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Focus and scope

As new technologies and therapeutic interventions are continually being developed, Ophthalmology has become a field of rapid change, particularly in the Asia-Pacific region, where disease patterns and health care delivery differ greatly from those seen in the West. Asian Journal of Ophthalmology was established in 1998 with the aim of disseminating information relevant to Ophthalmology and glaucoma throughout Asia and to interested groups worldwide.

The objectives of Asian Journal of Ophthalmology are as follows:

- To provide a platform for the publication of information with a focus on Ophthalmology in Asia.
- To disseminate information that will improve the care of patients with all types of ophthalmological disorders, with a special focus on glaucoma.
- To increase the understanding of such disorders through reporting of educational activities.
- To publish the results of research programmes to expand knowledge about the causes, prevention, and treatment of ophthalmological disorders.
- To work closely with Asian and international researchers to achieve these aims.
- To provide a forum for young and relatively inexperienced researchers to present their research results as Original Articles via an international platform.
- To maintain and promote relationships with any organization with similar goals.

Although the focus of Asian Journal of Ophthalmology mainly was on glaucoma with close ties to the South-East Asian Glaucoma Interest Group (SEAGIG) in the past, the journal now focuses on the entire spectrum of Ophthalmology. This resulted in collaboration with the Asia Pacific Ophthalmic Trauma Society (APOTS).

The Asian Journal of Ophthalmology and Kugler Publications have started to collaborate since mid 2012 on the publication of the journal. A new website has been launched (www.asjoo.com), which facilitates all aspects of the peer-review and publication process, from manuscript submission to publication.

For further information and manuscript submissions please visit our website: www.asjoo.com.

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Asian Pacific Glaucoma Guidelines 3

The Asia Pacific Glaucoma Society (APGS) is moving ahead with preparation of the 3rd Edition of our popular Glaucoma Guidelines that are distributed and read widely across the Asia-Pacific Region. The last edition (then known as the SEAGIG Guidelines was published 6 years ago), this version was downloaded thousands of times per year since 2003. The APGG are a very important educational tool for the Asia-Pacific region and are widely used.

This latest edition of the Guidelines will be co-chaired by Profs. Aung Tin (Singapore) and Jonathan Crowston (Melbourne). Currently the Working party is researching and preparing the necessary updates.

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Outcomes following orbital decompression surgery for dysthyroid optic neuropathy associated with Graves' ophthalmopathy

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Abstract

Purpose: *To investigate the outcomes of orbital decompression surgery for dysthyroid optic neuropathy associated with severe Graves' ophthalmopathy.*

Design: *Ten years (2000-2010) retrospective case series.*

Methods: *Thirty-eight orbits (with dysthyroid optic neuropathy) of 119 surgical orbital decompressions. Patients with dysthyroid optic neuropathy associated with Graves' ophthalmopathy, who underwent orbital decompression surgery at Sydney Eye Hospital (Sydney, Australia), were investigated for outcome measures.*

Results: *Thirty-five orbits were eligible for data analysis. Orbital decompression surgery improved visual acuity in 29 orbits and maintained visual acuity in four orbits. In patients with dysthyroid optic neuropathy, there was a statistically significant mean improvement in visual acuity of 2.8 lines postoperatively (standard deviation = 3.2; 95% confidence interval 3.9 to 1.7, p-value < 0.05). There were no statistically significant differences in visual acuity amongst different combinations of orbital walls being decompressed, with the majority of orbits had the medial orbital wall decompressed. This may reflect the small number of decompressions performed in each subgroup. Orbital decompression surgery reduced proptosis by a mean of 3.2 mm (standard deviation = 2.9; 95% confidence interval -4.32 to -2.07; p-value < 0.05). Medial and lateral orbital walls decompression resulted in the greatest mean reduction in proptosis. There were no severe visual impairment cases postoperatively (VA worse than 6/60). There were two patients with new onset diplopia postoperatively. There were three orbits with bleeding and one orbit with CSF leakage, all without major sequelae postoperatively.*

Conclusion: *Regardless of surgical access, orbital decompression surgery is effective and safe in the management of dysthyroid optic neuropathy and in reducing proptosis in patients with Graves' ophthalmopathy.*

Key words: *Dysthyroid optic neuropathy, surgical decompression, Graves' ophthalmopathy, visual acuity, Hertel's exophthalmometry, adverse outcomes*

Introduction

Dysthyroid optic neuropathy (DON) occurs in 5-6% of patients with Graves' ophthalmopathy{McNab, 1997 #33}{Leong, 2009 #10},[1] which could be threatening to vision.[2] Systemic glucocorticoids and orbital decompression surgery are

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This study was approved by the Human Research Ethics Committee of the Northern Hospital Network of New South Wales Health, New South Wales, Australia.

the treatment of choice for DON.[2] Orbital decompression surgery usually results in resolution of DON with a relatively acceptable adverse outcomes profile.[2]

Previous studies have demonstrated the efficacy and relative safety of surgical orbital decompression.[3-6] A systematic review recommended reporting of surgical outcomes based on one indication, in order to facilitate future meta-analysis of outcomes.[7]

With this in mind, the present study aims to report main outcome measures which include change in visual acuity, change in proptosis as measured by exophthalmometry measurements and new onset diplopia, after orbital decompression surgery for DON.

Methods

Consecutive patients who underwent orbital decompressions for dysthyroid optic neuropathy at a single tertiary referral centre between January 2000 and December 2010 were retrospectively identified. The decision to operate on individual patients was made by the consultant surgeon in charge, if there were evidence of reduction in vision from baseline, reduction in color vision, presence of afferent pupillary defect and orbital imaging evidence of crowding of the orbital apex. Data was obtained by subsequent review of the medical records.

Patient information recorded included sex, age at the time of surgery, smoking status and thyroid status (thyroid function test). The surgical approach and any complications of surgery were also recorded. The main outcome measures include pre-operative and postoperative best corrected Snellen visual acuity, proptosis measurement using Hertel exophthalmometry (Zeiss, Jena, Germany) and the presence of diplopia. The Snellen visual acuity was converted to the log of the minimum angle of resolution (LogMAR) values in order to perform statistical analysis for visual acuity.[8]

These data were analyzed for change in visual acuity, change in proptosis as measured by exophthalmometry measurements, new onset diplopia and other operative adverse events. The statistical analysis performed included paired T-test verified with the Wilcoxon Signed-Rank test. Subgroup analysis was performed using the two-sample T-test. Results were considered significant if $P \leq 0.05$.

The research questions are:

1. Does orbital decompression surgery preserve and/or improve visual acuity in patients with DON associated with Graves' ophthalmopathy and if so, is there any difference in visual outcome amongst subgroup of orbits (*i.e.*, comparisons of combinations of orbital wall(s) being decompressed)?
2. Does administration of preoperative glucocorticoids influence final visual outcome?
3. Does orbital decompression surgery reduces proptosis in patients with DON associated with Graves' ophthalmopathy and if so, which combination of orbital walls decompression results in the highest amount of reduction in proptosis?
4. What are the adverse outcomes in this cohort of patients?

Results

Over the ten- years study period, there were a total of 119 surgical decompressions for Graves' ophthalmopathy on 69 patients (Fig. 1). Of these, there were a total of 38 orbits of 26 patients for which the indication for surgery was dysthyroid optic neuropathy (Fig 1). Thirty-five orbits were eligible for analysis. Two orbits were excluded due to incomplete visual acuity data. One orbit was excluded as this data was from a subsequent surgery (*i.e.*, the orbit required a second operation due to recurrence of dysthyroid optic neuropathy).

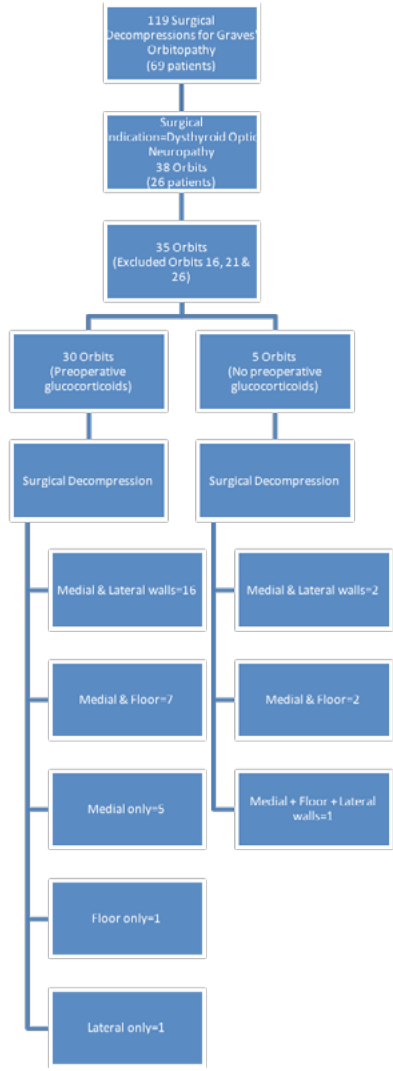

Fig. 1. Illustration of our case series of 35 orbits which underwent orbital decompression surgery for dysthyroid optic neuropathy associated with Graves' ophthalmopathy.

There were 20 female patients (31 orbits) and six male patients (seven orbits). The patients' age ranged from 28 years to 74 years, with an average age of 53.6 years. Fifteen patients had unilateral surgical decompression (16 orbits), one patient requiring repeated surgery on the same side. This patient had repeated surgery on the same side six weeks after the initial surgery due to recurrence of DON whilst steroids were weaned. Eleven patients had bilateral surgical decompressions (22 orbits). Within the bilateral surgical decompressions group, five patients had simultaneous surgery (on the same day) and six patients had sequential surgery (on different days, ranging from five days to three months). The average postoperative follow-up period was 9.9 weeks (range one to 36 weeks).

Preoperatively, the majority of orbits were treated with glucocorticoids (Fig 1). The mean preoperative VA within the group treated with glucocorticoids preoperatively was 0.45 ± 0.51 LogMAR units (Snellen equivalent 6/16.9 ± 5.1 lines). The mean postoperative VA within this group was 0.14 ± 0.30 LogMAR units (Snellen equivalent 6/8.3 ± 3.0 lines). Thus, there was an average improvement of 3.1 ± 3.2 lines of VA. The oral prednisolone therapy was weaned off postoperatively. On the other hand, the mean preoperative VA within the group not treated with glucocorticoids preoperatively was 0.28 ± 0.17 LogMAR units (Snellen equivalent 6/11.4 ± 1.7 lines). The mean postoperative VA within this group was 0.19 ± 0.25 LogMAR units (Snellen equivalent 6/9.3 ± 2.5 lines). Thus, there was an average improvement of 0.9 ± 2.8 lines of VA.

Of the orbits, 73.7% have had two walls decompressed (Table 1).

Table 1. The proportion of orbital decompression surgeries involving different orbital walls.

Orbital walls	Orbital fat	Number of orbits	Percentage of cases	
	Removed	Not Removed		
Medial, Lateral & Floor	0	3	3	7.9%
Medial & Lateral	0	18	18	47.4%
Medial & Floor	5	5	10	26.3%
Medial only	1	4	5	13.2%
Lateral only	0	1	1	2.6%
Floor only	1	0	1	2.6%

Outcomes in visual acuity (after any orbital decompression surgery)

Twenty-nine orbits showed improvement in VA postoperatively (Table 2), 24 out of 29 orbits (83%) with postoperative VA equal to or better than 6/9 . Four orbits had maintained VA postoperatively (6/9; 6/18; 6/6; 6/6), with the majority with VA of 6/9 or better. Two orbits had worsened VA (6/12 to 6/24; 6/5 to 6/6). Three patients (orbits 16, 21 and 26; Fig. 1) were excluded due to aforementioned reasons.

VA will be converted into LogMAR to facilitate comparison and statistical analysis.[8] The LogMAR value will be subsequently converted back to the Snellen equivalent. The mean preoperative visual acuity was 0.43 LogMAR units (standard deviation = 0.48), whereas the mean postoperative visual acuity was 0.15 LogMAR units (standard deviation = 0.29). In Snellen notation, the mean preoperative visual acuity was 6/16 ± 4.8 lines; the mean postoperative visual acuity was 6/8.5 ± 2.9 lines.

Paired T-Test was performed to measure the overall outcome of VA following surgical decompression in DON. In patients with DON, there was a statistically significant mean improvement in VA of 2.8 lines postoperatively (standard deviation = 3.2; 95% confidence interval 3.9 to 1.7, p-value < 0.05). The power ($\alpha = 0.05$) was 0.99. The Wilcoxon Signed-Rank Test confirmed the findings from the Paired T-Test. There was a positive correlation between pre-operative VA and postoperative VA (Correlation Coefficient = 0.75).

Table 2. The outcomes in visual acuity after any type of orbital decompression surgery in this case series.

Outcomes in VA	Number of orbits
Improvement	29
Maintained	4
Worsened	2
Excluded	3
Total	38

Outcomes in VA (comparisons of different surgical techniques)

Two-sample T-test was utilized to compare postoperative VA amongst four comparison groups (Table 3). There were no statistically significant differences amongst these comparison groups.

Table 3. Two-sample T-test results of different comparison groups (outcomes in VA).

Comparison groups	Mean difference (LogMAR units)	Standard deviation	95% Confidence Interval	P-value
Orbital walls				
Medial & Lateral vs. Medial & Floor	-0.07	0.35	-0.35 to 0.21	0.55
Medial & Lateral vs. Medial	0.11	0.38	-0.29 to 0.52	0.57
Medial & Floor vs. Medial	0.18	0.27	-0.14 to 0.50	0.24
Orbital fat				
Orbital fat excision (n = 5) vs. No orbital fat excision (n = 5)	**-0.22**	**0.21**	-0.52 to 0.08	0.13

Outcomes in proptosis (after any orbital decompression surgery)

Using the Paired T-Test, there was a statistically significant mean reduction in proptosis of 3.2 mm after orbital decompression surgery (standard deviation = 2.9; 95% confidence interval -4.32 to -2.07; p-value < 0.05). The power ($\alpha = 0.05$) was 0.99. The Wilcoxon Signed-Rank Test confirmed the findings from the Paired T-Test. There was a positive correlation between pre-operative proptosis and postoperative proptosis (Correlation Coefficient = 0.70).

Outcomes in proptosis (comparisons of different surgical techniques)

Medial and lateral orbital walls decompression resulted in mean reduction of 3.9 mm in proptosis postoperatively, whereas medial wall and floor decompression resulted in mean reduction of 1.1 mm in proptosis postoperatively (Table 4). This is likely associated with incorporating the lateral orbital wall during decompression.

Using the Two-sample T-test, there was a statistically significant difference between these two subgroups (mean difference = -2.81; P-value < 0.05) (Table 5). There was no statistically significant difference between orbital fat excision and no orbital fat excision (mean difference = -0.73; P-value = 0.40) (Table 5).

Table 4. Orbital decompression surgeries involving different orbital walls and the outcomes in proptosis.

Orbital walls	Number of orbits	Mean change in proptosis postoperatively (mm)	Range	Standard deviation	95% Confidence Interval
Medial & Lateral	18	-3.9	-11.0 to 1.0	3.2	-5.66 to -2.21
Medial & Floor	10	-1.1	-2.5 to 1.0	1.1	-2.04 to -0.21

Table 5. Two-sample T-test results of different comparison groups (outcomes in proptosis).

Comparison groups	Mean difference	Standard deviation	95% Confidence interval	P-value	Power (α = 0.05)
Orbital walls **Medial & Lateral vs. Medial & Floor**	-2.81	3.41	-4.68 to -0.94	< 0.05	0.85
Orbital fat **Orbital fat excision (n = 5) vs. No orbital fat excision (n = 3)**	-0.73	1.11	-2.71 to 1.25	0.40	

Adverse outcomes

There were no severe visual impairment cases postoperatively (VA worse than 6/60) (9). There were also no cases of stroke postoperatively. There were two patients with new onset diplopia postoperatively. No patients within this cohort had pre-operative diplopia. There were three orbits which had bleeding (7.9%) and one orbit which had cerebrospinal fluid (CSF) leakage (2.6%), all without major sequelae postoperatively.

Discussion

Graves' ophthalmopathy may be thought of as a heterogeneous autoimmune orbital reaction, characterized by the presence of thyroid stimulating immunoglobulins (TSIgG), typically affecting patients of middle ages.[10] Risk factors associated with severe forms of Graves' ophthalmopathy include genetic,[11] increasing age,[12] male sex[13] and high levels of thyrotropin receptor autoantibodies.[14] Cigarette smoking can affect the response to treatment (steroids and orbital irradiation) in a dose-dependent fashion.[15] Orbital decompression surgery may be considered when medical decompression has failed to relieve dysthyroid optic neuropathy associated with severe Graves' ophthalmopathy. Wakelkamp et al suggested that

in severe Graves' ophthalmopathy with compressive optic neuropathy, immediate orbital decompression surgery does not appear to result in better outcomes and therefore recommended immediate high doses of systemic glucocorticoids therapy.[3] Urgent orbital decompression surgery is considered if immunosuppressive therapy has failed to halt the progression of Graves' ophthalmopathy.[10] Urgent orbital decompression is considered on the basis of several important parameters including VA reduction, contrast sensitivity reduction, significant colour vision loss, pupil function and orbital imaging (looking for evidence of loss of fat effacement in the posterior orbit with significant extraocular muscles enlargement).

The surgical approaches were chosen pre-operatively and this may introduce bias in the analysis of outcomes. The chosen surgical approaches may be influenced by surgeons' preferences, orbital anatomy (assessed pre-operatively by imaging), visual acuity, amount of proptosis and anticipated complications (including new onset diplopia).

VA outcomes

Orbital decompression surgery is effective in improving VA postoperatively. In our study, the majority of orbits had improved VA postoperatively and this was similar to previous report in the literature.[16,17] In our cohort of patients with DON, there was a statistically significant mean improvement in VA after orbital decompression surgery. Goh and McNab also reported significant improvement in median VA postoperatively in orbits with DON.[5]

There were no statistically significant differences amongst Medial & Lateral orbital walls decompression, Medial orbital wall & Floor decompression and Medial orbital wall decompression subgroups. Of note, all three groups had the medial orbital wall decompressed. In this case series, surgical access to the medial orbital wall is predominantly transcaruncular, with the remainder via endoscopic and cutaneous methods. We suggest that the medial orbital wall should be decompressed in orbits with DON, as this creates space for decompression of the optic nerve located at the postero-medial orbit. Cruz and Leme reported similar rate of reversal of optic neuropathy in both the inferomedial transfornix/transcaruncular approach and inferomedial plus lateral coronal approach.[18] McNab also suggested that in patients with DON, the method of surgical decompression did not influence visual acuity.[4] {McNab, 1997 #33}{McNab, 1997 #33}{McNab, 1997 #33}{McNab, 1997 #33}In our study, there was no statistically significant difference between orbital fat and no orbital fat excision within the Medial orbital wall & Floor decompression subgroup (in relation to postoperative VA). Kazim *et al.* reported orbital fat decompression was successfully performed in eight orbits to reverse dysthyroid optic neuropathy.[19]

Glucocorticoids may have influenced the final visual outcome in patients who underwent orbital decompression surgery for CON. It should be noted that the group pretreated with glucocorticoids had worse mean preoperative VA compared to the group not pretreated with glucocorticoids. Therefore, perhaps within this cohort of patients with more severe CON, the surgeon might have prescribed preoperative glucocorticoids.

Proptosis outcomes

Shepard *et al*. reported a mean improvement of proptosis by 4.9 mm in patients who had compressive optic neuropathy who underwent medial and extended lateral wall decompressions.[20] In our study, it appears that the mean reduction in proptosis was greater for the Medial & Lateral orbital walls decompression subgroup (3.9 mm) compared to that of the Medial orbital wall & Floor decompression subgroup (1.1 mm), with statistical significance (P-value < 0.05). These results suggest that incorporating the lateral orbital wall may result in higher reduction in proptosis. There was no statistically significant difference between orbital fat and no orbital fat excision within the Medial orbital wall & Floor decompression subgroup (in relation to postoperative proptosis). Adenis *et al*. reported a mean reduction in proptosis of 4.7 mm (standard deviation = 2.4) using the trans-septal approach to extraconal and intraconal fat excision.[21]

Adverse outcomes

As previously mentioned, there were no cases of severe visual impairment (VA worse than 6/60). There were two patients with new onset diplopia postoperatively. Patient 1 had bilateral sequential orbital decompressions involving the medial and lateral walls. Subsequent bilateral medical rectus recession resulted in improvement in the diplopia. Patient 2 underwent bilateral sequential orbital decompressions involving the medial and floor (with orbital fat removal). This patient had persistent diplopia at six months postoperatively. Graham *et al*. reported a 10% rate of occurrence of new-onset diplopia in patients who had Medial & Lateral orbital walls decompression surgery.[22] There were three orbits which had self-resolving bleeding. The first orbit developed postoperative bleeding associated with fat resection after Medial orbital wall & Floor decompression surgery.

The second orbit developed postoperative bleeding after Medial & Lateral orbital walls decompression (no orbital fat excision). The patient has a history of hypertension (treated) and had labile blood pressure levels both intra-operatively and during recovery. Immediate exploration and drainage of hematoma occurred and there was no visual loss postoperatively. The third orbit developed perioperative ethmoidal bleeding during Medial orbital wall & Floor decompression (with orbital fat excision), which resolved spontaneously. The patient's VA improved from 6/12 to 6/6 postoperatively. Lund *et al.* reported three cases of moderate bleeding occurring out of 20 cases who underwent orbital decompression surgery by the external Patterson approach, all of which had resolved without any major issues.[23] There was one orbit which had CSF leakage during Medial & Lateral orbital walls decompression surgery (no orbital fat excision). During the Lateral orbital wall decompression, the bone was removed with a drill and the temporal fossa was opened postero-laterally. CSF leakage was seen from the postero-lateral wall and was controlled with a fat plug, without significant complications. The patient had a successful orbital decompression otherwise, with VA improved from 6/12 to 6/6 postoperatively. Graham *et al.* also had two cases of CSF leak which were repaired intra-operatively without further complications.[22]

Future research may include comparing outcomes of patients who had received medical intervention (high dose glucocorticoids) alone versus medical and surgical interventions, preferably with a prospective study design and with sufficient power to show a difference between the two groups.

Conclusion

Our series of 35 orbits supports the established surgical approach of orbital decompression in sight threatening cases of dysthyroid compressive optic neuropathy. In most orbits, preoperative glucocorticoids were prescribed. Visual improvement occurred in the majority of cases. We further demonstrate that complications occurred rather uncommonly and when they do occur, they are usually self-limiting. Balanced medial and lateral orbital walls decompression demonstrate a greater reduction in proptosis compared to other techniques.

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Cryo-compression of sclerotomy sites after transconjunctival sutureless vitrectomy*

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This study was presented at the 108th annual meeting of KOS in Ilsan, Korea, on November 2-4, 2012.

Abstract:

Purpose: *Transconjunctival sutureless vitrectomy(TSV) has become more commonly performed, but the incidence of sclerotomy site leakage is becoming an issue. We have developed a new and easy sclerotomy closure technique using cryotherapy, and named it 'cryo-compression'.*

Methods: *After the removal of the cannula, sclerotomy sites' cryotherapy was performed with the setting of one cryospot for each site and ten seconds for each spot. After cryotherapy, firm pressure was maintained for more than 30 seconds. Immediately after compression, when any degree of leakage was detected, a single transconjunctival suture with 8-0 vicryl was placed. Postoperatively, topical steroid and antibiotics eyedrops were administrated.*

Results: *Sixteen patients undergoing 23-gauge vitrectomy with this technique were reviewed retrospectively. The postoperative one- and six-hour intraocular pressures (IOPs) were significantly lower than preoperative IOP, but postoperative one-day and one-week IOPs were not different from preoperative IOP. Incidence of hypotony was 12.5% (N = 2/16 eyes) at only one hour but all eyes recovered. Intraoperative suture at sclerotomy sites was placed in eight of the 48 sclerotomies(16.7%) and suture placement was not required postoperatively. No cases of severe intraocular inflammation or endophthalmitis were indentified.*

Conclusions: *Our short-term results are fairly respectable, so we think that the 'Cryo-compression' technique is helpful to obtain sclerotomy closure in TSV.*

Keywords: *Cryocompression, sclerotomy, transconjunctial sutureless vitrectomy*

Introduction

Since the small-gauge vitrectomy had been introduced by Fujii *et al*.[1] and Eckardt,[2] transconjunctival sutureless vitrectomy (TSV) became the standard vitrectomy technique in many retinal surgeries. Conventional 20-gauge pars plana vitrectomy (PPV) had been shown to have some suture material-related complications, such as postoperative inflammation or prolonged patient discomfort, but TSV has overcome these problems by self-sealing small-diameter sclerotomies.[3]

However, disadvantages such as postoperative hypotony, conjunctival bleb formation are attributed to poor sclera closure. With the advent of TSV, it has been

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postulated that the risk of choroidal detachment and endophthalmitis may be increased compared with that of conventional 20-gauge PPV.[4-7]

In case of leaking sclerotomies, many surgeons put in a transconjunctival or transscleral suture. Alternative skills to avoid leaking wounds were use of tissue glue,[8] a polyethylene glycol–based hydrogel bandage[9] or transconjunctival plain gut 'tape'.[10] But all of these techniques add cost or are still under investigation. Therefore, we propose another easy surgical technique to obtain sclerotomy closure.

Materials and methods

Patients who received a 23-gauge sutureless vitrectomy during the period between May 2012 and February 2013 were included, but excluded from the study if they had any past history of a PPV. The patients who needed the combined buckling procedure, silicone oil injection, gas injection or phacoemulsification were also excluded from the study. These patients were followed for at least one month after the operation. The potential benefits and possible risks of the technique were explained to the patients, and informed consent was obtained.

We have used technique in all cases with Total Plus 23Ga Vitrectomy Pak® (Alcon Laboratories Inc, Fort Worth, Texas, USA). Three transconjunctival sclerotomies were made parallel to the limbus using a two-step beveled approach. A total vitrectomy was done using a visualizing agent such as triamcinolone with external scleral depressor. At the end of surgery, microcannulas were withdrawn using a forceps, following the angled entry path. And then firm pressure were applied with a cryoprobe onto the sclerotomy sites. Cryostar® (D.O.R.C. International BV, Zuidland, The Netherlands) that we have used had a curved retinal probe with small, hard and round tip(2.5 mm) for conventional retinal reattachment surgery. In case of control group, after microcannula removal, firm pressure was applied with a cotton-tip applicator instead of a cryoprobe.

Sclerotomy sites' cryotherapy was performed with the setting of one cryospot for each site and 10 seconds for each spot. After cryotherapy, firm pressure was maintained for more than 30 seconds (Fig. 1). Immediately after compression, most sclerotomy sites turned concave and no significant leaking signs such as conjunctival bleb were observed (Fig. 2). A few seconds later, concave wounds were *defrosted* and became flat. When any degree of leakage was detected, a single transconjunctival suture with 8-0 vicryl was placed. Postoperatively, topical steroid and antibiotics eyedrops were administrated. To identify early postoperative hypotony(intraocular pressure, IOP ≤ 5 mmHg), we checked IOPs postoperatively. Number of intraoperative or postoperative sclerotomy sutures was collected and any complications related to sclerotomy leakage were noted.

Postoperative IOPs were compared with preoperative IOPs using Mann-Whitney test. P values of < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS for Windows (Ver. 15.0, Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL).

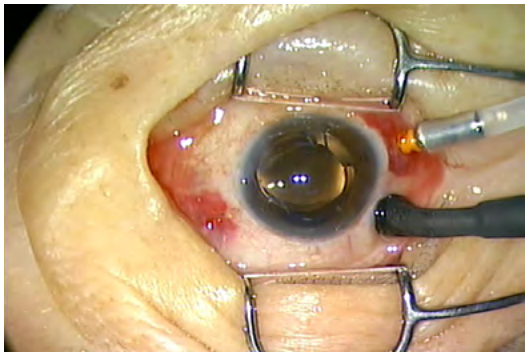

Fig. 1. External photograph of 'Cryo-compression' technique, being performed onto the sclerotomy site after cannula removal.

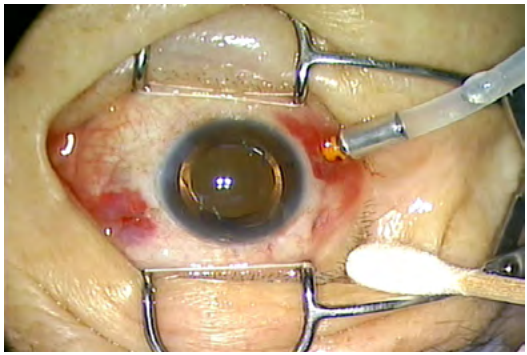

Fig. 2. Immediately after compression, the sclerotomy sites turned concave and no wound leakage was detected.

Results

16 patients undergoing 23-gauge vitrectomy with this technique were reviewed retrospectively, and 15 patients with a cotton-tip applicator were reviewed as a control group. Surgeries were performed by a single surgeon(Ho Young Lee) at a single hospital. The demographics and clinical data of the patients are shown in Table 1.

Intraocular pressures before and after operation are shown in Figure 3. In cryo-compression group, the mean postoperative IOPs at 1 and 6 hours were significantly lower than preoperative IOP. Whereas, in control group, the 1, 6 hour, and 1 day IOPs were significantly lower than preoperative IOP. 1 week and 1 month IOPs were not different from preoperative IOP. So, cryo-compression group eyes were recovered earlier than control group eyes.

Incidences of postoperative hypotony (IOP ≤ 5 mmHg) at 1 and 6 hours, 1 day, 1 week, and 1 month after 23-gauge TSV are illustrated in Figure 4. In cryo-compression group, the incidence of hypotony was 12.5%(N = 2/16 eyes) at only 1 hour and all eyes recovered. But, in control group, the incidence of hypotony was 26.7% at 1 hour (N = 4/15 eyes), 13.3% at 6 hours (N = 2/15 eyes, 6.7% at 1 day (N = 1/15 eyes), and 0% at 1 week and 1 month post-TSV. All eyes with hypotony during the early postoperative period recovered normal IOP at 1 week post-TSV without postoperative suture placement.

The intraoperative and postoperative complications are summarized in Table 2. In cryo-compression group, intraoperative suture at sclerotomy site was placed in 8 of the 48 sclerotomies(16.7%) and suture placement was not required postoperatively. In control group, suture placement was performed in 8 of the 45 scleotomies(17.8%) and no postoperative suture placement was done. Suture placement rate was similar between two groups. In cryo-compression group, one choroidal detachment case was detected but recovered as soon as intraocular pressure was elevated. No cases of severe intraocular inflammation, endophthalmitis or retinal detachment were indentified.

Table 1. Clinical features of cases.

	Cryo-compression group (n = 16)	Control group (n = 15)
Sex (Male : Female)	10 : 6	8 : 7
Age at operation(mean ± SD, year)	55.8 ± 12.05	57.5 ± 17.05
Laterality (OD : OS)	10 : 6	10 : 5
Surgical Indications for PPV		
Vitreous hemorrhage/opacity	6	12
IOL dislocation	7	2
Crystalline lens dislocation	3	1

Table 2. Intraoperative and postoperative complications.

Complications	Cryo-compression group (n = 16)	Control group (n = 15)
Intraoperative suture placement at sclerotomies	8 (8/48, 16.7 %)	8 (8/45, 17.8 %)
Postoperative suture placement at sclerotomies	0	0
Choroidal detachment	1	0
Retinal detachment	0	0
Endophthalmitis	0	0
Vitreous hemorrhage/opacity	0	0
Severe chamber reaction	0	0

Discussion

Making a good beveled incision, such as two-step technique and applying firm pressure onto the seclerotomy sites immediately after cannula removal were key points for tight wound closure in a small-gauge vitrectomy system.[11]

Many retinal surgeons use a cotton-tip applicator to apply firm pressure onto the sclerotomy sites soon after the removal of the cannulas. But a cotton-tip applicator has a little bit soft and large end so it often cannot seal the sclerotomy sites properly. Besides a few strands of cotton may enter the subconjuctival space.

Woo *et al.*[12] recently reported, in a retrospective study including 322 eyes of 292 patients who underwent 23-gauge TSV, that intraoperative suture placement was required for leaking sclerotomies in 36 cases (11.2%) and the incidences of postoperative hypotony were 11.3% at 2 hours, 6.5% at 5 hours, 3.8% at 1 day, and 0% at 1 week. They used a cotton-tip applicator.

Cryotherapy is very popular method to create a chorioretinal adhesion during retinal detachment surgery. During freezing, extracellular and intracellular ice crystal forms, thereby causing mechanical effect and cellular damage. And during thawing, water and electrolytes separate, causing dissolution of cellular membrane. This effect results in the choroidal and retinal scar.[13]

Some retinal surgeons use cryotherapy for other purposes. Yeh *et al.*[14] concluded that cryotherapy of the sclerotomy sites might be a helpful adjunct procedure in diabetic vitrectomy for inhibition of fibrovascular ingrowth, and hence prevention of recurrent vitreous hemorrhage. Their operative technique was a standard 3-port 20-gauge PPV and sclerotomy sites' cryotherapy was performed with the setting of 2 cryospots for each site and 6 seconds for each spot. As their results, there was no significant complication, such as postoperative inflammation reaction. So we decided to apply cryotherapy to seal the sclerotomy sites of TSV. Since the tip of the cryoprobe was harder and smaller than that of the cotton-tip applicator, we thought we could use a cryoprobe instead of a cotton-tip applicator, and finally found out ways to seal the sclerotomy sites with cryotherapy. Moreover only 3 cryospots that we applied were less than their methods.

At first, cryotherapy was performed in the same way that Yeh *et al.*[14] had described, but the setting of cryospot was modified after many trials and errors. In some cases that was applied only cryotherapy shortly without firm pressure, wound leakage was happened several times. So we performed cryotherapy much longer and maintained pressure on the wound sites much harder. After that procedure, we found that small concave-shaped sclerotomy sites meant good surgical wound integrity. That is the reason why we named this technique "cryo-compression" not just cryotherapy.

The technique that we introduce shows several advantages as compared with other methods. Most of all, it can reduce suture-related problems, such as postoperative inflammation, patient discomfort, and delayed visual recovery. In case of leakage after "cryo-compression", placing a single suture is very easy because the wound is compressed. And this technique makes the cost of surgery less than that of cases of suture placement, tissue glue, and a polyethylene glycol–based hydrogel bandage. Moreover, cyrotherapy and cryoprobe are familiar with retinal surgeons, so this technique is very easy to perform.

Our reasons for the sclerotomy sites' cryo-compression were described as below. First, a cryoprobe with a small and hard tip is good for applying firm pressure, so we can use instead of a cotton-tip applicator. Second, freezing just inside and outside the surgical wound by cryotherapy helps to prevent wound leakage. Even though the ice crystal melts into water soon, if firm pressure is applied onto the beveled sclerotomy wound, we expect freezing procedure to fill a small space around the conjunctival and scleral wound. Third, as a delayed effect of cryotherapy, cryo-compression can cause focal scar formation of the pars plana without shrinkage or other damage to the sclera. It is a well-known fact that cryotherapy has little effect on the vitreous and sclera.[15,16]

In our study, intraoperative sclerotomy suture rate was 16.7%(8/48), relatively higher than that reported by Woo *et al.*[12] (11.2%). But the incidence of postoperative hypotony(12.5%, 2/16 eyes at only 1 hour) was lower than their results. Because this study is non-randomized and has small number of subjects, our results can't be directly compared with theirs. Furthermore, there is another limitation that long-term results are lacking. But to our knowledge, this is the first report to describe "cryo-compression" technique for 23-gauge sclerotomy closure in TSV. So we think "cryo-compression" is worth attempting and it can be seen as a useful technique to obtain sclerotmy closure.

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Keratoconus associated with cone-rod dystrophy

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Abstract: *Keratoconus is known to be associated with a variety of ocular and systemic disorders. The common posterior segment disorders known to be associated with keratoconus are retinitis pigmentosa, macular coloboma, Leber's congenital amaurosis, retinal aplasia and retrolental fibroplasias.*[1-3] *Occurrences of keratoconus in association with tapetoretinal degeneration is rare and has been reported infrequently.*[4-5] *Visualization of the fundus is often difficult in cases of keratoconus due to the associated refractive error and corneal opacities. This may make it difficult for the ophthalmologist to clinically diagnose associated macular degenerative changes preoperatively. We report a case of keratoconus who was diagnosed to have cone-rod dystrophy following successful corneal transplantation.*

Key words: *Keratoconus, bull's eye maculopathy, retinitis pigmentosa, electroretinogram*

Case report

A 29-year-old man presented to the outpatient clinic with complaints of sudden painless decrease of vision, associated with watering in the right eye for the past one month. There was no history of any recent trauma. The patient was a known high myope since 15 years and a contact lens wearer for the last ten years. On examination, his best corrected visual acuity in the right eye was counting fingers at one meter and 20/200 in left eye. Slit lamp biomicroscopy of both eyes revealed features suggestive of advanced keratoconus, with acute hydrops in the both eye (right more than left eye). Fundus examination through the hazy cornea revealed pigmentary changes at the macula in both eyes.

Following medical management of the hydrops in the right eye, best corrected visual acuity with contact lens did not improve beyond 20/200. He underwent corneal transplantation in the right eye one year later. Postoperatively, despite a clear graft (Fig. 1), his best corrected visual acuity in the right eye did not improve beyond 20/120. Keratometry readings in the right eye were 48.25 x 128 deg/44.12 X 38 deg. Fundus examination of both eyes revealed minimal temporal pallor of optic disc associated with pigmentary changes at the macula giving the appearance of bull's eye maculopathy (Fig. 2). An electroretinogram of both the eyes was done. Grossly delayed implicit time with reduced amplitudes of the rod response and extinguished cone waveforms were noted, indicating cone rod dystrophy (Fig. 3). Color blindness was also noted with the Ishihara's pseudoisochromatic color plates. Genetic counseling revealed it to be an isolated defect with negative family history.

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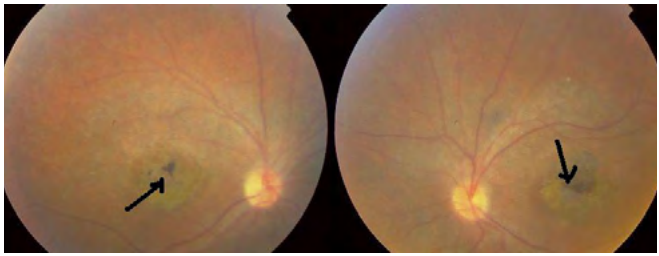

Fig. 1. Slit-lamp photograph of left eye showing healed acute hydrops (arrow) and clear corneal graft post PKP (right eye).

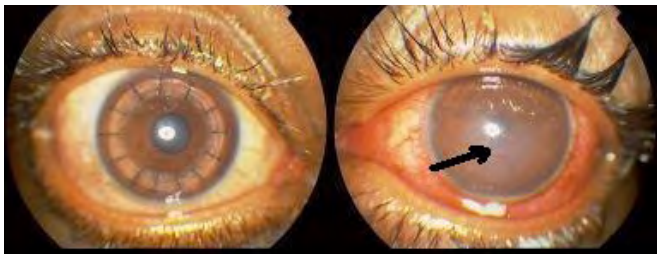

Fig. 2. Fundus photograph of the both eyes with Bull's eye maculopathy(arrow) and minimal temporal pallor.

Discussion

A correlation between keratoconus and tapetoretinal degeneration has been reported by Moschos and coworkers.[4] Progressive cone dystrophy in association with keratoconus has also been reported in a 33 year old woman.[5] Coexistence of these two conditions, especially photoreceptor dysfunction, has prognostic implications on the outcome of corneal transplantation in these cases. High refractive error and corneal opacities in keratoconus may often prevent visualization of the fundus. In our case a clear view of the fundus was not possible due to the corneal scarring which occurred following resolution of corneal hydrops. However, following corneal transplantation, it was possible to make a clinical diagnosis of bull's eye maculopathy, which was confirmed to be cone rod dystrophy on electro physiologic study.

Preoperative electro physiologic studies have been advised to evaluate retinal photoreceptor function, when a clear view of the fundus is not possible. Moschos and coworkers recommend avoiding corneal transplantation if electro physiologic studies show an abnormal response as it indicates photoreceptor dysfunction, usually associated with poor visual potential.[4]

Although corneal transplantation has not been advocated for patients of keratoconus with tapetoretinal degeneration, it may improve the quality of vision in these patients if not the absolute visual acuity, as was noted in our patient. After explaining the nature of disease and the visual outcome of corneal transplantation, our patient is now awaiting corneal transplantation in the left eye. Our case also strengthens the association between keratoconus and cone rod dystrophy. Hence it is essential to perform preoperative electro physiologic studies to evaluate the retinal activity and possible visual outcome, in patients with keratoconus associated with corneal opacity, which precludes a detailed fundus examination preoperatively.

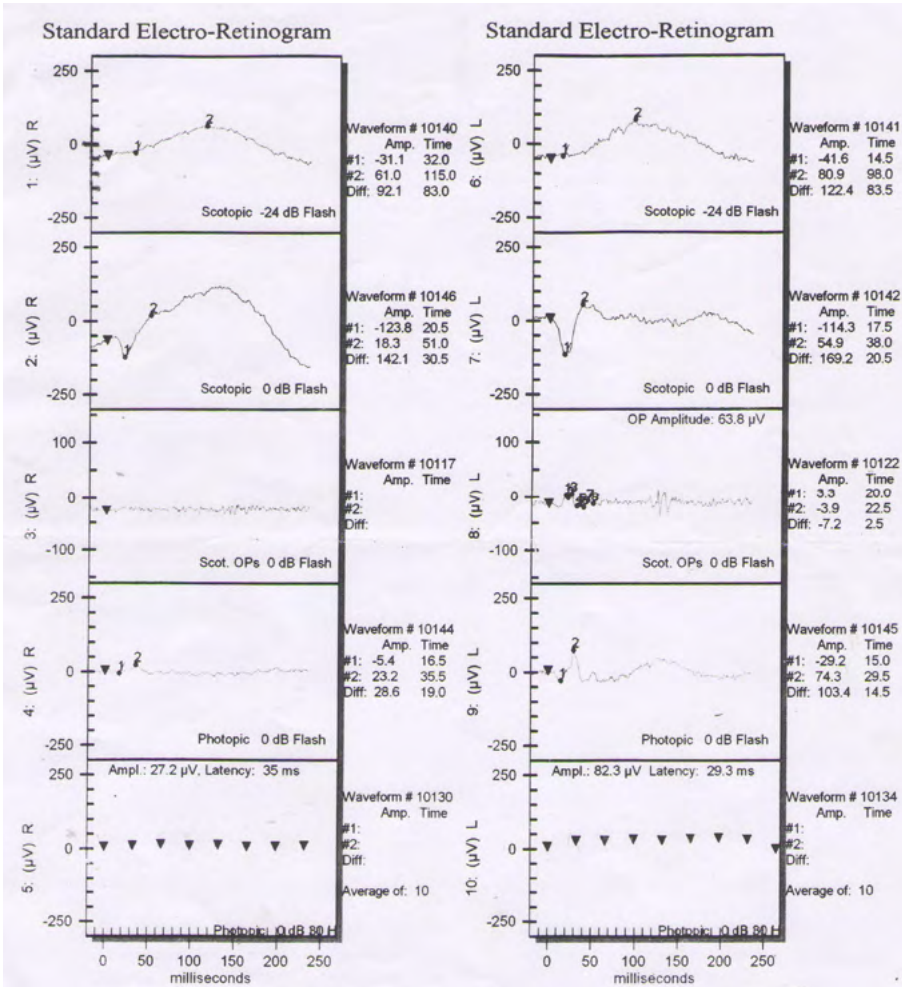

Fig. 3. ERG showing abnormal waveforms. Scotopic/blue flash-showing reduced amplitude and delayed implicit time in both eyes. Photopic/30Hz showing extinguished waveforms in both eyes.

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Embolization of dural carotid cavernous fistula via the superior ophthalmic vein approach

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Abstract: *In this case report, we present a patient with Type B dural carotid-cavernous fistula (CCF), who had failed cannulation via the transfemoral route and subsequently underwent CCF occlusion via the anterior orbital approach through the superior ophthalmic vein (SOV). Successful occlusion of CCF was achieved, with excellent visual and cosmetic outcomes postoperatively. When all venous routes have been exhausted, the SOV approach is an excellent and viable alternative in the treatment of dural CCFs. Close cooperation between the orbital and neuro-interventional teams in a hybrid operating theatre setting is essential in ensuring success of the operation.*

Key words: *Carotid cavernous sinus fistula, hybrid operating theatre, superior ophthalmic vein, cavernous sinus coiling*

Introduction

Carotid cavernous fistula (CCF) is an abnormal vascular shunt, which connects the intracranial carotid artery and cavernous sinus. With the advancement of liquid embolic agents[1] and metallic coils,[3] endovascular obliteration is now the treatment modality of choice for closure of CCFs. The transvenous approach is recommended for indirect CCF closure, and this is conventionally achieved transfemorally via the inferior petrosal sinus (IPS). If the IPS is inaccessible due to occlusion or lack of visualization, the cavernous sinus may be approached via the facial vein. However, this method is often unsuccessful due to tortuosity of the facial venous system. When all venous routes have been exhausted, surgical exposure and direct cannulation of the superior ophthalmic vein (SOV) is an excellent alternative to access the cavernous sinus, with good results and minimal complications reported in previous studies.[3] In this case report we present a patient with Type B dural CCF, who was treated successfully using the SOV approach.

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Case report

A 47-year-old Malay lady with a past medical history of diabetes and hypertension presented with a six-month history of left eye prominence, associated with pain, swelling, tearing, retro-orbital headache and intermittent diplopia (Fig. 1).

Fig. 1. Mild proptosis (4 mm) and eyelid edema of the left eye at presentation.

A CT-scan (Fig. 2A) and MRI (Fig. 2B) revealed a dilated superior ophthalmic vein and enlarged extraocular muscles in the left eye. Preoperative intracranial angiogram showed a Type B dural CCF supplied by many fine feeder vessels from the internal carotid circulation (Fig. 3). Conservative management did not relieve her symptoms of pressure and discomfort behind the left eye and headaches even after six months. An attempted closure of her CCF via the transfemoral approach was unsuccessful resulting in referral to the Orbit and Oculofacial Service.

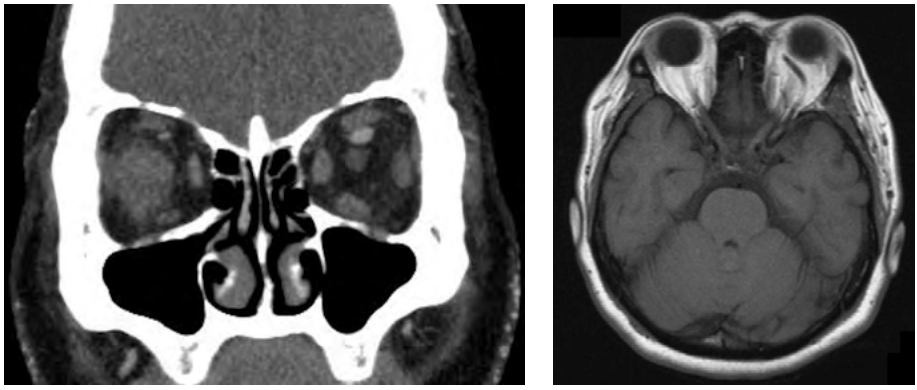

Fig. 2A(left) & 2B(right). Pre-operative imaging revealed a dilated superior ophthalmic vein and enlarged extra-ocular muscles in the left orbit. (2A) CT scan (2B) MRI (axial view).

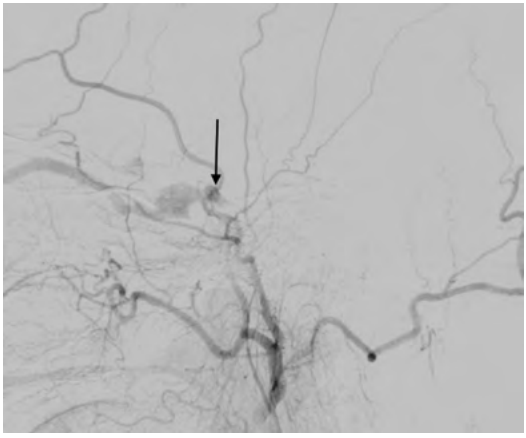

Fig. 3. Pre-operative intracranial angiogram showed a left dural CCF, supplied by many fine feeder vessels from the internal carotid circulation.

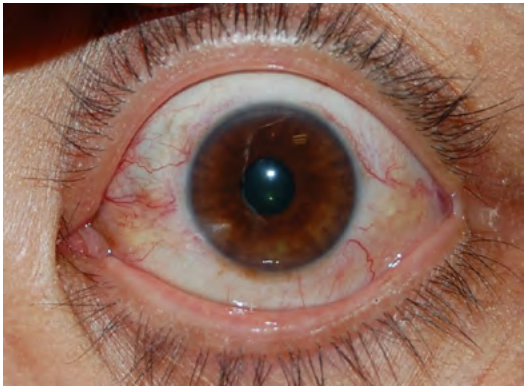

Fig. 4. Left eye demonstrating tortuous corkscrew-type conjunctival blood vessels

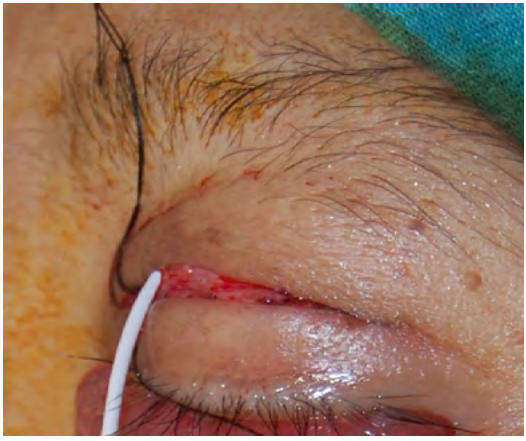

Fig. 5. Intra-operative photograph demonstrating the superior ophthalmic vein cannulation.

On examination, tortuous corkscrew-type blood vessels were seen in her left eye (Fig. 4). Best-corrected visual acuity (BCVA) was 6/6 bilaterally. Ocular motility was full in the right eye (OD), and there was mild global limitation in the left eye (OS). Pupillary reaction was sluggish, with a grade-2 relative afferent pupillary defect (RAPD) and proptosis of 4 mm in the left eye. Confrontational and static, automated visual field testing and color vision was normal. Intraocular pressure (IOP) was 14 mmHg (OD) and 21 mmHg (OS). Fundus examination was normal in the right eye, and showed dilated retinal veins in the left eye. After obtaining informed consent, she underwent a left anterior superior orbitotomy through an upper eyelid crease incision, in a Hybrid Operating Theatre under general anesthesia. The orbital septum was opened and dissection and exploration performed to identify the dilated SOV, which was then cannulated with a 4Fr Angiocatheter (Fig. 5). After confirmation of patency by intra-operative angiography, CCF obliteration was carried out using detachable HyperSoft neuro-coils (Microvention). Once adequate closure of the fistula was confirmed by angiography (Fig. 6A, 6B), the catheter was withdrawn and the wound closed. Postoperatively, she recovered well. BCVA was 6/6 bilaterally, with restoration of full ocular motility, no RAPD and normal color vision. In addition, IOP was normal and her proptosis resolved completely.

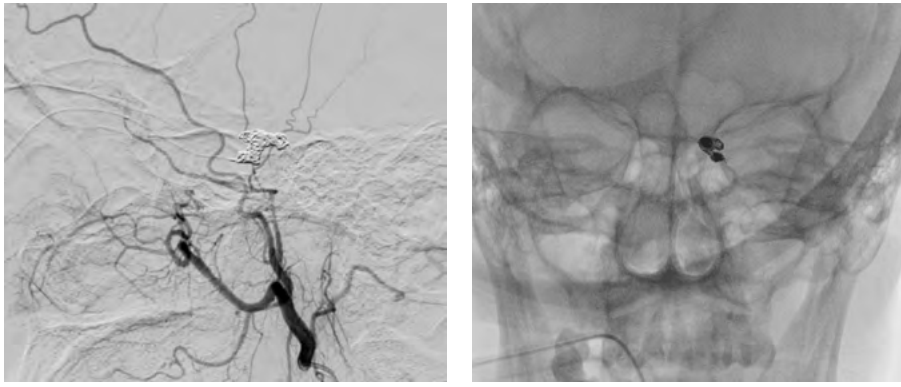

Fig. 6A(left) & 6B(right). Postoperative angiogram revealed successful obliteration of CCF by coiling (A) Lateral view; (B) Anterior view.

Discussion

CCFs may be anatomically and hemodynamically classified into four types based on the Barrow classification.[4] Type A CCFs are direct, high-flow lesions, which result from a direct connection between the intracavernous carotid artery and cavernous sinus. Type B, C and D CCFs are indirect, low-flow lesions that vary anatomically – the arterial supply of Type B lesions originate from meningeal branches of the internal carotid artery (ICA), Type C from meningeal branches of the external carotid artery (ECA), and Type D from meningeal branches of both the ICA and ECA.

Compared to direct CCFs, dural CCFs tend to have an insidious onset, with fewer and milder symptoms. Meyers *et al.*[5] noted that the commonest presenting signs and symptoms of dural CCFs were conjunctival injection (93%), chemosis (87%), proptosis (81%), diplopia (68%), cranial bruit (49%), retro-orbital headache (34%), raised IOP (34%) and decreased visual acuity (31%). Dural CCFs pose a major diagnostic dilemma and are often initially misdiagnosed as allergic or infective conjunctivitis. Accurate diagnosis is usually only made once the patient develops more severe symptoms such as visual loss or diplopia. This delay in diagnosis can be seen in our patient, who was misdiagnosed by several doctors and was unresponsive to conservative treatment initially. As dural CCFs may potentially lead to devastating complications such as stroke or intracranial hemorrhage secondary to retrograde cortical venous flow, all physicians should maintain a high index of suspicion in cases refractory to initial treatment. CT/MRI scans should be conducted to look for findings suggestive of dural CCF such as proptosis, expansion of the cavernous sinus, dilated SOV and enlargement of extraocular muscles. Digital subtraction angiography is used as the gold standard for diagnosis, and also to identify feeding vessels and drainage patterns.[5]

Although 20-60% of patients with dural CCF have spontaneous fistula closure and may be treated conservatively, endovascular obliteration is indicated in patients with progressive visual decline, refractory elevation of IOP, cortical venous drainage with neurological symptoms, and intractable headache/ocular pain.[6] As our patient experienced worsening symptoms and a decreased quality of life, she opted for surgical treatment. The conventional transfemoral approach via the IPS was carried out, but was unsuccessful due to occlusion of the IPS. As such, the patient underwent a surgical cut down approach with direct cannulation of the SOV. There were no intra-operative complications noted and the patient had excellent functional and cosmetic outcomes postoperatively. As interventional radiological and surgical techniques become more precise, with delivery of good outcomes with minimal morbidity and minimal invasiveness, such procedures may be considered in refractory cases of carotid-cavernous fistula even without disabling and severe proptosis and visual loss.

In most cases of carotid cavernous fistula, regardless of chronicity, the superior ophthalmic vein is dilated and patent. The superior ophthalmic vein is formed by the fusion of the supraorbital vein and the angular vein of the face, behind the trochlea of the superior oblique tendon. It then courses intraconally beneath the superior rectus-levator complex from medial to lateral and then enters the cavernous sinus through the annulus tendinus of Zinn.

We believe that our illustrated case report is unique in several ways. Unlike previously published case reports elsewhere where such patients had the initial surgical access performed in the operating theatre, then wheeled to the interventional suite under general anesthesia for intraluminal coiling before finally returning to the operating theatre for completion of the procedure, the availability of the Hybrid Operating Theatre with high-risk cardiac anesthesia support made this possible, highlighting a patient-centered approach rather than a systems-based approach.

Finally, all of this was possible because of the excellent understanding and cooperation between the various teams involved, common goal of patient's best interest, and the ability to perform a delicate and skillful procedure in a facility that permits the above with least inconvenience to the patient.

In conclusion, dural CCFs may potentially lead to severe visual dysfunction and should be diagnosed and treated promptly. When all venous routes have been exhausted, the transorbital approach via the superior ophthalmic vein remains an excellent and viable alternative to access the fistula. Close cooperation between the orbital, anesthetic and radiological teams is essential in ensuring success of the operation.

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Sterile keratitis post collagen cross-linking (CXL) therapy for treatment of keratoconus

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Abstract: *Corneal collagen cross-linking therapy is a relatively new treatment for progressing corneal ectasias such as keratoconus. Here the authors discuss the case of a 22-year-old male who underwent collagen cross-linking for treatment of progressive keratoconus, who then developed a serious post operative complication of a sterile keratitis.*

Key words: *Collagen cross-linking, keratoconus, sterile keratitis*

Introduction

Corneal collagen cross linking therapy is a relatively new treatment for progressing corneal ectasias such as keratoconus. The concept is to strengthen the cornea by inducing stronger bonds between collagen fibres in the corneal stroma.[1] As initially described, UV A radiation is applied for 30 minutes to a de-epithelialised cornea that has been saturated with riboflavin. In the original trials no adverse effects were reported, but the authors were keen to note that as the technology and its application were new, practioners should only use this treatment for documented progressive disease only, until further experience and data were collected.[1]

Since its introduction, further studies have attempted to assess the safety and efficacy of the treatment.[2,3] It is considered a safe technique for the operator,[4] however, there are now case reports suggesting some complications associated with this treatment.[5-7] These complications may be associated with certain steps in the procedure, de epithelialisation or irradiation of the cornea, or a combination of steps.

Here we will discuss the case of a patient who underwent CXL for treatment of progressive keratoconus, and presented two days post treatment with a significant complication from the procedure.

Case report

A 22-year-old male of Fijian-Indian background presented to our clinic less than 48 hours post CXL treatment for keratoconus in the right eye (RE). He reported bilateral keratoconus, with previous hydrops in the left eye (LE). He reported no previous surgery to the RE or treatment to the RE. There was documented progression of his keratoconus in the right eye and he underwent CXL treatment. The technique used followed that published by Wollensak *et al*.[1] After the treatment, a bandage contact lens was applied and he was commenced on ketorolac trometamol (Acular 5mg/5ml) TDS and Tobramycin 0.3% (Tobrex) TDS.

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On presentation, his visions were RE hand movements only (HM) and LE < 6/60. On examination, the contact lens was not found. His RE showed severe ciliary injection, slit lamp microcopy revealed a large central epithelial defect, multiple small to medium sized corneal infiltrates, posterior synechiae and an endothelial plaque. The anterior chamber showed 3+ cells, consistent with an acute keratouveitis. The LE showed a central scar, with central stromal thinning (Fig. 1).

Initial management consisted of corneal scrape and swab to attempt to identify causative pathogen (MC&S including fungal culture, PCR for HSZ/VZV) and commencement of intensive presumptive treatment. This consisted of cephazolin 5% eye drops, gentamicin 0.9% eye and natamycin 5% eye drops hourly in the RE. He was also commenced on oral voriconazole (400 mg BD for 24 hrs as induction, then reduced to 200 mg BD for maintenance) Ciprofloxacin (750 mg BD orally) and atropine 1% eye drops BD.

Microscopy showed a gram-negative organism, indicating a bacterial keratitis as the main differential. In light of this, his antibiotic regimen was changed from cepahazolin 5% eye drops to ceftazidime 5% eye drops for better gram-negative cover.

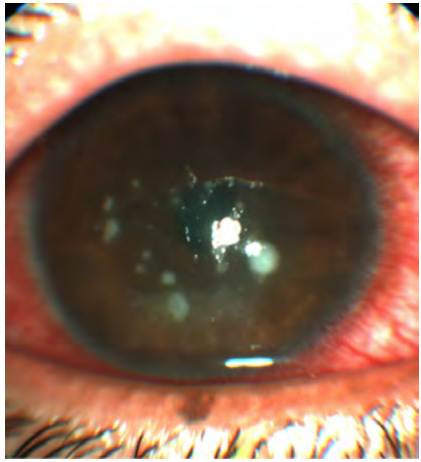

Fig. 1. Photograph of RE on presentation. After seven days of treatment there was no clinical improvement. Final microbiology analysis suggested that the initial gram-negative source was likely due to sampling contamination; final culture studies and PCR testing were negative. Examination of the RE revealed persistent anterior stromal infiltrates and white cell recruitment (WCR) centrally, and no change in the epithelial defect.

To identify the causative pathogen, confocal microscopy and corneal biopsy were performed post cessation of antibiotics for 24 hrs. Figure 2 shows the confocal microscopy image, this was reported as hyper-intense cyst-like lesions in deep stroma. This was consistent with Acanthamoeba keratitis. In light of this, the patient was commenced on PHMB (Polyhexamethylene biguanide) and brolene eye drops hourly.

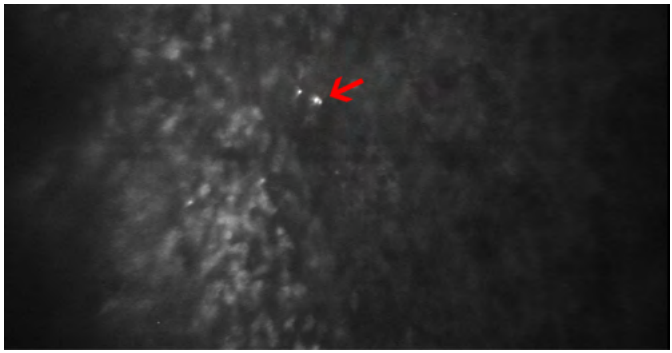

Fig. 2. Confocal microscopy image showing cyst.

Over the following days, the patient reported less pain in the RE. On examination the ciliary injection began to improve. On day 13, the appearance of the infiltrates improved, but the epithelial defect remained unchanged (Fig. 3). Corneal biopsy results were returned and were negative for Acanthamoeba. In light of the partial response to PHMB treatment, it was decided to continue this in the short term.

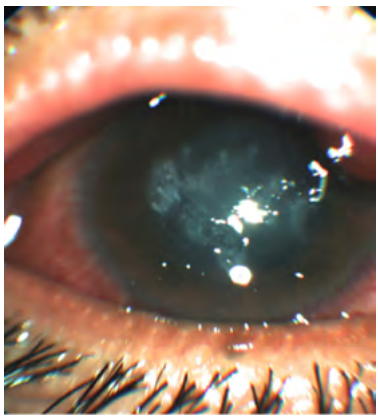

Fig. 3. Photograph of RE cornea at day 13.

The patient was discharged with outpatient follow-up, but at three days post discharge he reported worsening pain. He was referred to a specialized eye hospital. Examination showed that the epithelial defect was worse, with persistent central stromal infiltrates. All his drops were ceased for 24 hours and further corneal scrapings were obtained and sent for microbiological assessment.

Repeat corneal cultures and PCR were performed; results were negative for micro-organism, fungi and HSV PCR. He was then commenced on a topical steroid, and was monitored. He showed improved corneal appearance. Unfortunately, the patient self-discharged. He re-attended for follow-up approximately two weeks post self-discharge, on examination he had re-epithelialized the cornea, but best corrected vision was unchanged at hand movements only in the RE.

Discussion

The initial presentation, in regards to the onset post procedure, presents limited differentials. There have been reports of bacterial keratitis and infiltrates post CXL.[8-10] In these reports, causative organisms have penetrated the to the stroma of the cornea due to the absence of the protective layers of the cornea which are removed to allow absorption of the riboflavin or through intra or early post procedural contamination. These cases present with similar infiltrates, and in a similar time frame, but in the absence of a clear causative pathogen (initial gram negative was thought to be due to sample contamination rather than the causative organism of the keratitis) and the slow response to treatment targeting presumptive organisms, a hypersensitivity reaction to the either the riboflavin or the UVA radiation source was suspected to have caused the keratitis. Sterile keratitis is a known complication of CXL,[11,12] but sterile infiltrates are associated with contact lens wear, autoimmune disease, immune mediated local reaction, non steroidal anti inflammatory drug use and corneal surgery. This patient had some of these risk factors, namely the commencement of NSAID drops post procedure (Acular) and placement of bandage contact lens.[11] In this case we cannot rule out a causative organism that was not detected by standard culture media, but sensitive to the prescribed treatment.

The confocal microscopy complicated, rather than contributed to diagnostic process. There have been reported cases of AK post CXL,[7] but definitive exposure to tap water was noted in the presenting history. The onset of our patient's symptoms was not consistent with AK. AK is usually seen as a progressive, slow onset with atypical features of bacterial or fungal keratitis.[13] The appearance of cysts on the confocal microscopy, in the absence of positive tissue diagnosis presented a diagnostic quandary. The diagnosis of AK by PCR has been shown to have a sensitivity of 80% and a specificity of 100% in one study,[14] and in another study 24 out of 31 cases (77.4%) of AK diagnosed by confocal microscopy were confirmed by PCR.[15] Tissue diagnosis with PCR remains the gold standard for diagnosis of AK.

The apparent response to treatment after the introduction of PHMB is difficult to assess given the entirety of the treatment regimen at that stage. The response was marginal, and may not indicate treatment of AK.

Arora *et al.*[12] describe a similar progression in their case study of a child post CXL for progressive keratoconus. In their case, there was no confounding confocal microscopy finding and they instigated a regimen of topical steroid early in the presentation, within 48-72 hours post CXL procedure, with good results. In another case, corneal infiltrates were seen on day 5 post CXL[16] and topical steroids were commenced to good effect. Sterile corneal infiltrates have been described in several clinical settings and probably occur as a result of enhanced cell mediated immunity to staphylococcal antigens deposited in high concentrations in areas of static tear pooling.[12,16]

CXL is an increasingly popular treatment for progressive keratoconus. It is growing in popularity, and the body of literature surrounding CXL is growing. Our experience highlights a potential risk of sterile keratitis after CXL treatment.

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Purtscher-like retinopathy in a 56-year-old Thai female with anti-glomerular basement membrane glomerulonephritis

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Abstract

Purpose: *To report a case of Purtscher-like retinopathy in an anti-glomerular basement membrane glomerulonephritis in a 56-year-old Thai female.*

Method: *Observational case report.*

Results: *A 56-year-old Thai female was referred to Naresuan university hospital with anemia and pitting edema in both legs. She had underlying diseases of hypertension, hypercholesterolemia and chronic renal failure with anemia. Before her referral, she was treated by an internist at a provincial hospital. Because of deterioration of creatinine level and anemic symptoms, she was advised to see a nephrologist for the diagnosis of causative pathology and treatment. A re-evaluation of chronic renal failure was done. The results of laboratory investigation were creatinine level of 2.42 mg/dl, blood urea nitrogen (BUN) 44 mg/dl and the urinalysis found microscopic hematuria. Further evaluations for hematuria; vaginoscopy, cystoscopy and ultrasonography of genitourinary system were performed, but the outcome was normal. The result of a renal biopsy was anti-glomerular basement membrane glomerulonephritis. Hemodialysis and total plasma exchange were done several times to reduce the circulating antibody of the anti-glomerular basement membrane level.*

During her admission, the patient complained of sudden blurred vision in both eyes after the ninth total plasma exchange. She had no previous ocular problems nor physical trauma. The ocular examination showed visual acuity of counting fingers in both eyes. Anterior segment was normal for her age. The posterior segments showed retinal thickening around the posterior poles with clear intervening zones in both eyes with some intra-retinal hemorrhage, which was consistent with the earlier-diagnosed Purtscher-like retinopathy. The pathogenesis of Purtscher-like retinopathy was investigated with negative results. During counseling, the patient and her family chose observation instead of active treatment. The patient was discharged and followed-up at the out-patient unit of the ophthalmology department of the Naresuan university hospital.

Conclusion: *Purtscher-like retinopathy is a rare ocular disease with unknown pathogenesis. There are many diseases reported to be associated with Purtscher-like retinopathy. In this case, we found Purtscher-like retinopathy in a patient with anti-glomerular basement membrane glomerulonephritis.*

Key words: *Purtscher-like retinopathy; Anti-Glomerular Basement Membrane Glomerulonephritis; Total plasma exchange*

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Introduction

Purtscher's retinopathy is a rare ophthalmologic disease. It was first described by Otmar Purtscher in 1910, in a patient with a history of head trauma resulting from falling from a tree.[1] The patient showed retinal whitening and retinal hemorrhage around the posterior pole of both eyes. Causes other than trauma, with the same ophthalmic findings are diagnosed as Purtscher-like retinopathy. The most common cause of Purtscher-like retinopathy is acute pancratitis.[2,3] Long-bone fracture, connective tissue diseases such as systemic lupus erythromatosus (SLE), chronic renal failure and orbital anesthetic injection are also reported to be causes of Purtscher-like retinopathy.[2,3] The main pathogenesis is thought to be associated with micro-embolization of the retinal arterioles from various causes.[2-7] The pathogenesis of hyperviscosity and vascular autoregulation are now under investigation.[8,9] Recently, computational fluid dynamic simulation software has shown the role of wall shear stress as a new mechanism in the development of Purtscher's and Purtscher-like retinopathies.[10] Treatment of Purtscher-like retinopathy is to correct the causative systemic pathology and for ocular treatment, observation is usually advised.[2] The visual prognosis of Purtscher-like retinopathy is guarded.

Anti-glomerular basement membrane glomerulonephritis is a rare kidney disease with an incidence of one case per million.[11] The affected patients usually come in with symptoms of acute or sub-acute renal failure with varied clinical forms from mild severity to rapidly progressive glomerulonephritis (RPGN). The anti-glomerular basement membrane antibody circulates in the serum of the patients and destroys the basement membrane of the renal glomeruli.[11,12] The antibody affects collagen type IV, which is the composition of the renal glomerular basement membrane. In some cases, the antibody also affects the respiratory system. Because of the same collagen component, it causes alveolar hemorrhage.[13] Renal failure combined with alveolar or pulmonary hemorrhage is called Goodpasture's syndrome. Due to the circulating antibody in the patient's blood stream, the treatment modalities of anti-glomerular basement membrane glomerulonephritis are plasmapheresis, corticosteroids, and immunosuppressive drugs. Plasmapheresis is used for the reduction of the circulating anti-glomerular basement membrane antibody found in the patient's plasma.[11]

Material and methods

The patient was referred from a provincial hospital to the Naresuan university hospital with an increasing level of serum creatinine and deterioration of anemic symptom. The history and physical findings were reported. The patient was re-evaluated because of the sub-acute renal failure. Special investigations, such as renal biopsy, were done and reported. The renal pathological specimens were shown and detailed in this report. The ocular diagnosis and differential diagnosis of its cause were detailed through the treatment of the patient.

Case history

A 56-year-old Thai female with underlying diseases of essential hypertension, hypercholesterolemia and the recent diagnosis of chronic renal failure for a few months prior to her referral. She was followed-up and treated at a provincial hospital by an internist. Medication consisted of amlodipine, enalapril, furosemide, hydralazine, gemfibrozil, aspirin, folic acid and calcium supplement. In this follow-up, an increasing level of serum creatinine was found, up to the level of 2.42 mg/dl and her hematocrit dropped from 26% to 20% without blood loss. She also experienced mild dyspnea from chronic anemia and increasing swelling of her legs from chronic renal failure. She was referred to a nephrologist for further evaluation and treatment at Naresuan university hospital.

The vital signs were within normal limits; blood pressure 107/65 mmHg, pulse rate 75/min. The physical examination showed a moderately pale conjunctiva and moderately pitting edema in both legs. The medication was adjusted and the follow-up was done at Naresuan university hospital by a nephrologist. Re-investigation showed hematocrit 24.2%, blood urea nitrogen (BUN) 20.3 mg/dl, creatinine 2.4 mg/dl. Urinalysis results showed proteinuria 1+, and red blood cells (RBC) 50-100 cells/HPF. The hematocrit, blood urea nitrogen and creatinine levels were compatible with the diagnosis of chronic renal failure/chronic kidney disease stage IV, but the microscopic hematuria was not explained. The urinalysis was redone with the same findings, so she was sent to evaluate the cause of microscopic hematuria due to its possibility to correlate with the cause of her worsening signs of chronic kidney disease. A vaginoscopy was done with the result of normal mucosa and no bleeding. The cystoscopy result was normal without blood or bladder stone(s). The ultrasonography of genitourinary system was normal. A renal biopsy was done after follow-up without the improvement of microscopic hematuria. The result of the renal biopsy with the immunofluorescent study showed positive linear staining for IgG (3+) along glomerular basement membrane with foci of breaks in glomerular basement membrane, presence of fibrocellular and fibrous crescent. The circulating antibody was also found in the patient's blood circulation, with titer of 1:160. All these findings were compatible with the diagnosis of anti-glomerular basement membrane glomerulonephritis.

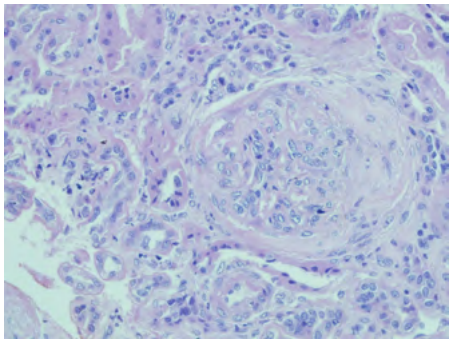

Fig. 1. *H-E 40x* **: Hematoxylin and eosin stain, 40x, fibrocellular crescent of glomerulus.**

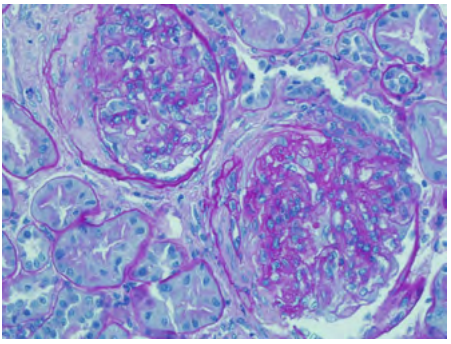

Fig. 2. *PAS-40x* **: Periodic acid schiff stain 40x, fibrocellular crescent of glomeruli.**

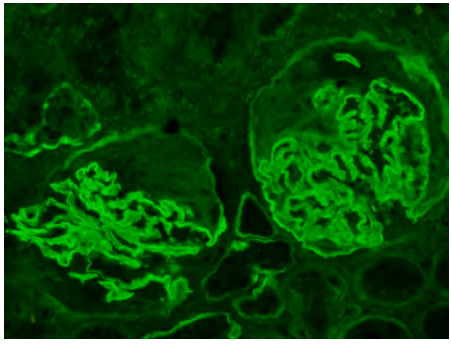

Fig. 3. *IgG-40x-2* **: Immunofluorescent IgG antibody, 40x, positive 3+ along GBM.**

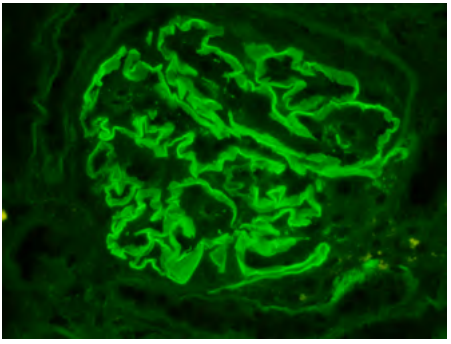

Fig. 4. *IgG-60x* **: Immunofluorescent IgG antibody, 60x, positive 3+ along GBM.**

The treatment for the patient was pulse corticosteroids (methylprednisolone 750 mg intravenously for three days) and cyclophosphamide (100 mg/day). There was no improvement of her condition and circulating antibody level after the treatment was started, so plasmapheresis was advised. The patient underwent total plasma exchange (TPE) ten times and after the sixth episode of TPE the antibody titer had reduced from 1:160 to 0.

The patient started complaining of blurred vision in both eyes after the ninth TPE, and was referred to the ophthalmology department. Ocular examination found visual acuity of counting fingers in both eyes, no relative afferent pupillary defect, nuclear sclerotic cataract in both eyes, no anterior chamber cells and flare. The fundoscopic findings were whitening of retina around posterior pole with clear intervening zones between the retinal arterioles compatible with Purtscher flacken, which is pathognomonic for Purtscher-like retinopathy, some retinal hemorrhages, and cotton wool spots in both eyes. No perivascular sheathing. No vitreous cells. Optic disc margins were not swollen and not pale. Based on these findings, she was diagnosed as Purtscher-like retinopathy. Optical coherent tomography (OCT)

of both eyes was done and retinal thickening around posterior pole and macular edema were found. Because she had already received a high dose of corticosteroids which was one of the reported treatment choices for the Purtscher-like retinopathy, the patient did not want any more treatments for her ocular problems. Special investigations, such as fundus fluorescent angiography (FFA), were discussed during treatment counseling, but the patient refused because of severe dizziness and her impaired renal function. The follow-up of her ocular symptoms was performed at the out-patient department of the ophthalmology department of the Naresuan university hospital.

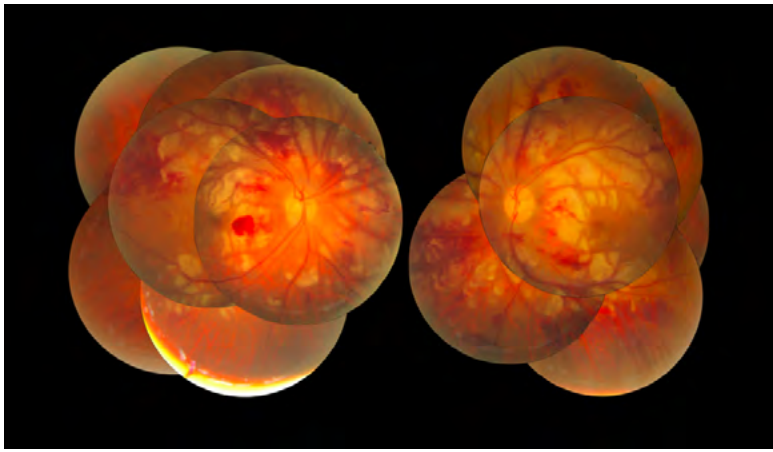

Fig. 5. Color fundus photography of both eyes showed whitening of the retina around the posterior pole with clear intervening zones between the retinal arterioles, retinal hemorrhages, and cotton wool spots. Disc margins were not swollen.

The first follow-up visit took place two months after the first diagnosis. There was improvement of the retinal thickening at the posterior poles in both eyes. Vision in both eyes was not significantly improved, the final visual acuity (BCVA) was 6/200,3/200. Optic discs were pale with the attenuation of retinal vessels.

The laboratory findings of circulating autoantibody was negative after the sixth of the ten total plasma exchanges that were performed during her admission. The hemodialysis was continued with the protocol of a chronic kidney disease patient. The immunosuppressive agents were continued; oral prednisolone and cyclophosphamide were administered.

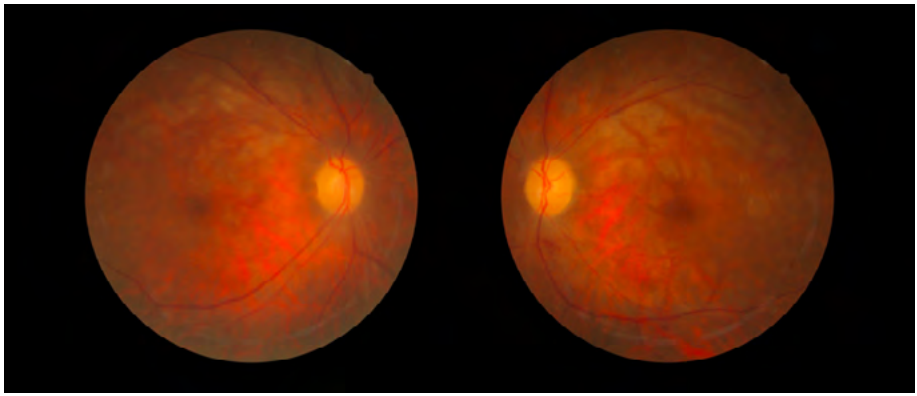

Fig. 6. Color fundus photography of both eyes (two months after the first diagnosis) showed improvement of the thickened retina around the posterior poles, less retinal hemorrhages, and cotton wool spots. Optic discs were mildly pale without swelling of the margins.

Discussion

This patient had already been diagnosed of renal insufficiency and microscopic hematuria. She was evaluated and treated by a nephrologist, but her condition did not improve despite the proper treatment. Also, the cause of microscopic hematuria was not explained by her underlying diseases. Therefore, a renal biopsy was done to investigate the cause of microscopic hematuria. The renal biopsy result revealed the underlying pathology of anti-glomerular basement membrane glomerulonephritis. The proper treatment was advised and the choice of plasmapheresis was given together with intravenous and oral corticosteroids and immunosuppressive drugs. After the ninth episode of total plasma exchange (TPE), the patient complained of acute blurred vision. The further review of the last episode of TPE was normal, without any complications. Ocular examination showed a visual acuity of counting fingers at three feet in both eyes. The anterior segment showed senile nuclear sclerotic cataracts which did not explain the cause of her visual loss. The relative afferent pupillary defect was negative. The fundoscopic findings were retinal whitening around the posterior pole with clear intervening zones in both eyes which was compatible with Purtscher flecken, cotton wool spots and retinal hemorrhage in both eyes. All of the described fundoscopic findings were consistent with the diagnosis of Purtscher's retinopathy. Without the obvious history of head or chest trauma, the diagnosis of Purtscher-like retinopathy was made.

The most common cause of Purtscher-like retinopathy is acute pancreatitis,[2] of which there was no clinical sign in this patient. From the systemic review of history and physical examination of this patient, there was only the diagnosis of anti-glomerular basement membrane glomerulonephritis with anemia, essential hypertension and hypercholesterolemia. As far as the authors know, there was no report of an association of anti-glomerular basement membrane glomerulonephritis and Purtscher-like retinopathy.[2,3]

Anti-glomerular basement membrane glomerulonephritis is an auto-immune disease caused by IgG autoantibodies against the glomerular basement membrane. It shows the clinical picture of renal insufficiency from mild severity to rapidly progressive glomerulonephritis (RPGN). With the same collagen type IV of glomeruli, it also affects the alveoli of the lungs and causes pulmonary hemorrhage (Goodpasture's syndrome). The presence of circulating auto-antibody level is needed for the immunological diagnosis of anti-GBM glomerulonephritis and its level is directly related to the disease severity.[11] The combination of renal and pulmonary systems is not always presented, there is a group of patients that referred to the clinic only for renal problems. In our patient, for determination of the cause of the microscopic hematuria, normal vaginoscopy and normal cystoscopy were performed. The renal ultrasonography was normal with normal size of both kidneys. After the renal biopsy (Figs. 1 and 2), the pathological findings showed the positive linear staining for IgG (3+) along the glomerular basement membrane with foci of breaks in the glomerular basement membrane (Figs. 3 and 4). The result suggested anti-glomerular basement membrane glomerulonephritis. The circulating autoantibody to glomerular basement membrane was positive with titer of 1:160. Consequently, the definite diagnosis of anti-glomerular basement membrane glomerulonephritis was made.

In experiments, the circulating microparticle of glass sphere, fat, platelet and leukocyte aggregates were injected in pigs' and cats' circulation, the intermediate sized of microparticles can cause the clinical picture of Purtscher-like retinopathy.[2-7] In anti-glomerular basement membrane glomerulonephritis the circulating particles or antigen-antibody complex are also found,[11,12] which can explain the pathophysiology of Purtscher-like retinopathy in our patient. However, as far as the author's knowledge, there is no previous report showing the association of these two diseases. This paper is the first report showing some association between Purtscher-like retinopathy and anti-glomerular basement membrane glomerulonephritis. The definite conclusion of the pathophysiology of the patient with anti-glomerular basement membrane glomerulonephritis with Purtscher-like retinopathy has to be further studied.

Our patient developed blurred vision after the ninth total plasma exchange before the Purtscher-like retinopathy was diagnosed. W.H. Reinhart *et al.* reported the change of hemorheology of the circulation after hemodialysis with the result of increased hematocrit and increased plasma and whole blood viscosity after the hemodialysis was done, due to the influence of the hemodialysis passage.[9]

Amit Nautiyal *et al.* reported a case of patient with Purtscher-like retinopathy with multiple myeloma.[8] In their case, hyperviscosity from multiple myeloma was mentioned to be the cause of Purtscher-like retinopathy. Then, the several times of total plasma exchanges in our patient could lead to the plasma hyperviscosity and thus, Purtscher-like retinopathy.

Conclusion

Purtscher-like retinopathy is a rare ocular disease with unknown pathogenesis. There are some systemic diseases which are known to be associated with Purtscher-like retinopathy, but there is no report about anti-glomerular basement membrane glomerulonephritis. This is the first case report of Purtscher-like retinopathy in anti glomerular basement membrane glomerulonephritis patient. The pathogenesis could be from the circulating autoantibody by the proposed mechanism of micro-embolisation. However, the hemodynamic and fluidic change after plasma exchange might also play a role in development of Purtscher-like retinopathy in this case. The mechanism of Purtscher-like retinopathy occurred in chronic renal failure could also be in differential of pathogenesis. Further study is needed to confirm the mechanism and possibility of the association. In complicated cases without obvious causes, the pathogenesis of the disease should be investigated which directs to the proper treatment and better visual prognosis.

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The role of the TB T-spot test in patients with tubercular retinal vasculitis

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Abstract

Purpose: *To report tuberculosis (TB) T-spot diagnosis and management of two cases of presumptive tubercular retinal vasculitis in Singapore.*

Method: *Retrospective case reports.*

Results: *Two patients were diagnosed with presumptive TB retinal vasculitis using clinical features, TB T-spot test and ancillary investigations. They were successfully treated with a combination therapy of oral steroids, anti-tuberculosis medications and pan retinal photocoagulation (PRP). Follow-up demonstrated resolution of symptoms and signs with no complications arising from anti-tuberculosis medications.*

Conclusions: *TB retinal vasculitis presents diagnostic and therapeutic challenges. Ocular TB diagnosis is often presumptive, as confirmatory evidence of organisms from the eye has low yield. The results of culture and Mantoux test require a long waiting period. TB T-spot provides rapid results with high sensitivity and specificity, thus holding promise as a diagnostic tool. Management of TB retinal vasculitis is multi-modal and multi-disciplinary requiring oral steroids and pan-retinal photocoagulation by the ophthalmologists and anti-tuberculosis medications by the Physicians.*

Key words: *Tuberculosis, retinal vasculitis, TB T-spot, Singapore*

Introduction

Tuberculosis (TB) is an infectious disease caused by various strains of mycobacteria, commonly *Mycobacterium tuberculosis*. It typically affects the lungs, but also causes extrapulmonary manifestations in the eye. In 2011, the World Health Organization (WHO) estimated 8.7 million incident cases of TB.[1] TB is endemic in Singapore, the incidence rate increased from 39.2 in 2010 to 40.5 per 100,000 in 2011.[2] Extrapulmonary incidence in Singapore accounts for 1.2% of all TB cases.[1] Sharma *et al*. reported ocular TB incidence ranging from 1.4-5.7%.[3] Incidence of ocular TB in Singapore is not known. In human immunodeficiency virus (HIV) patients, the incidence may increase to between 2.8-11.4%.[3] TB affects many ocular tissues, including retinal vasculitis.[4] The haematogenous route of spread is the most common.[4] Retinal vasculitis has been postulated to arise from delayed type hypersensitivity reaction to sensitized tuberculous protein in the vessel walls.[5]

The diagnosis of tubercular vasculitis is often presumptive as there may be no

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confirmatory evidence of tuberculosis in these patients.[5] To our knowledge and according to Gupta *et al.*,[5] there are no published studies yet on Interferon-gamma Release Assays (IGRA) (*e.g.*, TB T-spot) and ocular TB. We present a pilot study on two cases of presumptive unilateral TB retinal vasculitis discussing the management and role of TB-T spot in the diagnosis in Singapore.

Materials and Methods

Two patients with presumptive TB retinal vasculitis were diagnosed and identified by a specialist in an ophthalmology clinic in Singapore. The diagnosis was made according to Gupta *et al.*'s[5] presumptive diagnostic criteria as shown below. Additionally, the TB T-spot test was positive in both cases.

Presumptive ocular TB diagnostic criteria[5]

Any one or more clinical signs listed in Section I in combination with any positive tests under section II *or* a positive therapeutic trial section in section III *in combination* with section IV.

Section I – Clinical presentation in intraocular TB

1. Anterior uveitis	Granulomatous, nongranulomatous, iris nodules, ciliary body tuberculoma
2. Intermediate uveitis	Granulomatous, nongranulomatous with organizing exudates in the pars lana/ peripheral uvea
3. Posterior and panuveitis	Choroidal tubercule, choroidal tuberculoma, subretinal abscess, serpiginous-like choroiditis
4. Retinitis and retinal vasculitis	
5. Neuroretinitis and optic neuropathy	
6. Endophthalmitis and panophthalmitis	

Section II – Systemic investigations

1. Positive Mantoux reaction
2. Evidence of healed or active tubercular lesion on radiography of the chest
3. Evidence of confirmed active extrapulmonary TB (either by microscopic examination or by culture of the affected tissue for *M. Tuberculosis*)

Section III – Therapeutic test

A positive response to four drug anti-tuberculosis treatment (ATT) (Isoniazid, Rifampicin, Ethambutol and Pyrazinamide) over a period of 4 to 6 weeks.

Section IV – Exclusion of other Uveitis Entities

In the geographic regions where TB is low in incidence, other causes of uveitis must be excluded by various laboratory investigations including serology for syphilis, toxoplasmosis and others.

Results

Case 1

A 36-year-old Chinese man with no past medical history presented with two months of floaters in the left eye associated with low-grade fever and with cough of two months duration, four months prior. He was asymptomatic in the right eye. There was no travel history or prior contact with TB.

Visual acuity (VA) was 6/6 unaided in both eyes. The anterior segments were normal. However, fundus examination of the left eye revealed sheathing of vessels with flame-shaped haemorrhages noted in the superior and temporal quadrants (Fig. 1a). The right fundus was normal. Fundus fluorescein angiography (FFA) (Fig. 2a) showed capillary non-perfusion with perivascular leakage in the areas of haemorrhages. The only positive investigation was a reactive TB T-spot® (Oxford Immunotec/ United Kingdom) test. Chest X-ray (CXR) was normal. Additional investigations for infective and autoimmune causes were normal (Table 1). Mantoux test was not performed.

A provisional presumptive diagnosis of TB-associated supero-temporal retinal vasculitis was made. He was commenced on oral Rifampicin 10 mg/kg OD, Isoniazid 300 mg OD, Ethambutol 15 mg/kg OD, Pyrazinamide 25 mg/kg OD for a duration of six months. Oral prednisolone 1 mg/kg was commenced 48 hours later. Sectoral retinal photocoagulation was applied to the ischaemic areas. The haemorrhages resolved after 11 months with no neovascularisation or complications (Fig. 1b). A presumptive diagnosis of TB-associated retinal vasculitis was subsequently confirmed upon resolution of fundal changes with the four-drug ATT.

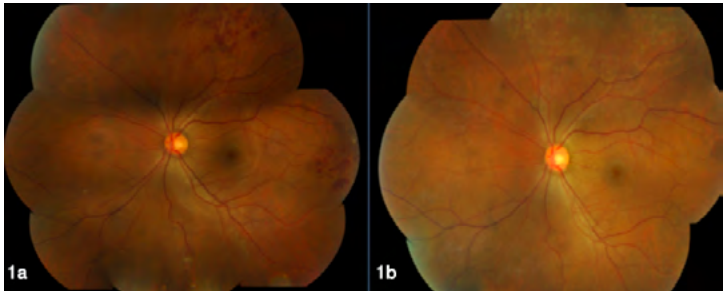

Fig. 1. Mosaic fundal photographs OU (Case 1). a. Superotemoral flame-shaped haemorrhages and sheathing and sclerosis of vessels. b. Resolved flame-shaped haemorrhages with photocoagulation scars, ten months later.

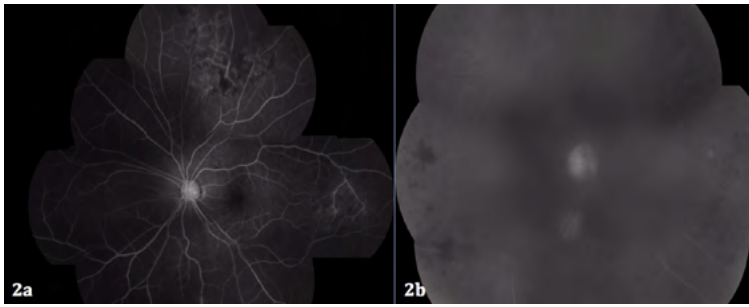

Fig. 2a. FFA OS showing leakage and blocked hypofluorescence and capillary non-perfusion in the superotemporal fundal region (Case 1).
Fig. 2b. FFA OD showing focal vasculitis with no capillary non-perfusion (Case 2).

Case 2

A 58-year-old Chinese man, who was a hepatitis-B carrier on Adefovir, presented with the first episode of right eye floaters of one-week duration. This was associated with on-off joint pains and swelling for one year. He had no rashes, mouth ulcers, loss of appetite or weight, cough or night sweats.

Visual acuity was 6/6 in both eyes. The anterior segments were normal. Dilated right fundus showed preretinal haemorrhage superiorly, cotton-wool spots inferiorly with diffuse clusters of dot-blot haemorrhages and small patches of retinal infiltrates, perivascular sheathing and vitreous clumps along the superior and inferior retinal vessel arcades but not vitritis (Fig. 3a). The left fundus was normal. FFA confirmed focal areas of vasculitis but no areas of capillary non-perfusion (Fig. 2b).

Investigations showed a reactive TB T-spot test and elevated inflammatory markers were raised (ESR 36 mm/hr, CRP 8.5 mg/L). His CXR showed three stable granulomas that were present in previous CXRs. Other investigations for infective and autoimmune causes were normal (Table 1). Mantoux test was not performed.

The presumptive diagnosis of right TB-associated vasculitis was made. A baseline AST and ALT were normal (Table 1). Patient was commenced on oral Rifampicin 10 mg/kg, Isoniazid 5 mg/kg and Pyrazinamide 25 mg/kg for duration of six months. Oral prednisolone 0.5 mg/kg was commenced 48 hours later. One month later, right eye panretinal photocoagulation (PRP) was done. Symptoms and fundus changes resolved after eight months (Fig. 3b) and patient no longer complained of floaters.

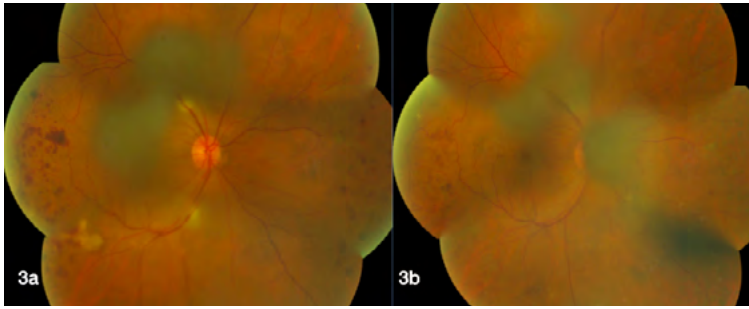

Fig. 3. Mosaic fundal photographs OD (Case 2). a. Dot blot haemorrhages, cotton wool spots and perivascular sheathing. b. Resolved fundal changes with PRP scars eight months later.

Table 1. Laboratory investigative results of two patients with presumptive tuberculous retinal vasculitis.

Laboratory test	Reference range	Case 1	Case 2
TB T-spot	Nil	Reactive	Reactive
Haemoglobin (g/dL)	13.0-17.0	14.6	10.52
White blood cells (10^9/L)	4.00-11.00	5.33	14.8
Platelets (10^9/L)	130-400	221	303
Erythrocyte sedimentation rate (ESR) (mm/hr)	1-10	3	36
C-reactive protein (CRP) (mg/L)	1.0-5.0	< 1.0	8.5
Rheumatoid factor (RF) (IU/mL)	< 14	< 10	< 10
Anti-myeloperoxidase (U/mL)	0-20	< 1	< 1
Anti-PR3 (U/mL)	0-20	< 1	2
Anti-nuclear antibody (ANA) (%)	< 100	17	60
Anti-double-stranded deoxyriboneuclotide acid (anti-ds DNA) (IU/mL)	1.0-25.0	0.9	6.5
Rapid plasma regain/venereal disease research laboratory (RPR/VDRL)	N.A.	Non-reactive	
Anti- hepatitis C virus (anti-HCV)	N.A.	Non-reactive	
Hepatitis B surface antigen (HBsAg)	N.A.	Non-reactive	Reactive
Human immunodeficiency syndrome antigen-antibody (HIV Ag-Ab)	N.A.	Non-reactive	
Alanine transaminase (ALT) (U/L)	10-44	10	15
Aspartate transaminase (AST) (U/L)	10-34	17	24

Discussion

TB remains a serious health problem in Singapore, especially with increasing rates of HIV and influx of migrant workers who have not been vaccinated.[6] Therefore, understanding TB-associated ocular complications is important for the ophthalmologist. The occurrence of isolated ocular TB in absence of systemic TB is not unusual.[7] Diagnosing TB retinal vasculitis requires a high index of suspicion as its features mimics other infectious and non-infectious intraocular inflammation including sarcoidosis, Behcet's disease and isolated retinal vasculitis.[8]

According to the WHO, a definite case of TB is when *Mycobacterium tuberculosis* complex is identified from a clinical specimen either by culture or a newer method such as molecular line probe assay from a patient.[1] However, the diagnosis of intraocular TB is difficult due to the large variations in clinical presentations, lack of uniformity in diagnostic criteria, and the low yield of organisms from the eye. One has to rely on the clinical presentations with investigations such as Mantoux test or molecular diagnostic techniques to make a diagnosis of presumed intraocular TB.[5] The TB T-spot test is a reasonably fast and accurate diagnostic test. Results are obtained within 24 hours with a high sensitivity of 97.2% and a specificity of 92%.[9] It can also differentiate latent from active TB, and eliminates false positives secondary to vaccinations.[10] It is also found to have a stronger correlation with the level of exposure to mycobacterium tuberculosis compared to the Mantoux test.[5]

The 'gold standard' of TB diagnosis is culture. However, this is not feasible in patients with TB-associated uveitis without respiratory symptoms as they would be incapable of producing sputum for culture. The four to eight weeks waiting time for the culture result[11] to guide the decision to initiate treatment may also be unpractical. Furthermore, culture result incubation time may prolong in multi-drug resistant mycobacterium.[12] The use of polymerase chain reaction (PCR) for TB in intraocular fluids is often not possible as TB particles are usually not present in TB retinal vasculitis, as it is usually immune-mediated. Additionally, aqueous or vitreous sampling may incur risks of procedural-related ocular injuries. IGRA tests such as TB T-spot test therefore hold promise as the diagnostic tool for ocular TB in the future.

The effective management of TB retinal vasculitis consists of a combination therapy of multidrug anti-TB therapy with systemic steroids. Isolated use of systemic steroids in a positive-TB patient may provoke the risk of miliary TB,[8,13] while isolated use of anti-TB therapy may not reduce the immune-mediated inflammation. PRP is required if there is occlusive vasculitis to prevent rubeosis from ischaemia and inflammation.[13] Regular ophthalmic assessment is recommended to follow-up for resolution of fundal changes and monitoring of ocular side effects of anti-TB therapy, especially when the total dosage of ethambutol received exceeds 25 mg/kg.[10]

Conclusion

TB retinal vasculitis is uncommon but demonstrating a resurgence. A high-index of suspicion with knowledge of its geographical prevalence combined with a thorough work-up to rule out other causes and multi-modal treatment is necessary for early and effective management.

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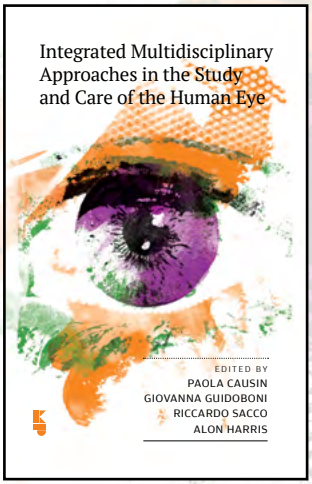

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