JOURNAL OF THE COLLEGE OF OPHTHALMOLOGISTS OF SRI LANKA

VOLUME 21 No. 2 2015

- TOPOGRAPHY GUIDED LASER ASSISTED SUB-EPITHELIAL KERATECTOMY (LASEK) WITH CORNEAL COLLAGEN CROSSLINKING (CXL) IN PATIENTS WITH THIN CORNEA

- 'AN UNDER DIAGNOSED CONDITION'

College of Ophthalmologists of Sri Lanka Annual ISSN 2345-9115

Journal of The College of Ophthalmologists of Sri Lanka

Editors

Dr. Mangala Gamage, DO, MS, FRCS
Consultant Eye Surgeon

Dr. Binara Amarasinghe, DO, MS, FRCS
Consultant Eye Surgeon

Published by

College of Ophthalmologists of Sri Lanka
National Eye Hospital, Colombo 10,
Sri Lanka.

Email: ophsleye@gmail.com
Telephone: 94+11-2693924
Fax: 94+11-2693924
Website: www.cosl.lk

Printed by

Ananda Press
82/5, Sir Ratnajothi Saravanamuttu Mawatha,
Colombo 13, Sri Lanka.
Tel: +94 11 2435975
E-mail: anpress@sltnet.lk

Journal of the College of Ophthalmologists of Sri Lanka is published annually in two volumes. It is clinically oriented, designed to keep ophthalmologists up to date. It contains peer reviewed articles, current research, case presentations and clinical challenges.

9 772345 911006

JOURNAL OF THE COLLEGE OF OPHTHALMOLOGISTS OF SRI LANKA

Instructions to Contributors

The College of Ophthalmologists of Sri Lanka publishes original articles in Ophthalmology, original work on Ophthalmology and related Sciences presented at meeting, congresses of the College as well as lectures, seminars and symposia associated with the College. Articles subject to editorial revision, may not be reproduced without permission after publication. Statements in the articles are the sole responsibility of the authors and not reflect the opinion or attitude of the College or the editors.

Manuscripts typed in double spacing with 1" margin on both sides in 12 point Times Roman font in Microsoft Word software should be e-mailed to the editors immediately after the Annual Congress in order that they could be included in the Journal of the same year. Any scientific paper or research paper related to ophthalmology, will be accepted for publication.

Title page should be typed on a separate page and should bear the names of authors, their present posts and the place where the work was carried out. The title should be brief and meaningful to facilitate indexing. If authorship is limited to direct participants, all other contributors to patient care must be acknowledged. The usual plan, a short summary, introduction, materials and methods, results, discussion and bibliography should be followed, whenever possible.

Wherever ethical clearance is needed, the obtaining of clearance must be acknowledged in the text.

Only standard abbreviations and SI units should be used in the text. Drugs should be designated by their generic names.

Illustrations such as graphs, charts and drawings should be prepared on the computer and cited in the text. Legends should be typed on a separate page.

Photographs, x-rays, photomicrographs must be of good quality suitable for publication and magnifications indicated. Legends and captions should be typed on a separate page. Authors may be called upon to bear the cost of colour illustrations.

Tables should have a title, numbered consecutively, typed in double spacing and submitted in separate page and cited in the text.

References should be double-spaced, arranged alphabetically, by author, and cited by superior numbers in the text. Reference must be to primary publications, not to citations of the articles in other publications.

Please provide complete publication data. Including first and last page numbers. "in press" articles may be included; the journal must be specified. *Presentations and manuscripts "submitted for publication" are considered unpublished communication* and, should be acknowledged in the text or footnotes, but should not be listed with published references. Published abstracts may be included but should be labeled "abstract". Use Index Medicus style of abbreviation, and punctuation. Some typical examples follow: note the **absence of periods after initials and abbreviations.** When there are 5 or more authors, name the first three, "et al" .

Journal Articles

1. Smith JD. Ophthalmology and the medical community. *Surv Ophthalmol* 1996; **41**: 1-30.
2. Smith JD, Jones TS. Ophthalmology and society. *Surv Ophthalmol* 1997; **42**: 65-78.

Books

3. Smith JD, Jones TS. Public JQ, et al. Ophthalmology and the World. Boston. Bayside Press, 1997, pp 1-9.

Chapters

4. Stevens JT. A transcendentalist's view of optics, in Smith JD (ed): Ophthalmology and the Universe, Vol. 6. Part 3. Boston, Bayside Press, 1997. ed 2, pp 230-245.

Proofs will be submitted to the first named author to be returned within 4 days. No major alterations could be accepted at this stage. Requests for reprints must be made direct to the printer and paid for by the author. No free reprints will be supplied.

Articles to be e-mailed to

The Editors,
Journal of the College of Ophthalmologists of Sri Lanka
E-mail: **ophsleye@gmail.com**

JOURNAL OF THE COLLEGE OF OPHTHALMOLOGISTS OF SRI LANKA

VOL. 21 2015 NO. 2

CONTENTS

Topography guided laser assisted sub-epithelial keratectomy (LASEK) with corneal collagen crosslinking (CXL) in patients with thin cornea

K. H. Wickramasinghe[1], S. K. G. S. Kurera[2], C. J. Kumarage[3], W. M. C. M. Andradi[4], D. H. H. Wariyapola[5]

The Journal of the College of Ophthalmologists of Sri Lanka 2015; 21: 47-48

Introduction

Refractive surgery allows short sighted people to see without glasses changing their total outlook. Unfortunately refractive surgery wyeakens the cornea and in a patient who already has a cornea susceptible to ectasia the risk is significantly high. Topography Guided Laser Assisted Sub-Epithelial Keratectomy (LASEK) can induce ectasia in patients with a susceptible cornea. Corneal Collagen Crosslinking (CXL) performed simultaneously with LASEK reduces this risk and allows patients to undergo LASEK without an added risk. Patients who have to have CXL because of conditions like keratoconus can get the refractive errors corrected at the same time if both CXL and LASEK are done at the same visit.

Method

A series of patients who underwent topography guided LASEK surface ablation with simultaneous CXL is presented. Dr DHH Wariyapola, Consultant Eye Surgeon selected the eligible patients and performed the procedures at Nawaloka Hospitals Pvt Ltd.

The procedure used in LASEK + CXL

Initially alcohol 20% is kept on the cornea for 40 seconds using a well. Then alcohol is washed off. Subsequently epithelium is peeled off. There is no need to preserve the epithelium. In conventional LASEK, epithelium is replaced on the stromal bed. Topolyser (Vario TM) guided ablation (Topography guided) is performed next. In this procedure we need to preserve a minimum corneal thickness of 400 micro meters for CXL. Therefore, patient corneal thickness and required correction influences the amount of ablation possible. After the ablation is completed CXL follows. Riboflavin drops are instilled for 30 mins. Then a 10 min UV exposure with 9 $mWcm^{-2}$ is done. Epithelium off ablation takes off the Bowmans layer of the cornea, which allows for better absorption of riboflavin. After the CXL, mitomycin C (MMC) 0.04% is kept for 12 s and washed off. Finally bandage contact lens is inserted and kept for 1 week.

Case details

Patient 1 – A male of 24 yrs who had his right eye (RE) LASEK done in 2010, was chosen. His current uncorrected visual acuity (UCVA) was RE 6/6 and left eye (LE) 6/60. His refraction showed RE Plano 6/6 and LE -4.50 -0.50 @ 160 6/9. His LE had keratoconus (Figure 1) and patient was chosen for LE LASEK + CXL. The patient was allocated the following treatment plan by the Wavelight EX 500 machine (Figure 2).

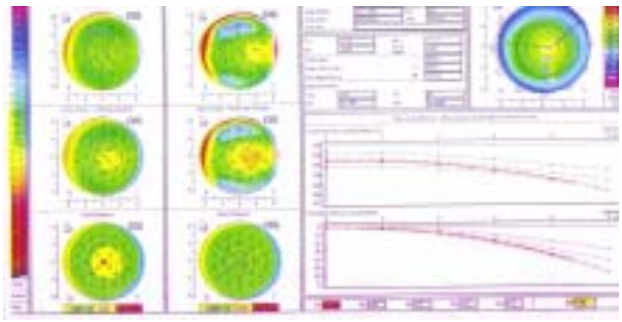


Figure 1. *Oculyzer image showing red flag for keratoconus for patient 1.*

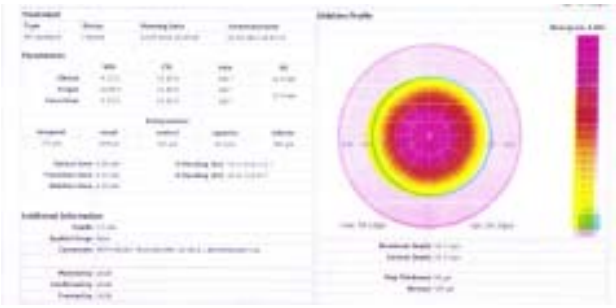


Figure 2. *Treatment plan given by the excimer machine for patient 1.*

Outcome – Pre op refraction in LE was -4.50 -0.50 @ 160 6/9 and post op refraction (2 weeks post op) showed LE Plano -0.75 @ 170 6/9.

[1]*Registrar in Ophthalmology,* [2]*Post Graduate Trainee in Ophthalmology,* [3]*Senior Registrar in Ophthalmology,* [4]*Reaserch Assistant,* [5]*Consultant Ophthalmologist, Sri Jayawardenapura General Hospital, Kotte, Sri Lanka.*

Patient 2 – A Male of 25 yrs with UCVA RE 6/60 and LE 6/36 was chosen and his refraction was RE -6.00 – 2.25 @ 15 6/12 and LE -1.00 -0.50 @ 165 6/6. He had keratoconus (Figure 3). He could not tolerate the refraction and wanted to be without glasses. Planned to do RE LASEK + CXL (Figure 4).

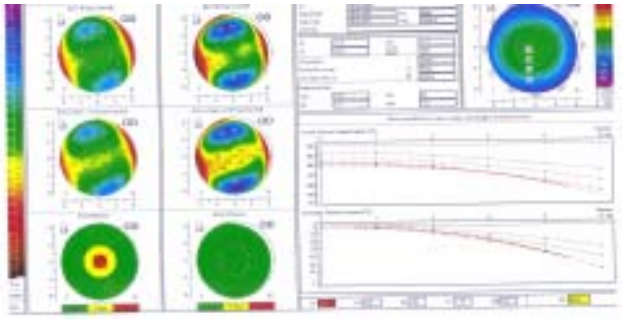


Figure 3. *Oculyzer image showing red flag for keratoconus for patient 2.*

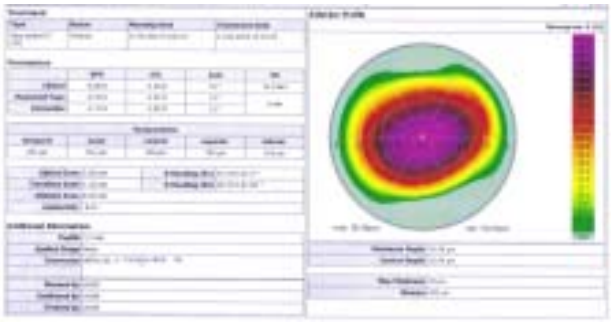


Figure 4. *Treatment plan given by the excimer machine for patient 2.*

Outcome – Pre op refraction was RE -6.00 - 2.25 @ 15 6/12 and post op refraction (2 weeks post op) was RE -3.50 -1.50 @ 10 6/9. Patient can tolerate the post op refraction.

Patient 3 – A Female of 28 yrs with UCVA in RE 6/60 and LE 6/9. Her refraction was RE -1.00 - 1.75 @ 80 6/24 and LE – 0.50 6/6. The patient had progressive keratoconus which needed CXL and was also offered LASEK for refractive correction (Figure 5 and Figure 6).

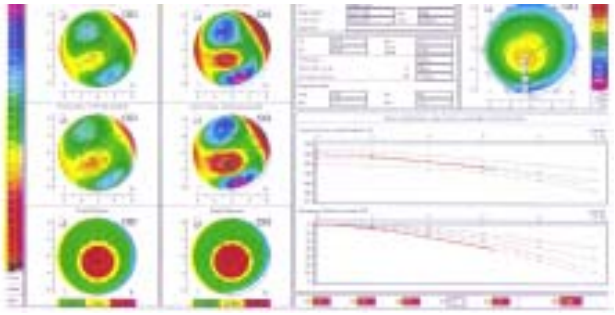


Figure 5. *Oculyzer image showing red flag for keratoconus for patient 3.*

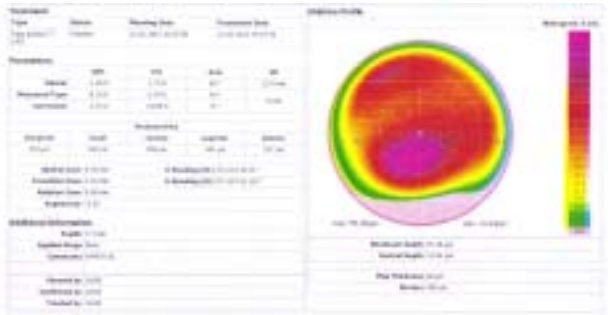


Figure 6. *Treatment plan given by the excimer machine for patient 3.*

Outcome – Pre op refraction of RE was -1.00 - 1.75 @ 80 6/24 and post op refraction (2 weeks post op) was RE Plano -2.00 @ 30 6/12. Patient has better best corrected visual acuity post OP.

Conclusions

CXL performed simultaneously with LASEK surface ablation allows patients who are keen to see without glasses; but who are susceptible to ectasia, to undergo refractive surgery safely. Patients who have to have CXL because of conditions like keratoconus can get the refractive errors corrected at the same time. Even if refractive error is partially corrected the regularization of the corneal surface enables the patient to have a better visual outcome.

The mechanisms of retinal ganglion cell injury in glaucoma

Nuwan Niyadurupola[1]

The Journal of the College of Ophthalmologists of Sri Lanka 2015; 21: 49-53

Abstract

Retinal ganglion cell death in glaucoma is multifactorial. In addition to intraocular pressure, ocular perfusion pressure and cerebrospinal fluid pressure have been found to be important factors associated with glaucoma. Excitotoxicity and inflammation may also have a role in retinal ganglion cell death in glaucoma.

Introduction

The principle pathology of glaucoma is the progressive death of retinal ganglion cells. The loss of retinal ganglion cells occurs at a faster rate than that which occurs with ageing. Irreversible visual loss may potentially result from the death of retinal ganglion cells. There are many theories for the mechanisms of retinal ganglion cell death in glaucoma. The main theories of mechanical, ischaemic, excitotoxic and inflammatory retinal ganglion cell death in glaucoma will be discussed further.

Mechanical theory

Elevated intraocular pressure (IOP) is a major risk factor for the development and progression of glaucoma.[1-7] Elevation of IOP has been shown to cause deformation of the lamina cribrosa of human eyes.[8] The deformation of the lamina cribrosa causes compression of the retinal ganglion cell axons that traverse through the pores of the lamina cribrosa. Compression of the retinal ganglion cell axons leads to disturbance of both anterograde and retrograde axonal transport at the optic nerve head.[9-12] Minckler and associates, showed that elevation of IOP in monkey eyes caused blockage of anterograde and retrograde axonal transport at the laminar cribrosa region of the optic nerve.[10] The disruption of axonal transport was associated with death of retinal ganglion cells.[10,11] However, IOP is not the only factor causing retinal ganglion cell death in glaucoma. Some patients have glaucoma despite normal IOPs (normal tension glaucoma) and some glaucoma patients continue to progress despite having their IOP reduced.[2-7] The cerebrospinal fluid pressure posterior to the lamina cribrosa may have an influence on deformation of the lamina cribrosa and death of retinal ganglion cells. Patients with normal-tension glaucoma have been found to have a significantly lower cerebrospinal fluid pressure than control subjects.[13] Furthermore, patients with both high- and normal-tension glaucoma have been found to have a high trans-laminar cribrosa pressure gradient compared to control subjects.[13] The extent of glaucomatous visual field loss was discovered to be negatively correlated with the cerebrospinal fluid pressure and positively correlated with the trans-laminar cribrosa pressure difference.[13] A lower cerebrospinal fluid pressure in relation to the IOP may contribute to the deformation of the lamina cribrosa in glaucoma. Potentially, therefore, the trans-laminar cribrosa pressure gradient may be more important than IOP alone in the mechanical changes at the optic nerve head that lead to glaucomatous retinal ganglion cell death.

Ischaemic theory

Perfusion of the optic nerve head is dependent on the blood pressure (together with the health of blood vessels supplying the optic nerve head) and the IOP. Mean ocular perfusion pressure (in mmHg) is defined as two-thirds mean arterial pressure minus IOP. Hence, a low blood pressure and/or high IOP may cause a reduction in ocular perfusion pressure. Poor perfusion of the optic nerve head may lead to retinal ganglion cell death from ischaemia. Chronic elevation of IOP has been shown to reduce optic nerve head blood flow and cause retinal ganglion cell death in monkey eyes.[14] Conditions associated with reduced ocular perfusion, such as hypotension,[15,16] cardiovascular disease,[16,17] Raynaud's disease[18] and migraine[19] have been shown to be associated with glaucomatous optic neuropathy. A low diastolic perfusion pressure (<50-55 mmHg) was found to be associated with glaucoma.[20] Additionally, a low systolic perfusion pressure has been shown to be associated with glaucoma progression.[16] Lowering blood pressure may cause worsening of glaucoma since patients treated with antihypertensive therapy that lowered diastolic blood pressure to <90mmHg were found to have worse optic disc parameters than those with diastolic blood pressures above 90 mmHg despite

[1]*Consultant Ophthalmic Surgeon and Honorary Senior Lecturer, Department of Ophthalmology, Norfolk and Norwich University Hospital, United Kingdom.*

treatment or those with normal diastolic blood pressures.[21] The relationship between blood pressure and glaucoma may be more important at night. Blood pressure has been shown to be lower at night than during the day.[22] Glaucoma patients who were found to have the greater fluctuations in mean arterial pressure and mean ocular perfusion pressure had the greater rates of visual field progression.[23] Furthermore, IOP has been found to be higher at night in glaucomatous, ocular hypertensive and normal eyes.[24] At night, a low mean arterial pressure and a high IOP contributes to a low mean ocular perfusion pressure. Hence, the risk of ischaemic neurodegeneration of retinal ganglion cells may be greater at night. It is therefore, important that in addition to IOP control in glaucoma patients, the mean arterial blood pressure does not drop too low at night. Twenty-four hour blood pressure monitoring may be useful in determining whether antihypertensive therapy should be changed, reduced or withdrawn to prevent night time dips in blood pressure in glaucoma patients who continue to progress despite good IOP control.

Excitotoxic theory

The involvement of glutamate excitotoxicity in the pathogenesis of glaucoma has been suspected since 1957 when it was discovered that subcutaneous injections of glutamate in mice caused selective and severe damage to the inner layer of the retina, primarily representing the retinal ganglion cells.[25] Glutamate mediates excitotoxicity through activation of the *N*-methyl-D-aspartate (NMDA) receptor. The intravitreal injection of NMDA was found to cause the death of retinal ganglion cells in rat eyes *in vivo*.[26,27] In the human retina, Niyadurupola and co-workers showed that NMDA caused a significant increase in retinal ganglion cell death.[28] Memantine, an antagonist of NMDA receptors, was found to prevent the death of retinal ganglion cells in rat[29] and primate[30] *in vivo* models of elevated IOP. In monkeys treated with memantine there was less change in optic disc cup and neuroretinal rim measurements following elevated IOP compared with eyes from monkeys treated with vehicle alone.[30] Memantine also protected neurones in the ganglion cell layer from IOP-induced retinal ischaemia in rat eyes *in vivo*.[31] Unfortunately, despite the success of memantine in experimental glaucoma, a randomised, double-masked, placebo-controlled clinical trial of memantine failed to show a significant benefit in human glaucoma patients (Allergan® Press Release 30th January 2008). The lack of a significant clinical response to memantine may reflect poor study design, inadequate dosing, insufficient follow up, or may confirm the complexity of glaucoma pathophysiology.

More recently, research studies have investigated adenosine 5'-triphosphate (ATP) excitotoxicity in relation to retinal ganglion cell death in glaucoma. Although ATP is well known for being an intracellular energy molecule, it also has a role in extracellular cell-to-cell signalling.[32-34] Furthermore, ATP may have a role in the pathogenesis of glaucoma. Mechanical stimulation of isolated rat retinas caused ATP release from Müller cells.[35,36] The elevation of IOP in rat eyes led to a significant increase in the ATP concentration in the vitreous *in vivo*.[37] Similarly, an increase in pressure in bovine retinal eyecups caused a significant increase in the ATP concentration in the vitreal compartment.[38] The ATP concentration in the aqueous of human eyes with acute primary angle closure glaucoma has been shown to be significantly elevated compared to control eyes.[39] The ATP concentration in the aqueous was correlated with the level of IOP in patients with acute primary angle closure glaucoma.[39] Retinal ganglion cell death by ATP excitotoxicity is mediated by activation of the $P2X_7$ receptor. The $P2X_7$ receptor agonist, 2',3'-O-(4-benzoylbenzoyl)-ATP (BzATP), caused the death of rat retinal ganglion cells *in vitro*[40] and *in vivo*,[41] an effect that was inhibited by the $P2X_7$ receptor antagonist, Brilliant Blue G (BBG). In addition, the rapid elevation of IOP in rat eyes caused an increase in the concentration of ATP in the vitreous that led to the death of retinal ganglion cells.[37] The intraocular injection of apyrase, an enzyme that causes the degradation of extracellular ATP, significantly protected the retinal ganglion cells from the pressure-induced cell death.[37] Work on human organotypic retinal cultures by Niyadurupola and associates, found that BzATP caused a significant increase in retinal ganglion cell death and this effect was inhibited by BBG, showing that ATP excitotoxicity via the $P2X_7$ receptor may have a role in retinal ganglion cell death in the human retina.[42] Excitotoxicity by ATP may also have a role in ischaemic neurodegeneration in the human retina. Oxygen and glucose deprivation of human organotypic retinal cultures caused death of retinal ganglion cells that was inhibited by the $P2X_7$ receptor antagonist BBG.[42]

Inflammatory theory

Cytokines, such as tumour necrosis factor-α (TNFα) and interleukin-1β (IL-1β), have been shown to be involved in retinal ganglion cell neurodegeneration. The upregulation of TNFα in the glial cells of the optic nerve head and retina and the upregulation of the TNFα receptor-1 in the retinal neuronal cells have been demonstrated in the retina of glaucomatous human eyes.[43] High IOP-induced retinal ischaemia caused an increase in TNFα expression in rat retinas *in vivo*.[44] The intravitreal injection of anti-TNFα antibody significantly reduced the number of apoptotic cells in the retina following pressure-induced ischaemia in rat

eyes *in vivo*.[44] Increased pressure and ischaemia in rat primary co-cultures of retinal ganglion cells and glial cells caused apoptotic retinal ganglion cell death due to TNFα secreted by the glial cells.[45] In an *in vivo* rat model of increased IOP, inhibition of TNFα protected retinal ganglion cells from cell death.[46]

Increased retinal expression of IL-1β has been identified in an *in vivo* rat model of high-IOP-induced retinal ischaemia and reperfusion.[47] The interleukin-1 receptor antagonist (IL-1ra) and anti-IL-1β antibody reduced retinal neuronal damage following ischaemic and excitotoxic insults suggesting that the neurotoxicity was IL-1β-mediated.[47] It is, therefore, likely that cytokines, such as TNFα and IL-1β, are involved in neurodegeneration of retinal ganglion cells in glaucoma.

Apoptosis of retinal ganglion cells

The final common pathway for retinal ganglion cell death in glaucoma is through the process of apoptosis. Elevated IOP in rats and primates *in vivo* has been shown to cause changes in retinal ganglion cells that are characteristic of classical apoptosis.[48-51] Human eyes with primary open angle glaucoma were found to have significantly more apoptotic cells in the retinal ganglion cell layer than in control eyes.[52] Apoptotic retinal ganglion cells have also been identified in normal tension glaucoma.[53] Apoptotic cell death relies on two interlinked pathways, the intrinsic (mitochondrial-mediated) pathway and the extrinsic (receptor-activated) pathway. Retinal ganglion cells may undergo apoptosis as a result of activation of either of the intrinsic or extrinsic apoptotic pathways.[54]

Recovery of retinal ganglion cells

There is growing evidence that there is a loss of retinal ganglion cell function in glaucoma prior to the death of retinal ganglion cells. Niyadurupola and co-workers,[55] have investigated retinal ganglion cell function using electroretinograms in patients with ocular hypertension and glaucoma. The photopic negative response (PhNR), the negative response following the b-wave of the photopic electroretinogram, has been shown to be associated with retinal ganglion cell function.[56-65] The lowering of IOP in patients with ocular hypertension and glaucoma led to an improvement in the amplitude of the PhNR, suggesting an improvement in retinal ganglion cell function.[55] The magnitude of the increase of PhNR amplitude was correlated with the degree of IOP reduction.[55] The greater the reduction of IOP in eyes with glaucoma and ocular hypertension, the greater the increase in the amplitude of the PhNR. Eyes with ocular hypertension and glaucoma that did not have significant IOP lowering did not have an improvement in PhNR amplitude.[55] The reversibility of retinal ganglion cell dysfunction with lowering of IOP has also been investigated using the pattern electroretinogram.[66-69] It appears, therefore, that adequate lowering of IOP in patients with glaucoma and ocular hypertension can improve retinal ganglion cell function, thus perhaps protecting retinal ganglion cells from glaucomatous cell death.

References

1. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002; **120**: 701-13.

2. Heijl A, Leske MC, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2002; **120**: 1268-79.

3. Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. *Arch Ophthalmol* 2003; **121**: 48-56.

4. The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol* 2000; **130**: 429-40.

5. Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. *Am J Ophthalmol* 1998; **126**: 487-97.

6. Collaborative Normal-Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma. *Am J Ophthalmol* 1998; **126**: 498-505.

7. Garway-Heath DF, Crabb DP, Bunce C, et al. Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial. *Lancet* 2015; **385**: 1295-304.

8. Quigley HA, Addicks EM, Green WR, Maumenee AE. Optic nerve damage in human glaucoma. II. The site of injury and susceptibility to damage. *Arch Ophthalmol* 1981; **99**: 635-49.

9. Anderson DR, Hendrickson A. Effect of intraocular pressure on rapid axoplasmic transport in monkey optic nerve. *Invest Ophthalmol* 1974; **13**: 771-83.

10. Minckler DS, Bunt AH, Johanson GW. Orthograde and retrograde axoplasmic transport during acute ocular hypertension in the monkey. *Invest Ophthalmol Vis Sci* 1977; **16**: 426-41.

11. Quigley HA, Addicks EM. Chronic experimental glaucoma in primates. II. Effect of extended intraocular pressure elevation on optic nerve head and axonal transport. *Invest Ophthalmol Vis Sci* 1980; **19**: 137-52.

12. Quigley HA, McKinnon SJ, Zack DJ, et al. Retrograde axonal transport of BDNF in retinal ganglion cells is blocked by acute IOP elevation in rats. *Invest Ophthalmol Vis Sci* 2000; **41**: 3460-6.

13. Ren R, Jonas JB, Tian G, et al. Cerebrospinal fluid pressure in glaucoma: a prospective study. *Ophthalmology* 2010; **117**: 259-66.

14. Wang L, Cull GA, Piper C, Burgoyne CF, Fortune B. Anterior and posterior optic nerve head blood flow in nonhuman primate experimental glaucoma model measured by laser speckle imaging technique and microsphere method. *Invest Ophthalmol Vis Sci* 2012; **53**: 8303-9.

15. Pache M, Flammer J. A sick eye in a sick body? Systemic findings in patients with primary open-angle glaucoma. *Surv Ophthalmol* 2006; **51**: 179-212.

16. Leske MC, Heijl A, Hyman L, et al. Predictors of long-term progression in the early manifest glaucoma trial. *Ophthalmology* 2007; **114**: 1965-72.

17. Hayreh SS. The role of age and cardiovascular disease in glaucomatous optic neuropathy. *Surv Ophthalmol* 1999; **43** Suppl 1: S27-42.

18. Gasser P, Flammer J, Guthauser U, Mahler F. Do vasospasms provoke ocular diseases? *Angiology* 1990; **41**: 213-20.

19. Drance S, Anderson DR, Schulzer M. Collaborative Normal-Tension Glaucoma Study Group. Risk factors for progression of visual field abnormalities in normal-tension glaucoma. *Am J Ophthalmol* 2001; **131**: 699-708.

20. Leske MC. Ocular perfusion pressure and glaucoma: clinical trial and epidemiologic findings. *Curr Opin Ophthalmol* 2009; **20**: 73-8.

21. Topouzis F, Coleman AL, Harris A, et al. Association of blood pressure status with the optic disk structure in non-glaucoma subjects: the Thessaloniki eye study. *Am J Ophthalmol* 2006; 142: 60-67.

22. Veerman DP, Imholz BPM, Wieling W, Wesseling KH, van Montfrans GA. Circadian profile of systemic hemodynamics. *Hypertension* 1995; **26**: 55-9.

23. Sung KR, Lee S, Park SB, et al. Twenty-four hour ocular perfusion pressure fluctuation and risk of normal-tension glaucoma progression. *Invest Ophthalmol Vis Sci* 2009; **50**: 5266-74.

24. Grippo TM, Liu JH, Zebardast N, Arnold TB, Moore GH, Weinreb RN. Twenty-four-hour pattern of intraocular pressure in untreated patients with ocular hypertension. *Invest Ophthalmol Vis Sci* 2013; **54**: 512-17.

25. Lucas DR, Newhouse JP. The toxic effect of sodium L-glutamate on the inner layers of the retina. *AMA Arch Ophthalmol* 1957; **58**: 193-201.

26. Siliprandi R, Canella R, Carmignoto G, et al. N-methyl-D-aspartate-induced neurotoxicity in the adult rat retina. *Vis Neurosci* 1992; **8**: 567-73.

27. Lam TT, Abler AS, Kwong JM, Tso MO. N-methyl-D-aspartate (NMDA)-induced apoptosis in rat retina. *Invest Ophthalmol Vis Sci* 1999; **40**: 2391-7.

28. Niyadurupola N, Sidaway P, Osborne A, Broadway DC, Sanderson J. The development of human organotypic retinal cultures (HORCs) to study retinal neurodegeneration. *Br J Ophthalmol* 2011; **95**: 720-6.

29. WoldeMussie E, Yoles E, Schwartz M, Ruiz G, Wheeler LA. Neuroprotective effect of memantine in different retinal injury models in rats. *J Glaucoma* 2002; **11**: 474-80.

30. Hare WA, WoldeMussie E, Weinreb RN, et al. Efficacy and safety of memantine treatment for reduction of changes associated with experimental glaucoma in monkey, II: Structural measures. *Invest Ophthalmol Vis Sci* 2004; **45**: 2640-51.

31. Lagrèze WA, Knörle R, Bach M, Feuerstein TJ. Memantine is neuroprotective in a rat model of pressure-induced retinal ischemia. *Invest Ophthalmol Vis Sci* 1998; **39**: 1063-6.

32. Holton P. The liberation of adenosine triphosphate on antidromic stimulation of sensory nerves. *J Physiol* 1959; **145**: 494-504.

33. North RA. Molecular physiology of P2X receptors. *Physiol Rev* 2002; **82**: 1013-67.

34. Burnstock G. Purinergic signalling. *Br J Pharmacol* 2006; **147** Suppl 1: S172-81.

35. Newman EA. Propagation of intercellular calcium waves in retinal astrocytes and Müller cells. *J Neurosci* 2001; **21**: 2215-23.

36. Newman EA. Glial cell inhibition of neurons by release of ATP. *J Neurosci* 2003; **23**: 1659-66.

37. Resta V, Novelli E, Vozzi G, et al. Acute retinal ganglion cell injury caused by intraocular pressure spikes is mediated by endogenous extracellular ATP. *Eur J Neurosci* 2007; **25**: 2741-54.

38. Reigada D, Lu W, Zhang M, Mitchell CH. Elevated pressure triggers a physiological release of ATP from the retina: Possible role for pannexin hemichannels. *Neuroscience* 2008; **157**: 396-404.

39. Zhang X, Li A, Ge J, Reigada D, Laties AM, Mitchell CH. Acute increase of intraocular pressure releases ATP into the anterior chamber. *Exp Eye Res* 2007; **85**: 637-43.

40. Zhang X, Zhang M, Laties AM, Mitchell CH. Stimulation of P2X7 receptors elevates Ca^{2+} and kills retinal ganglion cells. *Invest Ophthalmol Vis Sci* 2005; **46**: 2183-91.

41. Hu H, Lu W, Zhang M, et al. Stimulation of the P2X7 receptor kills rat retinal ganglion cells in vivo. *Exp Eye Res* 2010; **91**: 425-32.

42. Niyadurupola N, Sidaway P, Ma N, Rhodes JD, Broadway DC, Sanderson J. P2X7 receptor activation mediates retinal ganglion cell death in a human retina model of ischemic neurodegeneration. *Invest Ophthalmol Vis Sci* 2013; **54**: 2163-70.

43. Tezel G, Li LY, Patil RV, Wax MB. TNF-α and TNF-α receptor-1 in the retina of normal and glaucomatous eyes. *Invest Ophthalmol Vis Sci* 2001; **42**: 1787-94.

44. Berger S, Savitz SI, Nijhawan S, et al. Deleterious role of TNF-α in retinal ischemia-reperfusion injury. *Invest Ophthalmol Vis Sci* 2008; **49**: 3605-10.

45. Tezel G, Wax MB. Increased production of tumor necrosis factor-α by glial cells exposed to simulated ischemia or elevated hydrostatic pressure induces apoptosis in cocultured retinal ganglion cells. *J Neurosci* 2000; **20**: 8693-700.

46. Cueva Vargas JL, Osswald IK, Unsain N, et al. Soluble Tumor Necrosis Factor Alpha Promotes Retinal Ganglion Cell Death in Glaucoma via Calcium-Permeable AMPA Receptor Activation. *J Neurosci* 2015; **35**: 12088-102.

47. Yoneda S, Tanihara H, Kido N, et al. Interleukin-1β mediates ischemic injury in the rat retina. *Exp Eye Res* 2001; **73**: 661-7.

48. Guo L, Moss SE, Alexander RA, Ali RR, Fitzke FW, Cordeiro MF. Retinal ganglion cell apoptosis in glaucoma is related to intraocular pressure and IOP-induced effects on extracellular matrix. *Invest Ophthalmol Vis Sci* 2005; **46**: 175-82.

49. Garcia-Valenzuela E, Shareef S, Walsh J, Sharma SC. Programmed cell death of retinal ganglion cells during experimental glaucoma. *Exp Eye Res* 1995; **61**: 33-44.

50. Johnson EC, Deppmeier LM, Wentzien SK, Hsu I, Morrison JC. Chronology of optic nerve head and retinal responses to elevated intraocular pressure. *Invest Ophthalmol Vis Sci* 2000; **41**: 431-42.

51. Quigley HA, Nickells RW, Kerrigan LA, Pease ME, Thibault DJ, Zack DJ. Retinal ganglion cell death in experimental glaucoma and after axotomy occurs by apoptosis. *Invest Ophthalmol Vis Sci* 1995; **36**: 774-86.

52. Kerrigan LA, Zack DJ, Quigley HA, Smith SD, Pease ME. TUNEL-positive ganglion cells in human primary open-angle glaucoma. *Arch Ophthalmol* 1997; **115**: 1031-5.

53. Tatton NA, Tezel G, Insolia SA, Nandor SA, Edward PD, Wax MB. In situ detection of apoptosis in normal pressure glaucoma. a preliminary examination. *Surv Ophthalmol* 2001; **45**: S268-72; discussion S273-66.

54. Almasieh M, Wilson AM, Morquette B, Cueva Vargas JL, Di Polo A. The molecular basis of retinal ganglion cell death in glaucoma. *Prog Retin Eye Res* 2012; **31**: 152-81.

55. Niyadurupola N, Luu CD, Nguyen DQ, et al. Intraocular pressure lowering is associated with an increase in the photopic negative response (PhNR) amplitude in glaucoma and ocular hypertensive eyes. *Invest Ophthalmol Vis Sci* 2013; **54**: 1913-19.

56. Viswanathan S, Frishman LJ, Robson JG, Harwerth RS, Smith 3rd EL. The photopic negative response of the macaque electroretinogram: reduction by experimental glaucoma. *Invest Ophthalmol Vis Sci* 1999; **40**: 1124-36.

57. Colotto A, Falsini B, Salgarello T, Iarossi G, Galan ME, Scullica L. Photopic negative response of the human ERG: losses associated with glaucomatous damage. *Invest Ophthalmol Vis Sci* 2000; **41**: 2205-11.

58. Machida S, Toba Y, Ohtaki A, Gotoh Y, Kaneko M, Kurosaka D. Photopic negative response of focal electoretinograms in glaucomatous eyes. *Invest Ophthalmol Vis Sci* 2008; **49**: 5636-44.

59. Machida S, Gotoh Y, Toba Y, Ohtaki A, Kaneko M, Kurosaka D. Correlation between photopic negative response and retinal nerve fiber layer thickness and optic disc topography in glaucomatous eyes. *Invest Ophthalmol Vis Sci* 2008; **49**: 2201-7.

60. Tamada K, Machida S, Oikawa T, Miyamoto H, Nishimura T, Kurosaka D. Correlation between photopic negative response of focal electroretinograms and local loss of retinal neurons in glaucoma. *Curr Eye Res* 2010; **35**: 155-64.

61. Drasdo N, Aldebasi YH, Chiti Z, Mortlock KE, Morgan JE, North RV. The s-cone PHNR and pattern ERG in primary open angle glaucoma. *Invest Ophthalmol Vis Sci* 2001; **42**: 1266-72.

62. North RV, Jones AL, Drasdo N, Wild JM, Morgan JE. Electrophysiological evidence of early functional damage in glaucoma and ocular hypertension. *Invest Ophthalmol Vis Sci* 2010; **51**: 1216-22.

63. Nakamura H, Hangai M, Mori S, Hirose F, Yoshimura N. Hemispherical focal macular photopic negative response and macular inner retinal thickness in open-angle glaucoma. *Am J Ophthalmol* 2011; **151**: 494-506.

64. Machida S, Tamada K, Oikawa T, Yokoyama D, Kaneko M, Kurosaka D. Sensitivity and specificity of photopic negative response of focal electoretinogram to detect glaucomatous eyes. *Br J Ophthalmol* 2010; **94**: 202-8.

65. Machida S, Tamada K, Oikawa T, et al. Comparison of photopic negative response of full-field and focal electroretinograms in detecting glaucomatous eyes. *J Ophthalmol* 2011; 2011: pii: 564131. doi: 564110.561155/562011/564131.

66. Papst N, Bopp M, Schnaudigel OE. The pattern evoked electroretinogram associated with elevated intraocular pressure. *Graefes Arch Clin Exp Ophthalmol* 1984; **222**: 34-7.

67. Ventura LM, Porciatti V. Restoration of retinal ganglion cell function in early glaucoma after intraocular pressure reduction: a pilot study. *Ophthalmology* 2005; **112**: 20-7.

68. Sehi M, Grewal DS, Goodkin ML, Greenfield DS. Reversal of retinal ganglion cell dysfunction after surgical reduction of intraocular pressure. *Ophthalmology* 2010; **117**: 2329-36.

69. Ventura LM, Feuer WJ, Porciatti V. Progressive loss of retinal ganglion cell function is hindered with IOP-lowering treatment in early glaucoma. *Invest Ophthalmol Vis Sci* 2012; **53**: 659-63.

Recurrent ROP after intravitreal bevacizumab and laser photocoagulation combined therapy

Hiranya Abeysekera[1], Dharma Irugalbandara[2], Charith Fonseka[3]

The Journal of the College of Ophthalmologists of Sri Lanka 2015; 21: 54-57

Abstract

Introduction and Objectives: *Retinopathy of prematurity (ROP) is a potentially blinding disease in premature infants. Laser monotherapy, bevacizumab monotherapy and combined therapy are currently employed treatment methods for ROP. All these treatment modalities have the risk of recurrence as an early complication. Combined Rx have been pursued to minimize the possible disadvantages of laser ablation and intravitreal anti-VEGF monotherapy.*

Methodology: *ROP treatment records from May 2014 to September 2015 from the Eye Unit at the Lady Ridgeway Hospital for Children, Colombo were evaluated to detect patients who developed recurrence of ROP following combined treatment with 532nm Green Laser and intravitreal bevacizumab.*

Results and Conclusion: *Out of the total number of 36 babies who were treated with combined laser and intravitreal injection of bevacizumab, 3 babies were noted to have recurrence of ROP. Two cases were detected early and treated successfully and the other baby went blind from severe zone 1 recurrence. Careful follow up and meticulous examinations can identify the recurrence early and treat successfully.*

Introduction

Retinopathy of prematurity (ROP) is a vision-threatening disease associated with abnormal retinal vascular development that occurs in premature infants. Prematurity and low birth weight are strongly associated with increased risk of the disease. ROP is a major cause of blindness despite advances in combined treatment.

Randomized treatment trial – ETROP established peripheral retinal ablation with laser photocoagulation for prethreshold ROP.[5] But, adverse anatomical outcome and high percentage of severe recurrence were reported in the laser mono-therapy, particularly in zone 1 ROP. A prospective randomized controlled stratified multicenter trial assessed intravitreal bevacizumab monotherapy (BEAT-ROP)[9] concluded that bevacizumab treatment was more effective than peripheral laser ablation and the rate of recurrence is statistically low for zone 1 and posterior zone 2 ROP.

To minimize the possible disadvantage of laser ablation and intravitreal anti-VEGF monotherapy, combined treatment have been pursued in several studies.[1-4]

All the above described treatment modalities have the risk of recurrence.[12] A recurrence of ROP is defined as an arrest of anterior progression of retinal vasculature associated with a new demarcation line, ridge, or extraretinal fibrovascular proliferation (EFP). If fluorescein angiography is performed, it will demonstrate leakage. The plus disease also may recur.[11] Post-menstrual age (PMA) is defined as the gestational age (GA) at birth plus chronologic age in weeks.

Methodology

Ophthalmology Unit at the Lady Ridgeway Hospital for Children, Colombo is the main centre in Colombo which carries out screening and treatment for ROP. The Unit also receives tertiary level referrals from the Teaching Hospitals in most parts of the country. Management of ROP is carried out in collaboration with the Retinal Unit (CF) of the National Eye Hospital of Sri Lanka.

Premature infants born before 32 weeks of gestation or birth weight less than 1500g were screened for ROP. Furthermore, babies suffered with medical or neurological problems during the first 2-3 weeks of life were also seen. Babies were examined after installing tropicamide 0.5% and phenylephrine 2.5% eye drops three times each 5 minutes apart. Indirect ophthalmoscopy was performed with 20 diopter lens. Important findings were documented with RETCAM1 wide field digital imaging system. Indications for treatment for ROP is summarised in Table 1.

Opinion from the vitreo-retinal surgeon was obtained for babies with zone 1 stage 3 or worse ROP. More posterior disease was treated with intravitreal injection

[1]*Acting Consultant Paediatric Ophthalmologist,* [2]*Consultant Paediatric Ophthalmologist, Lady Ridgeway Hospital, Colombo,* [3]*Consultant Vitreoretinal Surgeon, National Eye Hospital of Sri Lanka.*

of Bevacizumab and combined 532nm laser treatment and the more anterior disease was managed with laser mono-therapy. All the treatments were carried out under topical anaesthesia.

Table 1. Indications for treatment for ROP

Zone 1 Stage 1 or 2 with plus disease
Zone 1 Stage 3 with or without plus disease
Posterior Zone 2 Stage 2 with plus disease
Zone 2 Stage 3 with or without plus disease

Results

This paper describes the experience of recurrence of ROP and their management at the Ophthalmology Unit at the Lady Ridgeway Hospital for Children during May 2014 and September 2015. Total number of 693 babies were screened during this period and a total number of 143 babies were treated according to the criteria mentioned in Table 1. 36 babies were managed with intravitreal injection of bevacizumab and 532nm green laser combined therapy (Table 2). One baby was lost to follow up at 48 weeks of PMA and further details were not available. One baby died following sepsis at 41 weeks of PMA. All the other 34 babies who received intravitreal bevacizumab therapy were followed up to 54-60 weeks of PMA with a mean 57 weeks (Table 3). Only three babies were found to have developed recurrence of ROP during the follow up. Out of the 3 babies who developed recurrence, 2 were local recurrence without plus disease and the other baby developed zone 1 recurrence with plus disease. The cases are described below.

Table 2. Indications to manage with intravitreal injection of bevacizumab and 532 nm green laser dual therapy

Indication	*Number of babies*
Zone 1 Stage 1 and 2 with plus disease	7 (19%)
Zone 1 Stage 3 with or without plus disease	4 (11%)
Zone 2 Stage 3 with or without plus disease	15 (42%)
Posterior Zone 2 Stage 2 with plus disease	10 (28%)
Total	36

Table 3. Follow up period for babies who received intravitreal bevacizumab treatment

End of follow up post menstrual age (weeks)	*Number of babies*
54	19 (53%)
55	3 (8%)
56	4 (11%)
57	1 (3%)
58	5 (14%)
59	1 (3%)
60	1 (3%)
Lost to follow up	2 (5%)
Total	36

Cases

Case 1

Baby girl, second of twins born at 30 weeks of GA was found to have Zone 1 Stage 1 with plus disease at 34 weeks of PMA. Intravitreal injection of bevacizumab was carried out soon after the diagnosis and three sessions of 532 nm laser treatment was performed. Local area of recurrence of ROP without plus disease was noted at the supero-temporal vascular arcade anterior to original ridge at 54 weeks of PMA (Figure 1). Laser treatment was carried out at the recurrence site. Patient was followed up 2 weekly till 60/52 PMA and no further recurrences were found.

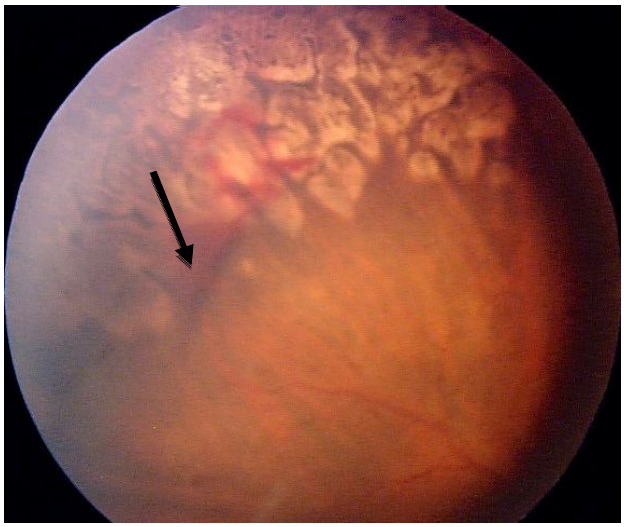


Figure 1. *Case 1, at the time of occurrence of recurrence. Arrow indicates the extraretinal fibrovascular proliferation (EFP).*

Case 2

Baby born at 27 weeks of GA was found to have posterior Zone 2 Stage 2 ROP with plus disease at 31 weeks of PMA. Intravitreal injection of bevacizumab and four sessions of 532 nm laser was carried out.

Local area of recurrence of ROP in the left eye iwas noted around the supero-temporal vascular arcade between the original ridge and the existing laser scars at 53 weeks of PMA (Figure 2a). Repeat laser treatment done at the site of recurrence and further problems were not noted during the follow up till 60 weeks of PMA (Figure 2b).

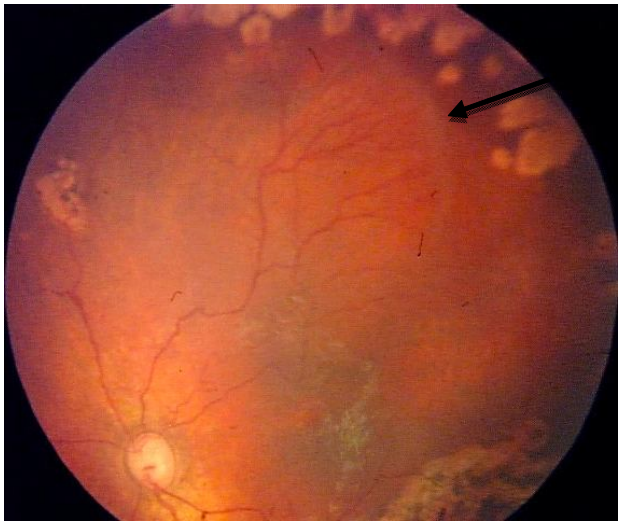


Figure 2a. *Case 2 at the time of occurrence of recurrence. Arrow indicates the extraretinal fibrovascular proliferation (EFP).*

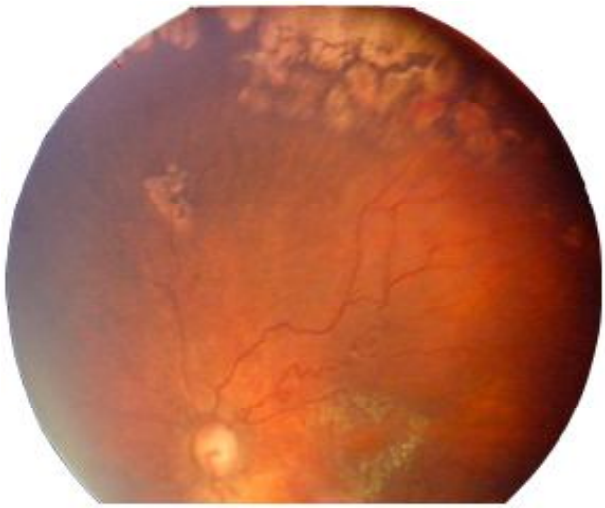


Figure 2b. *Case 2 after treatment for the recurrence.*

Case 3

Another baby girl born at 28 weeks of GA had Zone 1 Stage 2 with plus disease was managed with intravitreal injection of bevacizumab and 532nm laser. Recurrence of ROP with plus disease and vitreous haemorrhage was noted at 45 weeks of PMA (Figure 3). Patient was seen by the vitreoretinal surgeon and a repeat dose of intravireal bevacizumab was recommended. Further laser treatment was also carried out to the avascular area. Baby developed aspiration pneumonia and admitted to local hospital during the management of recurrence and the follow up was irregular. The recurrence progressed into Zone 1 Stage 5b which was inoperatable.

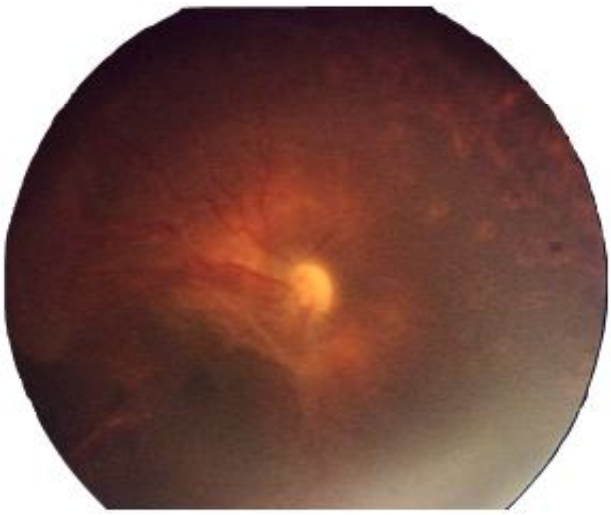


Figure 3. *Case 3 at the time of presentation with severe recurrence.*

Discussion and conclusion

Peripheral retinal ablation with conventional laser photocoagulation is a destructive treatment method that damages the majority of cells that produce proangiogenic factors, such as VEGF in the retina. Thus, laser treatment often causes complications, such as visual field constriction, and does not prevent all cases of visual impairment, especially in cases of Zone I ROP.[10]

The role of vascular endothelial growth factor (VEGF) in the pathophysiology of ROP is well studied.[6-8] But there are concerns about anti-VEGF (intravitreal injection of Bevacizumab) treatment for ROP regarding optimal dosage, timing of injection, recurrences, ocular and systemic safety, proper follow-up protocol, and long-term functional outcome. Even though the rate of recurrence is statistically less compared to laser mono

therapy, anti-VEGF therapy also reported to have severe recurrences.

The addition of laser therapy following intravitreal injection of bevacizumab hypothesised to decrease the risk of recurrence and obviate the need for prolonged follow-up. But there are case reports showing recurrence of ROP following dual therapy also.[12]

This case series shows that recurrence ROP can occur in small number of patients treated with combined bevacizumab and laser treatment. Therefore, prolonged follow up is required in these cases as well. Careful follow up and meticulous examinations can identify the recurrence early and treat successfully.

References

1. Jayerung Kim et al. Combined intravitreal Bevacizumab injection and Zone 1 Sparing laser photocoagulation in patients with zone 1 ROP. *Retina* 2014; **34**: 77-82.
2. Chung EJ et al. Combination of laser photocoagulation and intravitreal bevacizumab (Avastin) for aggressive zone I retinopathy of prematurity. *Graefes Arch Clin Exp Ophthalmic* 2007; **245**: 1727-30.
3. Lee JY et al. Effects of intravitreal bevacizumab and laser in retinopathy of prematurity therapy on the development of peripheral retinal vessels. *Graefes Arch Clin Exp Ophthalmol* 2010; **248**: 1257-62.
4. Nazari H et al. Intravitreal bevacizumab in combination with laser therapy for the treatment of severe retinopathy of prematurity (ROP) associated with vitreous or retinal hemorrhage. *Graefes Arch Clin Exp Ophthalmol* 2010; **248**: 1713-18.
5. Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. *Arch Ophthalmol.* 2003; **121**(12): 1684-94.
6. ChenJ, Smith LE. Retinopathyof prematurity. *Angiogenesis* 2007; **10**(2): 133-40.
7. Smith LEH. Pathogenesis of retinopathy of prematurity. *Acta Paediatric Suppl.* 2002; **91**(437): 26-8.
8. Mintz-Hittner HA, Best LM. Antivascular endothelial growth factor for retinopathy of prematurity. *Curr Opin Pediatr.* 2009; **21**(2): 182-7.
9. Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3 retinopathy of prematurity. *N Engl J Med.* 2011; **364**(7): 603-15.
10. Kychenthal A, Dorta P, Katz X. Zone I retinopathy of prematurity clinical characteristics and treatment outcomes. *Retina* 2006; **26**: S11-S15.
11. Jennifer Hu et al. Reactivation of Retinopathy of Prematurity After Bevacizumab Injection. *Arch Ophthalmol.* 2012; **130**(8): 1000-6.
12. Wendy Chen et al. Late recurrence of retinopathy of prematurity after treatment with both intravitreal bevacizumab and laser. *J AAPOS* 2014; **18**: 402-04.

Retrospective study of the patient profile and the incidence of post-operative endophthalmitis over a year (2014) at the National Eye Hospital

L. D. Jayathilaka[1], A. S. D. de Silva[2], R. A. K. Chinthaka[3], C. R. Fonseka[4]

The Journal of the College of Ophthalmologists of Sri Lanka 2015; 21: 58-61

Abstract

Introduction: *Cataract surgery is the most commonly performed surgical procedure in the National Eye Hospital (NEH). Endophthalmitis is the most serious complication of the cataract surgery. This study was conducted, because even a single case of post-operative endophthalmitis is challenging and stressful to treat.*

Objectives

I. To determine the reported incidence of Endophthalmitis following cataract surgery during the year 2014.

II. To compare ours with expected incidence (BOSU study-expected incidence of post cataract 1 in 700).

III. To assess patient profile.

Methodology: *Patients whose cataract operations were done at NEH and diagnosed with post-cataract endophthalmitis during the year 2014 were included. Retrospective cohort study design was used. Data were collected from the bed head tickets.*

Results: *During the year 2014, total of 21,819 operations were performed at NEH. Out of that 8480 were cataract operations. Ten cases of post-operative endophthalmitis were identified. Nine other cases were post cataracts. The incidence rate was 0.106. The age range was 60-77 years with male predominance. Five were diagnosed within 4 days, two within 5-7 days and three after 1 month of cataract operation. The results of microbiological cultures were one mixed growth (staphylococcus and streptoccocus), one staphylococcus aureus and six "no growth". On admission visual acuity (VA) varied from Snellen 6/18 to hand movement (HM). Final VA ranged from 6/60 to perception of light (PL). 2 patients were suffering from diabetes mellitus.*

Discussion and conclusion: *Our incidence of post cataract endophthalmitis is less than the BOSU expected incidence. (0.14% British Ophthalmological Surveillance Unit (BOSU) expected incidence). The limitations were its retrospective nature, and potential differences of the practices among surgeons.*

Introduction

Eye is vital for the human body. It is the organ of vision which gives us sense of light. Vision is an indispensable part of everyday life. Low vision and blindness have ominous effects not only on individuals, but also to the families, and to the society. These ominous effect expectrum starts from a decrease in quality of life, increased mortality to large-scale economic consequences. In addition there are cultural stigmas often associated with blindness, adding more distress to individuals and families leading to immense amount of social disadvantages. 50% of the blind in underprivileged countries report, a loss of social standing and decision-making authority, and 80% of blind women note a loss of authority within their families.[1] It is documented 45 million people in the world are blind, and 87% of visually impaired people live in developing countries. The economic consequences of blindness are enormous, as 90% of blind individuals cannot work.[2,3]

The most severe and dreaded complication of cataract surgery, is endophthalmitis. Fortunately the incidence is low. But the morbidity is noteworthy and visual recovery is indefinite. The BOSU study estimated the incidence in the UK to be 0.14% i.e. approximately one case per 700 cataract extractions, and the visual outcome for one third of these patients was less than 6/60.[4]

Objectives

1. To determine the reported incidence of endophthalmitis following cataract surgery during the year 2014.
2. To compare ours with expected incidence (BOSU study – expected incidence of post cataract 1 in 700).
3. To assess patient profile
   I. To explore age distribution
   II. To explore sex distribution

[1]*Medical Officer, Health Informatics,* [2]*Director, National Eye Hospital,* [3]*Consultant Paediatrician,* [4]*Consultant Eye Surgeon, National Eye Hospital, Colombo, Sri Lanka.*

III. To explore time of presentation (early, delayed, chronic, other)

IV. To explore aetiological distribution

V. To explore visual records on admission (pre-operative) and discharge

VI. To explore whether the patients were suffering from any other acute infection or immunocompromised diseases

Methodology

Since the post-operative endophthalmitis after cataract surgery is not a common occurrence retrospective cohort study design was selected. This design needs less time to complete and help in addressing diseases of low incidence. It is less expensive.

Patients whose cataract operations were done at NEH and diagnosed with post-cataract endophthalmitis during the year 2014 were included. Data were collected from the bed head tickets.

Results

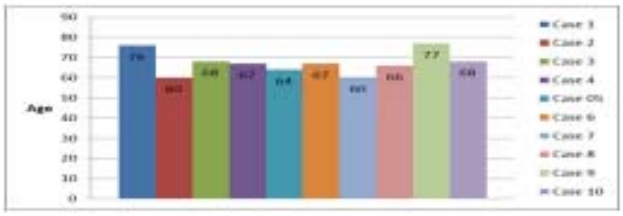
1. To determine the reported incidence of endophthalmitis following cataract surgery during the year 2014

- Period: 1st January 2014 – 31st December 2014
- Total No. of operations – 21,819
- Total No. of cataract operations – 8480
- Total No. cases reported – 10

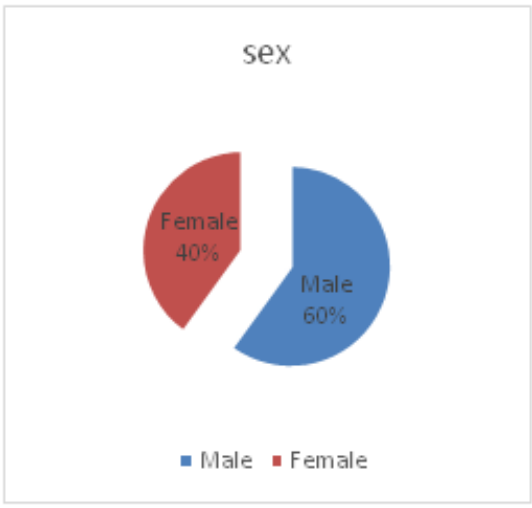
2. To compare ours with expected incidence (BOSU study – expected incidence of post cataract 1 in 700)

- Incidence = (10 / 21,819) × 100 = 0.0458
- Incidence = (9 / 8480) × 100 = 0.106 (cataract)
- Our incidence < expected incidence of post cataract (0.14%)

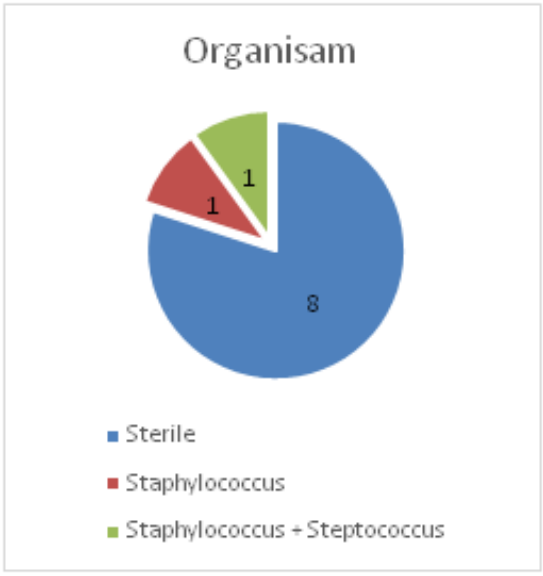
I. To explore age distribution



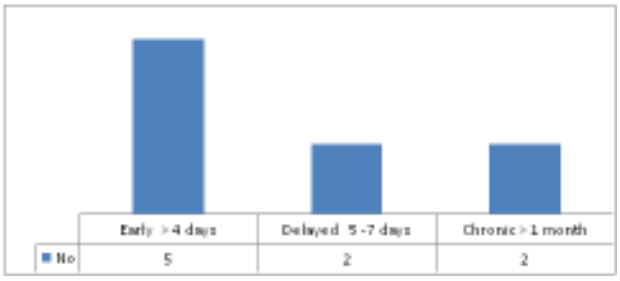
II. To explore sex distribution



III. To explore aetiological distribution



IV. To explore time of presentation (early, delayed, chronic, other)



V. To explore visual records on admission (pre-operative) and discharge

VI. To explore whether the patients were suffering from any other acute infection or immunocompromised diseases

Case	On admission V/A (pre-operative)	On admission V/A	Co- Morbidities
1	HM	2/60	HT
2	6/18	HM	DM, HT
3	1/60	PL	HT
4	HM	HM	None
5	6/60	6/60	None
6	No data	PL	DM
7	No data	PL	None
8	No data	HM	None
9	No data	No data	None
10	No data	No data	None

Discussion and conclusion:

Global situation

WHO, "Prevention of Blindness and Deafness Programme" had carried out a systematic search and review of all available data to obtain a global estimate of visual impairment for 2010.

Estimates of visual impairment had been derived at global level and in the six WHO Regions. The major causes of visual impairment and of blindness had been determined. This showed globally the primary causes of visual impairment were uncorrected refractive errors and cataracts, 43% and 33% respectively.[2]

Incidence of endophthalmitis is very low in western literature (0.08-0.02%.[5]

A population-based, prospective study with active surveillance of cases through BOSU had established the incidence of post cataract endophthalmitis following cataract surgery in UK was 0.085% (95% CI 0.073%, 0.097%) in 12-month period October 1999 to September 2000. The majority of patients were older than 70 years of age (mean = 73.5, median = 76, range = 7-94) and presented within the first week of cataract (81%).[6]

All cases of endophthalmitis occurring over a 10 year period within a single ophthalmic unit in the UK were reviewed in this study to find out post cataract endophthalmitis incidence. Over the 10 years, a total of 18191 cataract operations were performed. A total of 30 cases of endophthalmitis were recorded, giving an overall incidence of endophthalmitis of 0.16% (95% CI 0.11 to 0.24). The age range was 43-89 years, 73% of patients were female, and 50% of cases were in right eyes. Twenty one cases occurred after ECCE, eight after phaco, and one after secondary IOL insertion.[7]

A study done in United States of America to estimate endophthalmitis incidence after cataract surgery in year 2003 and 2004 had showed, the national rate in 2003 was 1.33 per 1000 surgeries (95% CI, 1.27-1.38) and decreased to 1.11 per 1000 (95% CI, 1.06-1.16) in 2004.[8]

A population-based cross-sectional study done to assess the visual outcome after cataract surgery in a south Indian population had demonstrated the occurrence of post-cataract endophthalmitis in India 0.6%.[9,10]

A study which had been done retrospectively by reviewing the medical records of patients with acute endophthalmitis following cataract surgery, which

were performed in local hospitals in China and later treated at the Zhongshan Ophthalmic Center between 1 January 1998 and 31 December 2009 had shown, delayed presentation, inappropriate treatment procedures, poor presenting VA, and causative organism virulence may account for the unfavorable visual outcome. In this study details of each case, including the interval from symptoms to presentation, initial treatment in local hospitals, microorganisms isolated, treatments, and visual outcome, were recorded.[11]

Sri Lankan situation

Even though cataract extraction accounts for a significant proportion of the surgical workload of most of the ophthalmologists and cataract surgery continues to be the commonest elective eye related surgical procedure performed in Sri Lanka, the studies on post cataract complications, including endophthalmitis is limited.

A retrospective case study, which had been done to compare the incidence rate of post-operative endophthalmitis after cataract surgery in three teaching hospitals in the UK, Sri Lanka and Paraguay had demonstrated, over a twelve month period between December 2003 and November 2004, over 8900 cataract surgeries were reported from Sri Lanka, around 2000 from Paraguay and approximately 2200cataract surgeries were performed in the UK. Of these, 18 cases (0.202%) of endophthalmitis were reported from Sri Lanka, 1 case (0.048%) from Paraguay and 3 cases (0.15%) in the UK. It was mentioned that elaborated and expensive method of asepsis was practiced in the UK.[12]

Conclusion

Our incidence of post cataract surgery endophthalmitis in year 2014 is less than the expected BOSU incidence of post cataract endophthalmitis (0.14% BOSU expected incidence). The limitations were retrospective nature of the study where we rely on others for accurate record keeping, and potential differences of the practices of different surgeons.

References

1. Wagner-Lampl A, Oliver GW. Folklore of Blindness. *J Vis Impair Blind.* 1994; **88**(3): 267-76.

2. Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. *Br J Ophthalmol.* 2011; bjophthalmol - 2011.

3. Chang MA, Congdon NG, Baker SK, Bloem MW, Savage H, Sommer A. The surgical management of cataract: barriers, best practices and outcomes. *Int Ophthalmol.* 2007; **28**(4): 247-60.

4. Managing-an-outbreak-of-postoperative-endophthalmitis.pdf [Internet]. [cited 2015 Aug 25]. Available from: https://www.rcophth.ac.uk/wp-content/uploads/2014/12/2011_PROF_104Managing-an-outbreak-of-postoperative-endophthalmitis.pdf

5. Grewal SS, Grewal RK, Gill AS. Endophthalmitis after cataract surgery. *Indian J Ophthalmol.* 1984; **32**(6): 501.

6. Kamalarajah S, Silvestri G, Sharma N, Khan A, Foot B, Ling R, et al. Surveillance of endophthalmitis following cataract surgery in the UK. *Eye.* 2004; **18**(6): 580-7.

7. Mayer E, Cadman D, Ewings P, Twomey JM, Gray RH, Claridge KG, et al. A 10 year retrospective survey of cataract surgery and endophthalmitis in a single eye unit: injectable lenses lower the incidence of endophthalmitis. *Br J Ophthalmol.* 2003; **87**(7): 867-9.

8. Keay L, Gower EW, Cassard SD, Tielsch JM, Schein OD. Postcataract surgery endophthalmitis in the United States: analysis of the complete 2003 to 2004 Medicare database of cataract surgeries. *Ophthalmology* 2012; **119**(5): 914-22.

9. Thomas R. Reducing endophthalmitis in India: An example of the importance of critical appraisal. *Indian J Ophthalmol.* 2010; **58**(6): 560-2.

10. Vijaya L, George R, A R, Raju P, Arvind H, Baskaran M, et al. Outcomes of cataract surgery in a rural and urban south Indian population. *Indian J Ophthalmol.* 2010; **58**(3): 223-8.

11. Ding Y, Lin M, Liu H, Zhang W, Wang L, Li Y. Outcomes of post-cataract surgery endophthalmitis referred to a tertiary center from local hospitals in the south of China. *Infection.* 2011; **39**(5): 451-60.

12. Syed RN, Ghosh YK, Berry-Brincat A, Brown RD, De Silva D, Khan S, et al. Incidence of Post-Operative Endophthalmitis in 3 Geographically Contrasting Populations – A Multicentre Study. *Invest Ophthalmol Vis Sci.* 2005; **46**(13): 5077.

An under diagnosed condition

Thisara Niyadurupola[1]

The Journal of the College of Ophthalmologists of Sri Lanka 2015; 21: 62-65

Abstract

A disease entity not commonly diagnosed in Sri Lanka is described. The possible secondary effects of this condition lead to a wide array of symptoms with a varying degree of severity. Early diagnosis and avoidance of the causative agent by changing dietary habits will result in almost complete recovery to normal health.

Case presentation

A fictitious name Mr. G.E., is given in this article to someone who suffered with this condition. A detail description of GE's symptoms throughout his life is described in chronological order.

G.E. was a very active young person who excelled in athletics and other physical activities and also excelled in his studies at school. He had a wide range of hobbies including cycling, playing musical instruments and other creative and constructive activities. G.E. frequently visited bakeries and his daily food intake had a variety of products sold in bakeries. He loved the aroma that emanated from bakeries.

G.E.'s maternal uncles developed premature male type baldness and maternal females had noticeable thinning of hair. The life expectancy of maternal relatives was around 60-70 years. The paternal relatives had full complement of hair with a life expectancy of 80-90 years.

G.E. first noticed his hair strands getting unusually thinner when he was in the GCE A/L class. During his first year in the university he became aware of developing accelerated male type of baldness.

One of his childhood hobbies was playing the guitar given to him by his mother on his twelveth birthday, but in his twenties he found it difficult to play the guitar because the tips of fingernails became brittle and became wasted as they rubbed against the strings of the guitar. The finger nails developed longitudinal ridges and small pits. Trivial daily activities made his fingernails and toenails split and break. In his thirties, his dentist became aware of excessive wear of teeth and suspected excessive grinding of teeth during sleep at night. He was given a tooth guard to be worn at night. Several years later the molar teeth became weak. They cracked and broke while biting into chicken bones.

While young, G.E. had no difficulty in having Sri Lankan spicy foods, but later on he found it difficult to tolerate spicy food. They were too hot and caused burning of mouth and tongue. Eating spicy food caused sweating and a runny nose as the food became excessively hot. He later thought this was due to inflammation of the oral mucosa and due to glossitis.

In his forties and in fifties he found it difficult to lie flat and woken up with regurgitation of food due to gastro-oesophageal reflux. He had to sleep with the head propped up with two to three pillows and on occasion he had to sit up and spend a couple of hours to get relief from his heartburn. He became bloated with gas in his intestines with increasing flatulence. His bowel habits changed and started passing frequent watery, frothy smelly stools.

G.E.'s prominent musculature around the base of the neck and shoulders became stiff leading to frequent muscle cramps. He resorted to move his neck and head in a gyratory fashion in an attempt to stretch and relax neck muscles. Doing any work stooping forward became impossible as his back muscles became stiff and painful. Returning back to normal erect posture became very difficult. Gardening, one of his past-time hobbies, had to be performed in short spells. He started having muscle cramps of his toes and feet especially at night.

G.E. was a very dextrous person doing many types of very fine manual hobbies. In his sixties he developed 'trigger fingers' on ring fingers of both hands limiting certain fine manual work. His sexual functions gradually diminished due to progressive impotence which he put down to advancing age. He developed tinnitus and lost high frequency hearing in both ears. Although he was prescribed hearing aids, he did not persevere wearing them.

G.E. developed persistent numbness in a circular patch of about two centimetre diameter on the inner aspect of both big toes. He thought he was developing diabetes, but his blood sugars at different occasions stayed normal. He underwent electro-physiological nerve conduction studies, but no abnormality was detected.

[1]*Retired Consultant Ophthalmologist, United Kingdom.*

He developed a habit of having an afternoon nap and felt somewhat lethargic, but he put this down to his disturbed sleep at night, over work and to his advancing age. On several occasions he almost fell asleep at wheel whilst driving his car especially returning home from work in the late afternoons. He had several experiences of suddenly becoming aware of his car veering off the edge of the road. Fortunately he escaped causing a road traffic accident.

Visual symptoms

G.E. started noticing blurring and disappearance of objects at and around the point of fixation. These strange visual symptoms lasted for few minutes before his eyesight returned to normal. He later developed much larger areas of loss of vision in his visual fields. These were of varying size and shape and distribution, ranging from uni-ocular to binocular, paracentral to quadrantanopic field loss. Each episode lasted for about 20-30 minutes with a slow gradual recovery. These symptoms were not associated with flashes of light, zig-zag patterns or nausea. G.E. had his visual fields tested on a few occasions but these did not demonstrate a persistent visual field abnormality. He also had a neurological workup including a magnetic resonance imaging (MRI) scan of the head. The MRI did not show any pathology except for usual 'age related changes' in the brain.

G.E. enjoyed a normal body weight of 65 Kg all through his adult life. However, he started losing weight which became accelerated lately, losing about 5Kg within a period of three months in spite of normal food intake. His work colleagues started commenting on his weight loss.

G.E.'s children had a good education and were able to support themselves. He was very happy and content with his achievements and working life and he had no reason to continue working at the same busy pace. He thought of giving up the heavy responsibilities he was handling at work. He had enough interests and commitments outside his job. He wanted to experience a multitude of other interesting and stimulating aspects of life. He made a positive decision to retire from work.

Within a few months into his retirement, his friend and next-door neighbour passed away due to bowel cancer. This incident and the multitude of symptoms he had, including loss of weight, prompted him to make a visit to his family doctor for a medical examination.

The family doctor found him to have normal blood pressure and normal cardiovascular system. His body weight recorded at the time was 59 kilogrammes. Initial laboratory tests revealed a haemoglobin level of 8.3% and a very low iron and ferritin level. His vitamin B12 level was very low. His fasting and postprandial blood sugars were normal. His thyroid and liver enzymes and renal functions were normal. The doctor referred him to the general hospital for a specialist's opinion. The gastroenterologist subjected him to an endoscopy and upper intestinal mucosal biopsy. While waiting for biopsy report he had further laboratory tests. Amongst them the tissue transglutaminase antibody (TTA) level was marginally elevated.

The endoscopy and upper intestinal mucosal biopsy revealed stunted intestinal villi with lymphocytic infiltration at the base of villi. A diagnosis of gluten enteropathy was made. He was advised to refrain from having any food items containing or contaminated with wheat flour, rye and barley. G.E. was treated with supplementary iron and vitamin B12 therapy. He had further advice from the professional dieticians. The dietary advice was directed towards a gluten-free diet for his malnutrition. He and his wife were given advice regarding providing the gluten-free diet and the prevention of cross contamination of his food with gluten from other food made at home. The dietary specialists provided him with prescriptions for gluten-free food items.

The British Coeliac Association provided him with a broader outlook of this condition.

Gluten is a protein found in wheat, rye and barley. Wheat flour, rye and barley are found in a large percentage of food items as a basic ingredient, bulk increasing agent or as a thickening agent. It also found as an inadvertent contaminant in a large number of food items.

Within two or three weeks of starting his gluten-free diet, G.E. felt an improvement in his general outlook. His main symptom of bloating and his bowel habits improved. He started passing well formed stools and had a great relief from flatulence. Gradually he was able to lie flat and have a normal sleep without being woken up with gastro-oesophageal reflux. He started gaining body weight over several months.

Over a period of few months, his finger and toe nails became shiny and strong and he started playing his guitar again. His sexual outlook improved over several months. The muscle rigidity and spasms got better. The trigger fingers became less troublesome. He was not troubled by hearing loss, but the tinnitus remained without much change. G.E. did not have further visual symptoms of transient visual field loss. The second endoscopy and biopsy a couple of months later showed normal regeneration of intestinal villi. He continued to have suplementory bimonthly vitmin B12 injections. Iron therapy was discontinued since his haemoglobin returned to normal.

Storing rice in old bags used to transport wheat flour

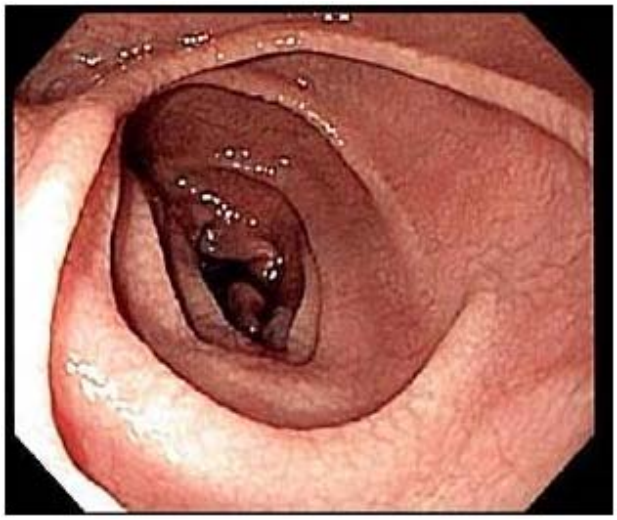
Main ingredient	Bulk increasing agent	Thickening agent	Drinks
Bread Biscuits Cakes Pastries String hoppers Hoppers Rotti Pasta Noodles Macaroni Godambara rotti	Chocolates (Barley & wheat) Sweets 'kevum' (Oil cakes) Other Coverings with bread crumbs – cutlets To make 'wade' smooth and crusty To make salt adherent on to surfaces like roasted cowpea and gram Grated cheese to prevent clumping	Gravy Soup Curry	Malted milk powder Beer Larger

Gluten enteropathy (Coeliac disease, US spelling – Celiac disease)

Gluten enteropathy is a chronic allergic immunologically mediated inflammatory response affecting the intestinal villi. In health, the villi provide an absorptive surface of the small intestine equivalent to the area of about three football grounds.

Normal villous structure (By courtesy of Science Picture Co.)

The chronic inflammation at the base of the villi in gluten enteropathy causes atrophy and stunting of villi making the intestinal lumen a flat-tube-like structure, thus greatly reducing the area available for absorption of nutrients. This leads to a chronic malabsorption syndrome.



Intestinal lumen of a coeliac. (Loss of villi and mucosal folds with mud cracked appearance). (Copied from Internet Marsh Histology Files)

Gluten enteropathy is mainly a childhood disease usually diagnosed around the age of 8 years, but 20% are diagnosed after the age of sixty years. There is a strong genetic component to this disease. The sufferers should possess the human leukocyte antigen, HLA-DQ2 and HLA-DQ8. Forty percent (40%) of UK population have these two genes but only about 1% of UK population is diagnosed with gluten enteropathy. The condition is prevalent in 10% of first degree relatives. New campaigns and improved awareness

amongst the general population has increased the rate of diagnosis. Five to ten percent of sufferers develop an itchy skin condition called dermatitis herpetiformis and all patients with dermatitis herpetiformis have gluten enteropathy.

It is the alcohol soluble prolamin gliadin which is antigenic in gluten in wheat. The prolamin in barley is hordein, in rye is secalin and some are allergic to prolamin avemin found in some oats. Avoiding gluten in the diet is very difficult as it is almost ubiquitous. Wheat flour is used in many food items either as the main ingredient, additive to thicken gravy and soup, increasing bulk of food items, as an adhesive agent to stick salt to roasted nuts or also as a contaminant.

An interesting research is being carried out in Nottingham University in Australia with hookworms to alter the immune response. (Reference: News Letter of British Coeliac Association October 2015). The initial results showed improved tolerance to gluten. The sufferers would be able to eat food containing gluten for a longer period without developing symptoms. A specific number of hookworm larvae are allowed to enter the skin at the antecubital fossa. The larvae penetrate the skin; enter into lungs via the blood stream. The larvae are swallowed as the phlegm reaches the throat. The larvae develop into adult worms inside the gut.

In Sri Lanka it is uncommon to hear the term gluten enteropathy or coeliac disease. The symptomatology described in the preceding sections of this article is wide-spread amongst the general population and is not considered as abnormal. Some people do complain of bloating, puffiness and reflux after eating bread and hoppers but they presume that increased gas is due to yeast added to make the dough to rise in bread making. It is very likely that these people would be suffering with this chronic condition. Natural hookworm infestation amongst Sri Lankan population could give some tolerance to gluten enteropathy. Better awareness amongst the general population may lead to an increase in the diagnosis of this debilitating chronic condition.

Reference

British Coeliac Association

10 year results of Ahmed glaucoma valve in refractory glaucomas in Asian eyes*

Deven Tuli[1]

The Journal of the College of Ophthalmologists of Sri Lanka 2015; 21: 66

Introduction

Ahmed glaucoma valve (AGV) is a valved glaucoma drainage device (GDD). It is designed to keep the pressure in range 8-12 mmHg. The commonly used model in adults (FP7) is relatively small and therefore fits in between two recti muscles (without dissection into the muscles). Its main limitation is hypertensive phase that results from scarring around base plate on sclera, the duration about 3 months and usually occurs 6 weeks to 6 months of surgery.

Baerveldt implant is the other popular GDD currently. That is a non valved shunt and therefore to prevent hypotony and flat AC requires restricting tube flow for first 4-6 weeks. Resulting, the IOP may remain uncontrolled in first 6 weeks period. Also with bigger size, it needs fitting behind two recti muscles and consequently requires more dissection.

Study

The current synopsis is a summary of AGV implanted in 50 eyes with completed follow up of 10 years. All subjects were of Asian origin mainly SAARC region and middle-east countries.

Eyes with refractory glaucoma underwent AGV implantation. 12 eyes had uncontrolled primary glaucoma with previously failed trabeculectomy. 38 eyes had uncontrolled secondary glaucoma (including neovascular glaucoma, post keratoplasty glaucoma, post vitreo-retinal surgery glaucoma and others).

Results

Mean IOP was 32 mmHg pre AGV implantation (on mean 4.3 medication) that dropped significantly to 12.1 mmHg at 1 year follow up post AGV (on mean 1.2 medication), 12.9 mmHg at 5 year follow up post AGV (on mean 2.3 medication) and 14.2 mmHg at 10 year follow up post AGV (on mean 2.5 medication) (Figure 1).

Vision remained stable or improved in all eyes and importantly no progression of glaucoma was noted. 4 eyes needed supplemental sector limited cyclophoto-coagulation and 2nd AGV was done in 2 eyes.

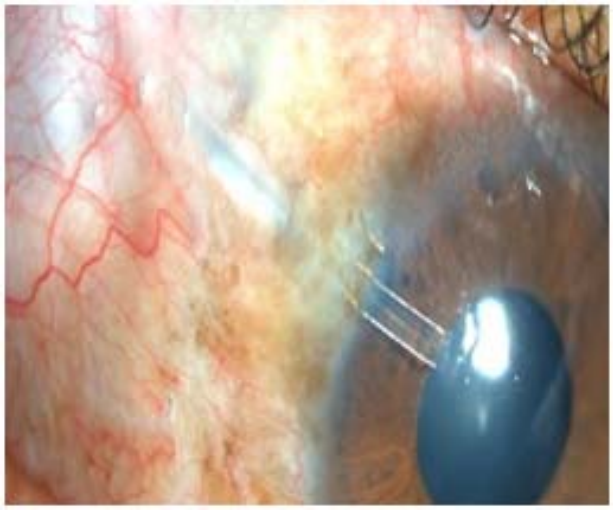


Figure 1. *Showing functional AGV implant at 10 years follow up visit.*

Complications were transient uveitis and hyphema in some eyes and managed appropriately. Silicone oil blocking tube (was aspirated or flushed), transient self limiting choroidal and cataract progression were seen in occasional eyes. More significant were tube exposure in 2 eyes (where scleral flap was fashioned to cover tube; no eye showed exposure in which cadaver sclera was used to cover tube externally).

Conclusion

We have had fairly good results with using AGV in refractory and difficult glaucoma eyes of our region. AGV provides immediate lowering of IOP that is a great asset in uncontrolled glaucoma. Given the resistant nature of the glaucoma in this cohort, supplementing the surgery with upto 1-3 medications is commonly required.

But importantly, we were able to meet target IOP in all eyes even with longer follow up of 10 years and save the optic nerve and prevent glaucoma progression and blindness.

Conflict of interests: Author declared none.

*Synopsis of the speach at COSL Annual Sessions, November 2015.

[1]*Surgical Glaucoma Specialist, New Delhi, India.*

Primary ocular adnexal large B cell lymphoma: A case study

H. K. A. Ruwanchinthani[2], N. Niroshan[1], S. Nanayakkara[3], B. Amarasinghe[4]

The Journal of the College of Ophthalmologists of Sri Lanka 2015; 21: 67-69

Introduction

The incidence of lymphoproliferative ocular diseases, especially malignant lymphoma, has increased over the years that lymphoma is the most common primary malignant orbital tumor in Asian countries like Japan and Korea[1,2,3] as well as in Europe.[4]

Intraocular lymphoma typically affects elderly patients and the incidence of ocular lymphoma increases with advancing age. In a study conducted in the United States, malignant lymphoma was the most common orbital tumor in the elderly age group, accounting for 24% of cases.[6] The median age at presentation for orbital and adnexal lymphoma is older than 60 years.

Case report

A fifty two year old female presented to the Out-patient Department at the National Eye Hospital, Colombo, with a history of slowly growing, reddish lump over the upper-lateral aspect of her left eye for 6 months duration. She denied any history of visual impairment, diplopia or pain. She was a diagnosed patient with Type 2 diabetes mellitus and hypertension for 3 years and was maintaining control with oral hypoglycaemic drugs and anti-hypertensives. She was otherwise healthy.

Her visual acuity was found to be 6/9 in both eyes. She had sub-conjunctival pink fleshy soft tissue mass over the superolateral aspect of the left globe and a less prominent similar lesion over the right globe with diffuse margins. Both lesions were extending post-eriorly into the orbit (Figure 1).

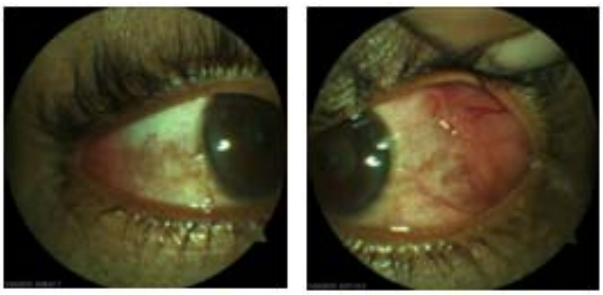


Figure 1. *Pink flesh colour denoted as "salmon-patch" lesions seen on patients' right and left eyes (respectively).*

Full range of extra-occular muscle movements were noted in both eyes. Both fundi appeared normal. There were no palpable lymph nodes, and the rest of the systemic examination was found to be normal, without any evidence of distant metastasis.

The investigations revealed that her ESR was 74 mm in the first hour. But her full blood count was within the normal range and the blood picture had no significant abnormality except for the rouleaux formation.

An incision biopsy was performed in the left sub-conjunctival lesion, which showed reactive lymphoid infiltration. However, as the clinical picture was more suggestive of a lymphoma, a repeat biopsy was performed and further immune-histochemical staining with CD markers was done. The tissue sections showed poly-poid lesions, lining stratified epithelium with under-lying connective tissue stroma showing dense lymphocytic infiltrate (Figure 2). Immune markers CD-3 (20%), CD-20 (80%), Ki-67 were positive. It was compatible with a Large B Cell lymphoma.

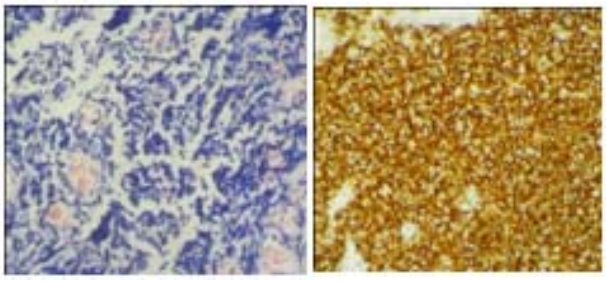


Figure 2. *The tissue sections showing polypoid lesions with dense lymphocytic infiltrate. Immune markers CD-3 (20%), CD-20 (80%), Ki-67 were positive.*

Patient was further investigated in view of excluding central nervous system and systemic involvement. Ultra sound scan of the abdomen was found to be normal except for the fatty liver. The Magnetic Resonance Imaging (MRI) of the brain (Figure 3) showed bilateral orbital involvement with neoplastic involvement of extraocular muscles. Irregular thickening of the extraocular muscles were noted with

[1,2]*Registrar in Opthalmology,* [3]*Consultat Pathologist,* [4]*Consultant Ophthalmologist, National Eye Hospital, Colombo, Sri Lanka.*

relative sparing of left medial rectus and right superior rectus muscles. Intracranial extension of the lesion was noted on right side with superomedial displacement of the optic nerve. No optic nerve compression was noted in MRI. Possible involvement of the lacrimal apparatus was seen bilaterally. Both globes appeared normal. There was no evidence of CNS involvement.

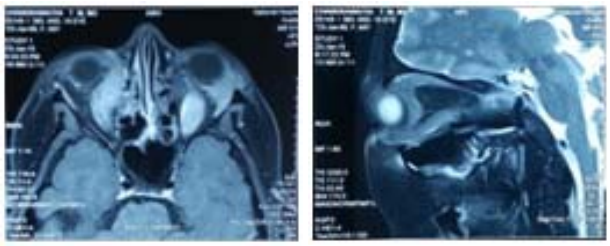


Figure 3. *Brain MRI shows neoplastic involvement of the extra-ocular muscles and intracranial extension of the lesion seen on the right side.*

According to Ann Arbor Staging of Non-Hodgkin's lymphoma, this patient can be classified Stage IIE, as she was having involvement of two or more lymphoid regions on the same side of the diaphragm and localized involvement of an extralymphatic site.

The patient was referred to National Cancer Institute at Maharagama, for oncological assessment and had undergone chemotherapy with six cycles of cyclophosphamide, vincristin and prednisilone and six cycles of rituximab for 6 months duration. A bone marrow biopsy was done, one month after completing the chemotherapy cycles, was found to be normal, and she is awaiting a CT head, neck and chest. Her eye lesion had resolved after chemotherapy.

Discussion

The peak age of presentation of orbital lymphomas had been identified as the sixth and seventh decades of life and the majority of it is non-Hodgkin's lymphomas. In the incidence of most of the subtypes of lymphomas, there is a female predominance, with a female to male ratio of 1.5:1. Early presentation, before the age of 20 is rare, and, in children, orbital leukemic infiltrates are more common than lymphoma.

Lymphoid lesions are commonly seen in superior and anterior aspects of the orbit. Usually, they progress over several months with painless proptosis, with no evidence of conjunctival chemosis or injection. The superior rectus-levator complex is the most commonly involved extra-ocular muscles.[7] Visual impairment is not a commonly recognized symptom while bilateral blindness is rare.[8]

Involvement of the lacrimal gland is seen in 30% of lesions, and they feel rubbery on palpation with a nodular consistency due to the lobular remnants of the gland. Presence of the native lymphocyte populations in the lobules may play a role. Lymphoid lesions of the epibulbar tissues show a characteristic pink fleshy color and are denoted as "salmon-patch" lesions. They are freely mobile and may be isolated or extend posteriorly into the orbit.

Palpable lymphadenopathy, if present, may indicate the presence of systemic disease. Literature reveals that 64% of lesions were found to be in the deep orbit, 28% were subconjunctival, and 8% were in the eyelid.[9]

The differential diagnosis for orbital lymphoma includes idiopathic inflammatory pseudotumor, orbital lymphoid hyperplasia, orbital sarcoidosis, Wegener granulomatosis, and chronic dacryoadenitis.

Lymphomas are thought to occur as the result of an immune-regulatory defect, caused by somatic mutations resulting either in loss of a tumor suppressor gene or in the up-regulation of a proto-oncogene or factor regulating mitosis and differentiation of naive lymphocytes to memory cells and plasma cells.

In a study done by Knowles and Jakobiec revealed that, out of the histological pattern of the primary orbital lymphoid lesions highlighted, 50% of them have been shown to be reactive or with atypical hyperplasia and the rest of the 50% as malignant lymphoma.[10] Of malignant orbital lymphomas, majority of 85% to 90% are diffuse, and only 10% to 15% are follicular and 50% of the diffuse lesions are well differentiated.[10]

Recent evidence, however, has shown that there is a continuous spectrum of disease in terms of prognosis, with systemic disease occurring in 15% to 25% of reactive hyperplasias, 40% of atypical hyperplasias, 20% of well-differentiated lymphomas, and 60% of poorly differentiated lymphomas.[9-15]

Lesions restricted to the orbit is treated with radiation, and they respond rapidly. However though radiotherapy may cause regression of lymphoid hyperplasia, steroids also play little role in treating lymphoid lesions.[16] Cure is not possible with surgical treatments, as lymphoid lesions are diffuse and locally infiltrative.

Regression of disease noted to occur approximately 1 month after completion of radiation therapy. In cases of diffuse large cell orbital lymphoma, chemotherapy generally is used in combination with local radiation. If there is evidence of systemic disease, chemotherapy is the treatment of choice, often in combination with localized radiotherapy. Follow-up of the orbital disease surveillance should be done at 6-month intervals for 2 years after treatment, after which patients

should continue to be followed regularly because of the risk of systemic involvement throughout their lifetime.

Acknowledgements

I wish to convey my heartfelt gratitude to Dr. Y. Ariyaratne, Consultant Onco-Surgeon at the National Cancer Institute, Maharagama, for his oncological management and further care.

References

1. Ioachim HL, Lerner CW, Tapper ML. The lymphoid lesions associated with the acquired immunodeficiency syndrome. *Am J Surg Pathol* 1983; **7**: 543.
2. Levine AM, Meyer PR, Begandy MK, et al. Development of B-cell lymphoma in homosexual men: Clinical and immunologic findings. *Ann Intern Med* 1984; **100**: 7.
3. Ziegler JL, Beckstead JA, Volberding PA, et al. Non Hodgkin's lymphoma in 90 homosexual men: Relation to generalized lymphadenopathy and the acquired immunodeficiency syndrome. *N Engl J Med* 1984; **311**: 565.
4. Sklar J, Cleary ML, Thielemans K, et al. Biclonal B-cell lymphoma. *N Engl J Med* 1984; **311**: 20.
5. Hansen JA, Good RA. Malignant disease of the lymphoid system in immunological perspective. *Hum Pathol* 1974; **5**: 567.
6. Foa R, Pelicci PG, Migone, et al. Analysis of T cell receptor gene rearrangements demonstrates the monoclonal nature of T cell chronic lymphoproliferative disorders. *Blood* 1986; **67**: 247.
7. Hornblass A, Jakobiec FA, Reiffler DM, et al. Orbital lymphoid tumors located predominantly within extraocular muscles. *Ophthalmol* 1987; **94**: 688.
8. Harris GJ. Bilateral blindness due to orbital lymphoma. *Ann Ophthalmol* 1981; **13**: 427.
9. Knowles DM, Jakobiec FA. Lymphoid hyperplasia and malignant lymphoma occurring in the ocular adnexa (orbit, conjunctiva, and eyelids): A prospective multiparametric analysis of 108 cases during 1977 to 1987. *Hum Pathol* 1990; **21**: 959.
10. Knowles DM, Jakobiec FA. Orbital lymphoid neoplasms: A clnicopathologic study of 60 cases. *Cancer* 1980; **46**: 576.
11. Medeiras LJ, Harris NL. Lymphoid infiltrates of the orbit and conjunctiva: A morphologic and immunophenotypic study of 99 cases. *Am J Surg Pathol* 1989; **13**: 459.
12. Cockerham GC, Jakobiec FA. Lymphoproliferative disorders of the ocular adnexa. *Int Ophthalmol Clin* 1997; **37**: 39.
13. Knowles DM, Jakobiec FA. Ocular adnexal lymphoid neoplasms: Clinical, histopathologic, electron microscopic, and immunologic characteristics. *Hum Pathol* 1984; **13**: 148.
14. Jakobiec FA, Knowles DM. An overview of ocular adnexal tumors. *Trans Am Ophthalmol Soc* 1989; **87**: 420, disc 442.
15. Gausas RE, Gonnering RS, Lemker BN et al. Identification of human orbital lymphatics. *Ophthal Plast Reconstr Surg* 1999; **15**: 252.
16. Kennerdell JS: Management of nonspecific inflammatory and lymphoid orbital lesions. *Int Ophthalmol Clin* 1991; **31**: 7.