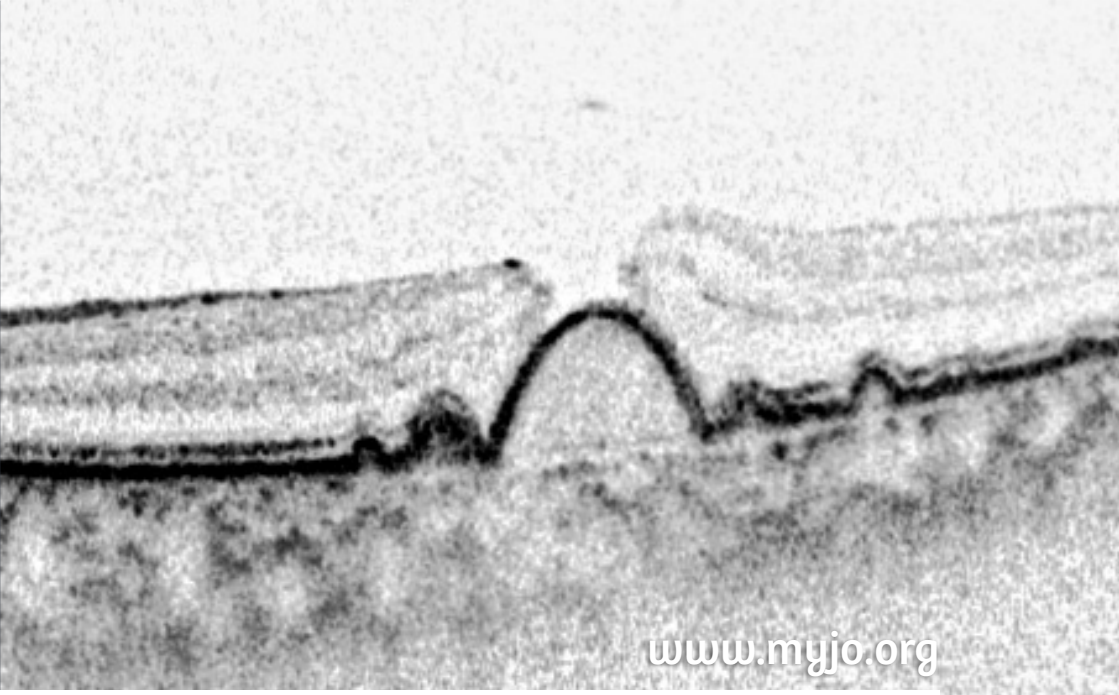

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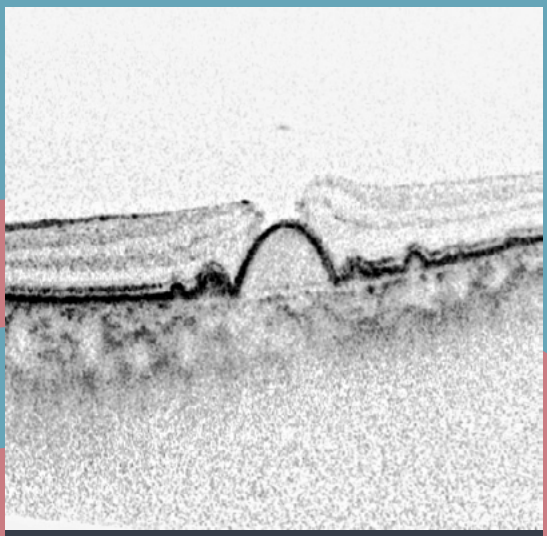

ABOUT THE COVER IMAGE

Button-hole features a button-shaped pigment epithelial detachment underlying a full thickness macular hole imaged by spectral-domain optical coherence tomography.

The image was taken by Dr. Ainal Adlin Naffi, consultant ophthalmologist, Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia.

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The perfect visual field test: does it exist?

Associate Professor Norlina Ramli

Glaucoma Specialist and Head of Ophthalmology Department, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia

The role of standard automated perimetry in glaucoma monitoring is irrefutable. White on white standard automated perimetry has been used in clinical practice since 1970 with the Octopus Perimeter.[1] Subsequently, Andres Heigl and his colleagues were instrumental in the development of what is arguably the most used perimetry test and analysis method in current clinical practice and research, the Humphrey Field Analyser.[2] It has undergone many improvements since its inception. Measures were developed to improve the accuracy, make the tests easier to perform, enhance efficiency, and establish a robust system to enhance the reliability.

In this current issue of Malaysian Journal of Ophthalmology, we have two articles which have highlighted the issue of enhancing the reliability of Humphrey visual field (HVF) results. In the first article, Mahayana *et al.* investigated the reliability parameters after three repeated HVF tests in the same patient spread over several days. They concluded that it required three perimetry examinations for the learning effect to diminish. Interestingly, while factors such as duration of test, fixation loss, and false-positive rates improved with each subsequent test, there was no statistically significant change in global indices. This indicates the robustness of the algorithm for glaucoma detection irrespective of the learning effect. In other words, the defects in pathological field loss are not possible to learn.

The second article investigated the effect of instructional videos on patients doing HVF for the first time. This is an important article which highlights how the artefact of learning effect can be minimised in perimetry through the use of demonstration videos. It is especially pertinent in patients undergoing perimetry for the first time. The findings of improved reliability parameters after watching the instructional videos were particularly evident in patients from lower educational levels.

Performing a HVF test is tedious at best for a patient. Factors such as lack of concentration, fatigue, and general health may result in inconsistent responses. While there have been significant advances made in the parameters for detection of glaucomatous field loss (visual field index and glaucoma hemifield test) and glaucomatous progression (Glaucoma Progression Analysis), there has been little

improvement in making the exercise simpler and easier for the patient. In this regard, deep learning and artificial intelligence may be the solution. Recently, Wen *et al.* successfully applied deep learning networks to predict future visual fields up to 5.5 years based on a single HVF.[3] The ability to predict future glaucomatous progression without the inconvenience of multiple confirmatory HVF tests as is current practice would be a significant advantage and bonus for both patients and ophthalmologists alike. Frequency of HVF testing and clinic visits could be minimised. The role of deep learning and artificial intelligence could also be extended to identify the optic disc associated with the visual fields loss as demonstrated by Ting *et al.*[4] Current clinical practice guidelines would have to be adjusted should deep learning and artificial intelligence technologies be applied in routine clinical practice.

These two articles serve as an important reminder that interpretation of visual fields test in patients should not be undertaken singly. The ophthalmologist should be cognizant of patient factors which may affect the reliability of this test and not make treatment decisions based on a single abnormal visual field result. Whilst we await further evidence supporting the robustness of deep learning and artificial intelligence in HVF interpretation, use of clinical data such as intraocular pressure, patient demographics, medical and surgical history, and central corneal thickness should all be taken into consideration when deciding on the appropriate personalised management for the individual patient.

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The learning effect in Humphrey Field Analyser testing in glaucoma patients: how many practice sessions are enough?

Bayu **Primahatmaja**, Krisna Dwi Purnomo **Jati**, Nyssa Alexandra **Tedjonegoro**, Indra Tri **Mahayana**

Department of Ophthalmology, Neuro-Ophthalmology and Glaucoma Division, Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada, Dr. Sardjito Hospital, Yogyakarta, Indonesia

Abstract

Purpose: The learning effect is an essential factor in many psychophysical tests. This study aims to examine the learning effects of Humphrey Field Analyser (HFA) in patients with glaucoma.
Study design: Cross-sectional study.
Methods: Twenty eyes of 12 patients (10 patients [83.4%] open-angle glaucoma, 1 patient [8.3%] angle-closure glaucoma, and 1 patient [8.3%] secondary glaucoma) were sent to HFA examination for three different sessions of examination. The inclusion criteria were patients with glaucoma who completed three HFA examinations. The results were analysed using ANOVA and Tukey's post hoc test. The primary outcomes were reliability, global indices, and the threshold sensitivity between the three sessions.
Results: Duration to complete the HFA test statistically decreased after the third session (first *vs* third session: 387 ± 96 *vs* 307 ± 93 sec; $p = 0.017$) as well as fixation loss (first *vs* third session: 0.25 ± 0.19 *vs* 0.05 ± 0.11: $p = 0.001$). False-negative results improved after the third session (first *vs* third session: 0.15 ± 0.15 *vs* 0.02 ± 0.03 $p < 0.001$). There was no statistically significant difference in false-positive,

Correspondence: Indra Tri Mahayana, MD, PhD, Department of Ophthalmology, Neuro-Ophthalmology Division, Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada, Dr. Sardjito Hospital, Jl. Kesehatan No.1, Senolowo, Sinduadi, Kec. Mlati, Kab. Sleman, Daerah Istimewa Yogyakarta 55281, Indonesia.
E-mail: tri.mahayana@gmail.com

mean deviation, pattern standard deviation, and visual field index within the three sessions.
Conclusions: There was shorter test duration, decreased fixation loss, and decreased false negatives in the third session of HFA, but there was no statistically significant change to the global indices. Experience has important effect on perimetry results. Thus, the learning effect should be taken into consideration for management of patients with glaucoma.

Keywords: glaucoma, visual field, learning effect

Kesan proses pembelajaran ke atas pesakit glaucoma yang melakukan ujian medan penglihatan menggunakan Humphrey field analysis: berapa kali ujian adalah memadai?

Abstrak

Tujuan: Proses pembelajaran adalah penting dalam mana-mana ujian yang melibatkan psikofizikal. Kajian ini bertujuan mengenalpasti proses pembelajaran minimum yang diperlukan oleh pesakit glaukoma bagi menghasilkan ujian medan penglihatan yang baik.
Kaedah kajian: Kajian keratan rentas
Metodologi: Dua puluh pesakit (dua puluh mata) telah menjalani ujian medan penglihatan mengunnakan Humphrey field analysia (HFA) untuk tiga sessi yang berlainan. Mereka terdiri dari 10 pesakit glaukoma bersudut terbuka, 1 pesakit glaukoma bersudut tertutup dan satu lagi adalah pesakit glaukoma sekunder. Kriteria utama adalah mereka perlu melengkapkan tiga sessi HFA. Keputusan ujian HFA telah dianalisa menggunakan one-way ANOVA dan Tukey post-hoc. Dapatan utama dari ujian ini adalah dari segi kebolehpercayaan, indeks global, dan ambang sensitivity di antara ketiga-tiga ujian HFA.
Keputusan: Waktu bagi melengkap ujian HFA berkurangan dengan signifikan pada ujian yang ketiga (ujian pertama: 387 ± 96 vs ujian ketiga:307 ± 93 sec; $p = 0.017$), begitu juga dengan kehilangan penetapan (fixation loss) (ujian pertama 0.25 ± 0.19 vs ujian ketiga 0.05 ± 0.11; $p = 0.001$). Kekerapan negatif palsu juga berkurangan selepas sessi ujian ke tiga (ujian pertama 0.15 ± 0.15 vs ujian ketiga 0.02 ± 0.03; $p < 0.001$). Tiada perbezaan signifikan secara statistik pada nilai positif palsu, min sisih, sisihan corak piawai dan indek medan penglihatan di antara ketiga-tiga ujian HFA.
Kesimpulan: Terdapat pengurangan masa ujian, kehilangan penetapan dan

kekerapan negative palsu pada ujian HFA yang ketiga tetapi tiada perubahan signifikan secara statistik pada indeks global. Pengalaman memberi kesan penting ke atas keputusan ujian perimetri. Dengan itu, proses pembelajaran perlu diambil kira dalam perawatan pesakit glaukoma.

Kata kunci: glaukoma, medan penglihatan, proses pembelajaran

Introduction

Glaucoma is the leading cause of non-reversible blindness.[1] Visual field analysis is a critical feature in diagnosing and managing glaucoma. The Humphrey Field Analyser (HFA) is one of the several methods available to measure the visual field. The learning effect is an essential factor that needs to be addressed when evaluating the visual field. It is assumed that experience might affect the result after performing several standard automated perimetry tests.[2]

Like other subjective psychophysical tests, the perimetry examination needs the patient's concentration and cooperation. The patient's performance may become better after several attempts. The more experience the individual has in perimetry, the better the result. An inexperienced subject might produce visual field results that show abnormality. Thus, this learning curve might mask the defect and create confounding results.[3] Gardiner *et al.* examined the learning effect for 6 years and concluded that it improved at each yearly visit.[4] The variability of test results decreased significantly with experience and began to appear after the second visit.[3] This learning curve has been reported consistently in other studies, and there is general agreement in the literature that at least three initial tests should be performed.[5,6] However, repeating the tests for reliable results is sometimes problematic, as glaucoma should often be diagnosed as quickly as possible.[5]

The learning curve is due to the psychological phenomenon of the visual system adapting to the process or improvement in the patients' recognition of the stimulus. Therefore, this study aims to evaluate the learning effect of HFA in patients with glaucoma.

Methods

This study was a cross-sectional study. Twenty eyes of 12 patients were recruited from routine follow-ups in the Glaucoma Clinic in Dr. Sardjito Hospital, Yogyakarta, Indonesia. No subjects had media clarity abnormalities (cornea, lens, and vitreous) or retinal diseases. Each participant was then enrolled for three perimetry examinations corresponding to their examination schedule in three different sessions

separated for at least 1 week. In each session, both eyes were examined using the Zeiss HFA (Zeiss Humphrey Field Analyser 3 Visual Field-Testing System, Carl Zeiss Meditec, Germany). Each patient was analysed using the 24-2 SITA Standard test pattern. Patients were excluded if they were not cooperative in each test session.

The HFA assessed the test duration, reliability indices, and global indices. The reliability indices recorded by this study were fixation loss as well as false negatives and false positives, while the global indices were Mean Deviation (MD), Pattern Standard Deviation (PSD), and Visual Field Index (VFI). Statistical analysis was performed using one-way ANOVA for all three sessions, continued by Tukey's post-hoc test.

Results

A total of 20 eyes from 12 patients were examined. The mean participant age was 41 ± 21 years old; seven participants (59%) were women and five (41%) were men. Based on the diagnosis, 10 patients (83.4%) were diagnosed with open-angle glaucoma, 1 patient (8.3%) with angle-closure glaucoma, and 1 patient (8.3%) with secondary glaucoma (Table 1).

The overall test duration was significantly improved on the third attempt compared to the first attempt ($p = 0.017$). The fixation loss also statistically improved in the third attempt compared to the first attempt ($p = 0.001$). Similarly, there was also statistically significant improvement in false-negative value ($p < 0.001$). Lastly, there was a statistically significant improvement in the first attempt compared to the second attempt ($p = 0.008$) and the first attempt compared to the third attempt ($p < 0.001$) (Table 2).

Table 1. Subject characteristics

Characteristics	**Value**
Age (mean ± SD)	41 ± 21 years
Sex	
Male	5 (41%)
Female	7 (59%)
Diagnosis	
Open-angle glaucoma	10 (83.4%)
Angle-closure glaucoma	1 (8.3%)
Secondary glaucoma	1 (8.3%)

Table 2. HFA parameters in three sessions

Parameter	a	b	c	P	a *vs* b	a *vs* c	b *vs* c
Test duration (sec)	387 ± 96	348 ± 77	307 ± 93	0.023	0.353	0.017	0.325
Fixation loss	0.25 ± 0.19	0.16 ± 0.16	0.05 ± 0.11	0.001	0.227	0.001	0.075
False negative	0.15 ± 0.15	0.05 ± 0.08	0.02 ± 0.03	0.000	0.008	0.000	0.639
False positive	0.09 ± 0.14	0.04 ± 0.06	0.02 ± 0.03	0.056	0.207	0.053	0.785
MD (dB)	-8.51 ± 10.26	-6.72 ± 9.85	-6.29 ± 9.52	0.754	0.835	0.759	0.990
PSD (dB)	5.02 ± 3.85	4.29 ± 3.42	3.45 ± 3.42	0.382	0.798	0.349	0.731
VFI (%)	77 ± 31	83 ± 28	84 ± 28	0.730	0.778	0.763	1.000

All data presented as mean ± SD. MD: Mean Deviation; PSD: Pattern Standard Deviation; VFI: Visual Field Index; a: first attempt; b: second attempt; c: third attempt

Discussion

In the present study, we found a significant improvement in test duration, fixation loss, and false-negative reliability indices on the second and third tests. The improvement in test duration indicates the learning effect experienced by the patients, showing that the patients understood how the test works and how to concentrate better compared to the first test. This learning effect was also shown in the improvement of reliability indices (fixation loss and false-negative). However, there was minimal improvement in false positives due to accurate machine settings and parameters used in this study. Global indices were unaffected by repeated examination. The same results were also observed in another study.[7] This might be because MD, PSD, and VFI represent the damage caused by glaucoma, which are reproducible and are not affected by the learning effect.

Perimetry is a subjective test that requires high concentration. Therefore, it is subject to a learning effect as the patient learns to respond consistently during the test, and high reproducibility of test measurements is often considered to diminish the learning effect.[8] Learning may be observed within a single examination of a given eye, between eyes at the same visit, or between subsequent examinations. In the present study, the learning effect diminished after the third session. This result is similar to a previous study that found changes in the threshold sensitivity in the first two sessions that were performed by an inexperienced individual.[9]

Fatigue should be taken into account since a prolonged test duration would produce worse results. Visual fatigue was suspected to be a factor behind result inconsistency. Therefore, patients were advised to rest prior to the first eye test and before beginning the second eye test.[10] One significant factor that creates a poor result on the first attempt is the patient's failure to understand the test.[11] Anxiety may have also influenced the first test results because the first test was conducted during the patients' first hospital visit. Aside from that, the patients may not feel comfortable when seated during the first test.[12] Therefore, this study's limitations were not considering the patients' cognitive level and fatigue for analysis. Further study is required to investigate the association between cognitive levels, anxiety, and patient's performance in HFA testing.

Conclusion

There was shorter test duration, decreased fixation loss, and decreased false negatives after the third HFA examination session, but there was no statistical change to the global indices. Many factors can affect the reliability of visual field examination in glaucoma patients. These factors are patient's cooperation, understanding, psychological condition, and fatigue. These factors should be considered prior to the tests. In addition, at least three perimetry examinations should be taken to obtain a reliable visual field result.

Declarations

Ethics approval and informed consent
The study was conducted in accordance with the Declaration of Helsinki. The authors declared no conflict of interest regarding this paper's publication. The authors were accountable for all aspects of work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved. The authors' institutional ethics board (The Ethics Committee of the Faculty of Medicine, Universitas Gadjah Mada-Dr. Sardjito General Hospital) approved the study by issuing the ethical clearance number KE/FK/0562/EC/2021.

Competing interests
None to declare.

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Fungal corneal ulcers: our 5-year experience in Bintulu

Loshni **Murugia**[1,2], Prem Ananth **Palaniappan**[3], Kenneth **Teow** Kheng Leong[4], **Choo** May May[1,2]

[1]University of Malaya Eye Research Center (UMERC), Department of Ophthalmology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; [2]Department of Ophthalmology, University of Malaya Medical Center (UMMC), Kuala Lumpur, Malaysia; [3]Mycology Section, Bacteriology Unit, Infectious Disease Research Centre, Institute for Medical Research, National Institutes of Health, Selangor, Malaysia; [4]Ophthalmology Department, Hospital Bintulu, Sarawak, Malaysia

Abstract

Purpose: The aim of this study is to investigate the epidemiological and aetiological pattern of fungal corneal ulcers treated in Hospital Bintulu, Sarawak.
Study design: Cross-sectional study.
Methods: This study is based on the data collected from clinical records of patients with culture-positive fungal corneal ulcer who presented to Hospital Bintulu from 2016 to 2020. Data was analysed using descriptive statistical methods.
Results: A total of 13 patients had fungal corneal ulcer. Males (84.6%) were more commonly affected compared to females (15.4%). The age of the patients ranged from 19 to 67 years. The commonest age group involved was 21–40 years, constituting more than half of the patients (53.8%). The mean age of the patients was 38 years old. *Fusarium* sp. was isolated in eight of them (61.5%), all of which had a history of palm oil dust insertion into the eye prior to presentation. Other fungal pathogens found include *Phellinus noxius* sp. in two cases (15.4%) as well as *Ascomyces* sp., *Nectriaceae* sp., and *Colletotrichum trunchatum* sp. in one case each (7.6%). Hypopyon was seen in eight cases (61.5%), where six cases were caused by *Fusarium* sp. while *Ascomyces* sp. and *Nectriaceae* sp. contributed one case each. Mixed fungal and bacterial infection was seen in two cases (15.4%).
Conclusion: This study showed that *Fusarium sp.* is the commonest pathogen causing

Correspondence: Dr. Loshni Murugia, MD, Department of Ophthalmology, University of Malaya, Jln Profesor Diraja Ungku Aziz, 50603, Wilayah Persekutuan Kuala Lumpur, Malaysia.
E-mail: loshni66@gmail.com

fungal corneal ulcer and affects predominantly young male plantation workers. The establishment of a proper framework to educate as well as strict enforcement of occupational safety may reduce the incidence of this disease in the population.

Keywords: blindness, fungal corneal ulcer, fungal keratitis, fungi, *Fusarium*

Ulser kornea akibat jangkitan kulat: pengalaman 5 tahun di Bintulu

Abstrak

Tujuan: Matlamat kajian ini adalah untuk menyiasat pola epidemiologi dan etiologi jenis kulat penyebab ulser kornea yang dirawat di Hospital Bintulu, Sarawak.
Reka bentuk kajian: Kajian keratan rentas.
Bahan dan kaedah: Kajian ini adalah berdasarkan data yang dikumpul daripada rekod klinikal pesakit dengan ulser kornea yang positif kultur untuk kulat, yang menerima rawatan di Hospital Bintulu daripada 2016 sehingga 2020. Data dianalisis menggunakan kaedah statistik deskriptif.
Keputusan: Sejumlah 13 pesakit mempunyai ulser kornea akibat jangkitan kulat. Lelaki (84.6%) adalah lebih kerap mendapat jangkitan ini berbanding wanita (15.4%). Umur pesakit yang terlibat adalah di antara 19 hingga 67 tahun. Umur 21-40 tahun merupakan julat umur yang paling berisiko dan mereka ini merangkumi lebih separuh daripada jumlah pesakit yang terlibat. Purata umur pesakit adalah 38 tahun. *Fusarium sp.* telah dikenalpasti dalam 8 pesakit (61.5%) di mana kesemua pesakit mempunyai sejarah kemasukan habuk kelapa sawit ke dalam mata sebelum hadir ke hospital untuk rawatan. Patogen kulat lain yang ditemui termasuk *Phellinus noxius sp.* dalam 2 kes (15.4%) serta *Ascomyces sp., Nectriaceae sp.* dan *Colletotrichum trunchatum sp.* dalam 1 kes setiap satu(7.6%). Kehadiran nanah (hypopyon) dilihat dalam 8 kes (61.5%) di mana 6 kes disebabkan oleh *Fusarium sp.* manakala *Ascomyces sp.* dan *Nectriaceae sp.* masing-masing menyumbang satu kes. Jangkitan kulat dan bakteria bercampur dilihat dalam 2 kes (15.4%).
Kesimpulan: Kajian ini menunjukkan bahawa *Fusarium sp.* adalah patogen yang paling kerap menyebabkan ulser kornea akibat jangkitan kulat dan kebanyakannya melibatkan pekerja ladang lelaki yang masih muda. Pembentukan satu rangka kerja yang boleh memberi kesedaran dan pengetahuan serta penguatkuasaan ketat keselamatan pekerjaan boleh mengurangkan kejadian penyakit ini di daerah Bintulu.

Kata kunci: buta, Fusarium, keratitis kulat, kulat, ulser kornea kulat

Introduction

Corneal ulcerations are described as corneal epithelium loss with underlying infiltration and suppuration of the stroma associated with signs of inflammation with or without the presence of hypopyon.[1] Corneal ulcers have been acknowledged as one of the most common causes of preventable blindness, second only to cataract in tropical countries.[1,2] In developing countries, approximately 1.5 to 2 million new cases of monocular blindness every year are partly attributed to corneal ulceration.[3] The causative organisms that infect the cornea includes bacteria, viruses, fungi, and parasites.[2]

Fungal keratitis forms a prime component of this disease spectrum and its incidence has been noted to vary from 17% to 36% in various regions worldwide.[4] Various clinical series set in tropical, warm climates such as south Florida, Africa, the Middle East, South Asia, India, and Singapore have described the predominance of fungal keratitis.[5] While India recorded an incidence rate of 44% to 47% due to its tropical climate, Ghana reported an incidence of 37.6 %.[6,7] This is followed by Bangladesh, 36%, and subsequently by south Florida and Nepal with a rate of 35% and 17%, respectively.[7] Geographic regions with temperate climates, however, showed a low incidence as depicted by Great Britain and northern United States.[7]

More than 105 species, classified into 56 genera have been recognized as the causative agents of mycotic keratitis.[8-10] Filamentous fungi, mainly *Fusarium* sp. and *Aspergillus* sp., as well as yeast-like fungi, particularly *Candida* sp., are the two medically important forms of fungi identified.[10] Fungal infections of the cornea often exhibit yellowish-white or greyish-white infiltrates with soft, creamy, raised exudates at the base of the ulcer.[7] Hypopyon is present in 55% of cases, hyphate edges or feathery borders are seen in 70% of cases, and satellite lesions appear in 10% of patients.[7] However, some fungal infections tend to mimic other types of stromal inflammation, posing a challenge in choosing the treatment regime.[6] In addition to the clinical findings, laboratory diagnosis by detection of fungal pathogens on direct microscopy and their isolation by culture is crucial.[6] Prompt diagnosis and treatment are essential to save vision and prevent complications such as endopthalmitis.[10] While current advances in diagnosis and pharmacological treatment are in place, 15–27% of patients still require surgical interventions such as keratoplasty, evisceration, or enucleation due to advanced disease at presentation or failure of medical treatment.[4]

The ophthalmological services in Bintulu Hospital receive emergency eye referrals from many interior primary care facilities. Cases of corneal ulcers contribute to the number of referrals apart from trauma and thus present an opportunity to study the disease from a single health facility. This study is intended to investigate the epidemiological and aetiological pattern of fungal corneal ulcers treated in Hospital Bintulu, Sarawak.

Methods

This study was conducted in compliance with ethical principles outlined in Declaration of Helsinki as well as Malaysian Good Clinical Practice Guideline and has obtained ethical clearance from the country's Medical Research and Ethics Committee. In this cross-sectional study, case records of all patients with fungal corneal ulcers who presented to the Department of Ophthalmology of Bintulu Hospital, Sarawak in the 5-year study period from January 2016 to December 2020, were analysed. All patients underwent a thorough medical history with complete clinical and microbiological examination during presentation. After a clinical diagnosis of infectious corneal ulcer was made, corneal scrapings were taken under slit lamp from the edge and base of ulcers, and were smeared onto two separate slides for direct microscopic examination with gram stain and 10% KOH preparation. Corneal scrapings were also directly inoculated onto Sabouraud agar for fungal culture, and McConkey agar, blood agar, and chocolate agar for bacterial culture.

A fungal corneal ulcer diagnosis was achieved after a positive result in gram stain or culture agar. All patients were started on empirical treatment; the treatment was modified according to response and microbiological tests. Information on possible predisposing factors, demographic data, microbiology results, treatment received, treatment continuity, and visual outcome at the end of 3 months or at the completion of the treatment (whichever happened earlier) were collected from the case records and analysed. Visual impairment of the affected eye was classified according to the International classification of Diseases 11, where the patient is defined to have no visual impairment when visual acuity (VA) is 6/12 and better; mild impairment when VA is worse than 6/12 but better than or equal to 6/18; moderate impairment when VA is worse than 6/18 but better than or equal to 6/60; severe visual impairment when VA is worse than 6/60 but better than or equal to 3/60; and the affected eye is defined as blind when VA is worse than 3/60.[11] Patients with incomplete data in case records, immune-compromised patients, and those who were partially treated prior to presentation were excluded. Descriptive analysis was used in this study.

Results

In the span of 5 years, from January 2016 to December 2020, a total of 13 patients were treated for fungal corneal ulcer. The first 3 years, from 2016 to 2018, recorded only one case each year. Subsequently there was a surge to six cases in 2019 and a slight drop to four cases in 2020. Males (84.6%) were more commonly affected compared to females (15.4%) (Table 1). Foreigners comprised 69.2% of total patients, with the majority coming from Indonesia. The age of the patients ranged from 19 to 67 years old (Table 2). The commonest age group involved was 21–40

Table 1. Gender and ethnicity distribution of fungal corneal ulcer cases

Gender	Ethnicity				Total
	Malay	Iban	Chinese	Foreigner	
Male	1	2	0	8	11
Female	0	0	1	1	2

Table 2. Age distribution of patients with fungal corneal ulcers

Age distribution (years)	Total
0–20	2
21–40	7
41–60	2
61–80	2

years, constituting more than half of the patients (53.8%). The mean age of the patients was 38 years old.

Fusarium sp. represented the highest proportion of fungal pathogen, accounting for eight patients (61.5%). Other fungal pathogens found included *Phellinus noxius* sp. in two cases (15.4%), *Ascomyces* sp., *Nectriaceae* sp., and *Colletotrichum trunchatum* sp. in one case each (7.6%). Hypopyon was seen in eight cases (61.5%): six cases were caused by *Fusarium* sp., while *Ascomyces* sp. and *Nectriaceae* sp. contributed one case each. Mixed fungal and bacterial infection was seen in two cases (15.4%).

Table 3 summarizes the preceding trauma and isolated organisms among patients. Oil palm dust was found to be the most common source of trauma in our patients. A total of nine patients (69.2%) claimed to have experienced dust particles from palm oil fruit or leaves falling into their eye before their painful ordeal begun. Most of them were Indonesian palm oil workers and none of them wore goggles or personal protective gear. Of these patients, Sabouraud culture grew *Fusarium* sp. in eight and the remaining one grew *Nectriaceae* sp. A patient whose preceding trauma was contact lens was infected with *Phellinus noxius* sp., while *Colletotrichum trunchatum* sp. was isolated from a patient injured by a plant branch while gardening. The remaining two patients were unsure of any presence of trauma.

Table 4 summarizes the percentage of visual impairment among patients. More than one-third (38.5%) of our cases were blind (as per ICD 11) in the affected eye at the time of discharge or default to follow-up. Severe visual impairment affected 7.7% cases. Recovery with no visual impairment was observed in 30.7% of patients, while the remaining 15.4% and 7.7% were categorized under moderate and mild visual impairment, respectively. Patients presented to the hospital at an average of 6.9 days after onset of symptoms and a regrettable 69.2% either requested an “at own risk” discharge or defaulted follow-ups prior to treatment completion.

Table 3. Preceding trauma and organisms isolated from the corneal ulcers

Organism	Preceding trauma				Total
	Palm oil dust	Contact lens	Plant branch	Unknown	
Fusarium sp.	8	0	0	0	8
Nectriaceae sp.	1	0	0	0	1
Ascomyces sp.	0	0	0	1	1
Colletotrichum trunchatum sp.	0	0	1	0	1
Phellinus noxius sp.	0	1	0	1	2
Total	9	1	1	2	13

Table 4. Percentage of patients with visual impairment at the time of discharge or default to follow-up according to severity as per ICD 11

Severity	Visual impairment (%)
None (VA 6/12 and better)	30.7
Mild (VA worse than 6/12 but better than or equal to 6/18)	7.7
Moderate (VA worse than 6/18 but better than or equal to 6/60)	15.4
Severe (VA worse than 6/60 but better than or equal to 3/60)	7.7
Blindness (VA worse than 3/60)	38.5

VA: visual acuity

Discussion

The prevalence of fungal corneal ulcer from various fungal pathogens has been estimated to be 1.3/100,000 people in Malaysia.[12] Most studies have addressed the role of geographic and climate variation in the predominance of certain fungal agents.[1,4,6,13-14] Bintulu, being a region with tropical climate, has been seeing a rise in fungal corneal ulcers. Therefore, it is crucial to identify the commonest fungal pathogen, correlate with risk factors, and manage the diseases before it progresses into a fulminating infection leading to blindness. While treatment of this debilitating disease has been costly and burdensome, the final visual outcomes are often

guarded.[15] The ability of fungal infections to masquerade as other infections leads to delayed diagnoses and makes treatment more challenging.

Fusarium sp. was the commonest species found to have infected our patients. This concurs with many previous studies that have yielded similar results.[16-18] It is important to note that all patients whose fungal isolates were *Fusarium* sp. were Indonesian palm oil workers in Sarawak. Agriculture is closely related to the incidence of fungal corneal ulcer in many countries.[19-21,20] Initial history from these patients revealed that symptoms were preceded by traumatic injury caused by palm oil dust or leaves while working. *Fusarium* sp. is known to be found in almost all ecosystems and commonly infects agricultural crops, therefore explaining our findings.[22] In addition, this species is said to be found in organic debris and all plant parts, from highest flowers to deepest roots.[23] Interestingly, a study in Malaysia on crown disease, a disease affecting palm oil trees that has been reported from palm oil plantations worldwide, isolated five different types of *Fusarium* sp. from palm oil leaves.[24] Moreover, a study has quoted that humid and warm climates are favourable to the growth of this fungus, which explains its prevalence in this part of the world.[25]

Our mean age of 38 years old does not follow trends in other studies performed worldwide, where the mean ranged from 40 to 56.1 years of age.[26-29] The lower figure may be attributed to the fact that most of the study subjects were young palm oil plantation workers. According to a study conducted in east Malaysia in 2019, the mean age of palm oil plantation workers was 30 years old, with males dominating the industry by 80%.[30] Male preponderance in this infection was evident with a male-to-female ratio of 5.5:1, mostly related to occupational ocular trauma. Men are also known to be more actively involved in outdoor activities and frequent contact with soil and nature, predisposing them to a greater exposure to fungal pathogens.[17]

Infection involving *Fusarium* sp. and *Aspergillus* sp. is a significant risk factor for hypopyon, a common finding in fungal keratitis.[31] Ocular examination findings in our study revealed hypopyon in 61.5% subjects. In China, Xu *et al.* observed hypopyon in 52.6% of fungal keratitis patients, while Shi *et al.* noted hypopyon in 47.9% of patients diagnosed with fungal keratitis.[31-32] A similar study in Mexico revealed hypopyon in 65.5% patients with *Fusarium* keratitis.[33] In this study, we noticed hypopyon in 75% of patients with *Fusarium* keratitis. On that account, hypopyon may be considered as a clinical indicator for commencing empirical antifungal regime after correlation with presenting history, which may improve prognosis of this debilitating disease.

According to the ICD 11, 38.5% of our patients were classified as blind and 7.7% as severely visually impaired in the affected eye at the time of discharge or default to follow-up. This was further worsened by a high “at own risk” discharge and default to follow-up rate of 69.2%, with 77.8% of defaulters being foreigners. The financial constraints following the need for a long hospital stay, travelling for follow-up, and costly antifungal medications may be contributing factors for this high rate, especially among foreigners. A study based on medical treatment for Fusarium keratitis reported that patient may require long hospital stay with an average of 31.5

days with a mean fee of USD 1,559.39.[34] The need for frequent travel for follow-up in certain cases may also be a major barrier, particularly for those travelling from the interiors of Sarawak. Furthermore, in severe cases such as corneal perforation, patients are required to travel approximately 1,200 km to west Malaysia by flight for a penetrating keratoplasty.

Bintulu has the third largest palm oil plantation in Sarawak, with foreigners comprising 47% of the workers employed.[35] As observed in our study, most of our patients were foreign palm oil plantation workers. A study done in west Malaysia reported that most palm oil plantation workers are on low incomes.[30] Many palm oil companies subscribe insurance for their employees. However, some faile to do so, leading to inability to afford medical expenses when unfortunate events occur. This problem arises commonly among foreigners who commonly request an "at own risk" discharge to return to their native country for further treatment, as observed in many of our study patients. Some studies have also addressed socioeconomic status as a potential risk factor of fungal corneal ulcers; this should be taken into account considering the fact that Sarawak has recorded a gross household income lower than the national average in the nation's recent socioeconomic report.[2,9,36] Tackling these financial burdens may lead not only to a reduction of fungal corneal ulcer cases but also improve prognosis of those suffering from this disease.

Most palm oil workers are not provided with protective gear for use at work.[30] According to national guidelines, the Department of Occupational Safety and Health (DOSH) Malaysia stressed the need for personal protective equipment wear for pesticide sprayers in the agricultural field, whereas there were no clear guidelines for fresh fruit harvesters.[37] Within palm oil plantations, DOSH should create awareness and enforce the use of protective goggles as preventive measures also among fresh fruit harvesters, now that it is evident that trauma from palm oil dust is a major preceding factor for fungal corneal ulcers. A direct referral pathway to specialist hospitals from these plantations via their DOSH team may also hasten the commencement of treatment, as patients only present to the hospital 6.9 days after initial symptoms. Early treatment may reduce ocular morbidity, reduce duration of hospitalization, and increase national work productivity.

Conclusion

This study showed that the *Fusarium* sp. was the commonest pathogen causing fungal corneal ulcers and affected predominantly young male plantation workers. The establishment of a proper framework to educate as well as strict enforcement of occupational safety may reduce the incidence of this disease in the population.

Declarations

Ethics approval and consent to participate

This is a retrospective study of the medical records of patients in Hospital Bintulu from 2016 to 2020. This study adhered to the tenets of the Declaration of Helsinki and ethical approval was obtained from the Medical Research and Ethics Committee, Ministry of Health Malaysia (Research ID: 59201).

Competing interests

The authors declare no conflicts of interest with respect to the publication of this article.

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Effect of a patient educational video on visual field test reliability

Lee Hsin Yi[1,2], Norlina **Ramli**[2], **Nurul Akma** bt Saharuddin[1], **Siti Faeza** Hanim Syed Yaziz[1], **Ong** Poh Yan[1]

[1]Department of Ophthalmology, Hospital Selayang, Selangor, Malaysia; [2]Department of Ophthalmology, University Malaya, Kuala Lumpur, Malaysia

Abstract

Purpose: Standard automated perimetry (SAP) is the gold standard for detecting and monitoring visual field (VF) defects in glaucoma, but frequent re-testing due to unreliable results increase the burden on this frequently used service. This study aims to assess the reliability of the Humphrey visual field (HVF) test in glaucoma-suspect patients with no previous SAP experience and to determine the effect of a VF test educational video on reliability.
Study design: The study was conducted as a full cycle audit.
Methods: The audit cycle was carried out in four phases: pre-intervention audit, intervention, monitoring, and post-intervention audit. The pre-intervention audit was carried out from January 2020 to May 2020 and the post-intervention audit was carried out from September 2020 to December 2020. The intervention was in the form of a VF test educational video. A post-video assessment pertaining to the contents of the video was given to patients in the intervention group to complete after they watched the video. The results were then tabulated and analysed.
Results: The pre-intervention audit showed that only 66.7% of glaucoma-suspect patients with no previous SAP experience had reliable HVF tests. Post-intervention, HVF reliability improved to 87.5% of patients. Based on the reliability parameters, the main reason for the HVF test being classified as unreliable in both the pre- and post-intervention was fixation loss greater than 20% in 36 (90%) and 11 (73.3%) patients, respectively. There were 76.9% of patients with unreliable fields who had < 4 correct answers on the post-video assessment; all patients who had > 4 correct answers had reliable HVF results.

Correspondence: Lee Hsin Yi, MD, Department of Ophthalmology, Hospital Selayang, Lebuhraya Selayang - Kepong, 68100 Batu Caves, Selangor, Malaysia.
E-mail: adrianne0786@gmail.com

Conclusion: HVF reliability performance in glaucoma-suspect patients improved with the introduction of a pre-test educational video. It is a simple and inexpensive method which may reduce the need for repeat HVF tests for those with unreliable tests.

Keywords: glaucoma suspect, standard automated perimetry, visual field test reliability

Keberkesanan video pendidikan terhadap prestasi kebolehpercayaan ujian medan penglihatan

Abstrak

Pengenalan: Perimetri automatik ialah ujian piawaian emas untuk mengesan dan memantau kecacatan medan penglihatan Humphrey Visual Field (HVF) dalam penyakit glaukoma, tetapi keperluan ujian ini untuk diulang kerana keputusan yang kurang memuaskan akan meningkatkan beban perkhidmatan di klinik. Kajian ini bertujuan untuk menilai kebolehpercayaan ujian medan penglihatan di kalangan pesakit yang disyaki glaucoma yang tiada pengalaman menjalani ujian perimetri. Kajian juga bertujuan menentukan keberkesanan video pendidikan terhadap kebolehpercayaan hasil ujian ini.
Reka bentuk kajian: Kajian audit pra dan pasca intervensi.
Kaedah: Kitaran audit telah dijalankan dalam empat fasa bermula dengan audit pra-intervensi, diikuti dengan fasa intervensi dan pemantauan. Akhir sekali, fasa pasca intervensi dijalankan. Audit pra-intervensi telah dijalankan dari Januari 2020 hingga Mei 2020 dan audit pasca intervensi dijalankan dari September 2020 hingga Disember 2020. Intervensi adalah dalam bentuk video pendidikan ujian medan penglihatan. Penilaian siaran video yang berkaitan dengan kandungan video telah diberikan kepada pesakit dalam kumpulan intervensi untuk dilengkapkan selepas mereka menonton video tersebut.
Keputusan: Audit pra-intervensi menunjukkan bahawa hanya 66.7% pesakit disyaki glaukoma tanpa pengalaman ujian perimetri mempunyai ujian HVF yang memuaskan. Selepas intervensi, angka ini meningkat kepada 87.5% pesakit.
Berdasarkan parameter kebolehpercayaan, sebab utama ujian HVF tidak memuaskan dalam kedua-dua kumpulan pra dan pasca intervensi ialah kehilangan arah penglihatan 'fixation loss' (FL) lebih daripada 20% iaitu 36 (90%) dalam kumpulan pra-intervensi dan 11 (73.3%) dalam kumpulan pasca intervensi. 76.9% pesakit yang mempunyai HVF kurang memuaskan mendapat skor <4 dalam penilaian video, padahal semua pesakit yang medapat skor >4 menghasilkan HVF yang memuaskan.

Kesimpulan: Prestasi kebolehpercayaan HVF di kalangan pesakit yang disyaki glaukoma bertambah baik dengan pengenalan video pendidikan pra-ujian. Ia adalah kaedah yang mudah dan murah yang mampu mengurangkan keperluan untuk ujian HVF berulang bagi mereka yang mempunyai ujian HVF yang tidak memuaskan.

Kata kunci: glaucoma syak, kebolehpercayaan ujian medan penglihatan, ujian medan penglihatan

Introduction

Glaucoma is a progressive optic neuropathy with characteristic changes in the optic nerve head and corresponding visual field (VF) loss. It is a debilitating disease and the leading cause of global irreversible blindness.[1–3] Its insidious onset is often associated with diagnostic delay.

Management of glaucoma aims to maintain maximal functional vision by reducing its rate of progression; reduction of intraocular pressure is the only modifiable risk factor to prevent glaucoma progression.[4,5] To date, no single test or combination of tests has been identified as optimal in screening for glaucoma.[6] However, a combination of VF testing, assessment of optic disc and retinal nerve fibre layer, and tonometry may be used.[7]

Standard automated perimetry (SAP) is the gold standard for detecting and monitoring VF defects in glaucoma, but abnormal reliability parameters will render the test inaccurate. An unreliable test result cannot be used for clinical decision making and hence requires repeated testing. To tackle this issue, multiple studies have been conducted in an effort to identify possible factors that influence VF test reliability and ways to improve it.[8–11] Humphrey visual field (HVF) analyser (Carl Zeiss Meditec, Dublin CA, USA) is a commonly used static automated perimetry to measure VF.

A study conducted by Sherafat *et al.* looked into the reliability of VF test results with the introduction of a patient training video.[10] Although the results seemed promising, their patient group included various ocular pathologies and 82% of them were not HVF-naïve. Furthermore, test performance by technicians was also not standardized.

An audit is part of continuous quality improvement process that focuses on specific aspects of health care and clinical practice with the aim to highlight discrepancies between standards and actual practice in order to identify the changes needed to improve the quality of care. They consist of measuring a clinical outcome or process against well-defined standards set on the principles of evidence-based medicine. A full cycle audit identifies and implements changes to improve the clinical outcomes and re-audits the clinical practice to see whether the outcomes have changed for the better.

The main aim of this study was to assess whether the introduction of an educational video prior to testing improved the reliability of HVF tests in glaucoma-suspect patients with no previous SAP experience.

Methods

This audit was conducted in the Ophthalmology Clinic, Selayang Hospital. Only glaucoma suspects with no prior SAP tests were included. Inclusion criteria were patients aged 18 and above who underwent automated VF testing for the first time. Based on the National Clinical Practice Guideline for Glaucoma published in 2018, glaucoma suspects are individuals with suspicious glaucomatous optic disc appearance regardless of intraocular pressure and/or risk factors that increase the likelihood of developing glaucoma.[7] Risk factors include older age, positive family history of glaucoma, obstructive sleep apnoea syndrome, and diabetes mellitus. These patients were thoroughly examined in the Ophthalmology Clinic and subsequently scheduled for a HVF test.

Exclusion criteria included presence of ocular diseases affecting central vision, such as macular scarring, age-related macular degeneration, and diabetic maculopathy, and presence of dementia, stroke, severe arthritis, hearing loss, or any other systemic conditions that result in physical difficulties to perform a reliable VF test.

The study was conducted in accordance with the Declaration of Helsinki and adhered to Good Clinical Practice guidelines. Approval for the study was obtained from the local Medical Research and Ethics committee (NMRR-19-3527-51947). All patients provided written informed consent prior to enrolment.

The 24-2 SITA Fast strategy was used for screening glaucoma suspects. Data from the first eye was collected, which was routinely fixed as the right eye. However, when vision in the right eye was poor and the patient was unable to perform the HVF test, the left eye was used as the first eye. Once the test was completed, the results were printed out and reviewed.

A standard set by the manufacturers of the SITA test was used, with a cut-off of less than 20% for fixation loss (FL) rate and less than 15%for false-positive (FP) response rate to define a VF test as reliable.[12] The false-negative (FN) response cut-off rate was initially set at 33%. However, it was no longer considered while flagging a test result as unreliable, as FN rate estimates are elevated in glaucomatous VF tests, even in highly attentive patients. A study conducted by Katz *et al.* found that 81% of normal study participants were reliable on their first C30–2 full threshold VF test.[11] Sherafat *et al.* also reported a of reliability of 80.3% for the first attempt of a VF test.[10]

The audit cycle was carried out as part of a continuous quality improvement exercise. It consisted of four phases, starting with the pre-intervention audit to collect data that was then analysed against set standards, followed by the interven-

tion and monitoring phase. Subsequently, a post-intervention audit was conducted. The patients in each phase comprised different groups of people.

The pre-intervention audit was carried out from January 2020 to May 2020. Demographic data, best-corrected visual acuity (BCVA) with Snellen chart, and HVF test results of all glaucoma-suspect patients with no previous SAP experience were collected and analysed. Demographic data collected included age, ethnicity, gender, and education level. In this phase, we identified the possible factors affecting VF test reliability and explored methods to overcome these issues.

The intervention phase was conducted in July 2020 on a new group of patients. The purpose of the intervention was to enhance the patient's understanding regarding the VF test they were about to undergo. All patients were individually shown a standard educational video explaining the procedures involved in a VF test. The educational video was produced in house in both English and Malay with a total duration of 4.5 minutes. The patients then completed a post-video assessment containing seven questions that evaluated the patient's understanding of the video contents prior to performing the VF test. After watching the educational video, patients still received instructions from the technician monitoring the VF test as per usual practice. The VF test was conducted within 30 minutes of watching the complete video.

During the monitoring phase in August 2020, the reliability of HVF results were reviewed and analysed. It served as an adaptation period for technicians supervising the test to ensure that new patients were shown the educational video prior to performing the HVF test. Reminders were sent via a messaging application to the technicians' handphone devices at the beginning of each week prior to the patients' VF appointment.

A final post-intervention audit was conducted from September 2020 to December 2020 to reassess the reliability of VF tests in glaucoma-suspect patients who had no prior VF tests. Results were tabulated and compared against the earlier audit.

Results

A total of 473 HVF test were performed by patients with no prior SAP experience in 2020. From January to May 2020, 120 HVF tests were performed by glaucoma-suspect patients from a total of 163 tests. Meanwhile, 147 HVF test were performed by glaucoma-suspect patients from a total of 191 tests from September to December 2020. In the post-intervention audit, the first 120 consecutive patients were recruited for direct comparison.

A summary of sociodemographic data for the pre-intervention and post-intervention audits is provided in Table 1, which shows no significant difference between the population groups in the pre- and post-intervention audits in terms of age, gender, ethnicity, and education level. BCVA was also not significantly different between the

Table 1. Sociodemographic data of patients

	Pre-intervention audit, *n* (%)	**Post-intervention audit, *n* (%)**	***p*-value**
Age (years)			0.713
21-40	15 (12.5)	16 (13.3)	
41-60	47 (39.1)	48 (40)	
61-80	58 (48.3)	56 (46.7)	
Gender			0.439
Male	63 (52.5)	57 (47.5)	
Female	57 (47.5)	63 (52.5)	
Race			0.569
Malay	51 (42.5)	57 (47.5)	
Chinese	50 (41.7)	42 (35.0)	
Indian	19 (15.3)	21 (17.5)	
Education level			0.273
Primary school	33 (27.5)	36 (30.0)	
Secondary school	49 (40.8)	57 (47.5)	
Tertiary education	38 (31.7)	27 (22.5)	

two groups, as shown in Table 2. There was a significant improvement in reliability noted after the intervention, from 66.7% to 87.5%. Figure 1 shows the reliability of HVF test results from the pre- and post-intervention audits. Based on the pre-intervention audit, 40 patients (33.3%) had unreliable HVF test results compared to only 15 patients (12.5%) post-intervention.

Reasons for the HVF being classified as unreliable in the pre-intervention audit were FL greater than 20% in 36 patients, and both FL greater than 20% and FP response rate greater than 15% in 4 patients. Meanwhile, in the post-intervention audit, FL was greater than 20% in 11 patients, FP response rate was greater than 15% in 2 subjects, and both FL greater than 20% and FP response rate were greater than 15% in 2 patients.

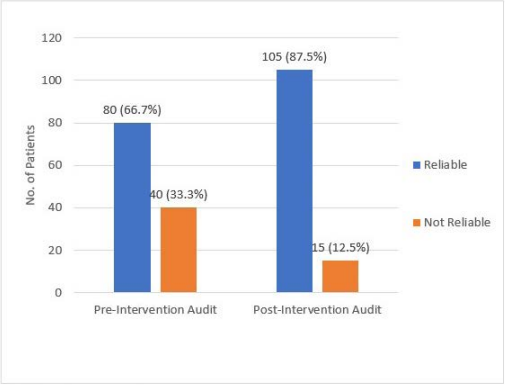
The overall performance and reliability parameters of the HVF test results are summarized in Table 3. The duration of VF test is shown in Table 4. Although the mean duration of HVF test was shorter in the post-intervention audit, the difference was not statistically significant. A summary of the post-video assessment results and the reliability of these VF tests are shown in Figure 2.

Binary logistic regression was used to further analyse age, race, gender, education level, and BCVA of patients to determine the factors affecting HVF test reliability. The results from the pre-intervention audit revealed that only education level was

Table 2. BCVA of patients in pre-intervention audit and post-intervention audit

BCVA	Pre-intervention audit, *n* (%)	Post-intervention audit, *n* (%)	*p*-value
> 6/9	93 (77.5)	77 (64.2)	0.075
6/12–6/18	21 (17.5)	33 (27.5)	
6/24–6/36	6 (5.0)	10 (8.3)	

BCVA: best-corrected visual acuity



*HVF: Humphrey visual field

Fig. 1. Reliability of HVF test results.

Table 3. Overall performance

Performance	Pre-intervention audit	Post-intervention audit	▲▼
Patients with poor reliability parameters (n = 120)			
FL > 20%	36 (30.0%)	11 (9.2%)	▼ 22.5%
FP > 15%	0	2 (1.7%)	▲ 1.7%
FL > 20% and FP > 15%	4 (3.3%)	2 (1.7%)	▼ 1.6%
Patients with good reliability parameters (n = 120)			
FL < 20% and FP < 15%	80 (66.7%)	105 (87.5%)	▲ 20.8%
Mean (SD) of reliability parameters			
FL	18.4 (1.68)	12.8 (1.17)	▼5.6
FP	3.6 (7.72)	3.7 (5.17)	▲0.1

FL: fixation loss; FP: false positive

Table 4. Comparison of Humphrey visual field test duration pre-intervention and post-intervention

	Pre-intervention audit	**Post-intervention audit**	***p*-value**
	Mean (SD)		
Duration (min)	5.1 (1.43)	4.2 (1.29)	0.792

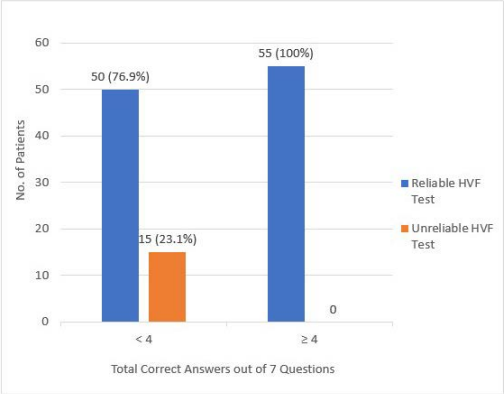


Fig. 2. Post-video assessment results from post-intervention audit. HVF: Humphrey visual field

associated with HVF test reliability ($p \leq 0.05$). The post-intervention audit showed that none of the factors above was significantly associated with HVF test reliability. These results are represented in Table 5 and Table 6.

Table 5. Factors affecting Humphrey visual field reliability in pre-intervention audit (*n* = 120)

Variables	**β**	**95% CI**	***p*-value**
Age group (years)	0.177	0.977, 1.457	0.083
Ethnicity			
Malay (Ref)			
Chinese	-1.109	0.109, 0.995	0.049
Indian	-0.196	0.208, 3.243	0.779
Gender			
Male (Ref)			
Female	-0.753	0.180, 1.232	0.125
Education Level			
Primary (Ref)			
Secondary	**2.251***	1.580, 57.079	*0.014*
Tertiary	**3.313***	3.662, 20.621	*0.001*
BCVA			
> 6/9 (Ref)			
6/12–6/18	0.625	0.594, 5.877	0.285
6/24–6/36	-1.593	0.019, 2.175	0.188

Hosmer and Lemeshow test p-value = 0.969
β: β-coefficient; 95% CI: 95% confidence interval; BCVA: best-corrected visual acuity

Table 6. Factors affecting Humphrey visual field reliability in post-intervention audit (*n* = 120)

Variables	β	95% CI	*p*-value
Age group (years)	-0.067	0.805, 1.087	0.385
Race			
Malay (Ref)			
Chinese	0.279	0.318, 5.499	0.701
Indian	-0.252	0.211, 5.704	0.913
Gender			
Male (Ref)			
Female	-0.252	0.223, 2.712	0.693
Education Level			
Primary (Ref)			
Secondary	0.636	0.304, 11.708	0.495
Tertiary	0.828	0.343, 15.270	0.932
BCVA			
> 6/9 (Ref)			
6/12 – 6/18	-0.546	0.130, 2.578	0.474
6/24 – 6/36	-1.014	0.028, 4.617	0.435

Hosmer and Lemeshow test p-value = 0.363

β: β-coefficient; 95% CI: 95% confidence interval; BCVA: best-corrected visual acuity

Discussion

This study shows that there was a significant improvement in VF test reliability post-intervention among glaucoma-suspect patients with no previous SAP experience. Results from this audit showed that the VF test educational video improved HVF performance reliability from 66.7% of patients pre-intervention to 87.5% post-intervention. This has also been demonstrated in a previous study conducted by Sherafat *et al.* which noted significant improvement of patients' VF test reliability after watching an educational video.[10]

The introduction of a standardised information video provides patients with information regarding the key points of the VF test and further reinforces the technician's instructions. The video contains clear explanations on how to perform the VF test correctly, which entails emphasising the importance of maintaining fixation and resisting the tendency to be "trigger happy" with responses. Furthermore, the video clarifies some of the uncertainties that may arise during the first VF test,

such as reminding the patient that, although they should maintain fixation, they are allowed to blink during the test, that the stimulus varies in brightness, and that they are allowed to pause if needed.

The SITA Fast algorithm was used for glaucoma screening of all patients in this study. Pierre-Filho *et al.* found there was no difference in sensitivities and specificities between SITA Standard and SITA Fast in perimetrically inexperienced individuals.[13] Although SITA Standard is a more precise testing algorithm than SITA Fast at lower VF sensitivities, it is unlikely to make a sizeable difference to improving the time to detect VF progression.[14] In this audit, the mean duration of the HVF test was similar to the average individual test time using SITA Fast, which is 5.0 minutes.[15]

The reliability parameters FL, FP, and FN were analysed; the percentage of FL was lower post-intervention. A previous study by Peracha *et al.* found that the majority of unreliable fields were due to FL.[16] FN was not used to flag a test as unreliable in this study as increased FN is strongly associated with glaucomatous VF status.[17] However, it is worth noting that even small frequencies of FN errors can lead to the inaccurate classification of a VF test as being glaucomatous.[18]

Patients were given a post-video assessment after viewing the VF educational video to evaluate their understanding of the test. There were 54.2% of patients who scored less than four answers correctly out of a total of seven questions. However, all patients who scored more than four answers correctly had reliable HVF tests. Based on this finding, it is possible that better understanding yields more reliable HVF results. Visualization and imagery have been noted to improve learning skills and transfer of knowledge.[19,20] Meanwhile, other studies have reported that adequate and careful patient instruction plays a major role in yielding reliable VF tests.[21,22]

Based on the results from the pre-intervention audit, only education level was associated with HVF test reliability ($p \leq 0.05$). On the other hand, the post-intervention audit revealed that none of the factors such as age, gender, ethnicity, education level, and BCVA was significantly associated with HVF test reliability. With the introduction of the educational video, education level was no longer a significant factor affecting reliability. This finding indicates that the VF educational video is beneficial for all patients regardless of their education level. Tan *et al.* reported that age, education level, and number of previous VF tests are major factors affecting the reliability of VF testing.[23] Another study by Bittner *et al.* found that level of vision loss was not significantly associated with HVF reliability.[24]

This study had several limitations. The technician's instructions were not standardised, as it is not representative of a typical hospital eye service clinic. All patients generally had their VF test done in the morning (8 am to 1 pm) but the waiting time was not considered in our analysis. The patient's performance might be affected by fatigue if the waiting time is longer. Despite the promising results obtained from this audit, patients who are repeating the VF test at a later interval

may not benefit as much from the patient educational video. Further studies can be conducted to establish the long-term effectiveness of the educational video. The effectiveness of the educational video in patients who are not VF-naïve would also be insightful.

Conclusion

HVF performance reliability in glaucoma-suspect patients undergoing VF tests for the first time improved with the introduction of an educational video prior to testing. It is a simple and inexpensive way of using available clinic time to enforce key points of the HVF test and may reduce the number of repeat tests due to unreliable results.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki and adhered to Good Clinical Practice guidelines. Approval for the study was obtained from the local Medical Research and Ethics Committee (NMRR-19-3527-51947). All patients provided written informed consent.

Competing interests
None to declare.

Funding
None to declare.

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The prevalence, clinical profile, and visual outcome of optic neuritis in Hospital Kuala Lumpur: a Malaysian perspective

Goh Ee Pian[1], Nurul 'Ain Binti **Masnon**[2], Lakana Kumar **Thavaratnam**[3], Shanthi Viswanathan **Shantakumar**[4], Tajunisah Begam Bt **Mohd Iqbal**[1]

[1]Department of Ophthalmology, UM Eye Research Centre (UMERC), University Malaya, Kuala Lumpur, Malaysia; [2]Department of Neuro-Ophthalmology, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia; [3]Department of Neuro-Ophthalmology, Sunway Eye Centre, Sunway Medical Centre Velocity, Kuala Lumpur, Malaysia; [4]Department of Neurology, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia

Abstract

Purpose: To study the clinical presentation, visual outcome, and predictors for both recurrence and poor visual recovery among optic neuritis (ON) patients in the Malaysian population.
Study design: Retrospective cohort study with longitudinal follow-up.
Methods: A total of 113 patients from the neuro-ophthalmology clinic fulfilling optic neuritis inclusion criteria within 4 weeks of onset were included. The study was conducted from May 2015 to June 2018. Demographic data, clinical findings, ophthalmological investigation, serological investigation, and imaging results were documented and tabulated. Patients were followed up to 1 year to assess the visual outcome and evidence of retinal nerve fibre layer (RNFL) thinning. Significant associative factors for recurrence and poor visual outcomes were identified using multivariate analysis.
Results: The age of the patients ranged from 13 to 71 years of age. The commonest age of presentation was 15–49 (67.3%) years of age. ON was predominant among Malays (65.5%), followed by Chinese (21.2%), and Indians (13.3%). The commonest form of ON was neuromyelitis optica spectrum disorder (NMOSD), which affected

Correspondence: Dr. Goh Ee Pian, M.Ophthal (UM), UM Eye Research Centre (UMERC) Department of Ophthalmology, University Malaya, 50603 Kuala Lumpur, Malaysia.
E-mail: nic85@live.com

all ethnicities. Significant predictors for recurrence of ON were presentation within the 15–49 age group (p = 0.013) and presence of RNFL thinning following 1 year of treatment (p = 0.001). Indians had significantly lower odds of recurrence, 0.063 (p = 0.015). Significant variables associated with poor visual outcome > 6/18 were poor presenting vision > 6/18 (p < 0.001) and evidence of RNFL thinning following 1 year of treatment (p = 0.003). Females had better visual prognosis (p = 0.005) than males.
Conclusion: NMOSD was the commonest form of ON in our study population. The presenting age group of 15–49 along with the presence of RNFL thinning within 1 year of treatment were significantly associated with recurrence. Additionally, evidence of RNFL thinning and poor presenting vision > 6/18 were associated with a poor visual outcome. This group of patients will require regular monitoring and early access to treatment.

Keywords: Malaysia, optic neuritis, recurrence, visual outcome

Prevalen, profil klinikal dan ketajaman penglihatan selepas optik neuritis di Hospital Kuala Lumpur: perspektif dikalangan rakyat Malaysia

Abstrak

Objektif kajian: Bagi mengkaji manifestasi klinikal, ketajaman penglihatan, dan faktor ramalan kepada kemungkinan serangan ulangan dan ketajaman penglihatan yang kurang baik dikalangan pengidap optik neuritis (ON) di Malaysia
Reka bentuk: Kajian kohort retrospektif
Metodologi: Seramai 113 pesakit dari klinik neuro-oftalmologi yang memenuhi kriteria penyakit ON dalam tempoh 4 minggu penyakit ini bermula, tanpa mengira umur, bilangan pengulangan dan laterality mata telah direkrut antara Mei 2015 sehingga Jun 2018. Data demografi, penemuan klinikal, hasil ujian oftalmologi, ujian serologi dan hasil pengimejan telah didokumentasikan dan dijadualkan menurut kepelbagaian etnik. Pesakit disusuli selama setahun untuk menilai ketajaman penglihatan dan perubahan ukuran ketebalan lapisan gentian saraf retinal (RNFL). Faktor-faktor yang meramalkan keberulangan dan ketajaman penglihatan yang teruk telah dikenalpasti menggunakan analisis multivariasi.
Dapatan kajian: Kebanyakan pesakit kita tergolong di antara umur 15-49 (67.3%). Sebahagian besar penyakit ini melibatkan kaum Melayu (65.5%), diikuti kaum

Cina (21.2%) dan kaum India (13.3%). Neuromyelitis Optica Spectrum Disorder (NMOSD) merupakan punca utama ON dalam populasi kami dan penyakit ini melibatkan sebahagian besar kaum Cina. Faktor-faktor penting yang berkait dengan ramalan keberulangan ON adalah umur di antara 15-49 (p = 0.013), dan ukuran RNFL yang menjadi semakin nipis selepas setahun dalam rawatan (p = 0.001). Kaum India didapati berkemungkinan rendah untuk keberulangan penyakit ON (p = 0.015). Pesakit yang mempunyai kenipisan RNFLyang semakin rendah selepas rawatan dalam setahun (p = 0.001) serta penglihatan teruk >6/18 pada awalnya (p < 0.001) berpotensi tinggi untuk mendapat penglihatan yang teruk selepas setahun dalam rawatan. Majoriti pesakit perempuan didapati mempunyai penglihatan yang baik selepas setahun dalam rawatan (p = 0.005).
Kesimpulan: Penyakit NMOSD merupakan punca utama penyebab ON di kalangan masyarakat di Malaysia, terutamanya di kalangan kaum Cina. Kajian kita menunjukkan golongan pesakit berumur diantara 15-49 tahun dan ketebalan RNFL yang nipis selepas setahun dalam rawatan berisiko untuk mendapat penyakit ON berulang. Ketebalan RNFL yang nipis selepas rawatan serta datang dengan penglihatan teruk pada mulanya berisiko mendapat dengan hasil penglihatan teruk selepas setahun dalam rawatan. Golongan pesakit ini perlu pemantauan yang lebih kerap dan mendapat rawatan awal.

Kata kunci: kaum Melayu, keberulangan, ketajaman penglihatan, optik neuritis

Introduction

Optic neuritis (ON) is defined as an inflammation of the optic nerve, which can present in an acute or subacute manner.[1] It is a rare disease with an incidence rate of 5.1 in 100,000 per year in central Europe.[2] The results of the Optic Neuritis Treatment Trial (ONTT) were instrumental in the study of the presentation and treatment of ON. The landmark study later introduced a standardised treatment for ON that has been adopted widely to date, which is mainly applicable to clinically isolated syndrome (CIS) and multiple sclerosis (MS).[3]

The ONTT study was conducted in a Caucasian population, whereby the majority of ON cases were found to be associated with MS.[4] Other forms of demyelinating ON diseases and treatment responses were not well studied. The advancement of serological markers contributed to the discovery of new antibody-related ON, such as anti-aquaporin 4 (anti-AQP4) antibody and anti-myelin oligodendrocyte (anti-MOG) antibody, which have been recognised as a separate entity of demyelinating disease.[5] The demyelinating disease presentation is atypical of ON and does not respond well to the standard ONTT treatment regime. They are associated with treatment resistance, frequent recurrences, and poorer visual prognosis.[6,7]

We aim to determine the prevalence, clinical presentation of ON, identify predictors for recurrence of ON, evaluate the visual outcome after 1 year of treatment, and identify associative factors of poor visual outcome among our diversified population.

Methods

A retrospective cohort study was conducted on the prevalence and presentation of ON among the three different major ethnics in Hospital Kuala Lumpur's (HKL) Neuro-Ophthalmology Clinic from May 2015 to June 2018 with a 1-year minimum follow-up to assess the visual outcome. The study was approved by the Medical and Research Ethics Committee from Ministry of Health, Malaysia. In view of the rare nature of the disease, all patients that met the inclusion criteria were included in the study.

We included patients who presented with ON features for less than 4 weeks, all ages, and any number of attacks fulfilling all four criteria of optic neuritis. The criteria were unilateral or bilateral decreased visual acuity measured using Snellen chart, unilateral or bilateral impaired colour vision using Ishihara test, presence of relative afferent pupillary defect (unless there was bilateral involvement), and the presence of visual field defect as evident in Humphrey visual field test. This included ON patients with evidence of infectious and autoimmune serological presentations, cerebrospinal fluid, oligoclonal band positive, and positive radiological evidence of demyelinating lesion.

We excluded patients with poor media clarity, ON of other causes, and patients who were unable to complete a 1-year follow up. A total of 113 patients with ON fulfilling the inclusion criteria were recruited and assigned to an anonymous research number. Relevant data obtained included demographic data, history of clinical presentation, clinical examination findings, ophthalmological investigation results such as Humphrey Visual Field Analyzer 30-2 and Heidelberg Spectralis optical coherence tomography (OCT) of the retinal nerve fibre layer (RNFL). Relevant investigation results were venereal disease research laboratory (VDRL), Mantoux, antinuclear antibody (ANA), rheumatoid factor (RF), anti-AQP4 antibody, oligoclonal bands immunoglobulin G (IgG), and anti-MOG antibody. Radio-imaging findings based on magnetic resonance imaging (MRI) with a number of sites of involvement (spine, brain, optic nerve) were recorded.

Patients were categorised based on diagnosis of ON as defined in Table 1. ON diagnosis was further subcategorised into typical and atypical ON. CIS and MS were classified as typical ON, whereas the remaining types of ON were classified as atypical ON. This classification is in accordance with a review for typical and atypical ON.[8]

Data obtained were tabulated and analysed via Statistical Package for Social

Table 1. Aetiological definitions of optic neuritis

No	Diagnosis	Definition of disease
1	Multiple sclerosis (MS)	Demyelination of the central nervous system (CNS) disseminated in time and space (Mc Donald's revised criteria 2017)
2	Neuromyelitis optica spectrum disorder (NMOSD)	Inflammatory CNS syndrome associated with serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG) fulfilling the International Panel for NMO Diagnosis (IPND) criteria (IPND)
3	Clinically isolated syndrome (CIS)	First episode of neurologic symptoms lasting for 24 hours as a result of inflammation or demyelination of CNS (National MS Society)
4	Chronic relapsing inflammatory optic neuropathy (CRION)	Relapsing inflammatory optic neuritis with steroid dependency; diagnosis of exclusion (Lee HJ, 2018)
5	Acute disseminated encephalomyelitis (ADEM)	Non-infectious, acute, inflammatory demyelinating events of the CNS, fulfilling the International Paediatric Multiple Sclerosis Study Group updated consensus. A diagnosis of exclusion (Daniela Pohl, 2016)
6	Parainfectious	Follows the onset of a viral infection by 1–3 weeks, can occur as a postvaccination phenomenon (Myron Yanoff, 2009)
7	Myelin oligodendrocyte glycoprotein (MOG) optic neuritis	Antibody-mediated demyelinating disease of the CNS, distinct from other demyelinating processes of the CNS *e.g.*, MS or NMOSD (AAO – Eyewiki)

CNS: central nervous system

Sciences version 26.0. Following 1 year of treatment, vision was reassessed based on Snellen chart and best-corrected vision via refraction. RNFL measurement by OCT was performed by the same operator during the follow-up. Vision based on Snellen chart was converted into logMAR and categorised based on WHO categorisation of visual impairment. For the purpose of analysing the visual outcome, vision was further classified into good vision ≥ 6/18 and poor vision < 6/18 for presenting vision and final visual outcome. Visual categorisation was based on a study on ON by Hansapinyo *et al.* Demographic data were analysed using descriptive analysis. All categorical data associated with recurrence and poor visual outcome were analysed using Chi-square test. Statistically significant variables were further analysed using multivariate analysis via binary logistic regression. A p-value < 0.05 was accepted as statistically significant.

Results

Demographics and types of ON

A total of 159 eyes of 113 patients who completed the 1-year follow-up were studied. None of the patients dropped out of the study. In the year 2015, the prevalence was 3.8977 per 100,000 outpatients over a period of 6 months. As for the year 2016, the prevalence was 5.001 per 100,000 outpatients, followed by a slight increment to 5.012 per 100,000 outpatients in year 2017. Table 2 summarises the prevalence of ON from 2015 to 2017.

Forty-one (36.3%) were diagnosed with neuromyelitis optica spectrum disorder (NMOSD), followed by 23 (20.4%) patients with CIS, 21 (18.6%) patients with MS, 15 (13.3%) patients with infectious ON, 6 (5.3%) patients with parainfectious ON, 3 (2.7%) patients with chronic relapsing inflammatory optic neuropathy (CRION), 2 (1.8%) patients with anti-MOG ON, and 2 (1.8%) patients with other causes of autoimmune ON.

In terms of age, the majority of patients 76 (67.3%) were between the ages of 15 and 49 years. Seventeen (15%) patients were below the age of 15 years and 20 (17.7%) presented above 49 years of age. In general, there was female preponderance, with 82 (72.6%) female patients and 31 (27.4%) male patients. The predominant race in our study was Malay with 74 (65.5%) patients, followed by Chinese with 24 (21.2%), and Indian with 15 (13.3%).

Table 2. Prevalence of ON in Hospital Kuala Lumpur

Year	Total ON patients (*n*)	Total outpatients (*n*)	Population (*n*/100,000 population)
2015 (May–Dec)	32	820,992	3.8977
2016	42	839,731	5.001
2017	37	738,228	5.012

ON: optic neuritis

Racial distribution of ON

Table 3 illustrates the racial distribution and clinical profile of ON diseases among the different races. Within the Malay group, the commonest cause of ON was NMOSD with 22 (19.5%) patients, MS with 18 (15.9%) patients, and CIS with 16 (14.2%) patients. However, within the Chinese group, we noticed a significant proportion of NMOSD 15 (13.3%) patients, followed by a minority in infectious ON 5 (4.5%) patients, and CIS 2 (1.7%) patients. As for the Indian group, CIS was found in 5 (4.5%) patients, NMOSD was found in 4 (3.5%) patients, and MS was found in 2 (1.7%) patients. The commonest age of presentation was 15–49 years old ($p = 0.017$) for all three races. The Malay group demonstrated a tendency of presentation at an earlier age < 15 (12.4%) compared to Chinese (0.9%) and Indian (1.7%). Female preponderance was

seen among all races. Most patients presented as unilateral ON (59.3%). Most did not have a history of recurrence (67.3%), did not experience pain (69.9%), and did not have disc swelling (75.2%). More than half (57.5%) our patients did not manifest RNFL thinning following 1 year of follow-up.

Table 3. Racial distribution of optic neuritis clinical profile

Variables	**Total** ***n*** **(%)**	**Malay** ***n*** **(%)**	**Chinese** ***n*** **(%)**	**Indian** ***n*** **(%)**	**Univariate** ***P*****-value***
Diagnosis					
MS	21 (18.5)	18 (15.9)	1 (0.9)	2 (1.7)	0.141
NMOSD	41 (36.3)	22 (19.5)	15 (13.3)	4 (3.5)	
CIS	23 (20.4)	16 (14.2)	2 (1.7)	5 (4.5)	
CRION	3 (2.6)	3 (2.6)	0 (0)	0 (0)	
ADEM	2 (1.8)	2 (1.7)	0 (0)	0 (0)	
Parainfectious	6 (5.3)	4 (3.5)	1 (0.9)	1 (0.9)	
Anti-MOG	2 (1.8)	1 (0.9)	0 (0)	1 (0.9)	
Infection	15 (13.3)	8 (7.2)	5 (4.5)	2 (1.7)	
Age (years)					
< 15	17 (15.0)	14 (12.4)	1 (0.9)	2 (1.7)	0.017
15–49	76 (67.3)	53 (46.9)	14 (12.4)	9 (8.0)	
> 49	20 (17.7)	7 (6.2)	9 (8.0)	4 (3.5)	
Gender					
Male	31 (27.4)	21 (18.5)	7 (6.2)	3 (2.6)	0.784
Female	82 (72.6)	53 (47.0)	17 (15.0)	12 (10.6)	
Laterality					
Unilateral	67 (59.3)	42 (37.2)	14 (12.4)	11 (9.7)	0.489
Bilateral	46 (40.7)	32 (28.4)	10 (8.8)	4 (3.5)	
Recurrence					
Yes	37 (32.7)	28 (24.7)	8 (7.1)	1 (0.9)	0.064
No	76 (67.3)	46 (40.7)	16 (14.2)	14 (12.4)	
Pain					
Yes	34 (30.1)	23 (20.4)	8 (7.2)	3 (2.6)	0.644
No	79 (69.9)	51 (45.0)	16 (14.2)	12 (10.6)	
OD swelling					
Yes	28 (24.8)	19 (16.8)	5 (4.5)	4 (3.5)	0.878
No	85 (75.2)	55 (48.7)	19 (16.8)	11 (9.7)	

Variables	Total *n* (%)	Malay *n* (%)	Chinese *n* (%)	Indian *n* (%)	Univariate *P*-value*
RNFL thinning (at year 1)					
Yes	48 (42.5)	28 (24.7)	12 (10.6)	8 (7.1)	0.381
No	65 (57.5)	46 (40.7)	12 (10.6)	7 (6.2)	

MS: multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorder; CIS: clinically isolated syndrome; CRION: chronic relapsing inflammatory optic neuropathy; ADEM: acute disseminated encephalomyelitis; ANTIMOG: myelin oligodendrocyte antibody; OD: optic disc; RNFL: retinal nerve fibre layer
*$P < 0.05$ is statistically significant (Chi-square test).

Comparing atypical with typical ON

As illustrated in Table 4, the common age group presenting with both typical and atypical ON was 15–19 years old. Atypical ON presented at near equal proportion for extreme age groups of < 15 years (14.2%) and > 49 years (15.0%) old. In contrast, typical ON rarely presented in the extreme age groups of > 49 years old (2.6%) and < 15 years old (0.9%). Atypical ON was shown to be predominantly affecting all the 3 major races. On the other hand, typical ON mostly affected the Malay group (15.9%) and rarely presented in the Chinese (0.9%) and Indian groups (2.6%). Female preponderance was still seen among both types of ON.

Table 4. Comparison of typical and atypical optic neuritis

Variable	Total (*n*) (%)	Typical ON (*n*) (%)	Atypical ON (*n*) (%)	Univariate	Multivariate	
				P-value	Odds ratio (95% CI)	*P*-value
Age						
< 15	17 (15.0)	1 (0.9)	16 (14.2)	0.259		
15–49	76 (67.3)	17 (15.0)	59 (52.3)			
> 49	20 (17.7)	3 (2.6)	17 (15.0)			
Race						
Malay	74 (65.5)	18 (15.9)	56 (49.5)	0.075		
Chinese	24 (21.2)	1 (0.9)	23 (20.4)			
Indian	15 (13.3)	2 (1.8)	13 (11.5)			
Gender						
Male	31 (27.4)	4 (3.5)	27 (23.9)	0.340		
Female	82 (72.6)	17 (15.0)	65 (57.5)			

Variable	Total (*n*) (%)	Typical ON (*n*) (%)	Atypical ON (*n*) (%)	Univariate	Multivariate	
				P-value	Odds ratio (95% CI)	*P*-value
Laterality*						
Unilateral	67 (42.1)	13 (8.1)	54 (34.0)	0.746		
Bilateral	92 (57.9)	16 (10.1)	76 (47.8)			
Recurrence*						
Yes	51 (32.1)	10 (6.3)	41 (25.8)	0.759		
No	108 (67.9)	19 (11.9)	89 (56.0)			
Pain*						
Yes	45 (28.3)	6 (3.8)	39 (24.5)	0.314		
No	114 (71.7)	23 (14.5)	91 (57.2)			
OD swelling*						
Yes	40 (25.2)	3 (1.89)	37 (23.2)	0.042		
No	119 (74.8)	26 (16.4)	93 (58.6)			
RNFL thinning (at 1 year)*						
Yes	67 (42.1)	11 (6.9)	56 (35.2)	0.612		
No	92 (57.9)	18 (11.3)	74 (46.6)			
Presenting vision*						
≤ 6/18	50 (31.4)	9 (5.7)	41 (25.8)	0.958		
> 6/18	109 (68.6)	20 (12.6)	89 (55.9)			
Visual outcome*						
≤ 6/18	111 (69.8)	25 (15.7)	86 (54.1)	0.033		
> 6/18	48 (30.2)	4 (2.5)	44 (27.7)		4.055 (1.264–13.009)	0.019
MRI sites*						
0	59 (37.1)	2 (1.3)	57 (35.8)	0.001		0.009
1	94 (59.1)	27 (17.0)	67 (42.1)		0.095 (0.021–0.425)	0.002
> 1	6 (3.8)	0 (0.0)	6 (3.8)			0.999

ON: optic nerve; OD: optic disc; RNFL: retinal nerve fibre layer; MRI: magnetic resonance imaging

$p < 0.05$ is statistically significant (univariate analysis = Chi square test; multivariate analysis = binary logistic regression).

*Calculated based on number of eyes.

Unilateral ON was the predominant presentation in both typical and atypical ON. Nevertheless, the fraction of bilateral ON presentation was slightly higher within the atypical ON group compared to the typical ON group. The majority of both typical and atypical ON did not have history of recurrence. However, as many as one-third of our ON patients had history of recurrence. Most of typical and atypical ON patients did not experience pain. Only one-fourth of our patients presented with pain, and the proportion of pain was greater in the atypical ON group compared to the typical ON group. In both typical and atypical ON, disc swelling was uncommon. Despite that, disc swelling was more frequently seen in the atypical ON group. In terms of presenting vision, both typical and atypical ON presented with nearly similar proportions of good vision ≤ 6/18 and poor vision > 6/18 within the respective groups. Good visual outcome, > 6/18 after 1 year of treatment was noted to be better in the typical ON group compared to the atypical ON group. Atypical ON, on the other hand, had a greater fraction of poor visual outcome ≤ 6/18 following 1 year of treatment. The presence of RNFL thinning at 1 year of follow-up was greater in the atypical ON group (35.2.%) compared to the typical ON group (6.9%). MRI lesions involving multiple sites (> 1) was only seen in atypical ON. Most typical ON had at least one MRI lesion. The proportion without MRI lesions was greater in the atypical ON group. From multivariate analysis, there seemed to be a significant association

Table 5. Positive laboratory results

Diagnosis	**Serology**					
	ANA	**RF**	**AntiSSARO**	**AntiAQP4**	**Oligoclonal band**	**ANTIMOG**
MS	1	0	0	0	2	0
NMOSD	1	2	2	26	0	0
CIS	0	0	0	0	0	0
CRION	0	0	0	0	0	0
ADEM	0	0	0	0	0	0
Parainfectious	0	0	0	0	0	0
ANTIMOG	1	0	0	0	0	2
Infectious	0	0	0	0	0	0
Total	3	2	2	26	2	2

MS: multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorder; CIS: clinically isolated syndrome; CRION: chronic relapsing inflammatory optic neuropathy; ADEM: acute disseminated encephalomyelitis; ANTIMOG: myelin oligodendrocyte antibody; ANA: antinuclear antibody; RF: rheumatoid factor; AntiSSARO: anti–Sjögren's-syndrome-related antigen A autoantibodies; AntiAQP4: aquaporin 4 antibody

of poor visual outcome > 6/18 following 1 year of treatment within the atypical ON group ($p = 0.019$) with an odds ratio of 4.055. There was also a significant association between MRI lesions in only one site within typical ON ($p = 0.002$) and absence of MRI lesion within the atypical ON group ($p = 0.009$)

Serology results

As shown in Table 5, NMOSD had the most significant association with other autoimmune serology. More than half of NMOSD patients (26/41, 63.4%) were positive for anti-AQP4 antibody. Among patients with positive anti-AQP4 antibody, two NMOSD patients had overlapping syndrome with positive anti-SSARO antibody, while two patients were positive for RF, and one patient had positive ANA. We only had two MS patients: one with positive oligoclonal band and one with positive ANA. Two of our patients had MOG antibody and of them, 1 patient had ANA serology positive. Our patients with CRION and CIS did not display any evidence of other autoimmune associations.

Infectious and parainfectious ON aetiology

We had 15 patients within the infectious ON group. All patients tested positive for *Mycobacterium tuberculosis*. There were six patients who were treated as parainfectious ON with a history of preceding upper respiratory tract infection.

Analysis of recurrent ON

As shown in Table 6, there was a statistically significant association between the 15–49 age group ($p = 0.013$) and ON recurrence. Conversely, patients who presented with ON below the age of 15 years were associated with reduced recurrence ($p = 0.024$). The Malay group showed significant association with ON recurrence ($p = 0.038$). In contrast, the Indian group was significantly associated with having no ON recurrence ($p = 0.015$). Additionally, there was also a significant association between the presence of RNFL thinning following 1 year of treatment with ON recurrence ($p = 0.001$).

Analysis of poor visual outcome

As seen in Table 7, female gender was significantly associated with having a better visual outcome ≥ 6/18 ($p = 0.005$) following 1 year of treatment. Poor presenting vision > 6/18 was significantly associated with a poor visual outcome > 6/18 ($p < 0.001$). Additionally, the presence of RNFL thinning after 1 year of treatment was significantly associated with a poorer visual outcome ($p = 0.003$).

Table 6. Variables associated with optic neuritis recurrence

Variables	Total (*n*)	Recurrence		Univariate analysis	Multivariate analysis	
		Yes (*n*) (%)	No (*n*) (%)	*P*-value	Odds ratio (95% CI)	*P*-value
Age*						
< 15	23 (14.5)	4 (2.5)	19 (11.9)	0.013	-	0.024
15–49	109 (68.5)	43 (27.0)	66 (41.6)		8.142 (1.548–42.829)	0.013
≥ 50	27 (17.0)	4 (2.5)	23 (14.5)		2.903 (0.393–21.438)	0.296
Race*						
Malay	106 (66.7)	40 (25.2)	66 (41.5)	0.019	-	0.038
Chinese	34 (21.4)	10 (6.3)	24 (15.1)		0.520 (0.168–1.610)	0.257
Indian	19 (11.9)	1 (0.6)	18 (11.3)		0.063 (0.007–0.579)	0.015
Gender*						
Male	44 (27.7)	12 (7.5)	32 (20.1)	0.422		
Female	115 (72.3)	39 (24.5)	76 (47.9)			
Laterality*						
Unilateral	67 (42.1)	23 (14.5)	44 (27.7)	0.603		
Bilateral	92 (57.9)	28 (17.5)	64 (40.3)			
Pain*						
Yes	45 (28.3)	16 (10.1)	29 (18.2)	0.555		
No	114 (71.7)	35 (22.0)	79 (49.7)			
OD swelling*						
Yes	40 (25.2)	7 (4.4)	33 (20.8)	0.022	0.680 (0.234 – 1.975)	0.478
No	119 (74.8)	44 (27.7)	75 (47.1)		-	-
RNFL thinning*						
Yes	67 (42.1)	33 (20.8)	34 (21.4)	< 0.001	4.020 (1.735 – 9.315)	0.001
No	92 (57.9)	18 (11.3)	74 (46.5)		-	-

Variables	Total (*n*)	Recurrence		Univariate analysis	Multivariate analysis	
		Yes (*n*) (%)	No (*n*) (%)	*P*-value	Odds ratio (95% CI)	*P*-value
ANA*						
Yes	5 (3.1)	4 (2.5)	1 (0.6)	0.02	12.072 (0.819 – 177.962)	0.070
No	154 (96.9)	47 (29.6)	107 (67.3)		-	-
AntiAQP4*						
Yes	33 (20.8)	17 (10.6)	16 (10.1)	0.007	2.483 (0.840 – 7.340)	0.100
No	126 (79.2)	34 (21.4)	92 (57.9)		-	-
RF*						
Yes	2 (1.3)	2 (1.3)	0 (0)	0.038		0.999
No	157 (98.7)	49 (30.8)	108 (67.9)			
AntiSSARO*						
Yes	3 (2.0)	3 (1.9)	0 (0)	0.011		0.999
No	156 (98.0)	48 (30.2)	108 (67.9)			
Oligoclonal band*						
Yes	3 (2.0)	1 (0.6)	2 (1.3)	0.962		
No	156 (98.0)	50 (31.4)	106 (66.7)			
ANTIMOG*						
Yes	3 (2.0)	2 (1.3)	1 (0.6)	0.195		
No	156 (98.0)	49 (30.8)	107 (67.3)			
MRI sites*						
0	59 (37.1)	13 (8.2)	46 (28.9)	0.034	-	0.612
1	94 (59.1)	34 (21.4)	60 (37.7)		1.205 (0.476–3.054)	0.694
> 1	6 (3.8)	4 (2.5)	2 (1.3)		2.962 (0.342–25.659)	0.324
Presenting vision*						
≤ 6/18	50 (31.4)	10 (6.3)	40 (25.2)	0.027	1.221 (0.444–3.356)	0.699

Variables	Total (*n*)	Recurrence		Univariate analysis	Multivariate analysis	
		Yes (*n*) (%)	No (*n*) (%)	*P*-value	Odds ratio (95% CI)	*P*-value
> 6/18	109 (68.6)	41 (25.8)	68 (42.7)		-	-
Visual outcome*						
≤ 6/18	111 (69.8)	28 (17.6)	83 (52.2)	0.005	1.340 (0.470–3.821)	0.585
> 6/18	48 (30.2)	23 (14.5)	25 (15.7)			

ANTIMOG: myelin oligodendrocyte antibody; ANA: antinuclear antibody; RF: rheumatoid factor; AntiSSARO: anti–Sjögren's-syndrome-related antigen A autoantibodies; AntiAQP4: aquaporin 4 antibody; OD: optic disc; RNFL: retinal nerve fibre layer; MRI: magnetic resonance imaging

$P < 0.05$ is statistically significant (univariate analysis = Chi-square test; multivariate analysis = binary logistic regression).

*Calculated based on number of eyes.

Table 7. Variables associated with poor visual outcome

Variables	Total (*n*)	Vision after 1 year of treatment		Univariate analysis	Multivariate analysis	
		Vision ≥ 6/18 (*n*) (%)	Vision < 6/18 (*n*) (%)	*P*-value	OR (95% CI)	*P*-value
Gender*						
Male	44 (27.7)	25 (15.7)	19 (12.1)	0.027	1	-
Female	115 (72.3)	86 (54.1)	29 (18.1)		0.244 (0.091–0.653)	0.005
Age*						
< 15	23 (14.5)	19 (12.1)	4 (2.5)	0.295		
15–49	109 (68.5)	75 (47.1)	34 (21.4)			
≥ 50	27 (17.0)	17 (10.6)	10 (6.3)			
Race*						
Malay	106 (66.7)	76 (47.9)	30 (18.9)	0.507		
Chinese	34 (21.4)	21 (13.2)	13 (8.2)			
Indian	19 (11.9)	14 (8.8)	5 (3.0)			

Variables	Total (*n*)	Vision after 1 year of treatment		Univariate analysis	Multivariate analysis	
		Vision ≥ 6/18 (*n*) (%)	Vision < 6/18 (*n*) (%)	*P*-value	OR (95% CI)	*P*-value
Laterality*						
Unilateral	67 (42.1)	43 (27.0)	24 (15.1)	0.187		
Bilateral	92 (57.9)	68 (42.8)	24 (15.1)			
Recurrence*						
Yes	51 (32.1)	28 (17.6)	23 (14.5)	0.005	1.291 (0.507–3.288)	0.593
No	108 (67.9)	83 (52.2)	25 (15.7)		1	-
Pain*						
Yes	45 (28.3)	30 (18.9)	15 (9.4)	0.587		
No	114 (71.7)	81 (50.9)	33 (20.8)			
OD swelling*						
Yes	40 (25.2)	29 (18.2)	11 (6.9)	0.669		
No	119 (74.8)	82 (51.6)	37 (23.3)			
RNFL thinning*						
Yes	67 (42.1)	35 (22.0)	32 (20.1)	< 0.001	3.856 (1.567 – 9.489)	0.003
No	92 (57.9)	76 (47.8)	16 (10.1)		1	-
ANA*						
Yes	5 (3.1)	2 (1.3)	3 (2.0)	0.140		
No	154 (96.9)	109 (68.6)	45 (28.1)			
AntiAQP4*						
Yes	33 (20.8)	17 (10.7)	16 (10.1)	0.010	1.556 (0.557 – 4.344)	0.399
No	126 (79.2)	94 (59.1)	32 (20.1)		1	-
RF*						
Yes	2 (1.3)	1 (0.6)	1 (0.6)	0.539		
No	157 (98.7)	110 (69.2)	47 (29.6)			

Variables	Total (*n*)	Vision after 1 year of treatment		Univariate analysis	Multivariate analysis	
		Vision ≥ 6/18 (*n*) (%)	Vision < 6/18 (*n*) (%)	*P*-value	OR (95% CI)	*P*-value
AntiSSARO*						
Yes	3 (2.0)	2 (1.3)	1 (0.6)	0.905		
No	156 (98.0)	109 (68.5)	47 (29.6)			
ANTIMOG*						
Yes	3 (2.0)	2 (1.3)	1 (0.6)	0.905		
No	156 (98.0)	109 (68.5)	47 (29.6)			
Oligoclonal band*						
Yes	3 (2.0)	2 (1.3)	1 (0.6)	0.905		
No	156 (98.0)	109 (68.5)	47 (29.6)			
MRI sites*						
0	59 (37.1)	41 (25.9)	18 (11.4)	0.762		
1	94 (59.1)	65 (40.9)	29 (18.2)			
> 1	6 (3.8)	5 (3.0)	1 (0.6)			
Presenting vision*						
≤ 6/18	50 (31.4)	49 (30.8)	1 (0.6)	< 0.001	1	-
> 6/18	109 (68.6)	62 (39.0)	47 (29.6)		37.647 (4.728 –299.799)	< 0.001

ANTIMOG: myelin oligodendrocyte antibody; ANA: antinuclear antibody; RF: rheumatoid factor; AntiSSARO: anti–Sjögren's-syndrome-related antigen A autoantibodies; AntiAQP4: aquaporin 4 antibody; OD: optic disc; RNFL: retinal nerve fibre layer; MRI: magnetic resonance imaging

P < 0.05 is statistically significant (univariate analysis = Chi-square test; multivariate analysis = binary logistic regression).

*Calculated based on number of eyes.

Discussion

The prevalence of ON in our study population was 5.001–5.012/100,000 per year. A similar incidence of 5/100,000 per year has been reported in a study conducted in central Europe.[2] Our study compared the clinical profile of ON among the three main races (Malays, Chinese and Indians) in our diverse population. We found that the main causes of ON in our study population were NMOSD (36.3%), CIS (20.4%), and MS (18.6%). Similarly, Hansapinyo reported that the main cause of ON in Thailand was NMOSD (38.7%) as opposed to MS (15.3%).[9] Additionally, a Singaporean population based study by Lim *et al.* concluded that the incidence of MS-related ON is significantly lower in Singapore in comparison to the ONTT study.[10] Moreover, a recent systematic review and meta-analysis demonstrated that the prevalence of anti-AQP4- and anti-MOG-related ON antibodies were more common in Asian than Western populations.[11] Hence, our study supports the growing evidence that NMOSD might be more common in South East Asia compared to Western countries.

In our study, a greater proportion of Chinese patients had NMOSD. This appears to be consistent with a local neurology study reported by Viswanathan that their Chinese cohort had a greater NMOSD to MS ratio of 2:1 with significant seropositivity of anti-AQP4 antibody. It was postulated that the Chinese group is genetically susceptible to the disease.[12]

We found that the 15–49 age group tends to experience ON recurrence. This is consistent with a recent international outcome prediction study of NMOSD showing that the age group below 35 years has the tendency to present with ON at onset and is associated with frequent recurrences and higher incidence of blindness. On the other hand, the older age groups often presented with myelitis.[13] However, in our study, the association with blindness in the younger age group was insignificant. Female preponderance was seen throughout all races. Consistently, Woung reported female predominance of ON groups in both Asian and Western countries. It was postulated that the female gender is more susceptible to autoimmune disease.[14]

Our study demonstrated that most of typical and atypical ON manifested with common overlapping clinical features that can hardly be differentiated. The common age group for presentation of both typical and atypical ON was 15–49 years of age. Atypical ON was shown to be affecting the extreme ages of < 15 years (14.2%) and > 49 years (15.0%) more than typical ON. This finding is consistent with the ONTT 1992 study. Atypical ON was shown to be the predominant disease affecting all three major races. However, typical ON mainly affected the Malay group (15.9%) and was rarely present in the Chinese (0.9%) and Indian (2.6%) groups. MRI lesions involving multiple sites (> 1) was only seen in atypical ON. Most typical ON had at least one MRI lesion. The proportion without MRI lesions was greater in the atypical ON group. The atypical ON group was significantly associated with poor visual outcome > 6/18 following 1 year of treatment ($p = 0.019$).

Most patients in our study group (75.2%) did not have disc swelling (retrobulbar ON). Our finding is in concurrence with the ONTT 1992 study, which reported that the majority (64.7%) presented without disc swelling.[3] Patients who presented with optic disc oedema were mostly associated with infectious ON (80%) and parainfectious ON (33.3%).

Presentation of pain appeared to be lower in our study population (30.1%), in contrast to the ONTT group (92%).[3] A possible reason is that most of our ON patients consisted of atypical ON as compared to the ONTT study.

As for association with recurrence of ON, the 15–49 age group was more susceptible to recurrence (p = 0.013). In contrast, patients < 15 years were found to have a lower risk of recurrence (p = 0.024). The Indian group seemed to have a significant lower odds ratio of 0.063 for recurrence (p = 0.015). The presence of RNFL thinning following 1 year of treatment was also associated with a higher likelihood of recurrence (p = 0.001).

In terms of poor visual outcome analysis, the female gender was associated with a greater potential of a good visual outcome (p = 0.005). The presence of RNFL thinning following 1 year of tratment was associated with a poor visual outcome. Most of the RNFL thinning in our study was found in the NMOSD group. In consonance, Noval *et al.* reported that NMOSD was associated with severe RNFL thinning and a poorer visual prognosis.[15] Poor presenting vision was found to have a great odds ratio (37.647) of developing poor visual outcome (p < 0.001). In agreement with our findings, Hansapinyo *et al.* similarly reported male gender and poor presenting vision to be independent predictive factors of poor visual outcome.[9]

The limitation of our study is its retrospective design involving a single institution review and limited sample size. However, the neuro-ophthalmology clinic in HKL is the only tertiary governmental neuro-ophthalmology centre to which most of the cases are referred. Some of the cases could possibly be recurrent or poorly responding ON with guarded prognosis.

Conclusion

Our study is the first in Malaysia to compare the clinical profile of ON among the diversified races in our study population. NMOSD was the main cause of ON in our study population. A significant factor associated with poor visual outcome was presenting vision worse than 6/18. A factor significantly associated with recurrence was presentation between the ages of 15 and 49 years. Evidence of RNFL thinning following 1 year of treatment may also predict recurrence and poor long-term visual outcome. Our patients require regular and combined neuro-ophthalmology and neuro-medical follow-up and immediate access to treatment to attain a better visual prognosis.

Declarations

Ethics approval and consent to participate

The study was approved by the Medical and Research Ethics Committee from Ministry of Health, Malaysia.

Competing interests

None to declare.

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Paediatric endophthalmitis: a 10-year retrospective study at Hospital Kuala Lumpur for incidence, risk factors, and outcomes

Tanusha **Dorairaja**[1,2], Azida Juana **Wan Ab Kadir**[2], Jamalia **Rahmat**[1]

[1]Department of Ophthalmology, Hospital Kuala Lumpur, Malaysia; [2]Department of Ophthalmology, University Malaya Medical Centre, Malaysia

Abstract

Purpose: Paediatric infectious endophthalmitis is a serious sightthreatening disease for children. The purpose of this study was to investigate the incidence, aetiology, microbiological spectrum, management, and visual outcomes of infectious endophthalmitis in children referred to the Department of Ophthalmology, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia.
Study design: Retrospective study.
Methods: The medical records of all patients under 18 years of age with histories of endophthalmitis treated at Hospital Kuala Lumpur from January 2009 to December 2018 were reviewed. The clinical characteristics, aetiology, microbiological spectrum, management, as well as the visual outcomes were analysed.
Results: A total of 23 children were identified, with a mean age of 3.15 (ranging from 20 days to 8 years of age). Previous ocular surgery (47.8%) and ocular trauma (30.4%) were the most common causes of endophthalmitis. Overall, eight (38.1%) cases with positive cultures were identified. The most commonly identified organism was *Staphylococcus* sp. comprising 50% of the isolates. Moreover, five isolates (62.5%) were grampositive organisms and three isolates (37.5%) were gramnegative organisms. The final visual outcome was 20/200 or better in one eye (4.3 %), hand movement in two eyes (8.7%), light perception in five eyes (21.7%), and no

Correspondence: Dr. Tanusha Dorairaja, Department of Ophthalmology, Hospital Kuala Lumpur, Jalan Pahang, 50586 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur, Malaysia.
E-mail: d_tanusha@hotmail.com

light perception in 13 eyes (56.5%). The visual outcome was not available for two patients (8.7%).
Conclusions: Previous ocular surgery and penetrating ocular trauma are the most frequent causes of paediatric endophthalmitis in our centre. *Staphylococcus* sp. was the most commonly identified organism in paediatric endophthalmitis. In this study, despite aggressive management with intravitreal antibiotics and vitrectomy, the visual prognosis was found to be generally poor.

Keywords: intravitreal antibiotics, Malaysia, paediatric endophthalmitis, visual acuity, vitrectomy

Endoftalmitis dikalangan kanak-kanak: kajian retrospektif selama 10 tahun di Hospital Kuala Lumpur

Abstrak

Tujuan: Endoftalmitis akibat jangkitan kuman dikalangan kanak-kanak merupakan penyakit serius yang mengancam penglihatan mereka. Tujuan kajian ini adalah untuk menyelidik kejadian, etiologi, spektrum mikrobiologi, rawatan dan penglihatan akhir jangkitan endoftalmitis di antara kanak-kanak yang dirujuk ke Jabatan Oftalmologi, Hospital Kuala Lumpur.
Kaedah kajian: Retrospektif.
Metodologi: Kajian ini berdasarkan rekod perubatan ke atas semua pesakit di bawah 18 tahun yang mempunyai sejarah endoftalmitis akibat jangkitan kuman, yang menjalani rawatan di Hospital Kuala Lumpur dari Januari 2009 sehingga Disember 2018. Manifestasi klinikal, etiologi, spektrum mikrobiologi, rawatan, dan juga ketajaman penglihatan terakhir telah dianalisakan.
Keputusan: Sejumlah 23 orang kanak-kanak telah dikenal pasti dengan purata usia 3.15 tahun (lingkungan antara 20 hari hingga 8 tahun). Endoftalmitis paling kerap terjadi selepas pembedahan okular (47.8%) dan trauma melibatkan tisu okular (30.4%). Kultur positif telah dikenalpasti dari lapan (38.1%) kes. Bakteria yang paling kerap dikenal pasti ialah *Staphylococcus* sp. (50%). Dari 8 kes berkultur positif, 5 (62.5%) adalah gram-positif dan 3 (37.5%) adalah gram-negatif. Ketajaman penglihatan terakhir adalah seperti berikut: 1 (4.3%) mata ≥ 20/200, 2 (8.7%) mata hanya dalam melihat pergerakan tangan, 5 (21.7%) mata hanya dapat mengamat cahaya dan 13 (56.5%) mata hilang penglihatan. Terdapat 2 pesakit yang ketajaman penglihatan terakhir tiada dalam rekod.
Kesimpulan: Kanak-kanak yang mempunyai sejarah pembedahan dan trauma

menglibatkan tisu okular adalah lebih kerap mendapat endoftalmitis akibat jangkitan. *Staphylococcus sp* adalah organisma yang paling kerap dikenal pasti. Dalam kajian ini, walaupun rawatan agresif dengan pemberian antibiotik secara intravitreal dan pembedahan vitrektomi, prognosis penglihatan secara keseluruhannya didapati kurang memuaskan.

Kata kunci: antibiotik intravitreal, endoftalmitis pada kanak-kanak, ketajaman penglihatan, Malaysia, vitrektomi

Introduction

Paediatric endophthalmitis is a devastating condition and a serious complication that may follow intraocular surgery, systemic infection, or penetrating ocular trauma. Open-globe injuries and glaucoma surgery are among the most common causes of paediatric endophthalmitis, whereas endogenous infection is the least common cause.[1-3] Unlike adults, who might complain of pain or blurred vision, children might not be able to either recognize or explain their symptoms, so it is more difficult to provide prompt diagnosis and treatment in the paediatric age group.

The reported incidence of paediatric endophthalmitis following cataract surgery ranges from 0.38% to 0.45%.[4] The incidence of paediatric post-traumatic endophthalmitis is estimated at 2.8–54.2%, which varies by country,[5,6] whereas, paediatric endogenous endophthalmitis is rare and constitutes only 0.1–4% of all endophthalmitis cases.[7]

Worldwide, infectious endophthalmitis is a rare but serious disease that frequently has a poor visual prognosis.[2,3] However, it is not as common in the paediatric age group as in adults, and less research has been devoted to this group. Available literature on paediatric endophthalmitis is limited and, to date, no studies on paediatric endophthalmitis have been conducted in Malaysia.

The aim of this study was to provide data on the incidence, aetiology, microbiological spectrum, management, and visual outcomes of infectious endophthalmitis in children referred to the Department of Ophthalmology of Hospital Kuala Lumpur, (HKL) Kuala Lumpur, Malaysia.

Methods

This was a retrospective observational study performed at the Department of Ophthalmology of HKL, which is the main tertiary referral centre for paediatric ophthalmology in Malaysia. We reviewed the medical records of patients 18 years and below with diagnosis of endophthalmitis who were seen and referred to the centre from

January 2009 to December 2018. Ethical approval for this study was obtained from Clinical Research Centre, HKL and Medical Research and Ethics Committee, Ministry of Health, Malaysia.

We retrieved records of 23 patients. All names and identification number of these patients were traced from the operation theatre and ward admission census and the medical records were retrieved from the record office. Information from both inpatient and outpatient records, including demographics, aetiology, underlying systemic and ocular comorbidities, time interval from the onset of ocular symptoms to presentation, clinical symptoms and signs, B scan findings, surgical procedures, vitreous and aqueous culture results, follow up treatment, complications, and final visual acuity were collected and recorded into the data collection sheet.

Statistical analysis

Data was analysed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive data was expressed as mean ± standard deviation (SD) for numerical data, and categorical variables were presented in frequencies and percentages. Statistical analysis was performed using Fischer's exact test for potential factors associated with phthisical eyes. $P < 0.05$ was considered significant.

Table 1. Demographic data of children with endophthalmitis

Parameter	***N* (%)**
Ethnicity	
Malay	15 (65.2)
Indian	4 (17.4)
Chinese	2 (8.8)
Orang asli	1 (4.3)
Others	1 (4.3)
Gender	
Female	8 (34.8)
Male	15 (65.2)
Age (years)	Mean: 3.15 (SD: 2.536)
Less than 1	6 (26.1)
1–5	11 (47.8)
6–8	6 (26.1)
9–18	0 (0)

Results

Demographic data

From this study, a total of 23 eyes of 23 children were identified. There were eight females (34.8%) and 15 males (65.2%) identified with a mean age of 3.15 years old (range, 20 days old to 8 years old). The racial distribution reflected the multiracial population in our country, with 15 Malay children (65.2%), four Indians (17.4%), two Chinese (8.8%) and one Vietnamese child. The demographic data are illustrated in Table 1. From these data, we noted that the peak age of incidence was 1–5 years of age and more specifically 2–3 years of age.

Aetiology

The aetiologies of paediatric endophthalmitis in this study are illustrated in Table 2, with the most common being previous ocular surgery, accounting for 11 (47.8%) of the 23 cases. Six out of 11 (26.1%) patients had a history of previous cataract surgery. Of these, four patients developed endophthalmitis within a month after surgery and two cases developed endophthalmitis at 5 weeks and 6 months post-

Table 2. Aetiologies of paediatric endophthalmitis

Aetiology	**Number of patients, *N* = 23**	**Percentage (%)**
Ocular trauma		
Toy gun pellets	1	4.3
Hair clip	1	4.3
Yoyo	1	4.3
Porcupine quill	1	4.3
Metal wire	1	4.3
Pencil	1	4.3
Others	1	4.3
Previous ocular surgery		
Cataract	6	26.1
Glaucoma	5	21.7
Endogenous		
Infected leg wound from scratch by cat	1	4.3
Thrombophlebitis	1	4.3
Haemophilus influenza meningitis	1	4.3
Respiratory tract infection	1	4.3
Urinary tract infection	1	4.3

operatively. Five out of 11 (21.7%) patients had glaucoma-related procedures, which included trabeculectomy with mitomycin C, Baerveldt tube repositioning, Baerveldt tube removal and reimplantation, and pupilloplasty for pupillary-block glaucoma. Of these five cases associated with glaucoma surgery, four patients developed delayed onset endophthalmitis, ranging from 2 months to 3 years. Risk factors identified in our patients were repeated and prolonged duration of surgery, bathing in well water, swimming at the beach, history of conjunctivitis, lack of proper postoperative care due to the patient being in an orphanage, and use of mitomycin C in filtering surgery.

Ocular trauma was the second leading cause of endophthalmitis in our study, which accounted for seven cases (30.4%). Of these, none had intraocular foreign body. The sources included hair clip, toy gun pellet, yoyo, metal wire, porcupine quill, pencil, and one unknown injury. In this group, the time from onset of ocular trauma to presentation to hospital was within 24 hours in six cases and 24 to 48 hours in one case.

Endogenous causes were the least common in children with five (21.7%) cases, two of which occurred in preterm babies. The primary sources in these cases are shown in Table 2.

A total of 753 paediatric cataract cases and 385 glaucoma-related procedures were performed at HKL from 2009 to 2018. Of the 11 postoperative endophthalmitis cases, ten were operated at HKL, whereas one was operated elsewhere and subsequently referred to HKL for endophthalmitis. The incidence of postoperative endophthalmitis in HKL for cataract cases was 0.6% and for glaucoma-related procedures was 1.3% over 10 years.

Comorbidities, risk factors, and ocular features

Eleven children had no ocular comorbidities, eight (34.8%) had glaucoma, four (17.4%) had congenital cataract, and one had retinopathy of prematurity. Two premature babies had developed endogenous endophthalmitis; the risk factors for these babies were urinary tract infection and *Haemophilus influenza* meningitis.

Most of the children presented with complaints of pain, redness, and eyelid swelling; however, two children were asymptomatic and noted to have low-grade endophthalmitis during their follow-up at the eye clinic. B scans performed in these children showed thickened sclera, loculation, and vitritis. Intraoperatively, these children were mostly found to have hypopyon and vitritis similarly as adults.

The patients' visual acuities (VA) at the time of the initial presentation and final follow-up are illustrated in Table 3. The initial VA could not be obtained because of non-cooperation in ten (43.5%) patients, nine had light perception, and four had hand movement vision. The final VA was recorded at 3 months, 1 year, and at last follow-up at the eye clinic. The final VA was not documented in two (8.7%) patients because these children were referred back to their original hospital for follow up at 1-month postoperative for continuation of care. Of the 23 eyes, only one patient

Table 3. Relationship between initial and final visual acuity

Final VA	Initial VA					
	Not available	NLP	LP	HM	20/200 or better	Total
20/200 or better	0	0	0	1	0	1
HM	0	0	1	1	0	2
LP	3	0	2	0	0	5
NLP	7	0	4	2	0	13
Not available	0	0	2	0	0	2
Total	10	0	9	4	0	23

VA: visual acuity; NLP: no light perception; LP: light perception; HM: hand movement

who had post-traumatic endophthalmitis achieved final VA of 20/200 or better and 20 patients had a final VA of hand movement or worse. Of the 20 eyes that had an unfavourable functional outcome, 13 (61.9%) eyes had phthisis bulbi. Overall, two patients had improved vision post-treatment and three maintained preoperative vision. Causes of poor vision included corneal scar, band keratopathy post-retinal detachment repair, advanced glaucoma, and macular scar.

Microbiology data

In all, there were eight positive cultures identified from 21 patients during this study. In two patients, the culture findings were not documented. Gram-positive organisms were isolated in five patients (62.5%). The most common organism isolated was coagulase-negative staphylococci, seen in two (8.7%) patients. In the postoperative group, coagulase-negative staphylococci and *Streptococcus pneumoniae* were the most common isolates. In the post-traumatic group, two (28.6%) of seven patients had positive culture results, and the isolated organisms were *Staphylococcus aureus and Enterobacter* sp. In the endogenous group, three of five patients had positive cultures identified, with *S. aureus* as the most common isolate. One patient with endogenous endophthalmitis secondary to urinary tract infection had *Pseudomonas aeruginosa* in urine sample and coagulase-negative staphylococci isolated from vitreous culture. Blood and urine cultures were sent for all patients with endogenous endophthalmitis. The microbiology of causative organisms is summarized in Table 4.

Table 4. Organisms isolated in paediatric endophthalmitis

Organism	Number, *n* = 23	Percentage %
Vitreous culture		
Coagulase-negative staphylococci	2	8.7
Staphylococcus aureus	1	4.3
Streptococcus pneumoniae	1	4.3
Enterobacter sp.	1	4.3
Blood sample		
Staphylococcus aureus	1	4.3
Urine sample		
Pseudomonas aeruginosa	1	4.3
Cerebrospinal fluid		
Haemophilus influenza	1	4.3
No growth	13	56.5
Not documented	2	8.7

Treatment

All patients received intravenous and topical antibiotics as soon as they were treated in HKL, although the antibiotic regime varied as there was no standard paediatric protocol available at the time. Of 23 children, 17 of them received intravenous cephalosporins (ceftazidime/ cephalexin/ ceftriaxone) and 6/23 received intravenous fluoroquinolones (ciprofloxacin).

Vancomycin and ceftazidime were used as intravitreal (IVT) antibiotics. IVT amphotericin B was given to one patient along with vancomycin and ceftazidime as fungal endophthalmitis was suspected. IVT dexamethasone was given to four patients. Primary pars plana vitrectomy (PPV) with IVT injection of antibiotics was directly performed in 19 patients (82.6%) due to severe vitreous inflammation. Four 4 (17.4%) patients were treated with vitreous sampling and IVT antibiotics alone. Of these, three patients presented with low-grade endophthalmitis that responded to IVT antibiotics and one patient had no fundus view due to opaque cornea, thus PPV could not be performed. None of the eyes were eviscerated/ enucleated. The number of IVT injections ranged from one to four.

As for topical antibiotic drops, 16 of the 23 were given topical moxifloxacin 0.5% and dexamethasone 0.1% drops and seven of 23 received topical moxifloxacin 0.5%, gentamicin, and dexamethasone 0.1 % drops.

Of the 19 patients who underwent PPV, nine (47.3%) cases were performed within 24 hours, seven were done within 1–7 days. and three were done after 7 days. Of the

Table 5. Analysis of possible factors associated with phthisical eyes

Variables (n)		**Non-phthisical eye, (*n* = 8)**	**Phthisical eye, (*n* = 13)**	***P****
Culture (21)	Positive (7)	2 (71.4%)	5 (28.6%)	0.656
	Negative (12)	5 (58.3%)	7 (41.7%)	
Time to hospitalization (21)	< 24 hours (12)	6 (50.0%)	6 (50.0 %)	0.274
	1–7 days (2)	1 (50%)	1 (50%)	
	> 7 days (7)	1 (14.3%)	6 (85.7%)	
Time of diagnosis to vitrectomy (18)	< 24 hours (8)	3 (37.5%)	5 (62.5%)	0.999
	> 24 hours (10)	4 (40%)	6 (60.0%)	
Vitrectomy (18)	Vitrectomy (18)	7 (38.9%)	11 (61.1%)	0.999
	No vitrectomy (3)	1 (33.3%)	2 (66.7%)	
Ocular comorbidity (21)	Yes (11)	8 (72.7%)	3 (27.3%)	0.438
	No (10)	6 (60%)	4 (40%)	

* Fischer's exact test

ten patients who had PPV after 24 hours, eight were referred from other hospitals and received multiple IVT injections prior to admission.

Table 5 summarizes the analysis of possible factors associated with phthisical eye using Fischer's exact test. There was no significant association found between culture, time to hospitalization, time from diagnosis to vitrectomy, whether vitrectomy was performed or not, and ocular comorbidities with phthisical eye in our study.

Discussion

In this retrospective study done at the HKL Department of Ophthalmology, 23 cases of endophthalmitis were identified in children under 18 years over a period of 10 years. This relatively low number of cases is consistent with the low rate of this complication. Previous ocular surgery (47.8%) consisting of cataract and glaucoma procedures was the most common causes of endophthalmitis. This is because they are the most common paediatric cases seen and managed at Hospital Kula Lumpur over the past 10 years. This differs from previously published papers by Zhang *et al.*[8] and Thordsen *et al.*,[9] where trauma accounted for a greater proportion of cases of endophthalmitis. The incidence of postoperative endophthalmitis in the study by Thordsen *et al.* was 38%,[9] while it was 3% in Zhang *et al.*[8]

Glaucoma surgery is a well-recognized risk factor for endophthalmitis. Previous studies have shown that endophthalmitis following glaucoma drainage device surgery usually occurs late, months to years after surgery, and is associated with tube repositioning, needling, and implant exposure, which was also seen in four of our patients.[3,9] In a series of 60 paediatric eyes with Ahmed implants, Parvizi *et al.* found that the rates of tube exposure and endophthalmitis were high, at 12% and 3%, respectively.[3] This emphasizes the importance of inspecting the overlying conjunctiva for tube exposure whenever the child is examined and parents being warned should there be only a thin layer of conjunctiva over the tube. The use of a 5% povidoneiodine solution has been proven effective in decreasing the incidence of infectious endophthalmitis.

Ocular trauma was the second leading cause of endophthalmitis, seen in 30.4% of our patients of which most were males (85.7 %). Rishi *et al.* reported almost similar rates (72%) in their series.[6] The higher incidence of traumatic ocular injuries in boys compared with girls puts them at a higher risk of developing endophthalmitis. Delayed repair of penetrating ocular trauma is among the major risk factors for development of infective endophthalmitis. Other risk factors are posterior location of the wound, lens disruption, vitreous prolapse, and eyes with retained intraocular foreign body.[5,10] Among our patients with ocular trauma, 71.4% had traumatic lenticular changes, which is one of the risk factors for developing endophthalmitis. Urgent referral of these cases to vitreoretinal surgeons is mandatory when penetrating eye injury is associated with signs of endophthalmitis. Aggressive management in the form of vitrectomy along with IVT antibiotics in paediatric post-traumatic endophthalmitis cases is associated with better clinical outcomes.[6,10,11]

Endogenous endophthalmitis is a rare but highly destructive infection of the eye, in which the pathogenic organisms reach the eye through the systemic circulation. Studies have shown that endogenous endophthalmitis accounts for 0.1% to 4% of all endophthalmitis cases.[7,12,13] Our study had five (21.7%) patients with endogenous endophthalmitis. It has been reported that the severity and rapidity of the progression of endophthalmitis are associated with the virulence of the infecting organism, and that more virulent organisms such as streptococci and gram-negative species usually lead to worse visual outcomes. However, in children it is not only the microbial virulence and exaggerated inflammatory response, but the inevitable delay in diagnosis and definitive treatment requiring general anaesthetic which are also likely to contribute to the poor outcome.[3,13]

The earliest symptoms of adult endogenous endophthalmitis include pain and decreased visual acuity. In adults, early symptoms may prompt patients to seek medical attention, allowing earlier diagnosis and a good outcome with appropriate management. However, because of poor communication in paediatric patients, it is difficult to diagnose endogenous endophthalmitis at an early stage and it may be misdiagnosed as uveitis, persistent foetal vasculature, cataract, retinopathy of

prematurity, toxocariasis, Coat's disease, retinal detachment, and retinoblastoma.[13] In a study by Basu *et al.*, six premature infants with extremely low birth weight developed endogenous endophthalmitis. They reported *Klebsiella pneumoniae* and *P. aeruginosa* in two cases each and *Candida albicans* and methicillin-resistant *S. aureus* in one case each.[14] Our study had two premature infants, of which one was secondary to urinary tract infection with coagulase-negative staphylococci and the other one was due to *H. influenza* meningitis. Since there is a usually a septic focus, systemic antibiotics seem to play a much definitive role in treatment in endogenous cases.

The most commonly identified organisms in our study were coagulase-negative staphylococci and *S. aureus*, comprising 50% of the isolates, as seen in other studies.[3,8,15] Culture-positive rates have been reported to range from 44% to 75% in Western studies.[11] Narang *et al.* reported 27% culture positivity from ocular specimens in India. In our study, culture positivity rate was 21.7%. The lower culture-positivity rates in our study may be due to the fact that most of the patients had received prior intravenous and IVT antibiotic treatment elsewhere before they were referred to our HKL.[5]

Therapeutic PPV was performed in 82.6% of cases in our study. Eyes with severe forms of endophthalmitis in the paediatric population benefit from PPV. Early PPV drastically decreases the microbiological load and aids the diffusion of IVT and systemic antibiotics within the eye. Patients undergoing PPV were more likely to have good anatomical outcome than those treated with antibiotics alone on presentation.[9,16] However, 13 (61.9%) of our patients had phthisis bulbi as a final outcome despite PPV being performed within 24 hours from diagnosis. The reason for this may be due to unfavourable presentation with corneal abscess, extensive retinal necrosis, subretinal abscess, and retinal detachment, which was noted intraoperatively in these patients. In addition, two of our patients developed retinal detachment post-PPV. It has been reported that corneal abscess and retinal detachment were associated with poor outcomes in children with endophthalmitis.[6] This may explain the poor outcomes in our cohort, where despite early and aggressive treatment, many did not have a favourable outcome.

The visual prognosis in paediatric endophthalmitis is generally poor, with most eyes having no residual functional vision. In our series, 13 (56.5%) cases were left with phthisical eye. Trauma portends a poor prognosis in children due to their greater risk of retinal detachment and subsequent development of proliferative vitreoretinopathy and amblyopia.[17] In contrast to previous reports, our study found that more children in the postoperative group ended resulted in phthisical eye compared to the post-traumatic and endogenous groups.

Study limitations

This study is limited by a retrospective study design of a rare condition. As the data was collected retrospectively, some data was unavailable. Lack of uniform guidelines

and treatment protocols were also limitations. While the study population is diverse, the numbers are small and do not allow for definitive comparison between groups.

Conclusion

This study provides information on a rare but sight-threatening complication in children. Paediatric endophthalmitis differs from adult endophthalmitis in many respects. First, the visual outcomes are generally poor. For some severe cases, even if visual acuity cannot be preserved, efforts should be made to retain the eyeball because eyeball contour is crucial for the development of the orbit and the children's psychological health. Second, diagnosis and treatment are likely to be delayed, as children are usually poor providers of case history, so they might not complain of symptoms promptly. Furthermore, treatment might be delayed by parents or by primary care doctors if the presenting signs are not obvious. Third, the paediatric vitreous cavity is filled with gel, which hinders the dispersion of drugs in the vitreous cavity, and children are more prone to retinal detachment complicated by proliferative vitreoretinopathy.

Treatment of paediatric endophthalmitis remains challenging and the visual prognosis is generally poor. Therefore, prevention of postoperative endophthalmitis is crucial and steps should be taken to reduce its occurrence. Regular maintenance of the air conditioning filters, use of povidone iodine 5% solution in the conjunctival sac a few minutes prior to surgery, proper construction of wound, use of prophylactic intracameral antibiotics or prophylactic subconjunctival antibiotic injection at the conclusion of surgery, and early initiation of topical antibiotics all help lower the frequency of postoperative endophthalmitis. Educating parents about the signs of endophthalmitis, especially lethargy, asymmetrical eye redness, eyelid swelling, and fever as well as proper postoperative care are also important. In the unfortunate event of endophthalmitis in children, prompt administration of systemic antibiotics with good intraocular penetration is more important due to the inevitable delay in arranging for intraocular injections in these group.

It is clear from our study that paediatric endophthalmitis is a serious condition that requires a high index of suspicion in children and aggressive management. We hope that this study will help to diagnose promptly, guide treatment, and improve the prognosis in this unique set of patients in future.

Declarations

Ethics approval and consent to participate

Ethical approval for this study was obtained from Clinical Research Centre, HKL and Medical Research and Ethics Committee, Ministry of Health, Malaysia. As this was a

non-interventional, retrospective study, informed consent was not required from subjects and/or their guardians.

Competing interests
None to declare

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Ab-externo XEN gel stent implantation in primary open-angle glaucoma: 6-month follow-up

Mohd Hasif **Mustafa**, Norshamsiah **Md Din**, Seng Fai **Tang**

Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

Abstract

Purpose: XEN gel stent (XGS) is one of the minimally invasive glaucoma surgery (MIGS) procedures offering substantial intraocular pressure (IOP)-lowering. We evaluated the efficacy and safety of XGS implantation via an ab externo approach in patients with primary open-angle glaucoma (POAG). We present 13 cases of successful XEN implantation via an ab externo approach in these patients.
Study design: Retrospective case series.
Methods: This was a retrospective case series involving patients diagnosed with POAG at a tertiary referral centre who underwent XGS implantation between February 2019 and June 2020 for uncontrolled IOP despite maximum topical medications. All patients underwent XGS implantation via an ab externo approach placed at the superotemporal quadrant. The main outcome measure was IOP reduction and number of antiglaucoma medications after XGS implantation, post-operative procedures, and surgical complications.
Results: Thirteen eyes of 13 patients were included in the analysis. At the 6-month follow-up, mean IOP reduction was 2.73 ± 3.66 mmHg and mean IOP was 13.8 ± 1.99 mmHg on an average of 1.6 antiglaucoma medications. Complications included transient hypotony and transient IOP spikes requiring needling. Two patients required stent removal due to recurrent conjunctival erosion and stent migration into the anterior chamber.
Conclusion: XGS implantation is able to achieve good IOP control with reduced need for antiglaucoma medications after a minimum follow-up of 6 months. Longer follow-up is needed to assess its long-term outcome.

Correspondence: Tang Seng Fai Tang, Dr Ophthal, Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, 9th Floor, Clinical Block, Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur, Malaysia.
E-mail: sengtangfai@gmail.com

Keywords: ab externo, minimally invasive glaucoma surgery, primary open-angle glaucoma, XEN gel stent

Implantasi gel sten XEN secara ab-externo pada pesakit glaukoma bersudut terbuka primer: lapuran pada 6 bulan rawatan susulan

Abstrak

Pengenalan: Gel sten XEN (XGS) merupakan prosedur pembedahan glaukoma invasif minima (MIGS) yang mampu menurunan tekanan intraokular (IOP).
Objektif: Kami menilai keberkesanan dan keselamatan implantasi XEN melalui kaedah ab-externo pada pesakit glaukoma sudut terbuka primer (POAG). Kami membentangkan 13 kes implantasi XGS yang berjaya dilakukan melalui kaedah ab-externo dalam pesakit POAG
Kaedah kajian: Siri kes retrospektif yang melibatan pesakit POAG yang telah menjalani implantasi stent gel XGS antara Februari 2019 dan Jun 2020 disebabkan oleh IOP yang tidak terkawal walaupun telah menggunakan ubat topikal secara maksimum. Semua pesakit menjalani implantasi gel sten XGS melalui kaedah ab-externo yang diletakkan di bahagian superotemporal. Kajian melihat kepada pengurangan IOP dan bilangan ubat antiglaucoma yang diperlukan selepas implantasi gel sten XGS, prosedur lain yang perlu dilakukan selepas pembedahan dan komplikasi pembedahan.
Keputusan: Tiga belas (13) pesakit yang melibatkan 13 biji mata terlibat di dalam kajian ini. Pada enam bulan, purata pengurangan IOP selepas pembedahan ialah 2.73 ± 3.66 mmHg dengan purata IOP pesakit adalah 13.8 ± 1.99 mmHg, dan purata ubat antiglaukoma ialah 1.6. Komplikasi termasuk hipotoni sementara dan lonjakan IOP sementara yang memerlukan bantuan cucukan (needling). Dua pesakit memerlukan pengeluaran sten kerana hakisan konjunktiva berulang dan penghijrahan sten ke dalam ruang anterior.
Kesimpulan dan rujukan: Implantasi gel sten XEN mampu mencapai kawalan IOP yang baik dengan pengurangan ubat antiglaukoma selepas rawatan susulan minimum 6 bulan. Kajian yang lebih lama diperlukan untuk menilai hasil jangka panjang.

Kata kunci: ab externo, bersudut terbuka primer, gel sten XEN, glaukoma pembedahan, glaukoma invasif minima

Introduction

Glaucoma is a progressive optic neuropathy causing irreversible blindness affecting more than 70 million people worldwide.[1] Intraocular pressure (IOP) is the only modifiable risk factor identified. Thus, reducing the IOP is the most effective option to slow down the progression of glaucoma.[2] Treatment for lowering IOP include oral and topical medications in addition to laser and surgical intervention. In open-angle glaucoma, conventional trabeculectomy, and glaucoma drainage devices are the most common procedures performed to lower IOP, but are associated with a range of complications including hypotony, leakage, choroidal effusion, and tube-related complications such as erosion, tube blockage, and bleb encapsulation.[3]

Minimally invasive glaucoma surgery (MIGS) is an emerging field of IOP-lowering procedures that provides fewer complications with reliable results. The XEN gel stent (XGS) is a type of MIGS which offers a good safety profile and faster recovery. In chronic open-angle glaucoma, the XEN device has been reported to provide IOP reduction of up to 56% and reduce antiglaucoma medications by up to 2.7 medications at 12 months,[4] with a lower rate of complications compared to conventional trabeculectomy.[5]

We evaluated the outcome of XGS implant via the ab externo approach in primary open-angle glaucoma (POAG) patients with regards to IOP-lowering effect, number of needlings, and number postoperative medications, as well as complications, including stent migration and endophthalmitis.

Methods

This retrospective case series was conducted at Hospital Canselor Tuanku Muhriz (HCTM), Pusat Perubatan Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia. The study included all XGS tube implantations via ab externo approach from February 2019 to June 2020. POAG was diagnosed based on IOP elevation of ≥ 22 mmHg, open angle on gonioscopy, glaucomatous optic disc changes, and a glaucomatous reproducible visual field defect on Humphrey visual field.

Best-corrected visual acuity (BCVA), IOP, and number of glaucoma medications were recorded at baseline. A minimum of 6-months of follow-up was required for each patient to be included in the study. The BCVA, IOP, medications, postoperative procedures, complications, and management were recorded after 1 week, and 1, 3, and 6 months postoperatively.

Primary outcomes were complete success (defined as IOP ≤ 21 mmHg without additional medication) and qualified success (defined as IOP ≤ 21 mmHg, with medication).[6] Secondary outcomes included percentage of IOP reduction, number of glaucoma medication required at 6-months postoperative, eyes achieving > 20%

IOP reduction with the same or fewer number of medications without secondary surgical intervention, and postoperative complications.

Surgical technique

All XGS implantations were performed via an ab externo approach at the superotemporal quadrant. If the preoperative IOP was > 30 mmHg, slow paracentesis was performed to avoid a sudden drop in IOP and to limit the bleb size after implantation. Topical proparacaine hydrochloride 0.5% was used for anaesthesia. Corneal traction with a vicryl 7-0 suture was placed at the intended quadrant. The sites for conjunctival and scleral entry wounds were marked at 7 mm and 2.5 mm behind the limbus, respectively. Subconjunctival lidocaine hydrochloride 2% injection separated the conjunctiva from Tenon's and provided further anaesthesia. The XGS injector needle was inserted 7 mm behind the limbus with the bevel facing up, directly beneath the conjunctiva and advanced towards the scleral entry wound. While applying countertraction with the corneal traction suture, the needle pierced the sclera until the needle tip was visible in the anterior chamber (AC). The slider was then pushed until the tip of the XGS tube could be seen in the AC. The needle was slowly withdrawn while still pushing the slider to complete tube deployment. Using this technique, the ideal tube placement can be achieved, with 2 mm each in the AC, scleral tunnel, and subconjunctival space. Subconjunctival mitomycin C 0.01% (30 µg/0.3 mL) was then injected posterior to the bleb.

Postoperative management

All patients received dexamethasone 0.1% and ciprofloxacin 0.3% every two hours, and all antiglaucoma medications were discontinued. Patients were seen weekly in the first month. When required, bleb needling was performed with 5-fluorouracil (5-FU) 5 mg/0.1 mL and dexamethasone 0.4 mg/0.1 mL when there were signs of subconjunctival fibrosis or high-risk bleb failure.[7] Steroid eyedrops were continued between 2 and 3 months postoperatively.

Needling

When needling was required postoperatively, the procedure was done in sterile conditions. Under topical proparacaine anaesthesia, a sterile 25-G needle was advanced into the subconjunctival space towards the bleb and subconjunctival and Tenon's adhesion was released. 5-FU 5% (5 mg/0.1 mL) and dexamethasone 0.4 mg/0.1mL were injected around the bleb at the end of the procedure.

Results

Thirteen eyes of 13 patients were included in this study. The mean age was 69 ± 5.3 years. There were eight males and five females. There were six patients each of

Table 1. Patient data

Parameter	Value
Age	69 ± 5.3 years
Ethnicity	6 Malays, 6 Chinese, 1 Indian
Baseline IOP (mmHg)	16.8 ± 3.2
Number of antiglaucoma medications (mean ± SD)	3.6 ± 0.6
Pseudophakia (%)	8 patients (61.5%)
XGS alone (%)	10 patients (76.9%)
XGS with phacoemulsification (%)	3 patients (23.1%)
Previous failed glaucoma procedure (%)	2 patients (15.4%) 1 Baerveldt 1 trabeculectomy

Malay and Chinese ethnicity, and one Indian. At baseline, eight patients were pseudophakic, while two patients had failed glaucoma drainage device procedure prior to XGS stent implantation (Table 1).

Only three of five phakic patients had combined XGS tube implantation with cataract extraction for concurrent cataract with high IOP. Their mean baseline IOP was 16.8 ± 3.2 mmHg and mean number of topical antiglaucoma medications was 3.6 ± 0.6.

All patients (100%) achieved IOP ≤ 21 mmHg. Only one patient achieved complete success, and the remaining patients achieved qualified success, requiring at least one antiglaucoma medication at 6 months postoperatively.

Effect of XGS on IOP and number of medications

At the 6-month follow-up, mean IOP was 13.8 ± 2.0 mmHg with a mean IOP reduction of 2.7 ± 3.7 mmHg, a 16.5% reduction from baseline IOP. The number of antiglaucoma medications was significantly reduced from 3.6 ± 0.6 preoperatively to 1.5 ± 0.7 at the 6-month follow-up, a mean reduction of 2.27 medications postoperatively. Five patients (45.5%) achieved more than 20% IOP reduction without requiring a secondary postoperative procedure.

Postoperative procedure

The postoperative interventions are summarized in Table 2. Postoperative procedures performed included AC reformation, XGS tube adjustment, conjunctival re-suturing, and needling. On average, all patients required 3.2 ± 1.2 needlings with 5-FU injection postoperatively. Three patients (23.1%) required AC reformation and one patient (7.7%) required XGS tube adjustment and conjunctival re-suturing due to tube migration (Table 2).

Table 2. Postoperative procedures

Procedure	
Anterior chamber reformation	3 patients (23.1%)
Tube re-adjustment	1 patient (7.7%)
Conjunctival re-suturing	1 patient (7.7%)
Average of needling procedures per patient	3.18 (± 1.19)

Complications

The most frequent postoperative complication was transient hypotony, which occurred in four patients (30.8%) but resolved within 2 weeks. There were also transient IOP spikes of > 30 mmHg in three patients (23.1%) requiring needling upon follow-up. Additionally, two patients (15.4%) had to undergo XGS explantation due to conjunctival erosion and tube migration to the AC due to eye rubbing. None of the patients had BVCA loss or postoperative endophthalmitis at 6 months.

Discussion

MIGS aim to provide a better safety profile with less invasive IOP-reducing procedure than traditional glaucoma surgery for patients with mild-to-moderate glaucoma as well as reduce the dependency on topical medication.[8] XGS is a porcine-based, 6-mm gelatine tube which allow aqueous drainage to the subconjunctival space through a 45 µm lumen. This dimension is able to reduce the occurrence of postoperative hypotony by providing a steady-state pressure of 6–8 mmHg at 2.25 µL/min flow rate.[9] It is highly debatable whether XGS via an ab externo approach is part of MIGS, as it requires conjunctival dissection, mitomycin injection, and filtrating bleb formation. To date, there are only a handful of articles in the literature discussing XGS implantation via the ab externo approach. In this retrospective study, we evaluated XGS implantation via an ab externo approach among POAG patients.

XGS were originally studied using an ab interno approach,[5,10,11] and recent studies have shown that the ab externo approach offers greater advantages with more predictable outcomes. The ab externo approach does not require corneal incision and involves less manipulation within the AC, which makes it theoretically safer in phakic eyes.[12] Even though the ab externo approach requires conjunctival resection, it also allows surgeon to direct aqueous outflow posteriorly in a more predictable fashion with a diffuse subconjunctival bleb compared to the ab interno approach. Moreover, in experimental studies, the ab externo approach demonstrated less outflow resistance and more predictable bleb formation, providing better prospects for long-term IOP control.[13]

IOP reduction after XGS implantion ranges from 25% to 56%. Galal *et al.*[14] and Perez-Terregrosa *et al.*[15] reported IOP reductions of 25% and 29.34%, respectively, after 1 year of XGS implantation in POAG patients. Patients in our study had a lower mean preoperative IOP of 16.8 mmHg, thus explaining the lower percentage of IOP reduction compared to other studies. Higher baseline number of antiglaucoma medications may also contribute to poorer conjunctival condition preoperatively. Moreover, we also included two patients (15.4%) who had previous failed glaucoma surgery with higher risk of postoperative fibrosis. XGS has been shown to have comparable surgical success and complications compared to trabeculectomy up to 12 months after surgery.[16,17]

We found transient IOP spikes that were well managed with needling postoperatively. However, we did not observe severe complications such as endophthalmitis or visual loss. Migration of the stent into the AC is possible, particularly if the patient rubs the eye, even several months postoperatively. If the XGS is implanted too superficially, stent erosion is possible and the XGS may have to be explanted.

The limitations of our study are the small number of patients and short duration of follow-up. However, the result of IOP reduction with fewer medications postoperatively provides a good predictive value for the long-term success of this approach. A longer follow-up period is required to assess long-term outcomes.

Declarations

Ethics approval and consent to participate
No ethics approval was required as this was a retrospective study.

Competing interests
None to declare.

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Autologous blood injection: alternative treatment for bleb leak

Nur Hafeela **Mohamad Rusli**, Safinaz **Mohd Khialdin**, Jemaima **Che-Hamzah**

Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Abstract

Background: To report a case of post-glaucoma drainage device (GDD) surgery with multiple small conjunctival defects treated with autologous blood injection.
Case presentation: A 28-year-old female with a history of juvenile open-angle glaucoma who had undergone multiple glaucoma surgeries with antimetabolite injections for uncontrolled intraocular pressure (IOP) of the left eye since 2006 underwent Baerveldt glaucoma implantation in 2017. One year postoperatively, she experienced persistent hypotony, which could not be resolved with a scleral bandage contact lens. Ocular examination revealed visual acuity of 6/9 and IOP of 8 mmHg. Multiple leakage points were identified with fluorescein at the junction between the plate and the tube. Subconjunctival injection of 1 ml autologous blood was administered near the conjunctival defects. Five months postoperatively, the leakage was sealed with IOP of 12 mmHg.
Conclusion: Autologous blood injection can be used as an alternative procedure for treating leaking blebs after a GDD surgery.

Keywords: autologous blood injection, bleb leak, glaucoma drainage device, glaucoma implant

Correspondence: Associate Professor Dr Jemaima Che-Hamzah, Department of Ophthalmology, 9th Floor, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, 56000 Cheras, Kuala Lumpur, Malaysia.
E-mail: jemaima@ppukm.ukm.edu.my

Suntikan darah autologous: rawatan alternatif untuk kebocoran bleb

Abstrak

Latar belakang: Melaporan satu kes kebocoran pada bahagian konjunktiva selepas pemasangan alat saliran glaukoma (glaucoma drainage device (GDD)) yang berjaya dirawat menggunakan suntikan darah autologous.
Pembentangan case: Seorang wanita berumur 28 tahun dengan sejarah glaukoma sudut terbuka juvana telah menjalani beberapa pembedahan glaukoma dengan suntikan antimetabolit bagi mengawal tekanan intraokular mata kiri sejak 2006 dan telah menjalani implantasi Baerveldt GDD pada 2017. Satu tahun selepas pembedahan, dia mengalami hipotoni yang berterusan dan tidak berjaya dirawat dengan kanta sentuh pembalut skleral. Pemeriksaan mata mendapati ketajaman penglihatan pesakit adalah 6/9 dengan tekanan mata 8 mmHg. Beberapa titik kebocoran dikenal pasti di persimpangan antara plat dan tiub menggunakan fluorescein. Suntikan subkonjunktival darah autologous sebanyak 1ml telah disuntik pada bahagian yang hampir kepada kawasan mengalami kebocoran konjunktiva. Lima bulan selepas suntikan, tiada lagi kebocoran dengan tekanan intraokular 12 mmHg.
Kesimpulan: Suntikan darah autologous boleh digunakan sebagai prosedur alternatif untuk merawat bleb yang bocor selepas pembedahan pemasangan alat saliran glaukoma.

Kata kunci: alat saliran glaukoma, kebocoran bleb, pembedahan implantasi glaukoma, suntikan darah autologous

Introduction

Glaucoma drainage devices (GDDs) are surgically implanted devices designed to drain aqueous humour from the anterior chamber through a long tube by its absorption into the tissues around the eye.[1] The leakage of aqueous from a filtration bleb is a rare complication after GDD surgery. The tube versus trabeculectomy (TVT) study showed only one case (1%) of wound leak.[2]

Bleb leaks can result in a series of issues, including a flat anterior chamber, cataract, corneal decompensation, synechiae, choroidal effusions, macular oedema, and endophthalmitis, if left untreated.[3]. Although endophthalmitis is a rare complication after GDD surgery, it can lead to significant vision loss.[3] Furthermore, the use of antifibrotic agents in glaucoma filtration surgery has led to an increase in the incidence of spontaneous bleb leaks due to the formation of extremely

thin, avascular blebs, and the highest risk was observed in those who received mitomycin-C (MMC) in comparison to 5-fluorouracil (5-FU).[3]

Bleb leaks can be managed conservatively by using aqueous suppressants such as carbonic anhydrase inhibitors and beta blockers. Pressure patching can be applied because it reduces eye and lid movement. Bandage contact lenses and collagen shields have also been used in bleb leaks.[3] When these methods fail, surgical repair is the definitive treatment to cover the conjunctival defect.[3] This can be done by transplanting or advancing healthy tissue from the conjunctiva, sclera, or amniotic membrane.[3]

Another treatment modality is autologous blood injections, wherein fibrin and erythrocytes can obstruct the fluid flow through defects, with plasma proteins diffusing to the defect and a subsequent cross-linking of the coagulating factors sealing the leak.[4] Autologous blood injections have been used to treat both overfiltering and leaking blebs.[5] This technique has been described as a safe procedure with fewer complications.[5] A small sample size of 10 patients who received autologous blood injections in Choudhri *et el.*[6] showed the average intraocular pressure (IOP) after autologous blood injection increased from 4.3 ± 2.5 mmHg to 6.4 ± 5.1 mmHg on the final visit, but this was statistically insignificant.[6] Another study done by Leen and associates showed a significant increase in IOP and visual acuity in 7 out of 12 eyes by a mean of 5.1 ± 2.9 mmHg and 5.3 ± 2.1 lines.[4]

We report a case of a young patient with multiple glaucoma surgeries for uncontrolled IOP who presented with multiple small conjunctival defects that were treated with autologous blood injection.

Case presentation

A 28-year-old female with a history of juvenile open-angle glaucoma had undergone multiple surgeries since 2006 for uncontrolled glaucoma in the left eye. The right eye had been enucleated for painful absolute glaucoma in 2015. Baseline IOP in the left eye was 38 mmHg. She initially underwent trabeculectomy with adjunctive 0.03% MMC applied into the conjunctival flap for 3 minutes, followed by a trabeculectomy revision and 5-FU a year later. Multiple needlings with subconjunctival 5-FU injection were administered and antiglaucoma medications were restarted, but IOP was still not under control.

The patient underwent 101-350 Baerveldt glaucoma tube implantation in 2017. The tube lumen was stented with prolene 4-0 and the tube was ligated with vicryl 7-0. MMC was not used during GDD implantation. Extensive superior fibrosis over the previous trabeculectomy site was noted intraoperatively. On day 2 postoperative, a slow leak was noted, but the leakage sealed completely after 3 weeks with IOP of 19 mmHg. Multiple leaking points were found at 4 months postoperative, followed by persistent hypotony for 1 year with IOP ranging between 6 and 9 mmHg. The leaks

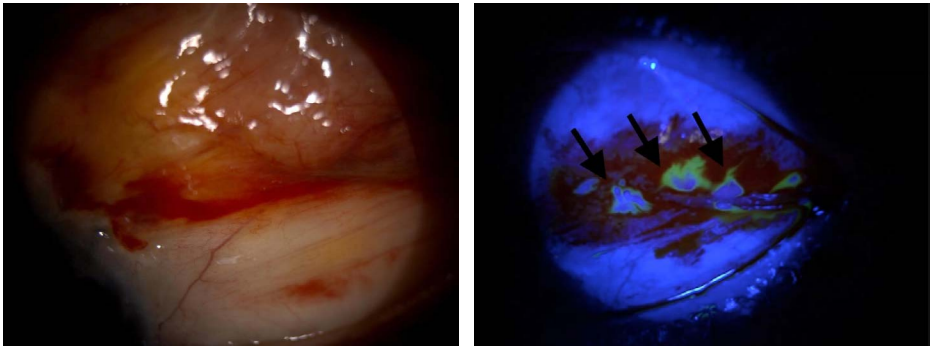

Fig. 1. Superotemporal conjunctiva of the left eye 1-week post-autologous blood injection. (*Left*) Subconjunctival haemorrhage surrounding the bleb area. (*Right*) Multiple slow leaks at the junction between the plate and the tube shown with black arrows.

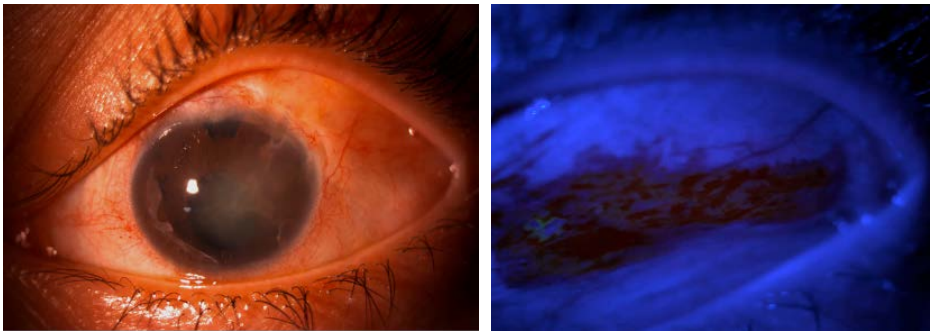

Fig. 2. Superotemporal conjunctiva 5 months post-autologous blood injection. (*Left*) White conjunctiva with resolved subconjunctival haemorrhage. (*Right*) Presence of minimal transconjunctival aqueous flow or "bleb sweating" at the junction between the plate and the tube.

could not be resolved with a scleral bandage contact lens, leading to the diagnosis of late postoperative leak with chronic hypotony.

Ocular examination revealed visual acuity of 6/9 and IOP of 8 mmHg in the left eye. The conjunctiva was mildly injected. The Baerveldt tube and plate were placed 10 mm from the limbus, with the elevated bleb seen above the implant. There was no exposed plate noted. Multiple leakage points were identified with fluorescein at the junction between the plate and the tube (Fig. 1). Eccentric central corneal opacity was observed due to the tube touching the cornea endothelium with a moderately deep anterior chamber and no cell activity. Peripheral anterior synechiae were present from 6 to 9 o'clock, and the pupil was round and reactive. Fundus examination revealed a pale optic disc with a cup-to-disc ratio of 0.9 with no sign of choroidal detachment or ocular hypotony.

The patient underwent a subconjunctival injection of 1 ml autologous blood near the conjunctival defects under topical anaesthesia. The left eye was anesthetized with proparacaine hydrochloride 0.5%. The area was then cleaned with povidone-iodine 5% and draped with a sterile eye surgical towel. A sterile lid speculum was placed on the eye. The antecubital fossa was cleaned with alcohol swabs and povidone-iodine 5%, and approximately 1 ml of venous blood was withdrawn in a 1 cc syringe. A 30-gauge needle was placed on a 1 cc syringe for injection of 0.5 to 0.75 ml of unclotted blood into the subconjunctival area near the defects. Antibiotic ointment and an ocular patch were then applied. Postoperatively, the patient was prescribed chloramphenicol ointment QID. At 5 months postoperative, the leakage was sealed (Fig. 2) with an IOP of 12 mmHg.

Discussion

A GDD is a drainage implant that is inserted under the conjunctiva to create an alternative pathway for aqueous humour from the anterior chamber, wherein a fibrous capsule forms around the reservoir for approximately 1 month after surgery.[1] GDDs can be associated with various postoperative complications such as hypotony, suprachoroidal haemorrhage, infections, valve malfunctions, and tube erosion, which increase the risk of endophthalmitis and strabismus that result from fibrosis around the surrounding muscle and corneal decompensation.[3]

Hypotony secondary to leaking bleb after GDD surgery is uncommon, but it is important to understand the treatments available to prevent further complications.[3] A serious complication such as endophthalmitis can happen as a result of the direct communication between the anterior chamber and the ocular surface.[3] Leaking blebs can be divided into early, occurring within 3 months of surgery, and late, occurring from 3 three months postoperatively.[3] Early postoperative bleb leaks are usually related to surgical trauma to the conjunctiva or inadequate conjunctival closure and can be avoided by careful and meticulous surgical technique.[7] Late-onset leaks are typically associated with thin, cystic, avascular blebs and occur months to years after surgery.[7]

It is believed that the use of augmenting antimetabolites such as MMC and 5-FU may further increase the risk of bleb leaks.[2,4] This was observed in our patient, who had a late-onset bleb leak 1 year post-Baerveldt tube implantation. She had received multiple antimetabolites at the bleb area, resulting in conjunctival thinning that predisposed the patient to persistent hypotony for more than 12 months with multiple small conjunctival defects. Conservative management failed to seal the leak. Post-autologous blood injection, IOP increased to 10–13 mmHg. The leakage was completely sealed after 5 months, especially in the surrounding area containing the blood. It is believed that red cells can slowly trigger fibroblastic transformation, which remains under the bleb for weeks or more.[4]

The management of late-onset bleb leaks can be divided into two categories: conservative and surgical.[3,8] Conservative treatments include medications or the use of therapeutic bandage contact lenses, application of cryotherapy or laser therapy, and autologous serum eye drops.[3,8] These methods can mechanically close the leak and induce a wound healing process.[3,8] A bandage contact lens can be applied for small leaks at the limbus.[9] However, bandage contact lenses do not act well on dry eyes, and standard contact lenses, with a usual diameter of 14 mm, can cause erosive damage to the bleb.[9] This latter method can lead to blebitis and endophthalmitis.[9]

Lynch *et al.* reported the efficacy of Nd:YAG laser to treat overfiltering and leaking blebs, but the long term success after 4 years was unsatisfactory.[8] This laser technique can also cause complications such as iatrogenic leaks, transient IOP spikes, corneal oedema, bleb pigmentation, pupil peaking, and late recurrences.[8] Another type of laser is the argon laser, which causes focal thermal damage and shrinkage of the conjunctiva.[8,10] Argon laser therapy has shown successful results in sealing the leaks requiring dyeing of the ischemic bleb with the use of large spot size, but this technique has not been universally accepted as it has not gained widespread use.[8]

When conservative treatments fail to seal the leaks, patients may require surgical intervention to prevent further complications. Surgical revision of late-onset bleb leak usually attempts to cover the blebs with various membranes such as conjunctiva-Tenon's flap, scleral patch graft, or amniotic membrane transplant.[8,11] A conjunctival-Tenon's flap has a long-term success rate for small blebs wherein the healthy conjunctiva is incised at the limbus and posteriorly and laterally.[8] A scleral patch graft is another alternative method.[8] The fragility of the conjunctiva after surgery may further increase the risk of bleb failure.[8] Amniotic membrane has also been used to cover and preserve leaking blebs; due to its antimicrobial activity, it causes less risk of infection and is easy to obtain.[12]

This was the first reported case of autologous blood injection in post-GDD surgery in Malaysia. It was hypothesized that fibrin and red cells would obstruct the fluid flow in the bleb and remain under the bleb for a few weeks.[13] At the same time, the blood cells can cause a fibroblastic transformation to replace inactivated Tenon capsule cells.[13] Few studies have shown an improvement of vision post autologous blood injection.[13,6] In the study done by Smith *et al.*, four of six eyes were leak-free and able to maintain IOP between 8 and 12 mmHg with no further complications.[13] In our patient, we opted to use autologous blood injection as the patient showed multiple small defects at the junction between the plate and the tube. This method is cheap, easily available, and safer since we utilized the patient's own blood. Furthermore, autologous blood injection enhances the healing process while maintaining bleb function.[4,13] It is believed that the whole blood, which consists of erythrocytes, leukocytes, white blood cells, and some clotting factors, can promote healing.[13] Bleb leakage was shown to be sealed 5 months after surgery and IOP remained stable until then.

Conclusion

Autologous blood injection can be used as an alternative procedure in treating leaking bleb after GDD surgery.

Declarations

Consent for publication
The patient has given informed consent for publication of the clinical data and images contained in this case report.

Competing interests
None to declare.

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None to declare.

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Treatment of primary vasoproliferative tumor of the retina using laser photocoagulation and intravitreal ranibizumab

Muhammad Syafiq **Ahmad Musthafa**[1,2], Wan Norliza **Wan Muda**[3], Norlina **Ramli**[2,4]

[1]Department of Ophthalmology, Hospital Sultanah Nur Zahirah, Kuala Terengganu, Terengganu, Malaysia; [2]Department of Ophthalmology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; [3]Department of Ophthalmology, Hospital Tengku Ampuan Afzan Kuantan, Pahang, Malaysia; [4]University Malaya Eye Research Centre, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Abstract

Background: Vasoproliferative tumours (VPT) of the retina are benign, uncommon tumours that occur mostly in patients with no other ocular pathology. Several treatment modalities are used to treat these tumours including cryotherapy, laser photocoagulation, anti-VEGF injection, and observation.
Case presentation: We present a case of a 40-year-old female with retinal VPT. The patient received a combination of selective laser photocoagulation of the tumour and serial intravitreal injections of ranibizumab that resulted in regression of the VPT and good visual outcome.
Conclusion: Laser photocoagulation treatment should be considered for treating primary retinal VPT as it is the most available treatment modality. Combination therapy laser photocoagulation treatment with anti-VEGF provides long-term tumour regression, which is effective for the macular oedema associated with this condition.
Keywords: epiretinal membrane, intravitreal ranibizumab, laser photocoagulation, vasoproliferative tumour of the retina

Correspondence: Muhammad Syafiq Ahmad Musthafa, MD, Department of Ophthalmology, Hospital Sultanah Nur Zahirah, 20400 Kuala Terengganu, Terengganu, Malaysia.
E-mail: syafiqmusthafa@yahoo.com

Laser fotokoagulasi dan suntikan intravitreal ranibizumab sebagai rawatan primer bagi penyakit tumor retina vasoproliferatif

Abstrak

Latar belakang: Tumor vasoproliferatif (VPT) pada retina merupakan tumor yang tidak merbahaya, jarang dijumpai dan sering terjadi tanpa penglibatan perubahan patologi pada tisu mata yang lain. Beberapa kaedah rawatan seperti kemoterapi, laser fotokoagulasi, suntikan intravitreal anti-faktor pertumbuhan vasoendotelial dan pemantauan klinikal didapati berkesan dalam merawat penyakit ini.
Pembentangan kes: Di sini kami melaporkan satu kes yang melibatkan seorang wanita berusia 40 tahun yang didapati mendapat VPT pada retina. Pesakit ini telah berjaya dirawat dengan laser fotokoagulasi selektif kepada tumor serta suntikan intravitreal ranibizumab yang bersiri. Hasil dari rawatan ini VPT pada retina hilang sepenuhnya dengan pengekalan penglihatan yang baik.
Kesimpulan: Rawatan laser fotokoagulasi merupakan modul rawatan yang sedia ada, perlu dipertimbangkan dalam perawatan VPT pada retina, yang mana terbukti dapat mengurangkan pertumbuhan penyakit ini. Suntikan intravitreal ranibizumab bertindak sebagi pelengkap untuk regresi tumor untuk jangka panjang terutamanya dalam mengurangkan edema di retina.

Kata kunci: fotokoagulasi laser, membrane epiretinal, suntikan ranibizumab, tumor vasoprolioferatif retina

Introduction

Vasoproliferative tumours (VPT) of the retina are benign, uncommon tumours that occur mostly in patients with no other ocular pathology. VPT has a predilection for the peripheral inferior temporal retina. It may cause decreased vision due to intra- or subretinal exudates, retinal detachment, vitreous haemorrhage, preretinal fibrosis, macular oedema, and epiretinal membrane. Several treatment modalities are used to treat these tumours including cryotherapy, laser photocoagulation, anti-VEGF injection, and observation.

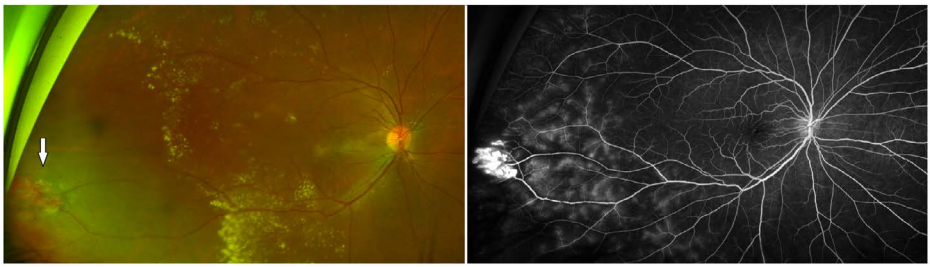

Fig. 1. (*Left*) White arrow showing elevated, telangiectatic aneurysmal vascular changes at temporal periphery, with hard exudates at temporal arcade. (*Right*) Fundus fluorescein angiography showing vascular leakage mainly at the temporal area with hyperfluorescent lesion corresponding to vascular tumour with area of significant capillary fall out area at temporal and inferotemporal quadrants.

Case presentation

A 40-year-old Malay female with no known medical illness presented with progressive blurring of vision in the right eye for 2 months, preceded by floaters and central scotoma. The patient had no history of eye redness, pain, trauma, or eye surgery.

Upon examination, her visual acuity (VA) was 6/30 in the right eye and 6/6 in the left eye. Intraocular pressure was 16 mmHg bilaterally. Bilateral anterior segment examination was unremarkable. Fundus examination of the right eye revealed epiretinal membrane at the macula with subretinal exudates measuring 9-disc diameters near the superotemporal and inferotemporal arcades, as well as a yellowish-red tumour at the temporal periphery. The tumour was fed by a minimally dilated retinal artery and drained by a slightly dilated vein (Fig. 1, left). In the left eye, there was minimal epiretinal membrane at the macula.

Fundus fluorescein angiography revealed a hyperfluorescent lesion corresponding to the vascular lesion temporally, with late leakage along the temporal and inferotemporal arcades and an area of capillary non-perfusion peripherally (Fig. 1, right). Optical coherence tomography (OCT) of the right macula revealed a central subfield thickness of 533 microns and macular oedema with epiretinal membrane (Fig. 2).

The right eye was diagnosed with retinal VPT with epiretinal membrane and macular oedema. Treatment consisted of selective focal and barricade argon laser photocoagulation (400 shots, 150–250mW) of the peripheral retinal telangiectasia with a combination of serial intravitreal anti-VEGF (ranibizumab).

At 1-month follow-up, the patient's VA improved to 6/18, and the VPT regressed (Fig. 3, left) with a reduction in exudates and oedema. The patient received four monthly and two bimonthly intravitreal injections of ranibizumab. At the 6-month follow-up, VA improved to 6/6 and the examination revealed regressed VPT vascu-

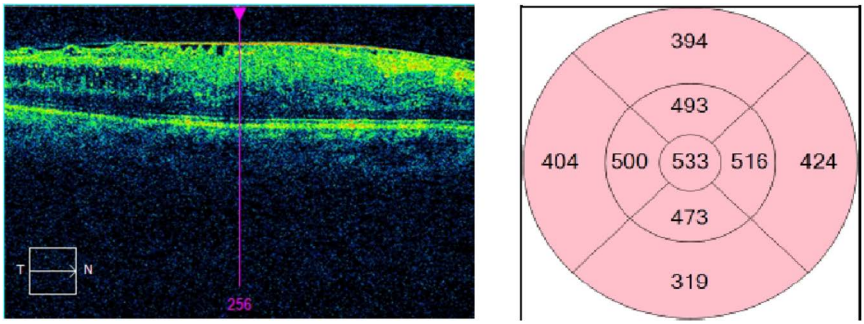

Fig. 2. Optical coherence tomography of the right eye showing epiretinal membrane and macular oedema.

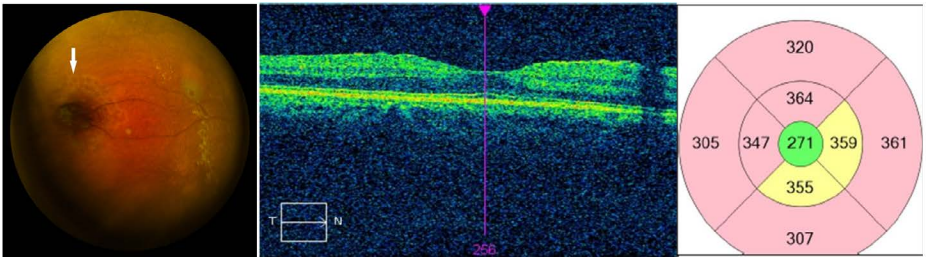

Fig. 3. (*Left*) Fundus photo 1 month after laser treatment showing regressed abnormal vessels surrounding laser marks (white arrow). (*Right*) Optical coherence tomography 6 months later showing marked reduction of macular oedema.

larization and reduced macular oedema based on OCT (Fig. 3, right). Upon 1 year of follow-up, VA remained at 6/6 and macula was dry with a central subfield thickness of 267 microns.

Discussion

Retinal VPTs are rare retinal lesions that usually present in the third or fourth decade of life. Its prevalence is equal in both sexes. Around 74% exist as primary tumours, while the other 26% are secondary to pre-existing vascular, inflammatory, dystrophic ocular diseases and degenerative ocular diseases.[1-3] Unlike secondary tumours, primary tumours usually present as solitary tumours.

Due to its rarity, there has been a lack of an evidence-based consensus pertaining to the optimal treatment of VPT of the retina. VPT treatment is based on the tumour's size and location as well as associated clinical features. Periodic observation of small, peripheral lesions with no evidence of macular involvement is recommended. In a report of 103 patients with VPTs, the primary treatment was observation (49%),

followed by cryotherapy (42%), laser photocoagulation (5%), or plaque radiotherapy (2%).[1] Several case reports have been published in the literature advocating for the use of photodynamic therapy to treat primary and secondary VPT.[4,5] Surgical management should also be considered for complications induced by retinal VPT, such as epiretinal membrane or tractional retinal detachment.[6,7]

The presence of significant exudates and epiretinal membrane along with macular oedema in our patient indicates the need for more than observation.[2] The patient received laser photocoagulation treatment for the tumour and an anti-VEGF injection to alleviate macular oedema and improve vision. Krivosic *et al.* reported that direct laser photocoagulation of the retinal telangiectasia to the VPT surface induced regression of the retinal exudates. This treatment was sufficient in half the cases.[8] A similar finding of tumour regression was revealed in our case report following laser therapy.

Due to their natural history, retinal VPTs could lead to neovascularization, exudate formation, and tractional retinal detachment. Hence, we postulated that it would respond to anti-VEGF. Visual acuity deterioration is mostly caused by macular oedema or epiretinal membrane formation; therefore, anti-VEGF should potentially be able to decrease leakage, thus improving macular oedema, as well as inhibit neovascularization and induce regression of new vessels. While some studies indicate that intravitreal anti-VEGF may be a useful therapeutic option for these complications secondary to vasoproliferative tumours of the retina, it is still unclear whether the initially promising results will be sustained over time.[9,10]

Conclusion

Numerous treatment modalities are available for retinal VPT depending on the lesion's manifestation and location. The treatment's objective is to preserve vision by avoiding complications such as exudative retinopathy and to induce lesion regression. In this case, we conclude that combining photocoagulation treatment with intravitreal anti-VGEF is effective at inducing long-term regression of the VPT and alleviating associated macular oedema.

Declarations

Consent for publication

Informed consent was obtained from the patient for the publication of the clinical information and images used in this case report.

Competing interests

None to declare.

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Unilateral exudative retinal detachment as the first manifestation of lung carcinoma

Thamarai **Munirathinam**, **Neoh** Pei Fang

Department of Ophthalmology, Hospital Enche' Besar Hajjah Khalsom, Kluang, Johor Malaysia

Abstract

Background: Exudative retinal detachment without ocular metastasis is extremely rare.
Case presentation: We report a case of sudden onset of painless vision loss in the left eye with relative afferent pupillary defect. Fundus features suggested exudative retinal detachment. Abnormal cutaneous findings and lung findings led to the suspicion of malignancy. Computed tomography of the brain and orbit showed no ocular metastasis; however, imaging of thorax, abdomen and pelvis revealed lung malignancy with distant metastasis. Immunohistochemistry profile of the skin biopsy was suggestive of metastatic adenocarcinoma.
Conclusion: A high index of suspicion, thorough physical examination and prompt intervention can be lifesaving.

Keywords: adenocarcinoma, exudative retinal detachment, lung carcinoma

Correspondence: Dr. Thamarai Munirathinam, MD, Department of Ophthalmology, Hospital Enche' Besar Hajjah Khalsom, KM 5 Jalan Kota Tinggi, 86000 Kluang, Johor, Malaysia.
E-mail: nitaraicz88@gmail.com

Lekang retina secara eksudatif tanpa tanda metasis pada bahagian okular sebagai manifestasi awal kanser paru-paru

Abstrak

Latar belakang: Lekang retina secara eksudatif tanpa tanda metasis pada tisu okular adalah amat jarang terjadi.
Kes: Kami melaporkan satu kes kehilangan penglihatan secara tiba-tiba tanpa rasa sakit di mata kiri dengan kehadiran kerosakkan pupil aferen secara relatif (relative afferent pupillary defect). Pemeriksaan fundus menunjukkan lekang retina secara eksudatif. Berdasarkan pemeriksaan dan kehadiran tanda abnormal pada kulit serta hasil dari pemeriksaan paru-paru, kanser merupakan salah satu penyebab utama. Walaubagaimanapun, pengimbasan tomografi otak dan orbit tidak menunjukkan tanda metastasis okular, namun pengimejan toraks, abdomen dan pelvis menunjukkan kehadiran kanser paru-paru dengan metastasis yang jauh. Profil imunohistokimia ke atas biopsi kulit menunjukkan ciri-ciri adenokarsinoma metastatik.
Konklusi: Dengan indeks kecurigaan yang tinggi, pemeriksaan fizikal yang menyeluruh dan intervensi yang cepat boleh menyelamatkan nyawa.

Key words: adenokarsinoma, kelekangan retina secara eksudatif, kanser paru-paru

Introduction

Exudative retinal detachment (ERD) is defined by Ghazi *et al.* as detachment of neurosensory retina from the underlying retinal pigmented epithelium, caused by fluid accumulation in the subretinal space due to leakage from retinal or choroidal vessels in the absence of retinal breaks or traction.[1] Inflammatory, infectious, infiltrative, neoplastic, vascular, and degenerative conditions may be associated with blood-retinal barrier breakdown and the sequential development of ERD. Retinal detachment occurs when the ability of the retinal pigment epithelium to pump the leaking fluid into the choroidal circulation is compromised.

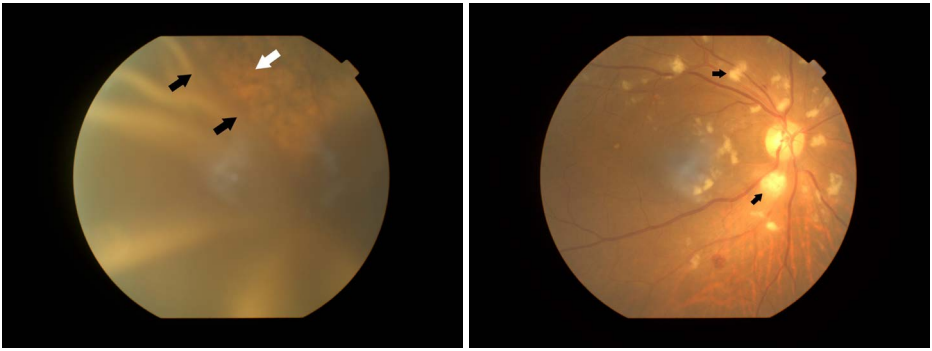

Fig. 1. (*Left*) Fundus photograph of the right eye shows scattered cotton wool spots (black arrows). (*Right*) Fundus photograph of the left eye shows near total retinal detachment (black arrows), with minimal flat retina associated with pigmentary changes superiorly (white arrow).

Case report

A 66-year-old man, former smoker with underlying type 2 diabetes mellitus, hypertension, and dyslipidaemia presented with sudden onset of painless decrease of vision associated with floaters in his left eye for 6 months. He had intermittent palpitation associated with dizziness. He had been unwell with constitutional symptoms such as loss of appetite and weight. Best-corrected visual acuity in the left eye was hand movement with presence of relative afferent pupillary defect; best-corrected visual acuity in the right eye was 6/12. Bilateral anterior segment examination and intraocular pressure were normal. Fundoscopy of the left eye (Fig. 1, left) revealed near total ERD with minimal flat retina superiorly. There was no retinal break at the peripheral retina on three-mirror examination and scleral indentation of the left eye. Shifting fluid sign was present in the left eye during the examination. Tobacco dust was not present in the affected eye. The patient also denied any history of high myopia, ocular trauma, previous ocular surgeries, or barricade laser done. Fundoscopy of the right eye (Fig. 1, right) showed multiple cotton wool spots at all four retinal quadrants. There was no associated intraocular inflammation such as anterior chamber cells or vitritis. Upon general examination, the patient was pale and showed sinus tachycardia. Multiple indurated skin lesions with central ulceration were seen on the scalp, neck, and chest (Fig. 2). There was reduced breath sound in the upper zone of the right lung.

Full blood count and peripheral blood film indicated severe normochromic normocytic anaemia with reticulocytosis. No blast cells were seen. Serum albumin level was low (30 g/L), indicating hypoalbuminemia of chronic illness,

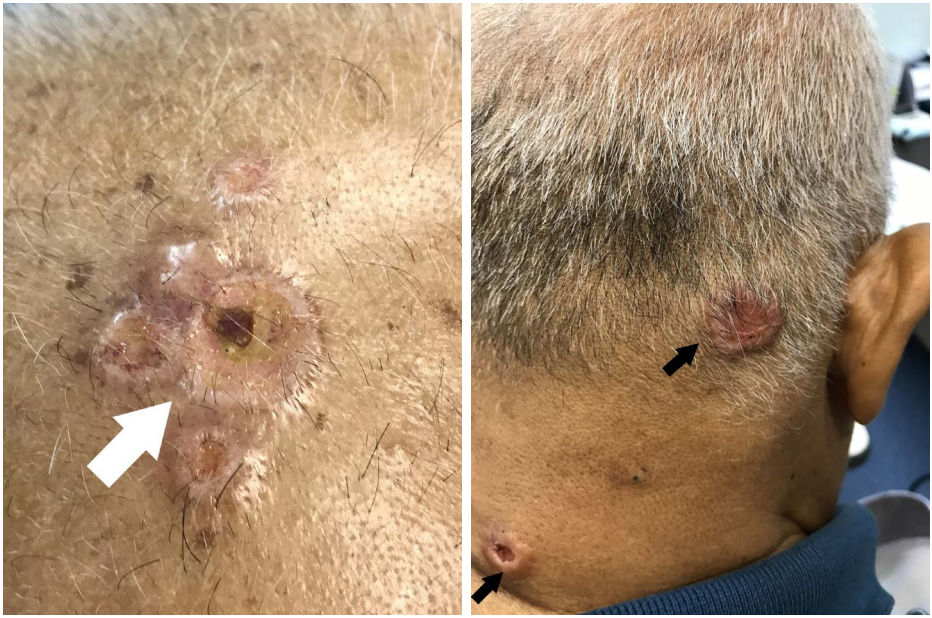

Fig. 2. Well-defined, indurated lesions (black arrow) with central ulceration (white arrow).

which may lead to ERD. Raised levels of C-reactive protein (58 mg/L) and lactate dehydrogenase (322 U/L) were found, which are associated with advanced lung carcinoma. Carcinoembryonic antigen (CEA), an important marker for malignant tumours, including non-small cell lung carcinoma, was 174 U/ml. High levels of urea (37.4 mmol/L) and creatinine (484 µmol/L) indicated acute or chronic renal failure in keeping with the advanced metastasis. There were no bacteria or fungi detected on blood and urine culture. Other tests including screening for tuberculosis, syphilis, hepatitis B and C, human immunodeficiency virus, toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus screening were negative.

Contrast-enhanced computed tomography of the thorax, abdomen and pelvis revealed right, upper lobe, contrast-enhancing mass measuring 7.5 x 7.0 x 5.5 cm with right pleural effusion (Fig. 3). Multiple mediastinal nodal, bone, peritoneal, and adrenal metastasis were present. There was no evidence of choroidal mass, orbital, or brain metastases.

Skin biopsy was reported to be most likely metastatic adenocarcinoma based on the immunohistochemistry profile of the tumour cells tested positive for EMA, Ber-EP4, CEA, cytokeratin 7 (CK7), and P63, with absence of transformation zone from the native adnexal structures. Infiltrative neoplastic epithelioid cells featured moderate to severe nuclear polymorphism.

Optical coherence tomography, ultrasound B-scan, and positron-emission

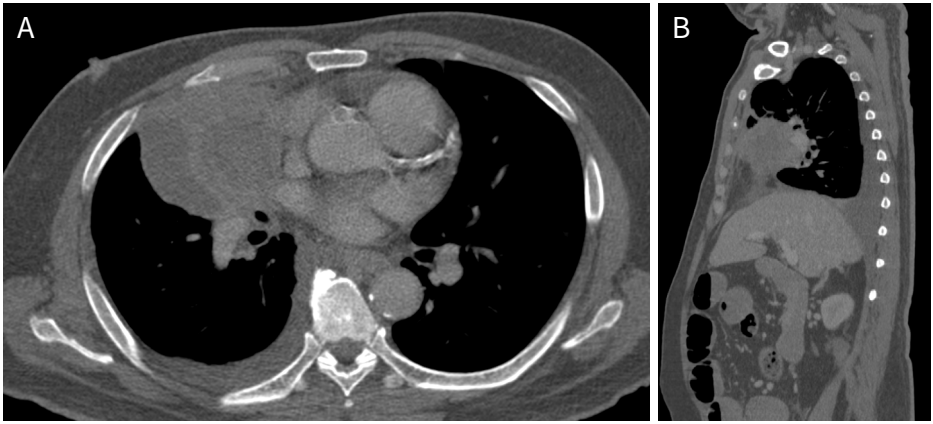

Fig. 3. (*A*) Axial section of contrast-enhanced computed tomography (CECT) of the thorax. (*B*) Sagittal section of CECT of the thorax shows enhancing mass (white arrow) with hyperdense centre arising from the anterior segment of right upper lobe.

tomography scan were not available at our health care centre, and the patient refused to be referred to tertiary centres for further workup. Thus, these investigations were not performed. He was diagnosed with ERD in the left eye secondary to metastatic lung adenocarcinoma. The patient died due to the illness 2 months later after refusing treatment and defaulting follow-up.

Discussion

Lung carcinoma is the second most frequently diagnosed cancer after breast cancer in women and prostate cancer in men.[2] It is common among men aged 55.1 ± 11.2 years and in former or active smokers. The most common histologic types are adenocarcinoma followed by squamous and small-cell carcinoma.[3]

Metastatic lung adenocarcinoma to the eye is very rare. The eye and orbit may be affected by cancer either directly, due to metastatic infiltration by neoplastic cells or compression, or indirectly from circulating antibodies associated with paraneoplastic retinal degeneration.

Our literature search showed that approximately 50 cases have been reported worldwide with ERD as the first symptom of lung carcinoma metastasis to the eyeball.[3] However, only three cases of ERD as the first symptom of lung carcinoma without concomitant ocular metastasis have been reported worldwide.[4-5] Thus, we report another case of ERD as the first manifestation of malignancy.

ERD develops when fluid collects in the subretinal space. There are numerous theories regarding the disruption of the integrity of blood-retinal barrier attributed by inflammatory, infectious, infiltrative, neoplastic, vascular, and degenerative

conditions and the sequential development of ERD.[6] Retinal vessel occlusion by tumour cells could lead to retinal ischemia, and increases the permeability of the vascular endothelium and subretinal fluid leakage. Other changes, such as hypercoagulability and hypoalbuminemia, may result in formation of thrombus within small retinal vessels.[7]

The detection of scattered cotton wool spots (CWS) in the right fundus indicates an ischemic retina.[8] It has been reported that CWS indicates blockage of a retinal arteriole caused by abnormalities in the vascular endothelium, abnormal erythrocytes, or emboli. The axoplasmic debris accumulates at the junction of healthy and anoxic retinas. In this case, the patient's blood pressure was within the normal range. There were no diabetic retinopathy changes noted in the right eye. Coagulation profile was within the normal range and there were no other retinal changes present to suggest hypercoagulable state. This should alert the ophthalmologist to arrange an extensive examination as it is usually a serious sign of vascular damage.

Cutaneous metastases from the lungs are rare but must be ruled out in patients with suspicious skin lesions, history of lung carcinoma, or tobacco exposure, as presented in our patient. The most common sites for cutaneous metastases are the scalp, head, neck, and chest, with the most common histological diagnosis being adenocarcinoma.[9] The percentage of patients with lung cancer that develop cutaneous metastases ranges from 1% to 12%, with an overall incidence of 5.3% for all cancers. Mean survival time from diagnosis of lung carcinoma is 10.3 months; for diagnosis of skin metastasis it is 4.9 months.[10] The prognosis for patients having lung cancer with skin metastasis is thus very poor.

The use of immunohistochemical markers is a useful method for ascertaining the site of origin in cases of adenocarcinoma. Cytokeratin 7 (CK-7) has a sensitivity and specificity of 93.8% and 50.0% in primary lung adenocarcinoma and 100% and 25.0% in metastatic lung adenocarcinoma.[11] In this case, the most useful immunohistochemical marker for diagnosis was CK-7, which is specific to primary lung adenocarcinoma. It has also been reported that, in cases of poorly differentiated adenocarcinoma, a decreased expression of Napsin A and TTF-1 was seen and a proportion of these tumours have been shown to be P63-positive as demonstrated in our case.

The choice of treatment varies depending on the underlying diseases, size, and location of lesion, number of satellite lesions, and the extent of the neoplasm. Treatment options include chemotherapy, immunotherapy, hormonal therapy, and radiotherapy. Gamma globulin, plasmapheresis, and interleukin-2 receptor blockade with a specific monoclonal antibody comprise the proposed first-line treatment in cases of ERD without ocular metastasis.

Conclusion

Our case report highlights a lung carcinoma that harbours behind an exudative retinal detachment. Malignancy should be suspected in atypical presentations of retinal detachment without obvious retinal tear. A thorough systemic evaluation, diagnostic imaging, and laboratory and immunohistochemistry tests are important to guide the ophthalmologist in identifying the primary site of neoplasia, as prompt intervention may be lifesaving.

Declarations

Consent for publication
Informed consent was obtained from the patient for the publication of the data and images contained in this case report.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare.

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Case report
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Cavernous sinus syndrome: a case report

Ong Jee Yan, Dennis **Ling** Chii Yih, **Tiong** Kiew Ing

Department of Ophthalmology, Sarawak General Hospital, Malaysia Ministry of Health, Kuching, Sarawak, Malaysia

Abstract

Background: Cavernous sinus syndrome (CSS) is a rare, but potentially life- and sight-threatening condition. We report a case of multiple cranial neuropathies with CSS.
Case presentation: A 70-year-old woman presented with unilateral complete ptosis, ophthalmoplegia, and diplopia. Examination showed left-sided multiple cranial nerve palsies, with the involvement of cranial nerve III (oculomotor nerve), IV (trochlear nerve), V1 and V2 (ophthalmic and maxillary branches of trigeminal nerve), and VI (abducens nerve). A clinical diagnosis of CSS was made. Neuroimaging revealed a left-sided cavernous sinus mass for further investigation.
Conclusion: In this case report, we highlight the clinical and radiological features of CSS to raise clinical suspicion for similar diagnosis in the future.

Keywords: cavernous sinus syndrome, cranial nerve palsies, ophthalmoplegia

Correspondence: Dr. Ong Jee Yan, MBChB, Department of Ophthalmology, Sarawak General Hospital, Jalan Tun Ahmad Zaidi Adruce, 93586 Kuching, Sarawak, Malaysia.
E-mail: jeeyan124@hotmail.com

Sindrom sinus cavernous: laporan kes

Abstrak

Latar belakang: Sindrom sinus cavernous (CSS) adalah jarang terjadi tetapi ianya berpotensi menyebabkan kehilangan nyawa dan penglihatan. Kami melaporkan kes (CSS) yang melibatkan neuropati kepada beberapa saraf kranial.
Laporan kes: Seorang wanita berusia 70 tahun mengalami ptosis yang teruk, oftalmoplegia dan diplopia. Hasil dari pemeriksaan klinikal terdapat penglibatan saraf kranial sebelah kiri di mana termasuk saraf kranial III (saraf okulomotor), IV (saraf troklear), V1 dan V2 (cabang oftalmik dan maxillari daripada saraf trigeminal) dan VI (saraf abdusen). Pengimejan neurologi telah dilakukan dan didapati terdapat ketumbuhan pada sinus cavernous sebelah kiri yang memerlukan siasatan lanjut.
Kesimpulan: Dari laporan kes ini, bagi meningkatkan pengesanan sindrom CSS, penekanan ke atas ciri-ciri klinikal dan radiologi adalah penting.

Keywords: sindrom sinus cavernous, palsi saraf kranial, oftalmoplegia

Introduction

Cavernous sinus syndrome (CSS) is a rare but potentially life and sight-threatening condition, by which the suspicion for diagnosis should be raised on clinical grounds. CSS presents as multiple cranial neuropathies with variable involvement of cranial nerves (CN) III, IV, V1, V2, and VI with or without additional signs and symptoms such as proptosis, conjunctival injection, retroorbital pain, and headache. Symptoms may be acute or progressive depending on the underlying aetiology. In some cases, clinical manifestation of CSS is non-specific with variable combinations of symptoms, further complicating the diagnostic process. A good understanding of the anatomical structures traversing the cavernous sinus, the pathophysiology of the disease process and the clinical manifestation of the disease can greatly assist in making a prompt diagnosis to improve prognosis.

Case presentation

A 70-year-old woman with underlying diabetes mellitus, hypertension, dyslipidaemia, and history of right occipital lobe infarction presented with left droopy eyelid and double vision for 2 weeks. She also complained of progressive blurring of vision in her left eye associated with intermittent headache. There were no symptoms of

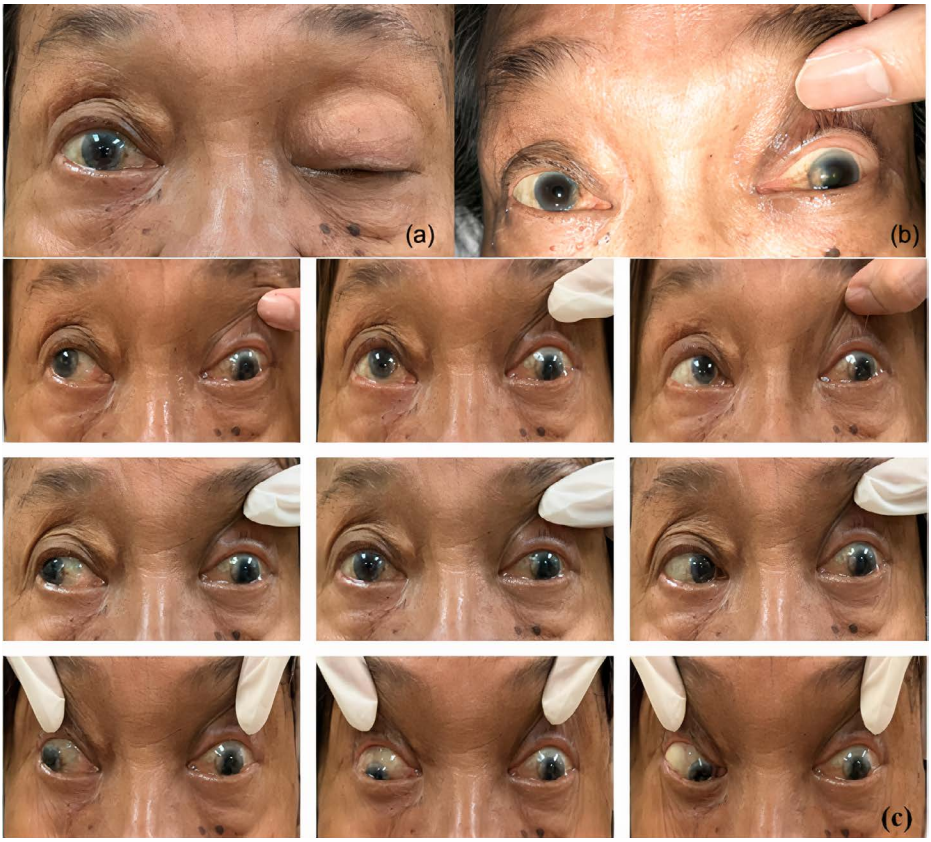

Fig. 1. Ocular manifestations of cavernous sinus syndrome in primary gaze. (*a*) Complete left eye ptosis. (*b*) Left eye exotropia and hypotropia. (*c*) Extraocular movement in nine cardinal positions of gaze. Presence of left eye ophthalmoplegia in all gaze directions.

increased intracranial pressure or other neurological symptoms. No prior history of trauma preceded the event.

On examination, her best-corrected visual acuity was 6/18 in the right eye and 6/120 in the left eye. The left eye showed complete ptosis and 15° exotropia on primary gaze with dilated pupil (Fig. 1 a, b). There was complete reduction of extraocular movement on all gaze directions with power of 1/5 remaining on left lateral gaze (Fig. 1c). There was no relative afferent pupillary defect. Conjunctiva was white with no dilated tortuous episcleral vessels. Corneal reflex was reduced in the left eye, with ipsilateral hypoesthesia over facial territories supplied by the ophthalmic and maxillary branches of the left trigeminal nerve. Otherwise, both the anterior and posterior segments of the left and right eyes were normal. The patient was clinically diagnosed with CSS.

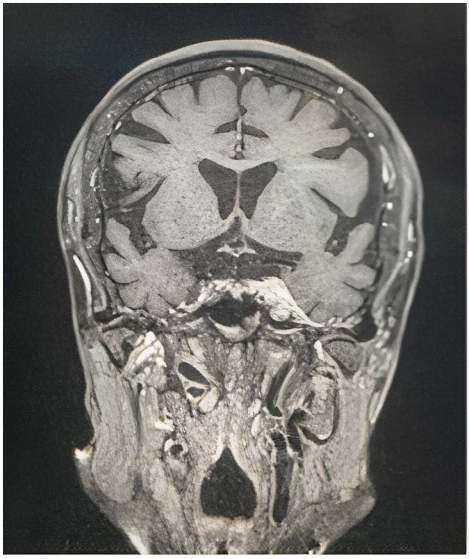

Fig. 2. Magnetic resonance imaging showed a heterogeneously enhancing lesion in the left cavernous sinus.

An urgent contrasted computerized tomography (CT) of the brain and orbit was performed. There was a heterogeneously enhancing lesion present in the left cavernous sinus with anterior extension to the orbital apex and left Meckel's cave. There were also radiological features of multifocal infarction, cerebral atrophy, and small vessel disease over the right occipital lobe, bilateral basal ganglia, right corona radiata, and centrum semiovale. Further magnetic resonance imaging (MRI) of the brain showed soft tissue thickening in the left cavernous sinus (Fig. 2). Differential diagnosis at this point included inflammatory changes, infectious causes, and tumour infiltration. Adjunctive tests performed included a complete blood count with differential counts, erythrocyte sedimentation rate, C-reactive protein, complete metabolic panel, tumour markers, intradermal tuberculin test, sputum for acid fast bacilli, syphilis, and chest X-ray. The tests were unremarkable. Our patient was co-managed with the neurosurgical and otorhinolaryngology teams following the imaging findings. A nasal endoscopy performed by the otorhinolaryngology team showed a right torus tuleres mass and a mildly bulging left fossa of Rosenmuller. Biopsy of the nasal mass showed enlarged lymphoid follicles with no trace of malignancy. Patient was counselled for further interventions, which included a lumbar puncture and a biopsy of the intracavernous lesion to guide further management. However, our patient refused further investigation in view of her old age and personal logistic issues. Follow-up to her condition was discontinued due to the patient's death to COVID 3 months following the diagnosis.

Discussion

The cavernous sinus is a small yet complex and important structure, which comprises the dural venous sinus located at the central base of skull on either side of the sella turcica containing the pituitary gland. It houses the CN III, IV, V1, V2, and VI, as well as the internal carotid artery and sympathetic fibres. CSS is defined as the involvement of at least two of the intracavernous CNs, or involvement of only

one CN in combination with radiologically confirmed cavernous sinus lesions.[1] It is caused by pathological lesions within the cavernous sinus leading to compression and compromise of the intracavernous neurovascular structures located within the small venous space. The true incidence of CSS is not well documented, with few studies conducted regarding its epidemiology. Approximately 5% of ophthalmoplegia in the United States were reported to be secondary to the CSS.[2] CSS affects both genders equally.

Diplopia and headache are the most common presenting symptoms reported among patients diagnosed with CSS, presenting in up to 90% of patients with CSS.[1,3] Other common presenting symptoms and signs reported include retro-orbital pain, facial paraesthesia, vision loss, hearing loss, proptosis, ptosis, painful or painless ophthalmoplegia, decreased corneal reflexes, and seizures.[3,4] Physical examination findings of CSS are dependent on CN involved, with the most common CN involved being CN III (85%), followed by CN VI (70%), V1, V2, and IV. The involvement of all CNs in CSS, as was evident in our case, is in fact uncommon. A study conducted by Fernández *et al.* in Spain showed that complete ophthalmoplegia was present in only 17% out of a series of 126 patients.[1] Painful ophthalmoplegia is less common and has been reported to be associated with inflammatory causes. The involvement of ophthalmic and maxillary branches of the trigeminal nerve embedded in the lateral walls of the cavernous sinus explains the ipsilateral upper facial hypoesthesia, sparing the lower facial dermatome, which is supplied by V3 branch. The involvement of pupil dilatation may or may not be present in CSS due to the concurrent presence of both sympathetic and parasympathetic innervations in the cavernous sinus.[5] In view of the direct venous drainage of the cavernous sinus from several facial structures including the eye, large cavernous sinus lesions may also exert mass effect leading to less commonly reported signs such as proptosis, conjunctival congestion, and ocular hypertension. These signs were not evident in our patient.

CSS can be caused by a broad category of diseases. Tumours account for the majority of CSS cases.[1,4,6,7] These neoplastic lesions can be primary or metastatic. Primary neoplastic lesions include meningioma, schwannoma of cranial nerves in the cavernous sinus, neurogenic tumour, and haemangioma. Metastatic lesions can arise from the breast, lung, and prostate, or via local spreading from facial structures, such as nasopharyngeal carcinoma with intracranial and cavernous sinus extension, which is highly prevalent in Southeast Asian countries and seemingly the culprit in our patient.[8] Other causes of CSS include trauma, vascular pathologies (*i.e.*, carotid-cavernous fistula, carotid-cavernous aneurysm, or cavernous sinus thrombosis), infections (*i.e.*, tuberculosis, mucormycosis, or Aspergillosis) and inflammation (*i.e.*, Tolosa-Hunt syndrome or Wegener granulomatosis). The wide variety of possible aetiologies contributes to the diagnostic challenge. Hence, the involvement of multidisciplinary teams in the diagnostic and management process is required to optimize the patient's outcome.

Neuroimaging plays a huge role in establishing a definitive diagnosis of CSS. Contrasted CT scan is useful in providing visualization of the cranial bones and the adjacent structures. MRI, on the contrary, is the most sensitive tool for visualizing soft tissues.[1] Both serve as valuable evaluation tools in the identification of causative lesion of CSS and its anatomical relations, as well as to identify the extent of local spread and source of metastasis in cases of tumours.[4] CT angiography and MR angiography can be acquired for further investigation of CSS of vascular aetiologies. Adjunctive investigation tools such as lumbar puncture and lesion biopsy are invasive and should be reserved for cases where diagnostic capability is limited based on clinical and imaging findings alone. In fact, some studies found lumbar puncture to be a poor diagnostic tool with low sensitivity in CSS cases.[1] Ancillary blood tests to rule out infectious and inflammatory causes are warranted in cases where common causes such as tumours and vascular aetiology have been excluded.

Conclusion

CSS presents as multiple CN III, IV, V1, V2, and VI palsies with variable combinations of symptoms. The diagnostic process can be challenging, yet crucial, given the life- and sight-threatening nature of the disease. Understanding the characteristic clinical features of CSS can assist in differential diagnosis. An early neuroimaging study is recommended in all patients with CSS. Prompt diagnosis of CSS and its underlying aetiology can improve prognosis.

Declarations

Consent for publication
The patient provided informed consent for the publication of this case report.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare.

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Eye-Quiz
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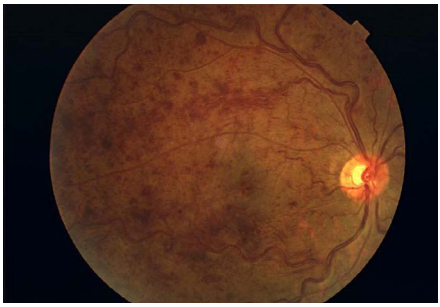
Intermittently blotchy

Mae-Lynn Catherine **Bastion**[1], **Lee** Mun Wai[2]

[1]Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre , Hospital Canselor Tuanku Muhriz, Kuala Lumpur, Malaysia; [2]LEC Eye Centre, Ipoh, Perak, Malaysia

Clinical context

A 40-year-old man with a history of fluctuating vision in his right eye for 1 year reported several blurring episodes lasting 1 hour, which resolved completely spontaneously between episodes. Visual acuity was 6/18, 6/12, N8 with no relative afferent pupillary defect. Intraocular pressure was normal.



Question 1
What are the signs shown in the photograph?

Question 2
What is your working diagnosis?

Question 3
Given that he has no other medical illness with normal systemic screen, and fundus fluorescein angiography (FFA) shows leakage of the peripheral veins and optic disc, what diagnosis would you most likely consider?

Correspondence: Dr. Mae-Lynn Catherine Bastion, Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Hosspital Canselor Tuanku Muhriz, Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur, Malaysia
Email: mae-lynn@ppukm.ukm.edu.my

Answer 1
Tortuous dilated superotemporal and inferotemporal vein, dot and blot, and flame-shaped haemorrhages in all four quadrants, hyperaemic optic disc, and dull macula.

Answer 2
Right central retinal vein occlusion (non-ischaemic) with macular oedema.

Answer 3
The feature of fluctuating vision, which returns to normal between episodes is the key history suggestive of papillophlebitis right (PP) in this patient. Another important observation is the lack of concordance between the good visual acuity and severity of retinal findings. Other features which point towards this diagnosis include the young age of the patient, unilateral presentation with disc hyperaemia and retinal venous engorgement, negative systemic screening, and FFA findings of optic disc and vein leakage.[1-3] PP is a rare form of partial central retinal vein occlusion (CRVO) affecting previously healthy women. It was first described by Lonn and Hoyt in 1966.[2] PP could be a form of inflammatory CRVO with more favourable outcomes. PP is postulated to be caused by inflammation of the optic disc, leading to central retinal vein compression and venous stasis. Although corticosteroids are the mainstay of treatment for PP, there is a lack of clear evidence to guide therapy. Some authors suggest combining it with anticoagulant therapy.[3,4] Treatment is needed to prevent progression to frank CRVO with its complications. In this patient, oral ciclosporin A 5 mg/kg/day or 300 mg per day was prescribed together with 40 mg oral prednisolone od for 1 week and then tailed at 5 mg/week. He gave a history of previous prednisolone therapy that required levels of 30 mg daily to prevent relapse. His visual acuity improved to 6/12, 6/9, N5 after 1 week of therapy.

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