In the event of acceptance of the manuscript for publication, the copyright of the manuscript will be automatically transferred from the author(s) to the *Hong Kong Journal of Ophthalmology*.

Format for Submissions

- The submitted article should belong to one of the following categories: Original Research, Review, Perspective, Brief Report, Photo Essay, Clinical Quiz, Letter to the Editor. Editorials are by invitation only.
- The format of the manuscript should be in line with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals,[1] a document issued by the International Committee of Medical Journal Editors.
- The manuscript should be accompanied by a title page and an abstract. The title page should carry: the title of the manuscript; the full name and 2 highest professional qualifications of each author; the department(s) and institution(s) to which the work should be attributed; the full name, address, telephone and fax numbers, and e-mail address, of the corresponding author; and acknowledgements of all sources of financial support and any financial interest on the part of the author(s). All subsequent correspondence between the Editorial Office and the corresponding author is by e-mail, so the corresponding author should ensure that a functional e-mail address is provided.
- An abstract of not more than 250 words should be on a separate page. For original research articles, the abstract should be structured using the following headings: Aim(s), Patients/Materials and Methods, Results, Conclusion(s). A maximum of 6 key words should be provided on this page.
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1. *International Committee of Medical Journal Editors (ICMJE). Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication. ICMJE; April 2010. www.icmje.org*

香 港 眼 科 醫 學 院

THE HONG KONG JOURNAL OF OPHTHALMOLOGY
BEST ORIGINAL ARTICLE AWARD

Purpose

To encourage submissions to the *Hong Kong Journal of Ophthalmology* (HKJO) by trainees and fellows of the College of Ophthalmologists of Hong Kong (COHK).

Awards and Prizes

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.

Eligibility

- One award is open to all fellows and members of the College; another one is limited to trainees only.
- Applicants must be a paid-up member or fellow of COHK at the time of submission.
- 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 of 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.
- Entries will be based on the article as a unit, but not the author. Because of this, it is possible that one single author wins both awards, given that he/she is the first author of the two best original articles published that year (but he/she has to be a trainee in this case as one award is open for trainees only).

Selection Panel

- Editor-in-Chief
- 1 representative from the University of Hong Kong
- 1 representative from the Chinese University of Hong Kong and
- President of the College

Selection Criteria

- Originality
- Scientific merit
- Methodology
- Presentation style

Award Presentation Ceremony

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

EDITORIAL

香 港 眼 科 醫 學 院

Challenges that lie ahead

Ian YH Wong, MBBS, M.Med (Oph)(Singapore), FRCSEd, FRCOphth, FCOphth HK, FHKAM (Ophthalmology)
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It has been my greatest honor and pleasure to have taken up the office of the Editor-in-Chief of the *Hong Kong Journal of Ophthalmology* (HKJO) since 2015. During the past two terms of service, we have seen leaps forward for our Journal. Some areas have had a facelift. For instance, HKJO has found its new home at hkjo.hk. Not only has this increased accessibility, it has also enabled authors to submit their manuscripts online. Since the launch of the website, HKJO has received 8362 visits from all over the world (as of 15 March 2019), including from the United States, India, China, the United Kingdom, Russia, and Singapore. Most visitors to the website are from Hong Kong (constituting around 30% of all visits), followed by the United States (11.8%) and India (7.5%) [**Table and Figure**]. We have also received submissions from different parts of the world. The original goal of setting up the website was to enhance international exposure of HKJO and to encourage submissions from outside of Hong Kong. I believe we have successfully achieved this goal. Although the setting up of the website was challenging, it was clearly the right decision. I wish to thank the Council of the College of Ophthalmologists of Hong Kong for endorsing this endeavor and for providing financial support. I would also like to acknowledge Dr Alvin Au Ka Hong for designing and setting up the website, and for providing technical support throughout the years.

Table. Number of visits to the *Hong Kong Journal of Ophthalmology* website (hkjo.hk)

Geographical location	No. (%) of visits
Hong Kong	2583 (30.87)
United States	990 (11.83)
India	630 (7.53)
United Kingdom	489 (5.85)
Russia	395 (4.72)
Singapore	283 (3.38)
Indonesia	216 (2.58)
Canada	201 (2.40)
China	193 (2.31)

Following the launch of the website, we had to find ways for our articles to be 'discoverable' by readers. Because HKJO is not indexed in MEDLINE, we made efforts to ensure the Journal was indexed in Google Scholar. Anyone searching Google Scholar can easily find our articles, and those who are interested are referred to our website so that the full article can be downloaded at no cost. Around 76% of visitors to our website were diverted from Google Scholar, whereas only 22% accessed the website directly (as of 15 March 2019). This shows the importance of being indexed by a popular search engine, as it can boost the number of visitors to our website and hence enhance the impact of our articles.

The three most downloaded articles on our website are: 'Thyroid eye disease: a 2017 update from the first thyroid eye clinic in Hong Kong' by Chong et al,[1] followed by 'Update on the management of non- infectious uveitis' by Ng et al,[2] and 'Small incision lenticule extraction: a review' by Yung et al.[3] May I take this opportunity to congratulate the authors on this achievement.

To encourage Fellows and trainees of the College to submit to HKJO, with generous support from the College and the Timothy Liu Kai Ching Memorial Fund, the Best Original

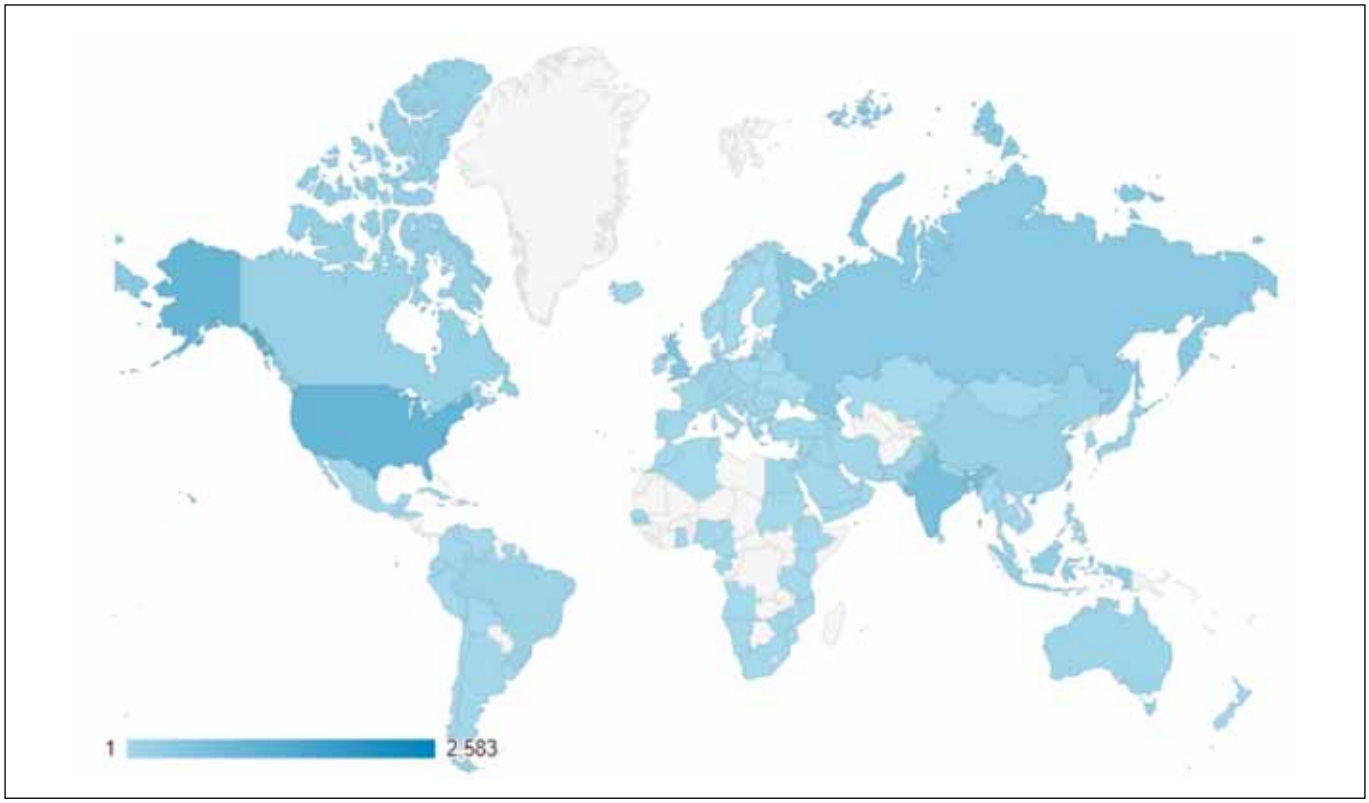

Figure. Frequency of visits according to the visitor's region.

Article Award was established in 2015. Original articles submitted to HKJO are evaluated by a panel appointed by the College Council, based on originality, novelty, clarity in presentation, and scientific impact of the results. Owing to the relatively low rate of submission, the Award is not given out yearly. I would like to take this chance to encourage more submissions from Fellows and trainees so as to make the selection process more competitive.

To be indexed by MEDLINE requires fulfilling several criteria.[4] The journal should demonstrate high quality of editorial work, showing objectivity, credibility, and quality of its content. The journal should also provide information about the methods of article selection and external peer review, publication policy requiring adherence to ethical guidelines, and proper disclosure of financial interests where appropriate.[4] The current Editorial Team has worked hard towards that goal. We truly believe that with collaborative efforts from all Fellows and Members of the College, HKJO will be indexed in MEDLINE one day.

This is the final issue for my current term of service as the Editor-in-Chief. I will step down after the upcoming Annual General Meeting of the College. I would like to show my heartfelt gratitude to all Editorial Board members and International Advisors for their continued support and input. I also wish my succeeding Editor-in-Chief every success, and I am sure he/she will bring HKJO to new heights.

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1. *Chong KKL, Lai THT, Chan R, Li CL, Young A. Thyroid eye disease: a 2017 update from the first thyroid eye clinic in Hong Kong. Hong Kong J Ophthalmol 2017;21:11-8.*
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4. *Medicine USN. FAQ: Journal Selection for MEDLINE® Indexing at NLM. Available from: https://www.nlm.nih.gov/lstrc/j_sel_faq.html. Accessed 1 April 2019.*

ORIGINAL ARTICLE

EX-PRESS shunt implantation in Chinese glaucoma patients: 1-year results

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Abstract

Aim: To report the safety and efficacy of EX-PRESS glaucoma filtration device implantation in Chinese glaucoma patients.

Methods: Records of 38 eyes from 38 Chinese glaucoma patients who underwent EX-PRESS shunt implantation between August 2012 and June 2014 with at least 1 year of follow-up were retrospectively reviewed. Main outcome measures included intraocular pressure (IOP), visual acuity, success rate, number of topical antiglaucoma medications applied, and postoperative complications.

Results: The mean IOP reduced significantly from 25.8±12.4 mmHg before surgery to 15.1±6.3 mmHg at 1 year after surgery ($p<0.005$). Repeated measures ANOVA showed that IOP at all time points after surgery was significantly lower than IOP before surgery. 73.7% of patients achieved complete or qualified success.

Conclusions: EX-PRESS shunt implantation is safe and effective in Chinese patients.

Key words: *Filtering surgery; Glaucoma*

Introduction

The EX-PRESS glaucoma filtration device (Alcon Laboratories, Fort Worth [TX], USA) is a non-valved stainless steel magnetic resonance imaging–compatible device.[1] With an external lumen of 400 μm and internal lumen of 50 μm, it facilitates minimally invasive surgery and promotes the postoperative consistency and predictability of trabeculectomy.[2-4] The EX-PRESS shunt was originally intended for subconjunctival implantation. Although this implant achieves significant reduction in intraocular pressure (IOP), complications related to excess outflow such as hypotony, flat anterior chamber, and suprachoroidal hemorrhage are frequent.[5,6] Therefore, subconjunctival implantation has been replaced by implantation under a scleral flap.[2]

The latest P50 model of the EX-PRESS shunt has a vertical channel in the back plate intended to direct aqueous flow more posteriorly to create a more diffuse posterior bleb. Compared with trabeculectomy, EX-PRESS shunt implantation demonstrates comparable IOP-lowering efficacy, faster visual recovery, and fewer postoperative complications,[7] as well as lower risk of postoperative hypotony.[8] In addition, EX-PRESS shunt negates the need for iridectomy, resulting in less inflammation and shorter operation time.[9] To the best of our knowledge, the surgical outcomes of EX-PRESS shunt implantation in the Chinese population have not been reported. Therefore, we evaluated the safety and efficacy of P50 EX-PRESS shunt implantation in Chinese patients.

Methods

The study was approved by the Institutional Review Board of The University of Hong Kong and was conducted in accordance with the Declaration of Helsinki. Medical records

of Chinese glaucoma patients who underwent EX-PRESS shunt implantation between August 2012 and June 2014 at Queen Mary Hospital with at least 1 year of follow-up were retrospectively reviewed. For patients with bilateral EX-PRESS shunt implantation, only information on the first eye was collected. Patients with cataract surgery within 1 year after EX-PRESS shunt implantation were excluded to avoid confounding IOP results. Patients with glaucoma surgery within 6 months before EX-PRESS shunt implantation were excluded to avoid the effect of scarring. Indications for EX-PRESS shunt implantation included suboptimal IOP control, disease progression despite maximally tolerated topical antiglaucoma medications, and topical medication intolerance.

Main outcome measures were IOP (measured by Goldman applanation), number of topical antiglaucoma medications applied, visual acuity, and postoperative complications requiring intervention. Each type of medication was counted as a single unit, with fixed combination eyedrops counted as two medications. Complete success was defined as IOP of 5-21 mmHg in high-tension glaucoma or a >20% decrease from preoperative IOP in normal-tension glaucoma, without antiglaucoma medications. Qualified success was defined using the same criteria, with patients on antiglaucoma medications achieving the target IOP. Failure was defined as hypotony with IOP of <5 mmHg or IOP of >21 mmHg despite topical medications, complete loss of light perception, or any further glaucoma drainage surgeries, excluding bleb needling.

All P50 EX-PRESS shunt implantations were performed by surgeons specializing in glaucoma surgery. Topical anesthesia with 0.4% oxybuprocaine was applied with or without subtenon anesthesia with 1% lidocaine. All conjunctival flaps were fornix based. Most shunts were implanted in the superonasal quadrant. In cases where the superonasal quadrant was not viable owing to conjunctival scarring or previous drainage surgery, the shunt was placed in other viable quadrants in the following order: superotemporal, inferotemporal, and inferior quadrant. A partial-thickness scleral flap of 4 mm × 3 mm was created. Mitomycin C (0.4 mg/mL) was applied subconjunctivally and underneath the sclera flap for 2 minutes, followed by irrigation with 50 mL of balanced saline solution. A paracentesis wound was created with a 15° stab knife at the temporal clear cornea. A 25- or 27-gauge needle was used to enter the anterior chamber just anterior to the scleral spur, at the posterior aspect of the blue zone, creating a track parallel to the iris plane. The EX-PRESS shunt was implanted. The scleral flap was closed with two 10-0 nylon sutures, and the conjunctiva was closed with either 8-0 or 9-0 vicryl. Postoperative topical medications included 0.5% levofloxacin four times a day and 1% prednisolone acetate six to eight times a day. Patients were followed up at day 1, week 1, and months 1, 3, 6, and 12.

Normality of data was tested using Q-Q plots. Outcomes at 1 year after surgery were compared with preoperative values using the paired sample *t*-test for continuous variables and Chi-squared test for categorical variables. Repeated measures ANOVA with Bonferroni post hoc test was used to compare continuous variables throughout the study period. Correlation between previous glaucoma surgery and the probability of success was determined using logistic regression analysis. Statistical significance was defined as $p<0.05$. All statistical analyses were performed using SPSS (Windows version 20; IBM Corp, Armonk [NY], US).

Results

45 EX-PRESS shunt implantations were performed during the study period. Two of the patients were lost to follow-up. Five of the patients underwent bilateral implantations and data from the second surgery were excluded to avoid statistical overestimation secondary to inter-eye correlation. A total of 21 right eyes and 17 left eyes from 28 men and 10 women (mean age, 59±17 years) were included for analysis (**Table 1**). The most common diagnosis was primary open angle glaucoma (44.7%), followed by uveitic glaucoma (28.9%). Previous ocular surgery was common, with 57.9% having had cataract surgery and 23.7% having had failed filtration surgery.

The mean IOP decreased from 25.8±12.4 mmHg before surgery to 15.1±6.3 mmHg at 1 year after surgery ($p<0.005$, paired *t* test, **Table 2**). The lowest mean IOP (9.2±6.0 mmHg) occurred approximately 1 week after surgery. The box and whisker plot revealed outliers that lay >1.5 times above the third quartile (**Figure**). Repeated measures ANOVA with and without outliers both showed that IOP at all time points after surgery was significantly lower than IOP before surgery

Table 1. Patient demographics

Variable	No. (%)
Sex	
Male	28 (73.7)
Female	10 (26.3)
Eye	
Right	21 (55.3)
Left	17 (44.7)
Diagnosis	
Primary open angle glaucoma	17 (44.7)
Uveitic glaucoma	11 (28.9)
Primary angle closure glaucoma	3 (7.9)
Congenital/childhood/juvenile glaucoma	3 (7.9)
Normal-tension glaucoma	2 (5.3)
Silicon oil–induced glaucoma	1 (2.6)
Neovascular glaucoma	1 (2.6)
Previous surgery	
Cataract surgery	22 (57.9)
Trabeculectomies	7 (18.4)
Pars plana vitrectomies	4 (10.5)
Ahmed valves	2 (5.3)

(**Table 3**). Patients who required a second glaucoma surgery within 1 year after of EX-PRESS shunt implantation were excluded from the ANOVA analysis.

The mean number of topical antiglaucoma medications applied was 3.3±1.5 before surgery, 1.0±1.4 at 6 months after surgery, and 1.2±1.3 at 12 months after surgery (p<0.0005, Wilcoxon signed rank test). 14 (37%) patients required oral acetazolamide before surgery and none required it after surgery.

Table 2. Intraocular pressure (IOP) at different time points

Time point	Mean±SD (95% CI) IOP, mmHg
Before surgery	25.8±12.4 (21.1-30.5)
After surgery	
1 day	10.1±6.4 (7.7-12.6)
1 week	9.2±6.0 (7.0-11.5)
1 month	10.6±4.6 (8.8-12.3)
3 months	12.3±4.6 (10.5-14.0)
6 months	13.7±4.8 (12.0-15.6)
12 months	15.1±6.3 (12.7-17.5)

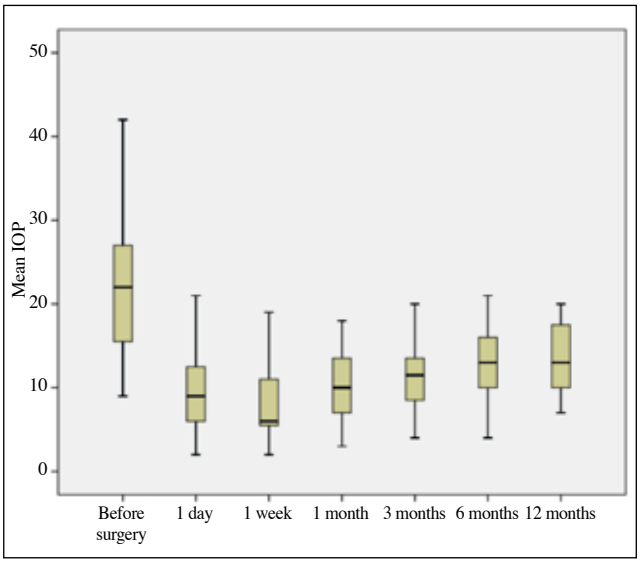

Figure. Box and whisker plot showing intraocular pressure (IOP) before surgery and at different time points after surgery

At 1 year after surgery, of 38 eyes, 14 (36.8%) achieved a complete success, 14 (36.8%) achieved a qualified success, and 10 failed. Of the 10 failed eyes, five had IOP of >21 mmHg despite medication and five underwent further glaucoma drainage surgeries (3 of which had secondary glaucoma). In subgroup analysis, of 17 patients with open angle glaucoma, 10 (58.8%) achieved a complete success, five (29.4%) achieved a qualified success, and two failed. Of 11 patients with uveitic glaucoma, four (36.4%) achieved a complete success, three (27.3%) achieved a qualified success, and four failed. Of three patients with primary angle closure glaucoma, two achieved a qualified success, and one failed. All four patients with neovascular or congenital glaucoma achieved a qualified success. The patient with silicon oil–induced glaucoma failed. The two patients with normal-tension glaucoma also failed. Logistic regression analysis showed no significant correlation between previous glaucoma surgery and the probability of success. No patients had hypotony or vision loss. Three patients required EX-PRESS shunt removal (**Table 4**).

There were no significant differences before surgery and at 1 year after surgery in terms of visual acuity (logMAR, 0.75±0.85 vs 0.61±0.73, p=0.09, paired t test), cup-disc ratio (0.67±0.2 vs 0.69±0.2, p=0.27, paired t test), and mean deviation on Humphrey 24-2 visual fields (-15.3±9.0 dB vs -18.4±9.7 dB, p=0.45, paired *t* test).

Discussion

Trabeculectomy has been the standard surgical treatment for glaucoma since the 1970s. However, it is associated with a wide range of postoperative complications and a lower success rate in patients with secondary glaucoma, non-Caucasians, and young patients.[10] Implantation of a tube shunt is an alternative option; however, shunts are associated with complications such as hypotony, diplopia, strabismus, tube erosion, and corneal decompensation.[11] Compared with trabeculectomy, EX-PRESS shunt implantation achieve

Table 3. Mean difference in intraocular pressure (IOP) between before surgery and at different time points after surgery

Repeated measures ANOVA	With outliers	P value	Without outliers	P value
Greenhouse-Geisser correction	F (2.282, 63.9)=25.94	<0.0005	F (2.514, 55.3)=23.6	<0.0005
Bonferroni post hoc test	Mean difference in IOP, mmHg		Mean difference in IOP, mmHg	
Before vs 1 day after surgery	15.7	<0.0005	13.0	<0.0005
Before vs 1 week after surgery	16.6	<0.0005	14.5	<0.0005
Before vs 1 month after surgery	15.2	<0.0005	12.0	<0.0005
Before vs 3 months after surgery	13.5	<0.0005	11.0	<0.0005
Before vs 6 months after surgery	12.0	<0.0005	9.2	<0.0005
Before vs 12 months after surgery	10.7	<0.0005	8.3	<0.001

Table 4. Postoperative complications requiring interventions	
Complication	**No. (%)**
Hypotony with shallow anterior chamber requiring anterior chamber reformation with viscoelastic	8 (21.1)
Bleb leak requiring conjunctival repair	8 (21.1)
Antimetabolite injection	
Mitomycin C	19 (50)
5 fluorouracil	4 (10.5)
Needling with antimetabolite injection	10 (26.3)
Inflammation requiring subtenon or oral steroids	2 (5.3)
Suture lysis	7 (18.4)
EX-PRESS shunt removal	3 (7.9)

similar efficacy, better tolerability, and fewer complications of hypotony and hyphema.[12]

Although the definition of success differs in different studies, the complete success rate of EX-PRESS shunt implantation at 1 year has been reported to be 60% to 87%.[13-16] The success rate was reported to be 50% lower among non-Caucasians patients (mainly patients of African or Indian origin).[14] For trabeculectomy, outcomes have been reported to be similarly poor among Chinese[17] and Malay[18] patients. Other risk factors include young age, previous glaucoma surgery, and use of antiglaucoma medications. Glaucoma type was not found to be a risk factor for failure, but the sample comprised >85% of open angle glaucoma cases and did not include secondary glaucoma or congenital glaucoma.[14]

In the present study, the complete success rate at 1 year was 36.8%, which is lower than that reported in other studies. This may be attributed to differences in case mix. Open angle glaucoma only constituted 44.7% of our patients. The remainder included uveitic glaucoma (28.9%), congenital or juvenile glaucoma (7.9%), angle closure glaucoma (7.9%), and other secondary glaucomas (10.5%). These patients were at risk of trabeculectomy failure, and thus EX-PRESS shunt implantation assumed the role of augmented trabeculectomy and was an alternative to tube shunt implantation. The complete success rate of 58.8% among patients with open angle glaucoma is comparable with that reported in the literature.

Most of our patients had previous ocular surgery. However, logistic regression analysis showed no significant correlation between previous glaucoma surgery and the probability of success of the current surgery. This may be attributed to the small sample size. Of the three patients with angle closure glaucoma, two were pseudophakic prior to implantation (one of them required shunt exchange for malpositioned shunt) and one was phakic and achieved a qualified success. Although an open angle is usually a prerequisite for EX-PRESS shunt implantation, EX-PRESS shunts have been used in patients with angle closure glaucoma, usually in combination with phacoemulsification.[14,19] To the best of our knowledge, there are no studies on EX-PRESS shunt implantation in patients with phakic angle closure glaucoma. The success in patients with angle closure glaucoma suggests that EX-PRESS shunt implantation in the area free of synechiae closure may be a viable option. The incidence of hypotony has been reported to be lower after EX-PRESS shunt implantation than after trabeculectomy.[8,19,20] One study reported a hypotony rate of 15.6% in the first week after EX-PRESS shunt implantation, but none of these eyes developed flat anterior chamber or lens corneal touch.[19] This may be because the 50-µm internal lumen diameter of the EX-PRESS shunt provides more resistance to aqueous outflow compared with the 750-µm smallest sclera punch in trabeculectomy, thus providing better anterior chamber maintenance, even in cases of hypotony.[3] None of our three patients with angle closure glaucoma developed hypotony, although two of them required anterior chamber reformation for shallow anterior chamber.

Limitations of our study include a heterogeneous sample, multiple surgeons, differences in anti-metabolite injection practices, and the retrospective nature.

Conclusion

EX-PRESS shunt implantation is effective and safe in primary open angle glaucoma and possibly in uveitic glaucoma. Further prospective and randomized controlled studies are recommended to clarify the efficacy of EX-PRESS shunt implantation in patients with angle closure glaucoma, neovascular glaucoma, or silicone oil–induced glaucoma.

Declaration

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ORIGINAL ARTICLE

Alcohol-assisted epithelial debridement for treatment of recurrent corneal erosion: a case series

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Abstract

Purpose: Recurrent corneal erosion is characterized by recurrent episodes of spontaneous breakdown of the corneal epithelium. Alcohol delamination of the corneal epithelium has a high success rate, but the procedure requires the use of an operating microscope in an operating theater. We present a case series of alcohol-assisted epithelial debridement in the clinic setting.

Methods: Records of eight consecutive patients aged >18 years who presented to a private ophthalmology practice clinic in Hong Kong between October 2012 and March 2018 with recurrent corneal erosion that did not respond well to conservative or surgical management with persistent symptoms of >3 months were retrospectively reviewed. 75% alcohol was applied directly to the site of abnormal epithelium under slit lamp, followed by debridement of the epithelium using a surgical sponge. A bandage contact lens was then inserted. Patients were followed up until complete healing of the epithelial defect.

Results: All eight patients achieved complete healing of the epithelial defect within 2 weeks with no major complication or recurrence.

Conclusion: Alcohol-assisted epithelial debridement is simple, safe, and effective for the treatment of recurrent corneal erosion. It can be performed in a clinic setting under slit lamp.

Key words: *Alcohols; Corneal ulcer; Epithelium, corneal*

Introduction

Recurrent corneal erosion (RCE) is characterized by the failure of epithelial cells to re-adhere tightly to the underlying stroma following injury,[1] owing to a combination of hemidesmosome weakness, pathological changes to the basement membrane, and excessive activity of matrix metalloproteinases.[2,3] To achieve proper adhesion between the epithelium and stroma, first-line options include intensive lubrication, padding, punctal plugs, bandage contact lens, and antibiotic ointment.[4] For those who do not respond well to conservative treatments, surgical options may be considered, including anterior stromal puncture, diamond burr superficial keratectomy, and phototherapeutic keratectomy (PTK).[5,6]

In 2006, Dua et al[7] reported a case series of 12 patients who underwent alcohol delamination for RCE, the area of affected

Table. Clinical characteristics and outcomes of patients undergoing alcohol-assisted epithelial debridement treatment for recurrent corneal erosion

Sex/age, y	Etiology	Duration of conservative management, mo	Time to complete healing, d	Follow-up, mo	Best corrected visual acuity		
					Before treatment	3-4 weeks after treatment	8 weeks after treatment
M/58	Idiopathic	7	8	39	0.8	0.6	0.8
M/36	Map dot fingerprint dystrophy	3	9	45	0.5	0.7	0.9
M/32	Traumatic	6*	8	14	1.0	0.7	1.0
F/27	Traumatic	12	14	7	0.9	0.9	0.9
M/58	Traumatic	5	8	45	1.0	1.0	1.0
F/35	Traumatic	4	7	0.25	1.0	0.7	1.0
M/37	Idiopathic	4	14	0.5	1.0	0.7	1.0
M/49	Traumatic	11	7	67	1.0	1.0	1.0

** Also underwent phototherapeutic keratectomy*

corneal epithelium was demarcated by an optical zone marker under an operating microscope and then delaminated using alcohol. Of those 12 patients, 11 had relief of symptoms over the follow-up period with no residual effects from the application of alcohol. Although alcohol delamination is effective and safe, it requires an operating theatre and an optical zone marker that may not be readily available in clinical practice. We propose a simpler and more convenient alcohol-assisted epithelial debridement method for the treatment of RCE in a private general ophthalmology clinic setting.

Methods

Records of eight eyes in eight consecutive patients aged >18 years who presented to a private ophthalmology practice clinic in Hong Kong between October 2012 and March 2018 with RCE that did not respond well to conservative or surgical management with persistent symptoms of >3 months were retrospectively reviewed (**Table**). Patients were excluded if they had concomitant keratitis or neutrophic ulcer.

The area to be treated was identified with fluorescein staining, and its size was measured using a slit lamp. Under the slit lamp, 75% rubbing alcohol (One Stop Medical Limited, Hong Kong) was applied to the affected area for 10 seconds using a surgical sponge tip. The abnormal epithelium was then peeled or scraped off, followed by rubbing of the debrided stromal bed with a dry sponge. A bandage contact lens was inserted and kept for 5 days. The affected eye was applied with topical levofloxacin, lubricant eyedrops, and nepafenac four times a day. Patients were followed up until complete healing of the epithelial defect.

Results

Two women and six men aged 27 to 58 years were diagnosed with RCE secondary to trauma (n=5), idiopathic RCE (n=2), and map dot fingerprint dystrophy (n=1). The duration of symptoms prior to alcohol-assisted epithelial debridement ranged from 3 to 12 months (mean, 6.5 months). The time to complete healing of the epithelial defect after debridement ranged from 7 to 14 days (mean, 9.38 days). The mean follow-up period was 27.2 months.

Seven of the patients failed conservative management; all had complete resolution of symptoms after alcohol-assisted epithelial debridement. One patient underwent PTK but had three recurrences within 4 months; had no recurrence 14 months after alcohol-assisted epithelial debridement. At week 8, all patients had either static or improved best corrected visual acuity. No patient had adverse effects, except that one developed a contact-lens related corneal abrasion 15 months later, which responded well to bandage contact lens and other conservative measures.

Discussion

A study by Singh et al[8] reported that 66% to 83% of patients were symptom-free after intervention and 91% to 100% of patients had decreased pain score. An electron microscope study showed that alcohol delamination of the corneal epithelium spares the Bowman's layer with well-preserved hemidesmosomes on the basal surface of the basal cell layer, and this may contribute to the high success rate of alcohol delamination.[9] In a randomized controlled trial by Chan et al[10] comparing 17 eyes treated with alcohol delamination with 16 eyes treated with PTK, the two techniques were comparable in terms of pain score and percentage of partial to complete resolution of RCE symptoms (65% vs 63%). A clinical audit reported that alcohol delamination meets the typical safety and efficacy standards.[11]

In our case series, alcohol-assisted epithelial debridement was effective and safe in the treatment of RCE. All our patients had complete resolution within 2 weeks and had no recurrence after a mean follow-up period of 27 months. However, a lack of a control group may be a limitation of this study. Further study is required to better evaluate the clinical efficacy of alcohol-assisted epithelial debridement, such as a prospective trial comparing this treatment with classical alcohol delamination, or other techniques such as PTK.

Declaration

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OPINION

Treat-and-extend regimen for management of neovascular age-related macular degeneration: recommendations from the Hong Kong Retina Expert Panel

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Abstract

Antivascular endothelial growth factor (anti-VEGF) agents are a safe and effective treatment option for neovascular age-related macular degeneration (nAMD). However, undertreatment related to the costs and route of administration of anti-VEGF agents remains a common problem for nAMD patients. The treat-and-extend (T&E) regimen for nAMD has proven to balance clinical effectivity with reduced numbers of injections. However, implementation of the T&E regimen depends on the capacity and resources of clinics and patient compliance. To determine the optimal T&E regimen for Hong Kong, a panel of retina specialists was initiated by MediPaper Medical Communications Limited to discuss the benefits and hurdles in adopting the T&E regimen and to develop recommendations for patient selection based on clinical needs, dosing criteria, and dosing regimen. Key recommendations included selecting patients with only-eye or recurrence for the T&E regimen, pre-booking clinic appointments to reduce patient visits, communicating the T&E regimen with non-vitreoretinal physicians and trainees, extending the maximum dose interval to 16 weeks, and actively engaging patients in decision making.

Key words: Aflibercept; Macular degeneration; Ranibizumab; Vascular endothelial growth factors

Introduction

Neovascular age-related macular degeneration (nAMD) owing to leakage or bleeding from choroidal neovascularization is a common cause of central vision loss in the developed world.[1] A meta-analysis in 2010 reported that the prevalence of nAMD among those aged 40 to 79 years was 6.8% for Asians and 8.8% for Caucasians.[2,3] Both of these populations share similar risk factors for nAMD, such as old age, smoking, obesity, sun exposure, and cardiovascular disease.[2]

Treatment goals for nAMD are to maximize and maintain visual acuity, reduce fluid and blood leakage, and induce regression of choroidal neovascularization.[2] The current gold standard treatment for nAMD is intraocular injection of anti-vascular endothelial growth factor (anti-VEGF) agents to inhibit the development of abnormal blood vessels.[4] Commonly used on-label anti-VEGF agents include ranibizumab and aflibercept.[5] These drugs are effective[4] but expensive and require frequent intraocular injections.

Based on pivotal phase-3 clinical trials, the initial recommended injection regimen was monthly or bi-monthly.[2,6-9] However, repeat injections put pressure on the overburdened eye clinics, and patients with reduced symptoms may halt the treatment. It is not uncommon for patients to be treated *reactively* (ie, as needed) upon symptom exacerbation. This may result in undertreatment and suboptimal outcomes.[10-12]

Therefore, physicians aim to balance the injection frequency with clinical outcomes and to determine an optimal, clinically feasible regimen. One strategy for patients responding well to anti-VEGF therapy is to use the treat-and-extend (T&E) regimen, which is a *proactive* regimen that allows for extension of visit intervals in patients without clinical evidence of recurring or worsening disease activity.[13] The T&E regimen has shown favorable results. The TREX-AMD and TREND studies using ranibizumab revealed that both monthly and T&E regimens achieved comparable visual acuity outcomes.[14,15] In the FLUID study, patients with significantly fewer ranibizumab injections had similar mean change in visual acuity.[16] The ALTAIR study reported similar efficacy between 2-week and 4-week adjustment of aflibercept.[17] A 1-year interim study of early versus late T&E regimen using aflibercept for nAMD showed similarly good visual acuity results.[18] The Fight Retinal Blindness! registry revealed that the T&E regimen using either ranibizumab or aflibercept resulted in improvements in visual acuity by 24 months.[19,20] Compared with the reactive regimen upon symptom exacerbation that may result in undertreatment and suboptimal outcomes,[10-12] the proactive T&E regimen enables significant visual improvement and significantly fewer clinic visits and injections, thus reducing the cost of treatment.[21]

In view of the similar effectiveness of T&E and monthly regimens, this position paper aims to summarize Hong Kong's T&E regimens in managing patients with nAMD and propose strategies for its implementation in the local setting.

Hong Kong Retina Expert Panel Selection

In October 2018, an expert panel comprising retina specialists from public, private, and academic institutions across Hong Kong was initiated by MediPaper Medical Communications Limited to discuss the current management of nAMD and implementation of T&E regimen in Hong Kong. The objectives were to investigate how the T&E regimen is practiced in Hong Kong and to identify benefits and hurdles of practicing the T&E regimen for nAMD patients. This paper presents the recommendations of the panel, which are based on a series of presentations and round-table discussions during the meeting.

Recommendations

General recommendations for T&E regimen in Hong Kong

In Hong Kong, different hospitals have different practices depending on capacity and resources. The proactive T&E regimen is beneficial as it provides better visual outcomes than reactive regimen and reduces the number of visits, patient expenses, and clinic burden compared with gold standard monthly or bimonthly regimens. The burden on facilities, including optical coherence tomography (OCT), varies among different hospitals.

Careful management of resources is recommended. All procedures performed in the operating theater are associated with additional workload related to admission and discharge; therefore, outpatient treatment is recommended unless clinically contraindicated. To reduce the number of visits and clinical workload, OCT assessment and anti-VEGF drug injection should preferably be performed on the same day and thus appointments should be scheduled 2 months in advance to ensure adequate resources and facilities available. Different specialists may be involved in the treatment of the same patient. The treatment plan may be considered complex to non-vitreoretinal physicians and trainees; retinal specialists are recommended to document the treatment plan in the case management system to enable non-vitreoretinal physicians or trainees to adhere.

Selection of patients for the T&E regimen

Identifying patients for the T&E regimen is based on clinical needs and patient preferences. Clinics may establish a set of criteria for patients to switch from the as-needed regimen to T&E regimen. In the current clinical setting, the T&E regimen is recommended for patients with only-eye or recurrent diseases.

Loading period - initiation of doses

All patients should receive three loading doses in the first 3 months.[2] The injection should preferably be performed

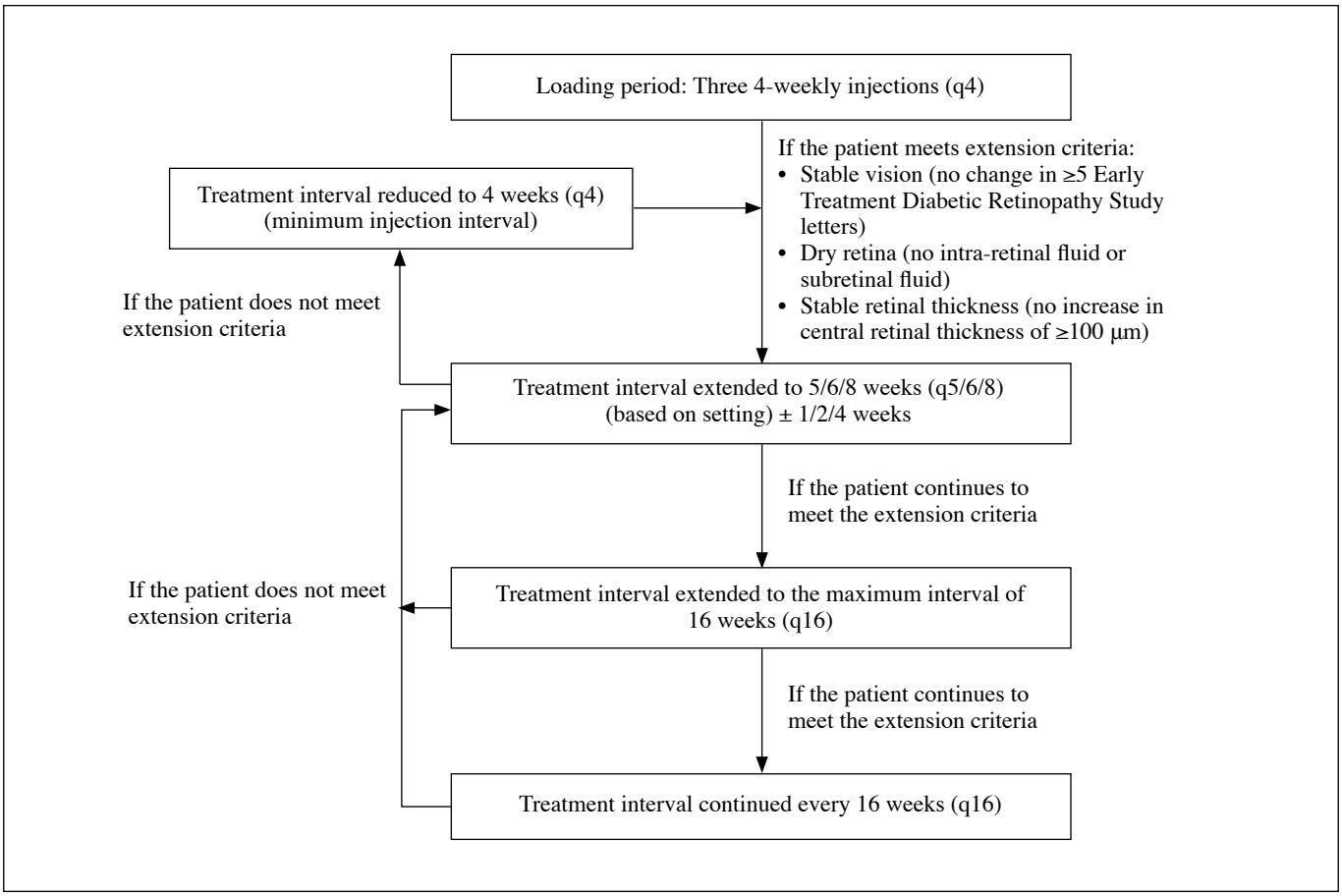

Figure. Proposed treat-and-extend regimen.

on the day of OCT assessment. If an OCT assessment is not feasible on the day of injection, it should be performed within 1 week before the injection date to assess the presence of any new or persistent fluid and to adjust the T&E regimen schedule when clinically indicated. Clinics should make efforts to fulfil the injection schedule, which may require careful scheduling of the operating theater. After three loading doses, patients are scheduled for an appointment 3 to 4 weeks later. Patients are briefed about the importance of adherence to the injection schedule to minimize rescheduling, which results in delayed schedule and interferes with the logistical planning.

Extension of treatment interval

A minimal interval for subsequent injections of 4 weeks (±1/2/4 weeks) is recommended.[2] In patients with stable vision (ie, no change in ≥5 Early Treatment Diabetic Retinopathy Study letters) and dry retina or stable retinal thickness (no increase in central retinal thickness of ≥100 μm), the treatment interval can be extended by 4 weeks (**Figure**). The treatment interval should either be maintained or reduced when fluid is present. The interval can be extended up to 16 weeks in patients who continue to meet the extension criteria.

Reduction of treatment interval

In patients not meeting the extension criteria or with presence of intraretinal fluid or subretinal fluid, the treatment interval should be reduced to 4 weeks (**Figure**).[2] Intraretinal cysts secondary to injection do not need to be treated. Pigment epithelial detachment may cause an increase in fluid, but it is not an immediate reason for reduction. However, such patients should be carefully monitored.

Maintenance criteria

In patients extended to the maximum interval of one injection per 16 weeks, the treatment interval should be maintained if the patient maintains a dry macula, has no loss of ≥5 Early Treatment Diabetic Retinopathy Study letters, has no increase in central retinal thickness of ≥100 μm, has no new neovascularization, and has no new macular hemorrhage.

Cessation of treatment

Neovascular age-related macular degeneration is a chronic condition and prolonged treatment for at least 2 to 3 years is recommended. All patients, including those who have ceased treatment, should be followed up indefinitely at least every 4 to 6 months and are advised to return for assessments upon symptom exacerbation. Even patients asymptomatic for

years may require treatment in later years owing to aging and further deterioration.

Limitations

These recommendations are limited to patients with only-eye or recurrent diseases. Patient selection should be based on clinical needs and patients' preferences. Patients with a non-resolving vitreous hemorrhage requiring vitrectomy are considered a special population,[22] although they are not excluded from the T&E regimen. Vitrectomy after anti-VEGF drug injection may reduce the effectiveness of the drug,[23] whereas anti-VEGF drug injection after vitrectomy may increase the risk of leakage.[24]

Conclusion

Adopting set criteria for selecting patients, improving patient retention, and optimizing resources will improve treatment outcomes and standard of care of patients with nAMD.

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Declaration

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CASE REPORT

Supraorbital nerve schwannoma in a young Chinese man: a case report and review of the literature

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Abstract

Schwannomas of peripheral branches of the trigeminal nerve are rare. We report a 23-year-old Chinese man who underwent anterior orbitotomy through an upper eyelid crease incision approach for resection of a supraorbital nerve schwannoma. Clinical features, imaging findings, and management considerations are discussed, and the literature reviewed.

Key words: *Eyelids; Neurilemmoma; Orbit*

Introduction

Schwannomas are benign, slow-growing tumors arising from the myelin sheath Schwann cells of the peripheral nerves. Orbital schwannomas are uncommon and account for 1% to 2% of all orbital tumors.[1] They usually originate from the ophthalmic division of the sensory branch of the trigeminal nerve, most commonly the supraorbital and supratrochlear nerves.[2] We report an anterior orbitotomy through an upper eyelid crease incision approach for resection of a supraorbital nerve schwannoma.

Case Presentation

In February 2015, a 23-year-old man with a history of recurrent craniopharyngioma and persistent visual impairment presented with a painless mass in the superomedial aspect of the left upper eyelid. He had no diplopia, ophthalmoplegia, proptosis or chemosis, or any deterioration in visual acuity. Confrontation testing revealed a left medial inferior quadrantanopia, which had been documented in 2008 as an old defect with optic atrophy, consistent with left optic disc pallor on fundi visualization. Ophthalmologic examination was unremarkable. Systemic evaluation excluded neurofibromatosis.

Contrast-enhanced computed tomography of the orbit demonstrated a well-circumscribed, homogenous, moderately enhancing ovoid solid mass of 1.2 cm × 0.8 cm × 0.8 cm at the superomedial aspect of the extraconal left orbit, anterosuperior to and abutting the globe. There were no aggressive features (bony destruction or invasion to surrounding structures), fluid, macroscopic fat component, or evidence of calcification. The left globe, lacrimal gland, and extraocular muscles were normal (**Figure 1**). Contrast-enhanced magnetic resonance imaging (MRI) showed a well-defined, homogenous, T1-hypointense and T2-hyperintense, avidly enhancing lesion of 1.1 cm × 1.0 cm × 1.0 cm, with no calcification or soft tissue or osseous invasion. There were no internal T1-hyperintense signals or fluid levels (**Figure 2**). The lesion had been identified on MRI in 2014. Owing to the static nature of the lesion, preliminary diagnoses included cavernous hemangioma and nerve sheath tumors.

In 2000, the patient had undergone craniotomy and excision of a craniopharyngioma. He had complications of panhypopituitarism and mild renal impairment but remained free of recurrence until 2015 when MRI of the pituitary gland incidentally found a well-circumscribed, T1-hyperintense mass of 1.7 cm × 1.9 cm × 1.8 cm at the pituitary fossa. A diagnosis of recurrent craniopharyngioma was made.

In January 2016, the patient underwent concomitant removal

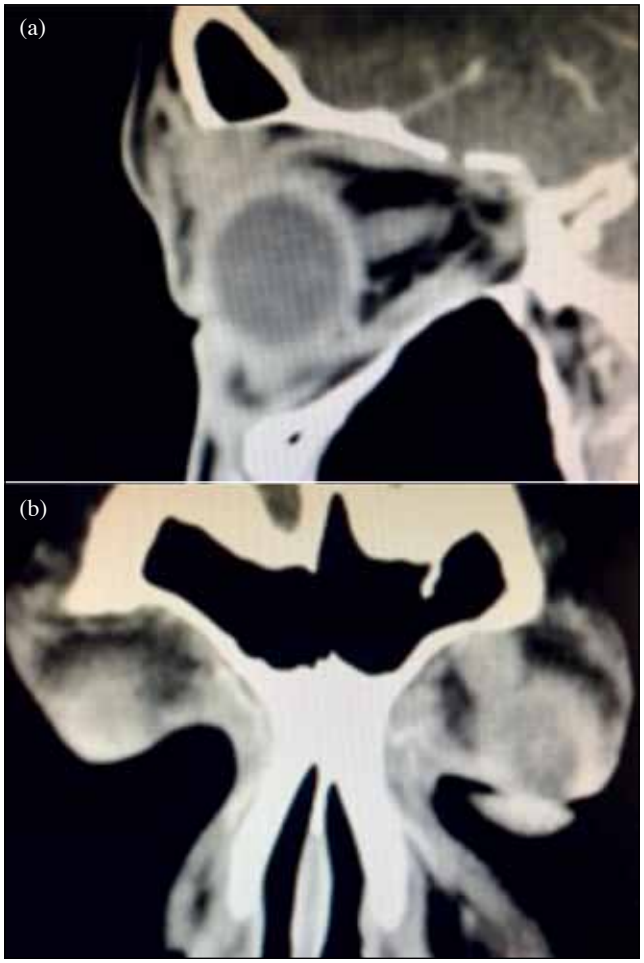

Figure 1. (a) Sagittal and (b) coronal views of contrast-enhanced computed tomography of the left orbit showing a moderately enhancing ovoid solid mass at the superomedial aspect of the extraconal left orbit. There are no aggressive features (bony destruction or invasion to surrounding structures), fluid, macroscopic fat component, or evidence of calcification. The left globe, lacrimal gland, and extraocular muscles are normal.

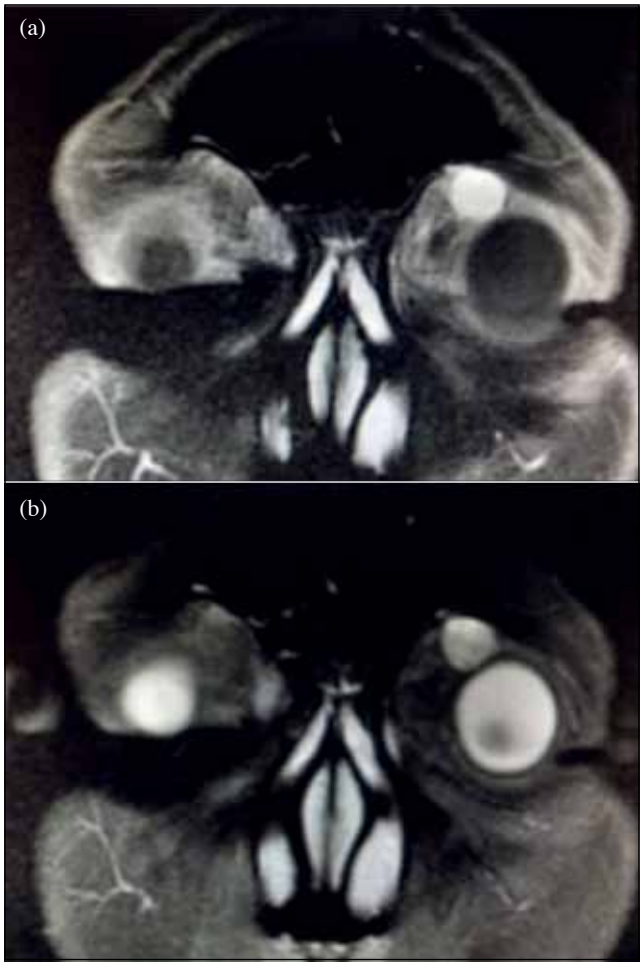

Figure 2. (a) T1-weighted and (b) T2-weighted contrast-enhanced magnetic resonance imaging of the orbits showing a T1-hypointense and T2-hyperintense, avidly enhancing lesion, with no calcification or soft tissue or osseous invasion. There are no internal T1-hyperintense signals or fluid levels.

of the pituitary and orbital masses in the same setting. For the orbital mass, anterior orbitotomy without bone flap through an upper eyelid crease incision was performed. Intra-operatively, the mass was noted to be arising from the supraorbital nerve. The resected oval mass was smooth and measured 1.2 cm × 1.0 cm × 1.1 cm, with a pale-yellow cut surface. Microscopic examination showed a circumscribed proliferation of spindle cells arranged in fascicles with nuclear palisading around fibrillary processes, consistent with Antoni A areas with Verocay bodies. The spindle cells contained elongated, wavy nuclei with tapered ends. There was no cytological atypia (**Figure 3a**). Immunohistochemical staining with S100 demonstrated diffuse positivity of the spindle cells for S100, establishing the diagnosis of schwannoma of the left supraorbital nerve (**Figure 3b**). Postoperatively, the patient reported mild sensory deficits over the distribution of the ophthalmic division of the left trigeminal nerve, which resolved after 6 months. Recovery was uneventful at 1-year follow-up.

Discussion

Supraorbital nerve schwannomas are rare and only 10 cases have been reported. Orbital schwannomas primarily affect individuals aged 20 to 40 years.[3] Approximately 10% to 15% of orbital schwannomas are associated with neurofibromatosis and this type has an earlier onset, compared with the isolated type. The age of onset of our patient was 23 years, which is relatively early, given no personal or family history of neurofibromatosis.

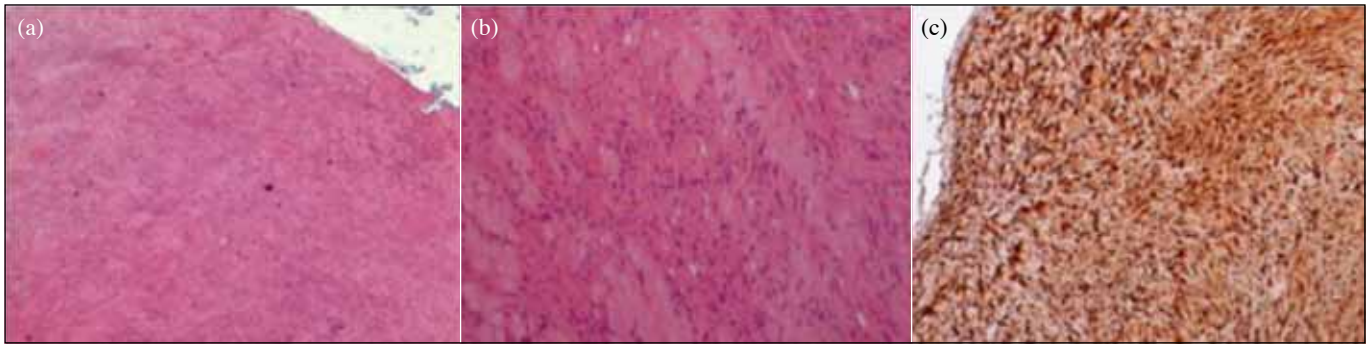

Figure 3. (a and b) Proliferation of spindle cells arranged in fascicles with nuclear palisading around fibrillary processes, consistent with Antoni A areas with Verocay bodies. The spindle cells contain elongated, wavy nuclei with tapered ends. There is no cytological atypia (hematoxylin and eosin, 40× and 100×, respectively). (c) Diffuse positivity of the spindle cells for S100 confirms the diagnosis of schwannoma (immunohistochemical staining with S100, 40×).

Table. 66 cases of orbital schwannomas reported in the literature[7-58]

Study	Sex/ age, y	History of neuro-fibromatosis	Tissue of origin / special feature	Location	Surgical approach	Treatment outcome
Skeoch,[7] 1956	M/41	-	-	-	-	Uneventful recovery
Horie et al.[8] 1982	F/41	-	Supraorbital nerve	-	Subfrontal orbitotomy	Uneventful recovery
Shields et al.[9] 1986	M/33	No	-	-	Lateral orbitotomy	Uneventful recovery
Grover et al.[10] 1993	F/45	-	-	Intraconal	Lateral orbitotomy	Uneventful recovery
Lam et al.[11] 1997	F/54	-	Ophthalmic nerve	Extraconal	Sub-brow incision	Uneventful recovery
Maesawa et al.[12] 1998	F/40	-	Ophthalmic nerve	-	Fronto-orbitozygomatic craniotomy	Residual sensory symptoms
Khwarg et al.[13] 1999	F/52	No	-	Intraconal	Lateral orbitotomy via an eyelid crease incision	Uneventful recovery
Tsuzuki et al.[14] 2000	F/62	No	Oculomotor nerve	Intraconal	Microsurgical lateral approach	Uneventful recovery
Goel et al.[15] 2003	M/18	No	Cavernous sinus	Extraconal	Lateral orbitotomy	Uneventful recovery
Schick et al.[16] 2003	M/36	Personal: type 2	-	Intraconal	Extradural pterional approach	Uneventful recovery
	F/24	Personal: type 1	-	Extraconal	Supraorbital approach	Resolution of proptosis but visual acuity remained poor
	F/43	-	-	Intraconal	Inferior-medial transconjunctival approach	Uneventful recovery
	M/50	No	Supraorbital nerve	Extraconal	Supraorbital approach	Uneventful recovery
	F/60	-	-	Intraconal and extraconal	Extradural pterional approach	Development of amaurosis with ptosis
Chang et al.[17] 2003	F/38	No	-	Intraconal	Lateral orbitotomy	Uneventful recovery
Barbagallo et al.[18] 2004	M/65	No	Supraorbital nerve	Extraconal	Fronto-orbitozygomatic craniotomy	Uneventful recovery
El-Bahy[19] 2004	M/40	No	Spheno-orbital	Extraconal	-	-
Subramanian et al.[20] 2005	F/18	-	- / With cystic degeneration	Intraconal	Combined medial and lateral orbitotomy	Resolution of proptosis but deterioration in vision
	M/40	-	- / With cystic degeneration	Intraconal	Lateral orbitotomy	Uneventful recovery
	F/78	-	- / With cystic degeneration	Intraconal	Enucleation	-
	M/48	-	- / With cystic degeneration	Intraconal	Lateral orbitotomy	Uneventful recovery
Tezer et al.[21] 2006	F/16	-	Infraorbital nerve	-	Subciliary incision	Residual sensory symptoms
Furuno et al.[22] 2006	F/74	-	Oculomotor nerve	Intraconal	Transcranial approach	Uneventful recovery
Boustred[23] 2007	F/5	Personal	Supraorbital nerve	-	Endoscopic approach	Uneventful recovery
Sales-Sanz et al.[24] 2007	F/49	No	- / Bilateral synchronous schwannomas	Extraconal	Subciliary inferior orbitotomy	Uneventful recovery
Colapinto et al.[25] 2007	M/68	No	Inferior oblique	Intraconal	Anterior orbitotomy	Uneventful recovery
Sugo et al.[26] 2007	F/34	No	-	Intraconal	Orbital unroofing by a frontotemporal approach	Uneventful recovery
Tanriover et al.[27] 2007	F/34	No	Oculomotor nerve	Extraconal	Pterional approach	Uneventful recovery

Table. (cont'd)

Shamim et al.[28] 2008	F/11	No	Oculomotor nerve	Intraconal	-	Uneventful recovery
Irace et al.[29] 2008	M/55	No	Abducens nerve	Intraconal	Modified microsurgical lateral orbitotomy	Uneventful recovery
Garg et al.[30] 2008	F/35	-	Infraorbital nerve	Extraconal	Inferior orbitotomy via an eyelid crease incision	Uneventful recovery
Youens et al.[31] 2008	F/51	No	- / Hybrid type	Extraconal	Anterior orbitotomy via an eyelid crease incision	Uneventful recovery
Kiratli et al.[32] 2008	F/12	Personal and family	Lateral rectus	Intraconal	Fractionated stereotactic radiotherapy	Uneventful recovery
Miliaras et al.[33] 2008	M/62	No	- / Malignant type	Intraconal	Anterior orbitotomy with radiotherapy	Intracranial recurrence, patient died 13 months after diagnosis
Karkas et al.[34] 2008	M/14	No	Infraorbital nerve	Extraconal	osteoplastic maxillotomy approach	Uneventful recovery
de Silva et al.[35] 2009	F/66	No	Lacrimal gland	Extraconal	Lateral orbitotomy	Uneventful recovery
	F/30					
Hironaka et al.[36] 2010	M/58	No	Ophthalmic nerve	Intraconal	Fronto-orbitozygomatic craniotomy	Residual sensory symptoms
de Jong et al.[37] 2010	M/44	No	Supraorbital nerve / ancient type	-	Superolateral orbitotomy	-
Birkholz et al.[38] 2010	F/23	No	-	Intraconal	Stereotactic radiosurgery	-
Hayashi et al.[39] 2010	F/46, F/46, F/46, M/46	No	Cavernous sinus	Extraconal	Gamma knife surgery	Uneventful recovery for tumor that was intracavernous; cases with dumbbell lesions exhibited visual deterioration
Brucoli et al.[40] 2011	F/75	No	-	Extraconal	Lateral orbitotomy	Uneventful recovery
Gunduz et al.[41] 2011	M/40	No	-	Intraconal	Orbitotomy via a superonasal skin approach	Uneventful recovery
Pushker et al.[42] 2011	F/62	No	-	Extraconal	Anterior orbitotomy	-
Denadai et al.[43] 2012	F/35	No	Supraorbital nerve	-	Supraorbital orbitotomy	Uneventful recovery
Izumo et al.[44] 2012	M/67	-	Supraorbital nerve	Extraconal	Anterior orbitotomy	Residual numbness
Nagashima et al.[45] 2012	M/5	No	Oculomotor nerve	Intraconal	Frontotemporal craniotomy	
Rato et al.[46] 2012	M/42	No	Abducens nerve	Intraconal	Lateral orbitotomy	Uneventful recovery
Kron et al.[47] 2012	M/59	No	- / Recurrence, possible schwannomatosis	-	Anterior orbitotomy	Diplopia and ptosis requiring surgical treatment
	F/5	No	- / Recurrence	-	Anterior orbitotomy	
Feichtinger et al.[48] 2013	F/53	-	Abducens nerve	Intraconal	Lateral orbitotomy	Uneventful recovery but with some permanent deficits
Bassily et al.[49] 2013	M/23	-	Ethmoidal air cell	Extraconal	Anterior orbitotomy via an eyelid crease incision	Uneventful recovery
Claros et al.[50] 2014	F/29	No	-	Intraconal	Lateral orbitotomy	Uneventful recovery
Mortuza et al.[51] 2014	M/56	No	Sclera / ancient type	Intraconal	Enucleation	-
Chacko et al.[52] 2014	F/66	-	Supraorbital nerve	-	-	Uneventful recovery
Comez and Muratli[53] 2014	F/65	No	-	Extraconal	Subciliary incision	Uneventful recovery
Koktekir et al.[54] 2014	F/41	No	Opthalmic, maxillary and supratrochlear nerves	Intraconal	Lateral orbitotomy	Recurrence a year later, completely resected. Unremarkable since
	F/29	No	Ophthalmic nerve	Intraconal	Anterior orbitotomy via an eyelid crease incision	Uneventful recovery
	M/57	No	-	Intraconal and extraconal	Anterior orbitotomy via an eyelid crease incision	Uneventful recovery
Taubenslag et al.[55] 2015	M/31	No	Supraorbital nerve / hybrid type	Extraconal	Anterior orbitotomy via an eyelid crease incision	-
Li et al.[56] 2015	M/27	No	Superior oblique muscle	Intraconal	Anterior orbitotomy	Uneventful recovery
Jacquesson et al.[57] 2015	M/49	-	Maxillary nerve	Extraconal	Expanded endoscopic endonasal approach	Uneventful recovery
Gupta et al.[58] 2017	F/39	No	- / Concomitant orbital cavernous hemangioma and schwannoma	Intraconal	Inferior transconjunctival orbitotomy	Uneventful recovery

Orbital schwannomas commonly present with a painless proptosis. Rarely, when the supraorbital nerve is affected, schwannomas may cause numbness and/or pain in the distribution of the trigeminal nerve, mimicking symptoms of sinusitis.[4] On MRI, the tumor is classically hypointense on T1-weighted and hyperintense on T2-weighted images, with avid post-gadolinium enhancement.[5] Histological examination demonstrates Antoni A or Antoni B areas, Verocay bodies, and positivity for S-100 immunohistochemical stain.

The surgical approach varies with the location and extent of the tumor as well as the nerve involved. The fronto-orbitozygomatic craniotomy allows wider access and exposure of orbital surfaces and content, and has been used for the removal of large intraorbital tumors. In our patient, anterior orbitotomy through an upper eyelid crease incision was used without a bone flap. This allows dissection of comparatively avascular tissue planes and minimizes transection of the orbicularis muscle and lymphatic channels, resulting in negligible scarring postoperatively.[6]

The literature was reviewed by searching the PubMed using keywords: 'orbital' and 'schwannoma'. In 32 cases, the diagnosis was not orbital schwannoma or information was inadequate. 66 cases in 27 men and 39 women were orbital schwannoma (**Table**).[7-58] The overall median age of onset was 41 years (41 years in women, 43 years in men). Only four cases had personal or family history of neurofibromatosis; 19 cases had unknown medical history. The median age of onset was earlier in those with personal or family history of neurofibromatosis than in those with isolated orbital schwannomas (18 vs 43 years). The orbital schwannomas were intraconal in 29 cases, extraconal in 21 cases, and unknown in the rest. In only 10 cases (including our patient) did the schwannoma arise from the supraorbital nerve. The eyelid crease incision approach has only been used six times, and only once for the resection of a supraorbital nerve schwannoma.[55]

Conclusion

Early diagnosis and accurate dimension determination of orbital schwannoma is essential for complete removal, preservation of normal anatomy, and reinstitution of pre-morbid visual acuity and ocular movements.

Declaration

The authors have no conflicts of interest to disclose.

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CASE REPORT

Nasolacrimal sac metastasis from colorectal carcinoma: a case report

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Abstract

We report a rare case of metastasis to the nasolacrimal sac from colorectal carcinoma in a 69-year-old man. Despite tumor removal and endoscopic dacryocystorhinostomy with stenting, the tumor recurred 3 months later, which was treated with chemotherapy and radiotherapy. Five months later, the patient eventually died from respiratory failure secondary to malignant pleural effusion.

Case presentation

In August 2016, a 69-year-old Chinese man presented with a 2-month history of bloody discharge associated with medial canthal swelling of the right eye. There was no proptosis, abnormalities of ocular motility, or palpable lymph nodes. Nasoendoscopy did not reveal any mass. Three years previously, he had metastatic colorectal cancer with regional lymph node and liver metastasis (stage T3N2bM1a, American Joint Committee on Cancer 7th edition). This was managed with laparoscopic anterior resection and open wedge resection of the involved liver segments, adjuvant chemotherapy, and targeted therapy. Despite aggressive treatment, there was recurrent liver metastasis and new pulmonary metastatic lesions 1 year after surgery.

Computed tomography with contrast of the orbit showed a cystic lesion at the right lacrimal sac measuring 8.7 × 14.7 mm, without evidence of bony erosion (**Figure 1**). The radiological appearance was consistent with nasolacrimal duct obstruction, likely secondary to metastatic colorectal cancer.

Figure 1. Computed tomography of the orbit showing right medial canthal swelling, a distended lacrimal sac, without evidence of bony erosion.

Endoscopic dacryocystorhinostomy was performed. A lacrimal mass was identified after opening the lacrimal sac (**Figure 2**). The mass was resected followed by standard

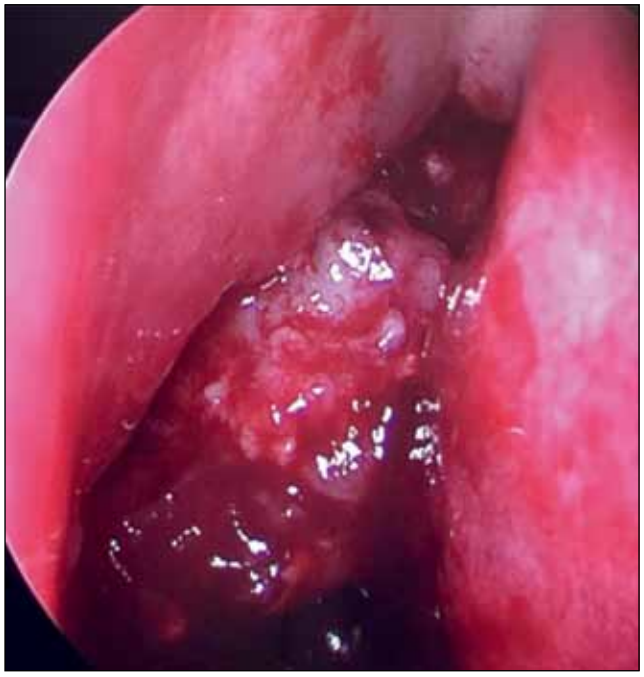

Figure 2. Intraoperative photograph of the lacrimal sac tumor.

silicon stent intubation. After surgery, the fistula remained patent and the silicone stent was removed 1 month later. At 1 month after surgery, no recurrence was seen on nasal endoscopy. Histopathology of the lacrimal sac tumor confirmed an adenocarcinoma with strongly positive immunohistochemical staining for CDX2, which was consistent with metastatic adenocarcinoma of intestinal origin (**Figure 3**). The tumor did not involve the resected margins. No palliative radiotherapy was performed, as recommended by the oncologist.

At 3 months after surgery, the patient had recurrent blood-stained tears. Nasal endoscopy revealed a recurrent right lacrimal sac lesion with contact bleeding. Computed tomography showed a recurrent lacrimal sac mass extending into the maxillary sinus and orbit. Targeted chemotherapy Regorafenib was given in view of multiple systemic metastases. However, the patient did not tolerate it owing to marrow toxicity. He subsequently underwent palliative radiotherapy (30 Gy) to the nasal and orbital mass. At 5 months after chemotherapy, the patient eventually died from respiratory failure secondary to malignant pleural effusion.

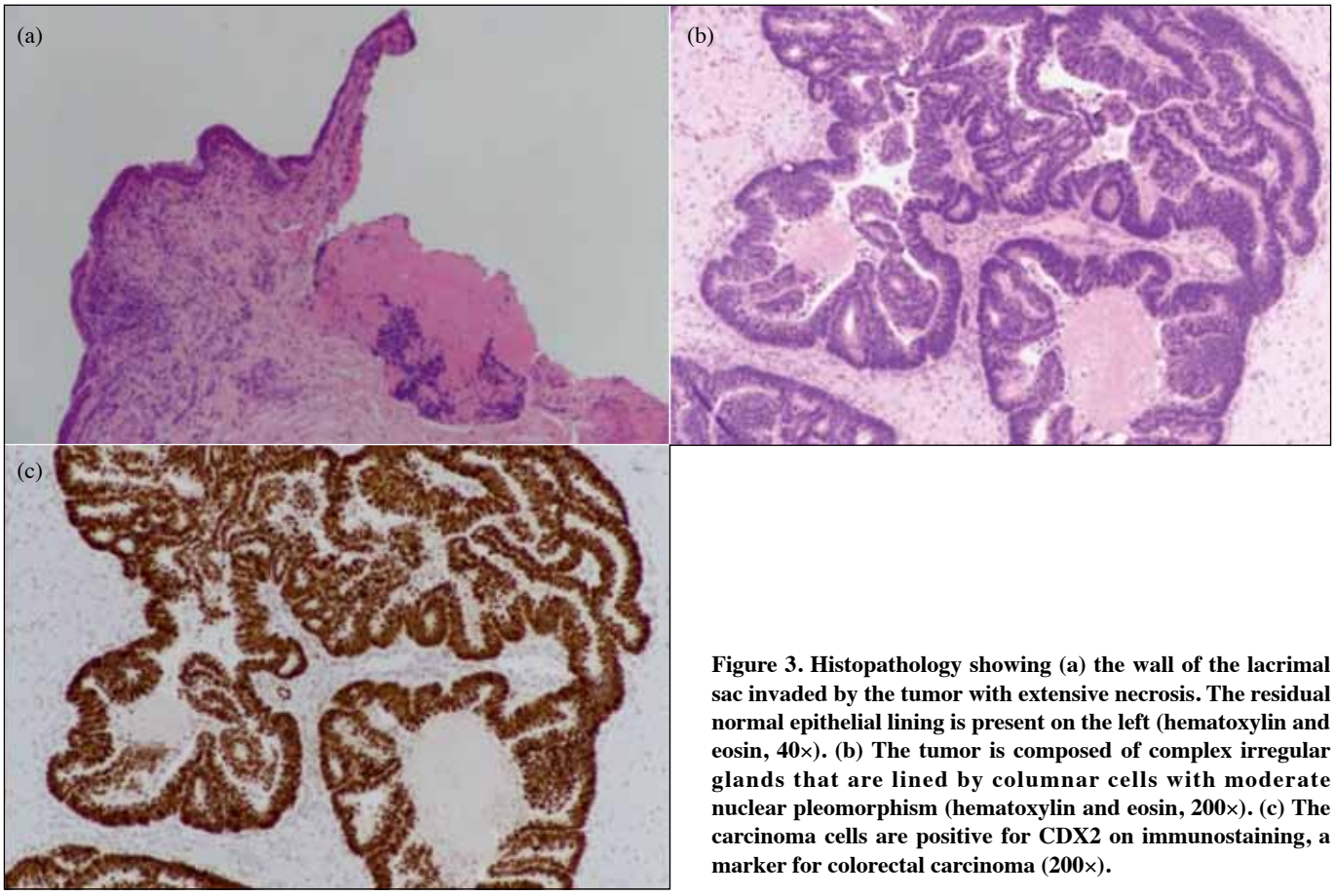

Figure 3. Histopathology showing (a) the wall of the lacrimal sac invaded by the tumor with extensive necrosis. The residual normal epithelial lining is present on the left (hematoxylin and eosin, 40×). (b) The tumor is composed of complex irregular glands that are lined by columnar cells with moderate nuclear pleomorphism (hematoxylin and eosin, 200×). (c) The carcinoma cells are positive for CDX2 on immunostaining, a marker for colorectal carcinoma (200×).

Discussion

Colorectal cancer is the third most common cancer in the world and in Asia.[1] Metastasis occurs most commonly in the liver and lung.[2-4] Colorectal cancer metastases to the orbit are uncommon.[5,6] Metastasis to the lacrimal sac has been reported to be secondary to carcinoma of the breast, lung, prostate, cutaneous melanoma, eye, liver, kidney, and nasopharynx.[5,7-10] To the best of our knowledge, colorectal cancer metastasis to the nasolacrimal sac has not been reported. Metastasis to the nasolacrimal sac is defined as metastasis to the space between the globe and bony orbital walls.[5]

Our patient presented with a bloody discharge and medial canthal mass. Other features of lacrimal sac metastasis include overlying skin changes or mass on nasal endoscopy. This is in contrast with orbital metastasis, in which patient presents with diplopia, proptosis, and decreased vision.[5] Because of the atypical presentation, computed tomography was performed and revealed a cystic lesion with no bony erosion. Imaging features of a malignancy in the nasolacrimal sac include a contrast-enhancing mass with expansion or erosion of nasolacrimal bone, and possible extension to the orbit, nasal cavity, and sinuses.[11-13] In a series of malignant lacrimal sac and nasolacrimal duct tumors, Kumar et al[13] reported that smooth expansion of the bony canal was more common than bony erosion, and that contrast enhancement was demonstrated in most cases on both computed tomography and magnetic resonance imaging. However, for locally advanced malignant lacrimal sac and duct tumors, it is difficult to distinguish primary tumors from secondary tumors by imaging alone.[13] The diagnosis of nasolacrimal duct metastasis must be confirmed by histology.

Staged management for lacrimal sac malignancy with secondary nasolacrimal duct obstruction is suggested. Lacrimal sac exploration and biopsy should be performed before proceeding to dacryocystorhinostomy. The histopathologic diagnosis and extent of the tumor helps plan definitive, individualized treatment. If the lacrimal sac mass is metastatic in nature, surgical resection would only be palliative.[11] For dacryocystorhinostomy, external approach is preferred as this does not breach the bones, which are natural barriers to tumor extension. In our patient, a one-stage endoscopic approach was performed for tumor removal and endoscopic dacryocystorhinostomy with stenting.

There is no consensus on the management of lacrimal sac metastases, because of their rarity. Current treatment options for metastases to the nasolacrimal duct include radiotherapy, chemotherapy, targeted therapy, and surgery.[5] Radiotherapy is effective in alleviating symptoms, but potential adverse effects include cataract, radiation retinopathy, and radiation-induced optic neuropathy. Surgical excision need not be complete or radical; the aim is to reduce symptoms, improve the quality of life, and maximize vision if possible. Our patient was treated with both chemotherapy and radiotherapy.

The median survival for colorectal metastasis to the orbit is reported to be 10 to 20 months.[9] Our patient with metastasis to the nasolacrimal duct also had a poor prognosis. Given the paucity of reported cases, further studies are needed to determine the prognosis of nasolacrimal sac metastasis.

Conclusion

Metastases to the lacrimal duct are rare. In atypical history and physical examination, clinicians should be aware of neoplastic causes and conduct early evaluation.

Declaration

The authors have no conflicts of interest to disclose.

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