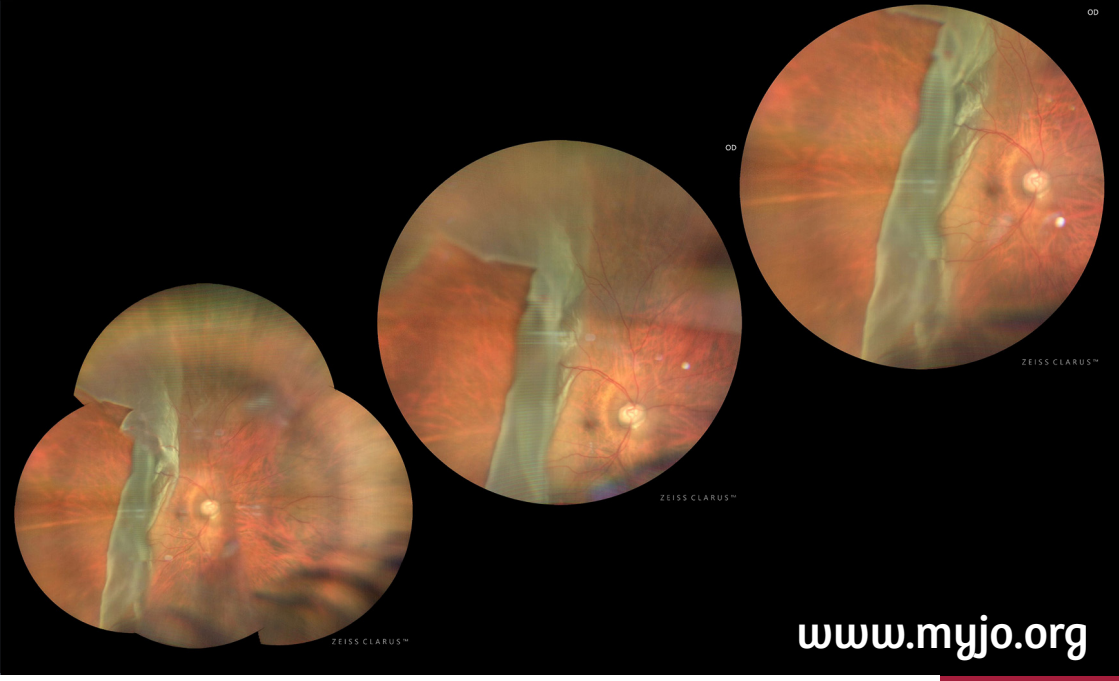

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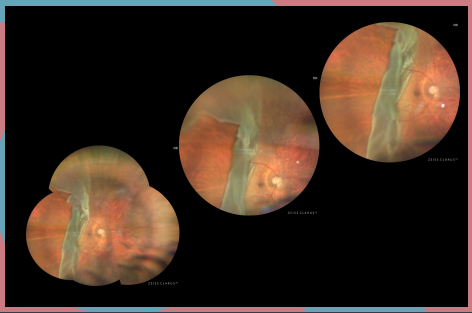

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Table of contents

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Editorial
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Phacoemulsification in acute angle closure glaucoma: when is the right time?

Norlina Ramli

Deputy Editor, Malaysian Journal of Ophthalmology

Abstract

Acute primary angle closure (APAC) remains one of the ophthalmological emergencies that is still very relevant currently. The numbers blinded globally by primary angle-closure glaucoma (PACG) exceed 5.3 million, with its destructive nature causing blindness disparity compared to primary open-angle glaucoma and disproportionately affecting Asian populations more severely. The clinical audit by Tan *et al.* from HTAR in this issue offers a timely and valuable contribution to our understanding of APAC management in real world Malaysian setting.[1]

The audit evaluated outcomes of 17 APAC patients who underwent phacoemulsification at Hospital Tengku Ampuan Rahimah (HTAR), Klang. Results were staggering; intraocular pressure (IOP) reduction from 50.44 mmHg at presentation to 18.24 mmHg after medical management and further reduction to a mean of 13.06 mmHg postoperatively. This confirms the efficacy of lens extraction as a powerful IOP-lowering intervention. Similarly, the improvement in mean logMAR visual acuity from 1.00 to 0.62 underscores the extra benefits that cataract surgery confers to APAC patients. These findings tally with the landmark EAGLE (Effectiveness in Angle Closure Glaucoma of Lens Extraction) trial, which demonstrated that clear lens extraction was superior to laser peripheral iridotomy in terms of IOP control, medication burden, health economics and quality of life.[2] Although the EAGLE cohort were patients with primary angle closure (PAC) or PACG, the findings could be applicable in patients with APAC too. This audit by Tan et al. add to the growing body of evidence that when phacoemulsification is performed in the quiescent phase following APAC, it is both safe and effective in addressing the angle crowding, and subsequently the intraocular pressure (IOP) component of the acute attack.

However, what is the optimal timing for cataract extraction in APAC? The Royal College of Ophthalmologists guidelines suggest approximately one to four weeks after presentation once the IOP is controlled and cornea clear.[3] In the HTAR cohort, 82.4% of patients underwent surgery within 6 weeks, reflecting a pragmatic approach that balances the need for timely intervention with the imperative to allow corneal clarity and inflammation to settle. This timing is also broadly consistent with Lam *et al.*, who suggested the ideal window is approximately one month post abortion of the acute attack.[4]

The ethnic distribution of the HTAR cohort—equal numbers of Malay and Chinese patients (41.2% each), with Indian patients comprising 17.6%—is noteworthy. Previous Malaysian studies have suggested that Malay patients may present with more advanced angle-closure glaucoma and progress faster than their Chinese counterparts.[5] Early lens extraction, especially following an APAC attack, may play a role in mitigating this ethnic specific risk profile.

One of the more interesting findings of this audit was the observation that up to 76.5% of the patients still required two or more topical IOP-lowering medications at final follow-up. This high rate of progression to chronic glaucoma despite phacoemulsification underscores an undeniable fact: while lens extraction is a powerful intervention, it is not curative in the majority. The underlying trabecular meshwork damage incurred during the acute attack—whether from prolonged IOP elevation, inflammation or the progressive formation of peripheral anterior synechiae—may leave a legacy of impaired aqueous outflow that persists even after the anatomical angle opens. It reinforces the findings that APAC is not an acute event to be aborted, but a harbinger of chronic disease that requires lifelong monitoring.

From a health systems perspective, the HTAR audit demonstrates that phacoemulsification can be delivered safely and effectively in a Malaysian public hospital setting. However, the authors acknowledge the limitation of the small number of cases reported may reflect under-reporting due to the manual system employed for card maintenance. A move towards integrated electronic health records would allow a better opportunity to understand the true burden of APAC outcomes to our health systems more accurately.

In conclusion, the HTAR audit adds to the growing consensus that phacoemulsification should play a central role in the management of APAC, offering significant benefits in terms of IOP control, visual rehabilitation, and reduction of systemic IOP-lowering medication. The high rate of persistent IOP elevation post phacoemulsification underscores the importance of continued monitoring of these patients in the long term. The question of optimal surgical timing remains open, but it is generally agreed that more importantly, the conditions such as adequate lowering of IOP, control of inflammation, and clear corneas should take precedence.

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Management and outcomes of acute primary angle closure with phacoemulsification: a clinical audit at hospital Tengku Ampuan Rahimah

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Abstract

Purpose: To evaluate the demographic characteristics, treatment effects, and timing of cataract extraction of patients with acute primary angle closure (APAC) in Hospital Tengku Ampuan Rahimah (HTAR), Klang, Malaysia.
Study design: Retrospective descriptive analysis.
Methods: This study included 17 patients with APAC in HTAR from 2021 to 2024. Data on demographics, visual acuity (VA), intraocular pressure (IOP), and antiglaucoma medications (including oral acetazolamide) were collected at presentation, preoperatively, and 3 months postoperatively following phacoemulsification with posterior chamber intraocular lens implantation (PCIOL).
Results: There were 10 females (58.8%) and 7 males (41.2%), with age ranging from 42 to 84 years. Seven patients (41.2%) were Malay, 7 (41.2%) were Chinese, and 3 patients (17.6%) were Indian. A total of 14 patients (82.4%) underwent phacoemulsification within 6 weeks of presentation. Mean IOP was 50.44 mmHg upon attack, 18.24 mmHg during abortion of attack, and 13.06 mmHg after surgery ($p < 0.001$). Mean logMAR VA improved from 1.00 to 0.62 ($p < 0.001$). Oral acetazolamide use declined significantly from 8 patients upon attack to 2 postoperatively ($p = 0.002$).

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However, 13 out of 17 patients (76.5%) of patients still required 2 or more topical IOP-lowering medications at final follow-up. No significant relationship was found between preoperative medication burden and early surgical timing.
Conclusion: Cataract surgery effectively improves VA and IOP and reduces dependency on systemic acetazolamide. Nevertheless, a high proportion of patients progress to require long-term topical therapy for chronic glaucoma, underscoring the need for ongoing monitoring. Further studies are required to determine the optimal timing for cataract surgery in APAC.

Keywords: acute primary angle closure, clinical audit, intraocular pressure, phacoemulsification

Pengurusan dan hasil rawatan penutupan sudut primer akut menggunakan fakoemulsifikasi: Audit Klinikal di Hospital Tengku Ampuan Rahimah

Abstrak

Tujuan: Untuk menilai ciri-ciri demografi, kesan rawatan, dan masa pembedahan ekstraksi katarak terhadap tekanan intraokular (IOP) pesakit dengan glaukoma sudut tertutup akut (APAC) di Hospital Tengku Ampuan Rahimah, Klang, Malaysia. Reka bentuk kajian: Analisis deskriptif retrospektif.
Kaedah: Kajian ini melibatkan 17 pesakit APAC yang menerima rawatan di HTAR dari tahun 2021 hingga 2024. Data demografi, akuiti penglihatan (VA), IOP dan penggunaan ubat antiglaukoma (termasuk acetazolamide oral) dikumpulkan semasa pesakit mula hadir ke hospital, sebelum pembedahan dan tiga bulan selepas pembedahan fakoemulsifikasi dengan implantasi kanta intraokular (PCIOL).
Keputusan: Terdapat 10 pesakit wanita (58.8%) dan 7 pesakit lelaki (41.2%), dengan umur antara 42 hingga 84 tahun. Pesakit Melayu 7 (41.2%), pesakit Cina 7 (41.2%) dan pesakit India 3 (17.64%). Seramai 14 (82.4%) pesakit menjalani pembedahan fakoemulsifikasi dalam tempoh enam minggu dari masa mula hadir ke hospital. Purata IOP adalah 50.44 mmHg semasa serangan akut, 18.24 mmHg selepas rawatan dan 13.06 mmHg selepas pembedahan ($p < 0.001$). Purata akuiti penglihatan logMAR bertambah baik daripada 1.00 kepada 0.62 ($p < 0.001$). Penggunaan ubat asetazolamide oral menurun secara signifikan dari lapan pesakit kepada dua selepas pembedahan ($p = 0.002$). Walaubagaimanapun, 13 daripada 17 pesakit (76.5%) masih memerlukan dua atau lebih ubat titis untuk menurunkan IOP pada rawatan

susulan terakhir di klinik. Tiada hubungan yang ketara ditemui antara penggunaan ubat anti-glaukoma sebelum pembedahan dan jangkamasa pembedahan awal.
Kesimpulan: Pembedahan katarak berkesan meningkatkan VA dan mengurangkan IOP serta kebergantungan pada asetazolamide oral. Walaubagaimanapun, sebahagian besar pesakit masih memerlukan ubat titis glaukoma pada jangka panjang untuk glaukoma kronik, sekaligus menekankan keperluan untuk pemantauan berterusan. Kajian lanjut diperlukan untuk menentukan pengaturan masa yang paling optimum untuk pembedahan katarak dalam situasi APAC.

Kata kunci: audit klinikal, fakoemulsifikasi, glaukoma sudut tertutup akut, tekanan intraokular

Introduction

Primary angle closure glaucoma (PACG) contributes 50% of the cases of blindness due to glaucoma even though it only accounts for 26% of all glaucoma cases.[1] Laser peripheral iridotomy (LPI) is the recommended initial therapy of PACG with the aim of eliminating pupillary block and prevent progression to acute primary angle closure (APAC).[2] However, Asian individuals with PACG after LPI alone have a 58.2% risk of developing APAC in the first 6 months despite LPI.[3]

APAC is within the spectrum of PACG and is an ophthalmic emergency in which intraocular pressure (IOP) increases due to aqueous humour outflow obstruction. It usually presents as a sudden onset of unilateral severe eye pain or headache, associated with blurred vision, rainbow-colored halos around bright lights, nausea, and vomiting. This medical condition requires immediate IOP lowering and LPI is usually performed to relieve pupillary blockage.

Lens extraction is the recommended management for primary angle-closure disease (PACD) based on the Effectiveness in Angle-closure Glaucoma of Lens Extraction (EAGLE) study, a randomized control trial published in 2016. The study concluded that clear lens extraction was superior to LPI in terms of IOP control, medication burden, health economic benefits, and quality of life.[4] Although the ideal timing of phacoemulsification for patients with APAC in Asia still remains undefined, the Royal College of Ophthalmologist guidelines suggest that early phacoemulsification should be offered once IOP is controlled and the cornea is clear, approximately 1 to 4 weeks after presentation.[2] This audit aimed to evaluate the outcomes of phacoemulsification in patients with APAC in Hospital Tengku Ampuan Rahimah, Klang, Malaysia.

Methods

The retrospective data of 17 eyes of 17 patients with APAC collected in Hospital Tengku Ampuan Rahimah from 2021 to 2024 were included in this audit. The inclusion criterion was APAC, diagnosed at IOP > 21 mmHg with occludable angle based on anterior chamber angle in the presence of any 2 of these 3 symptoms: history of blurring of vision and halos, ocular and periocular pain, nausea and/or vomiting, and any 3 of these 4 signs: conjunctival injection, corneal epithelial oedema, mid-dilated unreactive pupil, or shallow anterior chamber. Secondary lens-induced glaucoma, such as phacomorphic glaucoma, phacolytic glaucoma and phacoanaphylactic glaucoma, were excluded from this audit.

All eyes had cataract and underwent phacoemulsification with implantation of a single-piece posterior chamber intraocular lens (IOL) in the bag. All patients were followed up for 3 months. Visual acuity based on Snellen chart, IOP, and number of antiglaucoma medications with or without the usage of acetazolamide were recorded upon presentation, preoperatively, and 3 months postoperatively.

Statistical analysis

Chi-square goodness-of-fit test was used to compare visual acuity and usage of oral acetazolamide pre- and postoperatively. ANOVA was used to assess the mean difference of IOP across 3 groups of upon attack, upon abortion of APAC, and post-operative. *P*-value < 0.05 was considered significant.

Results

There were 10 females (58.8%) and 7 males (41.2%), with age ranging from 42 to 84 years old. Ethnic distribution was equal between Malay and Chinese 7 (41.18%) for both races, while 3 (17.64%) were Indian (Table 1). Follow-up period was 3 months. All surgeries were completed with no major complications. A total of 4 (23.53%) patients had no known medical illness. The most prevalent comorbidity identified in this audit was hypertension, found in 13 out of 17 patients (76.46%). Within the hypertension group, 7 patients (41.18%) also had diabetes mellitus. The audit shows a statistically significant ($p < 0.002$) treatment distribution among the 17 patients, with LPI being the standard intervention for 13 patients (76.47%), whereas 2 (11.77%) had argon laser peripheral iridoplasty (ALPI) as primary procedure and 2 (11.77%) had no procedure done prior to cataract extraction. The patients who did not have LPI or ALPI were planned for early cataract surgery by 17 days.

Table 1. Demographic data, comorbidities, duration of APAC upon presentation, and timing of phacoemulsification of patients with APAC

Variable	***n* (%)** **Total *N* = 17**	***p*-value**
Gender		
Male	10 (58.8%)	0.467
Race		
Malay	7 (41.18%)	0.390
Chinese	7 (41.18%)	
Indian	3 (17.64%)	
Laterality		
Left eye	9 (52.94%)	0.808
Comorbidities		
No known medical illness	4 (23.53%)	0.662
Hypertension	6 (35.29%)	
Diabetes mellitus & hypertension	7 (41.18%)	
Procedure		
Laser peripheral iridotomy	13 (76.47%)	0.002*
Argon laser peripheral iridoplasty	2 (11.77%)	
No procedure	2 (11.77%)	
Duration of APAC at presentation		
Less than 1 week	9 (52.94%)	0.567
2 to 4 weeks	3 (17.65%)	
4 weeks to 3 months	3 (17.65%)	
Longer than 3 months	2 (11.76%)	
Timing of phacoemulsification from APAC		
Less than 2 weeks	2 (11.8%)	0.057
2 to 4 weeks	4 (23.5%)	
4 to 6 weeks	8 (47.1%)	
6 weeks to 3 months	2 (11.8%)	
Longer than 3 months	1 (5.9%)	

* Statistically significant

Table 2. Mean difference in IOP upon attack, preoperative, and postoperative

IOP (mmHg)	Upon attack	Preoperative	Postoperative	*P*-value
	50.44	18.24	13.06	< 0.001

Table 3. Comparison of visual acuity improvement in mean logMAR upon attack and postoperativel

Category	Level of impairment	Visual acuity (mean logMAR)	Upon attack, *n* (%) Total *N* = 17	*p*-value	Postoperative, *n* (%) Total *N* = 17	*p*-value
0	None to mild	< 6/18	7 (41.2%)	0.221	14 (82.5%)	< 0.001
1	Moderate	6/24–6/60	4 (29.4%)		1 (5.9%)	
2	Severe	5/60–3/60	1 (5.9%)		0	
3	Blindness	2/60–1/60	0		0	
4	Blindness	>1/60	3 (17.65%)		1 (5.9%)	
5	Blindness	No light perception	1 (5.9%)		1 (5.9%)	

Table 4. Mean number of topical medications and oral acetazolamide upon attack, preoperative, and postoperative

Mean numbers of medications	Upon attack	*P*-value	Preoperative	*P*-value	Postoperative	*P*-value
1 antiglaucoma	2	0.346	2	0.475	4	0.392
2 antiglaucoma	2		3		4	
3 antiglaucoma	6		6		2	
4 antiglaucoma	5		5		7	
4 antiglaucoma + pilocarpine	2		0		0	
Oral acetazolamide	8	0.808	5	0.134	2	0.002*

* Statistically significant

Table 2 presents the mean IOP upon attack, 50.44 mmHg; during abortion of attack, 18.24 mmHg; and at 3 months postoperative, 13.06 mmHg ($p < 0.001$). There was 1 patient whose IOP remained 30 mmHg at 5 weeks postoperative with antiglaucoma eye drops, oral acetazolamide, and glycerol with logMAR of 0.54. Trabeculectomy with subconjunctival mitomycin C was then performed, and IOP subsequently was reduced to 12 mmHg.

Mean logMAR visual acuity was 1.00 during APAC attack and 0.62 at final follow-up ($p < 0.001$) (Table 3). The audit revealed a high pharmacological burden upon attack and in the preoperative phase, with all APAC patients in HTAR requiring multiple IOP-lowering medications. Phacoemulsification was highly effective in eliminating the need for systemic acetazolamide, from 8 patients upon attack to only 2 postoperatively ($p = 0.002$). The audit showed 13 patients still needing 2 or more topical IOP-lowering medications, indicating progression to chronic glaucoma (Table 4). Of the 17 patients with APAC managed in HTAR, 14 patients (82.4%) underwent phacoemulsification surgery by 6 weeks. However, three patients (17.6%) proceeded later than 6 weeks as 1 required 5 months to stabilize glucose control preoperatively, another refused early surgery after regaining good visual acuity following an attack, and 1 had a planned operation scheduled 8 weeks later.

Discussion

The mainstay treatment of APAC is LPI, as it relieves the pupillary block. However, LPI alone might not be sufficient, especially for Asian eyes, as shown by multiple studies in Asia— particularly Hong Kong, Singapore, Iran, and China—where higher percentages have persistently high IOP, suggesting that anatomical differences of eyes might play a role in this.[3] Asian eyes have heavily pigmented irises, which means that the laser needs more power to be able to penetrate effectively. This can cause more inflammation and pigment release, which could damage the trabecular meshwork and make it harder to control IOP.[5]

Phacoemulsification has been shown to be superior than LPI alone and can be a definitive treatment in APAC patients.[6] It significantly reduces peripheral anterior synechiae (PAS), effectively opens the drainage angle, deepens the anterior chamber, lowers IOP postoperatively, and requires fewer medications at the final visit.[3,5,6,7] All APAC patients in HTAR underwent uncomplicated phacoemulsification with IOL implantation. Topical dexamethasone 0.1% and a topical broad-spectrum antibiotic of the fluoroquinolone group (ciprofloxacine) were administered to all patients to reduce the intraocular inflammation, which prevents further formation of PAS that could lead to suboptimal IOP control. The visual acuity of the 2 patients who had neither LPI nor ALPI prior to phacoemulsification improved and the number of antiglaucoma medications decreased to a maximum of 2.

The optimal time frame of phacoemulsification for APAC remains uncertain. Lam *et al.* suggested the ideal timing for phacoemulsification is 1 month post-abortion of APAC, when the eye is quiescent, or before the formation of significant PAS.[6] On the contrary, some studies found no significant difference in outcomes for patients who underwent phacoemulsification a few weeks compared to a few days after an acute angle closure crisis.[7,8] HTAR implemented a mean time for phacoemulsification within 4 to 6 weeks, allowing more time for better corneal clarity and better control of inflammation, thereby reducing the formation of PAS. A well-planned cataract surgery anticipates zonulolysis with retropupillary IOL standby to overcome the risk of secondary angle closure. Biometry readings also achieve greater accuracy to prevent postoperative refractive surprises.

In this audit, there were no intraoperative complications, such as posterior capsule rupture or suprachoroidal haemorrhage, nor postoperative complications, the most common of which is pseudophakic cystoid macular oedema. Furthermore, patients have a risk of defaulting on appointments; arranging an early surgery is a way to curb further glaucomatous damage that could develop over time by 50%.[3] However more studies are required to establish the optimal timing for phacoemulsification in APAC patients. In our study, phacoemulsification showed significant reduction of IOP, improvement of visual acuity postoperatively, and reduced dependency on oral acetazolamide to control IOP ($p < 0.002$). This audit revealed only a small number of APAC patients treated in HTAR, which may be attributed to the manual system employed for card maintenance; this may have led to underreporting of cases.

Conclusion

Patients in HTAR underwent phacoemulsification when the eye was in the quiescent phase within 6 weeks of APAC. Cataract surgery can significantly improve VA, lower IOP, and reduce dependency on oral acetazolamide usage postoperatively in patients with APAC. However, further study is necessary to establish the optimal timing for cataract surgery in patients with APAC. A sustained commitment to professionalism and diligence is advocated in order to mitigate the prevalence of blindness among patients in Klang, Malaysia.

Declarations

Ethics approval and consent to participate

None to declare, as this was a retrospective descriptive analysis.

Competing interests
None to declare.

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Vision-related quality of life in patients suffering from coexisting glaucoma and cataract

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Abstract

Purpose: To evaluate the quality of life (QoL) and vision-related QoL in patients suffering from coexisting glaucoma and cataract.
Study design: Cross-sectional analytical study.
Methods: This study included a total of 222 cases: 163 patients suffering from coexisting glaucoma and cataract as the patient group and 59 healthy individuals as the control group. Data were gathered via EuroQol five-dimensional (EQ-5D) and National Eye Institute-Visual Functioning Questionnaire 39 (NEI-VFQ 39). The results were then compared before and one month after cataract surgery in the patient and control groups.
Results: The mean and 95% confidence interval of overall vision-related QoL scores in healthy individuals and patients in the pre- and postoperative phases were 86.65 (69.3–104.0), 48.7 (9.4–88.1), and 56.1 (12.2–100.0), respectively. There were significant differences among the 3 groups regarding all NEI-VFQ 39 items ($P < 0.05$). The mean and confidence interval of EQ-5D scores in the pre- and postoperative phases were 0.42 (0.21–0.64) and 0.58 (0.39–0.78), respectively ($P = 0.017$); for healthy individuals it was 0.70 (0.59–0.80). After surgery, all QoL items significantly increased among patients ($P < 0.05$). There were also significant differences in the scores compared to healthy individuals ($P < 0.05$). One month after surgery, all vision-related QoL item scores obtained by NEI-VFQ 39 and all QoL items scores

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obtained by EQ-5D were significantly lower in the treated patients than in healthy individuals ($P < 0.05$).
Conclusions: In patients suffering from coexisting glaucoma and cataract, The overall QoL and vision-related QoL scores improved after cataract surgery. However, there was a significant difference between patients and healthy individuals, with the healthy group having a superior score than the patients, both pre and postoperatively.

Keywords: cataract, glaucoma, quality of life, visual function

Kualiti hidup berkaitan penglihatan dalam kalangan pesakit yang menderita glaukoma dan katarak serentak

Abstrak

Tujuan: Untuk menilai kualiti hidup (QoL) dan QoL berkaitan penglihatan dalam kalangan pesakit yang mengalami glaukoma dan katarak secara serentak.
Reka bentuk kajian: Kajian analisis keratan rentas
Kaedah: Kajian ini merangkumi sejumlah 222 kes: 163 pesakit yang menghidap glaukoma dan katarak yang wujud bersama sebagai kumpulan pesakit dan 59 individu yang sihat sebagai kumpulan kawalan. Data dikumpul menggunakan EuroQol lima dimensi (EQ-5D) dan National Eye Institute-Visual Functioning Questionnaire 39 (NEI-VFQ 39). Keputusan kemudiannya dibandingkan sebelum dan sebulan selepas pembedahan katarak dalam kumpulan pesakit dan kawalan.
Keputusan: Purata dan 95% selang keyakinan keseluruhan skor QoL berkaitan penglihatan dalam individu yang sihat dan pesakit dalam fasa pra dan pasca operasi ialah 86.65 (69.3–104.0), 48.7 (9.4–88.1), dan 56.1 (12.2–100.0), masing-masing. Terdapat perbezaan yang ketara di antara 3 kumpulan berkenaan semua item NEI-VFQ 39 ($P < 0.05$). Min dan selang keyakinan skor EQ-5D dalam fasa pra dan pasca operasi ialah 0.42 (0.21–0.64) dan 0.58 (0.39–0.78), masing-masing ($P = 0.017$); untuk individu yang sihat adalah 0.70 (0.59–0.80). Selepas pembedahan, semua item QoL meningkat dengan ketara di kalangan pesakit ($P < 0.05$). Terdapat juga perbezaan yang ketara dalam skor berbanding individu yang sihat ($P < 0.05$). Sebulan selepas pembedahan, semua skor item QoL berkaitan penglihatan yang diperolehi oleh NEI-VFQ 39 dan semua skor item QoL yang diperoleh oleh EQ-5D adalah jauh lebih rendah bagi pesakit yang dirawat berbanding individu yang sihat ($P < 0.05$).
Kesimpulan: Bagi pesakit yang menghidap glaukoma dan katarak yang wujud

bersama, QoL keseluruhan dan skor QoL berkaitan penglihatan bertambah baik selepas pembedahan katarak. Walau bagaimanapun, terdapat perbezaan yang ketara antara pesakit dan individu yang sihat, dengan kumpulan individu yang sihat mempunyai skor yang lebih tinggi daripada kumpulan pesakit, sebelum dan selepas pembedahan.

Kata kunci: katarak, glaukoma, kualiti hidup, fungsi penglihatan

Introduction

According to the World Health Organisation (WHO), health is the absence of infirmity or disease and complete mental, physical, and social well-being.[1] Visual impairment, which is further categorised into low vision (best-corrected vision < 20/60) or blindness (best-corrected vision < 20/400), is one of the most common causes of disabilities.[2] Multidisciplinary management and early detection can minimise the effect of visual impairment on these patients' quality of life (QOL).

Eye practitioners mainly focus on clinical indicators, such as visual acuity impairment and visual field defects, to describe visual disabilities. However, the most important thing for patients is the treatment outcomes on functional status, which can affect emotional wellbeing and ultimately the vision-related quality of life (VRQoL).[3-7] VRQoL is defined as a person's satisfaction with their visual ability in their daily life. It reflects the social, emotional, and physical impact of visual impairment and economic wellbeing.[8,9]

The National Eye Institute Visual Function Questionnaire (NEI-VFQ) is one of the most commonly used patient-reported outcome measures to assess VRQoL. NEI VFQ is a reliable questionnaire used to determine the influence of vision on VRQoL. It is used in many countries worldwide to evaluate individuals' QoL.[7,10-13] This questionnaire can be used in both interview and self-reported formats. The validity and reliability of this questionnaire have been examined and approved by a research team in our country.[14]

Visual impairments increase the disease burden in countries and reduce the quality of life in individuals.[15-17] Previous studies have shown that many ocular diseases can affect QoL.[18-22] Cataract and glaucoma are two of the leading causes of visual impairment, which remain a major public health problem worldwide and have a significant impact on the QoL of patients, mainly due to reduced visual function and corresponding physical activity restriction.[21,23-26]

Although some studies have shown the effect of cataract surgery on visual function and QoL, these studies have been performed in different communities with different backgrounds.[13,27] Despite that, QoL is defined as an individual's perception of their position in the context of the culture and value systems in which they live, in relation to their goals, expectations, standards, and

concerns.[28] On the other hand, the coexistence of glaucoma and cataract in patients can signify the effect of disease on QoL, and the literature provides limited information about VRQoL in patients suffering from coexisting glaucoma and cataract.[29-32] In addition, most previously published papers on patients with coexisting glaucoma and cataract had a small sample size[30] did not involve original research.[29] Also, most studies were performed only on patients with cataracts or glaucoma.[11,13,19-21,25,26,30,33,34] Therefore, due to the lack of research results in the field of QoL and visual function in a group of patients suffering from coexisting glaucoma and cataracts compared to healthy individuals, we conducted a study to examine the QoL of these patients.

Methods

Study design

This cross-sectional-analytical study was performed in Khatam Al-Anbia Hospital in Mashhad, Iran, from 2017 to 2018. After explaining the study's objectives to the patients, consent forms were obtained, and the patients were asked to complete the questionnaire. The study was performed using the tenets of the Declaration of Helsinki and approved by the ethics committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1397.240).

Inclusion and exclusion criteria

All patients underwent a comprehensive ophthalmic examination, including best-corrected visual acuity (BCVA) assessment, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy using a Volk G-6 lens, and dilated fundus examination with a 78 D lens. Visual field testing was performed using 24-2 SITA Standard on the Humphrey Field Analyser (Carl Zeiss Meditec, Jena, Germany), and intraocular pressure (IOP) was recorded.

Patients were eligible for inclusion if they were 40 years of age or older, had a confirmed diagnosis of primary angle-closure glaucoma (PACG) based on gonioscopic evidence of at least 180° of angle closure (either appositional or synechial), elevated IOP (> 21 mmHg or controlled with medication), and characteristic glaucomatous optic neuropathy as evidenced by visual field defects or optic disc changes. In addition, participants were required to have a visually significant cataract, defined either by a BCVA of 20/30 or worse, or by subjective visual complaints interfering with daily activities, as judged by the examining physician. Cataract severity was graded using the Lens Opacities Classification System III (LOCS III), and only patients with nuclear or cortical cataracts of grade 2 or higher were included. In cases where both eyes met the inclusion criteria, the eye with more advanced disease or greater visual impairment was selected for analysis.

Exclusion criteria included a history of intraocular surgery, ocular trauma, secondary glaucoma (*e.g.*, neovascular, uveitic, pseudoexfoliative), corneal or iris abnormalities, angle neovascularisation, or any systemic or neurological condition that could affect visual function or QoL. Patients with acute angle-closure attacks, those on chronic miotic therapy, and monocular individuals were also excluded. To minimise confounding, individuals with significant systemic comorbidities such as uncontrolled diabetes or neurological disorders were not enrolled.

For the control group, visually healthy individuals were selected from companions of patients attending routine ophthalmic examinations. These individuals had no history of ocular disease, systemic illness affecting vision, or refractive error.[35]

Participants and group characteristics

Based on the data represented in Hatt's article[36] with a confidence interval of 95% and a test power of 80%, 163 adult patients participated in this study as a sample group. The first group included 163 patients who were diagnosed with glaucoma and cataracts. An expert glaucoma surgeon made the diagnosis. The second group included visually healthy individuals with no ocular, mental or musculoskeletal diseases, nor refractive error. This group was selected from the companions of patients recently undergoing ophthalmological examinations. The sampling was done randomly.

Questionnaires and data collection

These questionnaires have been translated into Persian, and their validity and reliability have been confirmed.[14,36] However, the reliability of the questionnaires (EQ-5D and NEI-VFQ 39) was evaluated using Cronbach's alpha test at a confidence level of 0.95 in SPSS software.

The questionnaire was the Persian version of NEI-VFQ (EuroQoL five-dimensional [EQ-5D] and 39-item Visual Functioning Questionnaire structure [NEI-VFQ 39]). The EQ-5D questionnaire measures the ability of individuals to perform tasks in five dimensions of mobility, personal care, normal activities (such as working, studying, doing household chores, having family or leisure activities), pain (discomfort), and anxiety (depression). This concise but comprehensive questionnaire takes one to five minutes to answer, depending on the situation. Then, each health condition is evaluated on a scale of 0 to 1. The NEI-VFQ 39 QoL is one of the most common questionnaires to measure the QoL and measures performance of various aspects of life, including general health, visual health, mental health, eye pain, distance and near vision activities, social performance, peripheral vision, color vision limitation of doing an activity, driving, and dependency. According to the questionnaire instructions, each question's answer is converted into a score between 0 and 100, in which 0 indicates the worst and 100 the best score.[37]

The interview format of the questionnaire was used to determine the QoL score. In addition to completing the questionnaire, demographic information affecting the QoL of patients (including age, sex, and education) was also obtained. Finally, compared to healthy individuals, the QoL score of patients suffering from glaucoma with cataract during the pre- and postoperative phases was evaluated.

Statistical analysis

The statistical package SPSS-24 (IBM Corp, Armonk, New York, USA) software was used for data analysis. The Kolmogorov-Smirnov test was used to evaluate the normality of the data, which is a prerequisite for the analysis of variance. For showing the QoL data, the mean with confidence interval, and for investigating and evaluating the difference in the QoL during pre- and postoperative phases, one-way analysis of variance was used at a confidence level of 0.95. A p-value less than 0.05 was considered a significant level. Cronbach's alpha test was used to examine the validity of the questionnaire used according to its main variables.

In addition to descriptive analyses and one-way ANOVA to compare mean QoL scores across the study groups, a multiple linear regression analysis was conducted to evaluate the independent impact of surgery after adjusting for demographic covariates. In this model, the composite score from the NEI-VFQ-39 and the overall score from the EQ-5D served as dependent variables. The independent variables included study group (preoperative, postoperative, and healthy controls), age, education level (categorised into five levels: illiterate, primary, secondary, diploma, and university), and occupation (categorised as employed, self-employed, and other). This analytical approach allowed simultaneous assessment of the surgical effect and the influence of demographic modifiers, enhancing the robustness and interpretability of the findings.

Results

Table 1 shows the difference in demographic characteristics between the two study groups. Table 2 presents the characteristics of descriptive statistics related to QoL items of 163 patients during the pre- and postoperative phases compared to 59 healthy individuals. The mean and confidence interval of overall NEI-VFQ 39 scores in the pre- and postoperative phases in patients and healthy individuals were 48.7 (9.4–88.1), 56.1 (12.2–100.0), and 86.65 (69.3–104.0), respectively ($P < 0.05$). The mean and confidence interval of EQ-5D score for patients during the pre- and postoperative phase were 0.42 (0.21-0.64) and 0.58 (0.39–0.78), respectively ($P = 0.017$), while for healthy individuals it was 0.70 (0.59–0.80). Table 2 shows the overall QoL score, vision-related QoL, and its components of patients during the preoperative and postoperative phases and healthy individuals. In pre- and postoperative, the lowest scores among patients were observed in general vision

Table 1. Demographic characteristics in patients and control groups.

Demographic variables		Control group number (%)	Patient group number (%)	*P*-value
Gender	Male	37 (63%)	99 (61%)	0.002
	Female	22 (37%)	64 (39%)	
Education	Illiterate	4 (7%)	15 (9%)	0.3
	Primary school	6 (10%)	21 (13%)	
	Secondary school	10 (17%)	23 (14%)	
	Diploma	24 (41%)	65 (40%)	
	University graduated	15 (25%)	39 (24%)	
Occupation	Employee	20 (34%)	62 (38%)	0.02
	Self employed	22 (37%)	48 (29%)	
	Others	17 (29%)	53 (33%)	
Visual outcomes	CDVA	0.05 ± 0.05	0.23 ± 0.14	0.04
	UDVA	0.05 ± 0.1	0.25 ± 1.5	0.03
	Spherical equivalent	-0.25 ± 0.75	-2.02 ± 0.5	0.001

CDVA: Corrected distance visual acuity; UDVA: Uncorrected distance visual acuity

(43.9 and 55.4, respectively), and the highest scores were found in color vision items (83.19 and 88.21, respectively). Cronbach's alpha test results for EQ-5D and NEI-VFQ were 0.79 and 0.77, respectively. These results indicate that Cronbach's alpha is higher than 0.7 in both questionnaires, indicating reliability (Fig. 1).

Based on the Scheffe post hoc test results, which are presented in Table 3, three comparisons have been made. The first comparison examined the QoL items among patients suffering from glaucoma with cataracts (during the preoperative phase) and healthy individuals. The second comparison examined the vision-related QoL items during the pre- and postoperative phases of patients with glaucoma with cataracts. Finally, in the third comparison, vision-related QoL items among patients suffering from glaucoma with cataracts during the postoperative phase compared to healthy individuals were examined. As can be noticed, the results of the variance analysis showed that the difference between the QoL items of these three groups was significant. As seen in Table 3, all vision-related QoL items among the three compared groups (preoperative phase, postoperative phase, and healthy individuals) were significantly different in all items. The results showed that all vision-related QoL items in the preoperative group were substantially lower than both the postoperative group and healthy individuals ($P < 0.05$). However, the second comparison between the QoL items scores among the postoperative phase was significantly lower than those of healthy individuals ($P < 0.05$).

Table 2. Comparison of vision-related QoL obtained by NEI-VFQ 39 and EQ-5D questionnaires between patients suffering from glaucoma with cataracts and healthy individuals

Questionnaire	Variables (number of questions)	Mean (± SD)		
		Patient group		Healthy control group
		Preoperative	Postoperative	
NEI-VFQ 39	General health (2)	59 (4.83)	70 (1.4)	84.62 (2.6)
	General vision (2)	43.9 (5.24)	55.4 (3.2)	87.53 (2.25)
	Ocular pain (2)	79.36 (3.92)	95.87 (2.6)	96.79 (1.26)
	Near activities (6)	51.45 (7.2)	63.21 (1.2)	95.9 (1.26)
	Distance activities (6)	59.83 (6.29)	74.76 (3.5)	98 (0.79)
	Vision-specific social functioning (3)	66.11 (5.76)	80.11 (0.9)	100(00)
	Vision-specific mental health (5)	51.63 (6.9)	61.87 (0.69)	95.84 (1.26)
	Vision-specific role difficulties (4)	59.65 (7.91)	73.2 (4.3)	94.9 (1.44)
	Vision-specific dependency (4)	62.72 (8.16)	78.5 (4.7)	98.89 (0.34)
	Driving (3)	50.97 (8.36)	61.8 (2.9)	91 (1.8)
	Colour vision (1)	83.19 (4.49)	88.2 (1.5)	97 (1.57)
	Peripheral vision (1)	62.09 (6.54)	75.12 (4.9)	99 (0.83)
	Composite score (39)	62.96	73.41 (3.2)	95 (0.72)
EQ-5D	Quality of life	0.42 (0.21–0.64)	0.58 (0.39–0.78)	0.70 (0.59–0.80)

NEI-VFQ 39: National Eye Institute-Visual Functioning Questionnaire; EQ-5D: EuroQol five-dimensional

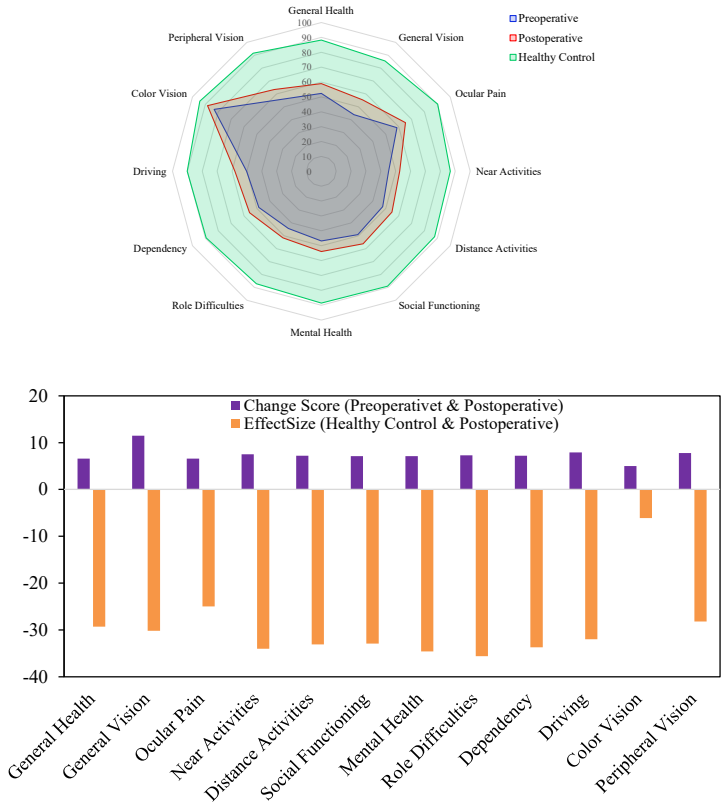

Fig. 1. (Top) Radar chart comparing NEI-VFQ 39 subscale scores across preoperative, postoperative, and healthy control groups. *(Bottom)* Bar graph showing change scores and effect sizes across the same subscales.

Multiple linear regression analyses were performed to assess the effect of surgery on the outcomes of both QoL instruments. Regarding the NEI-VFQ-39, the results showed that after adjusting for age, education, and occupation, patients in the postoperative phase scored an average of 7.3 points higher than in the preoperative phase ($P < 0.001$). Moreover, healthy individuals scored 37.8 points higher than the preoperative group ($P < 0.001$). Among the covariates, age was inversely associated with visual QoL ($\beta = -0.21$, $P = 0.028$), and individuals with university-level education had significantly higher scores than illiterate participants ($\beta = +6.1$, $P = 0.004$). Occupation was not statistically associated with outcome scores.

Table 3. The statistical difference (P-value) between patients suffering from glaucoma and cataracts (before and one month after surgery) and control groups

Questionnaire	Preoperative vs healthy control	Preoperative vs postoperative	Postoperative vs healthy control
National Eye Institute Visual Functioning Questionnaire			
General vision	0.002	0.033	0.02
Ocular pain	0.041	0.012	0.001
Near activities	0.001	0.001	0.015
Distance activities	0.005	0.001	0.03
Vision-specific social functioning	0.03	0.007	0.017
Vision-specific mental health	0.001	0.028	0.008
Vision-specific role difficulties	0.011	0.01	0.001
Vision-specific dependency	0.047	0.007	0.004
Driving	0.049	0.001	0.019
Color vision	0.004	0.036	0.021
Peripheral vision	0.03	0.028	0.048
Composite score	0.039	0.044	0.04
EuroQol five-dimensional			
Quality of life	0.001	0.02	0.037

Values are *p*-values.

The regression model for the EQ-5D showed similar patterns. Patients in the postoperative group had a 0.14-point increase in overall QoL scores compared to the preoperative group ($P < 0.001$). In contrast, healthy controls scored 0.28 points higher than the preoperative group ($P < 0.001$). Age again showed a negative association ($\beta = -0.006$, $P = 0.034$), and university education was associated with a 0.042-point increase compared to the illiterate category ($P = 0.012$). These findings confirm that cataract surgery's positive effect on visual and general QoL remains statistically significant even after adjusting for key demographic factors.

Discussion

This study evaluated the QoL and visual performance of patients suffering from glaucoma with cataract during the pre- and postoperative phases. According to the results of this research, although the overall QoL score and vision-related QoL score in glaucoma patients with cataract improved after cataract surgery, there was a significant difference between the results for patients in the postoperative patients and those of healthy individuals. Based on the results of this study, the total score of QoL VFQ 39 patients during the pre- and postoperative phase was 48.7 and 56.1, respectively; in healthy individuals it was 86.65. There was a significant difference between mean QoL VFQ-39 scores during the pre- and postoperative phases. Similar to our results, other studies have shown a significant improvement in the QoL VFQ scores observed after eye surgery. However, most have been conducted in different eye surgeries with different races and social factors.[29,38,39] The mean EQ-5D scores of patients during the pre- and postoperative phases were 0.42 and 0.58, respectively, which shows a significant difference between them. In this study, the QoL score was lower than in previous studies.[39-42] The main reason for this difference is the effect of economic, social, and racial factors on QoL scores. Also, this study's sample size was larger than that of the other mentioned studies.

Numerous studies have provided evidence of the advantages of phacoemulsification in treating. Phacoemulsification surgery yields a similar reduction in IOP compared to phacotrabeculectomy, but with a lower incidence of complications. However, individuals who undergo phacotrabeculectomy may experience slightly lower IOP levels and require fewer medications to lower IOP, which can be particularly beneficial for patients with advanced PACG or challenges in adhering to medication regimens.[43]

The lower QoL observed in patients with combined glaucoma and cataract may be attributed to the compounded impact of both conditions on visual function. Glaucoma causes irreversible damage to the optic nerve and visual field loss, while cataract impairs visual acuity and contrast sensitivity. Together, these conditions can significantly reduce functional vision and increase psychological distress, leading to lower QoL scores compared to patients with a single condition. Our findings align with previous studies that report reduced QoL in patients with coexisting ocular diseases.[29,38,39] These results underscore the importance of tailored clinical decision-making. For patients with both glaucoma and cataract, combined surgical approaches, such as phacotrabeculectomy, may offer better IOP control and reduce the need for medications, potentially improving long-term QoL outcomes. These QoL improvements following cataract surgery have important implications for clinical decision-making, especially in patients with coexisting glaucoma. While visual acuity and IOP remain key clinical metrics, integrating patient-reported outcomes such as vision-related QoL can help guide the choice between cataract extraction alone and combined cataract-glaucoma procedures.

For patients with moderate to advanced glaucoma or poor medication adherence, combined surgeries like phacotrabeculectomy may enhance IOP control and lead to more meaningful gains in functional vision and overall well-being. Incorporating QoL assessment tools into preoperative consultations may support more personalized surgical planning and improve long-term satisfaction with care. A previous study has shown that vision-related QoL increased following cataract surgery. In addition, increasing glaucoma severity had a negative impact on vision-related QoL.[29] However, other researchers have not evaluated the QoL and visual performance of patients suffering from glaucoma with cataract.

This study evaluated the QoL in 12 main subgroups with a total score. The results indicate a significant difference between patients and healthy individuals during the postoperative phase in all subgroups. Some studies aligned with this study's results and confirmed the correlation between QoL and visual performance in different eye diseases.[44]

In another study, education was significantly correlated to overall QoL and vision-related QoL. Due to the better awareness of patients with higher education about the need for surgery, QoL in these patients was higher than that of lower educated ones, which was in line with a previous study.[38] In examining QoL factors, including the psychosocial perspective, the cognitive environment among patients based on their education status can indicate that better-educated patients had better QoL than less educated ones. The correlation of age with these variables was inverse, which means that as age increases, the score of QoL decreases.[45]

This study has several limitations. First, its cross-sectional design restricts assessing long-term outcomes and causal relationships. Second, the absence of longitudinal follow-up limits insights into the sustainability of postoperative improvements in QoL. Third, potential selection bias may have influenced the findings, as participants were recruited from a single clinical setting. Additionally, cultural and socioeconomic factors may have affected self-reported QoL scores, introducing variability that is difficult to control. While this study focused on descriptive and comparative analyses, we acknowledge that multivariable statistical approaches, such as regression analysis, could have provided deeper insights by adjusting for confounding variables. Future research using this dataset may explore predictive modelling to assess the independent impact of demographic and clinical factors on QoL outcomes.

Conclusion

Several factors contribute to the observed differences, including the criteria for participant inclusion, disease severity and type, the participants' average age, random sampling, and individual and social factors. Overall, it can be inferred that both glaucoma and cataracts impact physical well-being and have psychosocial

implications. The combination of vision impairment and increased stress negatively affects the interpersonal relationships of patients. To summarise, while cataract surgery significantly improves the QoL and vision-related aspects for patients with glaucoma and cataracts, these measures remain lower than those of healthy individuals after the surgery.

Declarations

Ethics approval and consent to participate
The Helsinki Declaration and the Ethics Committee in Medical Ethics Committee approved the research protocol at Mashhad University of Medical Sciences (IR.MUMS.REC.1397.044).

Competing interests
None to declare.

Funding
None to declare.

Availability of data and materials
The datasets generated and analysed during the current study are not publicly available since all relevant data are included in the manuscript. However, they are available from the corresponding author upon reasonable request.

Author contributions
AA and FK were responsible for the study's conception and design. MF acquired the data. AM, AA, and FK analysed and interpreted the data. AM and FK wrote the draft. AA, MF, and revised the manuscript critically. All authors have read and approved the final manuscript.

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Differences in retinal ganglion cell layer and ganglion cell-inner plexiform layer thickness among haemodialysis patients with and without diabetes mellitus

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Abstract

Introduction: This study aimed to compare the thickness of the retinal ganglion cell layer (GCL) and the ganglion cell-inner plexiform layer (GC-IPL) in haemodialysis (HD) patients with and without diabetes mellitus (DM).
Methods: This was a single-centre cross-sectional study conducted in Indonesia. Comprehensive ocular examinations and demographic information were gathered from 110 eyes of 110 HD patients. The sample was divided into DM and non-DM groups. Optical coherence tomography was used to analyse GCL and GC-IPL thickness. The independent t-test or Mann-Whitney test was used to examine the difference between the two groups, and a *p*-value of less than 0.05 was deemed significant.
Results: We analysed 110 eyes of 110 HD patients and divided them into the DM group (27, 24.5%) and non-DM group (83, 75.5%). The average duration of HD in the DM group was lower at 30.8 months than in the non-DM group of 50.6 months

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($p < 0.05$). Hypertension was found in 24 (88.8%) patients in the DM group and 66 (79.5%) in the non-DM group ($p < 0.05$). HD patients with DM group showed significantly thinner GCL in all sectors ($p < 0.05$) and significantly thinner GC-IPL in 4 sectors ($p < 0.05$). In the hypertension cases, GCL and GC-IPL showed significant difference between the two groups ($p < 0.05$).
Conclusion: HD patients with DM demonstrated thinner GCL and GC-IPL. This finding indicates the importance of integrated ophthalmic evaluation in HD patients to prevent further damage of neural retina.

Keywords: biomarker, diabetes mellitus, haemodialysis, retinal ganglion cell, retinal imaging

Perbezaan ketebalan lapisan sel ganglion retina dan sel ganglion-lapisan pleksiform dalam antara pesakit hemodialisis dengan dan tanpa diabetes mellitus

Abstrak

Pengenalan: Kajian ini bertujuan untuk membandingkan ketebalan lapisan sel ganglion retina (ganglion cell layer, GCL) dan lapisan sel ganglion-lapisan pleksiform dalam (ganglion cell-inner plexiform layer, GC-IPL) dalam kalangan pesakit hemodialisis (HD) dengan dan tanpa diabetes mellitus (DM).
Kaedah: Kajian keratan rentas berpusat tunggal ini dijalankan di Indonesia. Pemeriksaan oftalmik menyeluruh dan maklumat demografi diperoleh daripada 110 mata bagi 110 pesakit HD. Sampel dibahagikan kepada kumpulan DM dan kumpulan bukan DM. Tomografi koheren optik digunakan untuk menganalisis ketebalan GCL dan GC-IPL. Ujian-t tidak bersandar atau ujian Mann-Whitney digunakan untuk menilai perbezaan antara kedua-dua kumpulan, dan nilai p kurang daripada 0.05 dianggap signifikan.
Keputusan: Sebanyak 110 mata daripada 110 pesakit HD dianalisis dan dibahagikan kepada kumpulan DM (27 pesakit, 24.5%) dan kumpulan bukan DM (83 pesakit, 75.5%). Purata tempoh HD dalam kumpulan DM adalah lebih pendek, iaitu 30.8 bulan berbanding 50.6 bulan dalam kumpulan bukan DM ($p < 0.05$). Hipertensi didapati dalam 24 pesakit (88.8%) dalam kumpulan DM dan 66 pesakit (79.5%) dalam kumpulan bukan DM ($p < 0.05$). Pesakit HD dengan DM menunjukkan ketebalan GCL yang secara signifikan lebih nipis dalam semua sektor ($p < 0.05$) serta ketebalan GC-IPL yang secara signifikan lebih nipis dalam empat sektor (p

< 0.05). Dalam kes hipertensi, GCL dan GC-IPL menunjukkan perbezaan yang signifikan antara kedua-dua kumpulan ($p < 0.05$).
Kesimpulan: Pesakit HD dengan DM menunjukkan GCL dan GC-IPL yang lebih nipis. Dapatan ini menunjukkan kepentingan penilaian oftalmik bersepadu dalam kalangan pesakit HD bagi mencegah kerosakan lanjut pada retina neural.

Kata kunci: biomarker, diabetes mellitus, hemodialisis, sel ganglion retina, pengimejan retina

Introduction

End-stage renal disease (ESRD), also referred to as stage 5 renal failure, is characterized by a glomerular filtration rate of less than 15 ml/min/1.73 m^2.[1] The primary cause of the illness is diabetes mellitus (DM), which is followed by polycystic kidney disease, glomerulonephritis, and hypertension (HT).[2,3] The United States Renal Data System recorded 124,411 new ESRD diagnoses in 2015. The disease's annual prevalence was approximately 20,000 cases.[4] Because ESRD results in irreversible loss of renal function, patients require dialysis or a kidney transplant as part of their renal replacement therapy in order to avoid uraemia. Lowered tear production, band keratopathy, lenticular opacities, conjunctival calcifications, variations in intraocular pressure (IOP), uremic optic neuropathy, and alterations in retinal microvasculature are a few of the many ocular findings.[5–7] The thickness of the ganglion cell-inner plexiform layer (GC-IPL) and retinal nerve fibre layer (RNFL) in ESRD patients was also significantly reduced in certain cases, measured by to optical coherence tomography (OCT).[8,9]

Over the past few decades, OCT has gained widespread usage as a diagnostic technique that can accurately depict retinal architecture. For instance, in individuals with glaucoma, diabetic retinopathy, age-related macular degeneration, and optic neuropathy, it can be used to measure the thickness of the retinal layer.[10–13] By measuring the thickness of each retinal layer, OCT has also emerged as a useful method for evaluating neurodegenerative diseases, which can be identified far sooner than with funduscopy.[14,15] Numerous theories demonstrated that ESRD treatments involving dialysis could alter the retinal microvasculature. Retinal ganglion cells may sustain damage from ischemia and elevated neurotoxic substances. The retinal ganglion cell layer (GCL), IPL, and RNFL are among the thinner retinal layers that result from it. Subsequently, this might have an impact on visual function, such as colour perception, visual acuity, and visual fields.

To our knowledge, there isn't much thorough documentation about the changes in GCL and GC-IPL in ESRD patients with and without comorbid conditions, including DM and HT. Thus, using spectral domain (SD)-OCT, the study assessed neuronal retinal profiles and differences, particularly between GCL and GC-IPL

thickness, in haemodialysis (HD) patients with and without DM. We expected that HD patients with and without DM would have different GCL and GC-IPL thicknesses, further emphasizing the value of comprehensive and routine ocular examinations in these patients.

Methods

Study design

The Ophthalmology Department and the Division of Nephrology, Internal Medicine Department, Dr. Soetomo General Academic Hospital, Surabaya, collaborated on this cross-sectional, single-centre study in May and June 2019. Participants were directly recruited from the HD unit is ESRD patients. Written informed consent was obtained from patients who fulfilled the study's inclusion and exclusion requirements. The principles of good clinical practice standards and the Declaration of Helsinki's tenets were followed when conducting the investigations. The Dr. Soetomo General Academic Hospital Surabaya's Institutional Review Board approved the study protocol (Komisi Etik Peneliti Kesehatan Rumah Sakit Dr. Soetomo No.1155/KEPK/V/2019).

Study population

Inclusion criteria were subjects with ESRD who underwent regular maintenance HD twice a week in our centre and in stable clinical condition to undergo eye examination related to the parameters studied. Exclusion criteria were subjects who did not consent, did not complete the required examinations, minors under 18 years of age, spherical equivalent refractive error based on Autorefracto Keratometer (ARK) below 6.00 D, and poor image score on SD-OCT (< 45).

Demographic, clinical characteristics, and laboratory data

The patients' demographic information was collected, including their age, sex, length of HD, intraocular pressure (IOP), spherical equivalent on ARK, best-corrected visual acuity (BCVA), and history of DM and HT. Following five minutes of rest, blood pressure (BP) was taken while seated using a validated equipment in the customary manner.

Ophthalmic examination

All participants had a thorough ocular examination on enrolment day conducted by the same team of skilled ophthalmologists. Using ARK, we measured BCVA, IOP, contrast sensitivity, anterior segment examination, posterior segment measurement in low light without pupillary dilation, and refractive parameters for both eyes. Additionally, fundus photos in colour were obtained.

SD-OCT measurement

One or two drops of tropicamide eye drop were previously injected into each eye before retinal layer measurements were performed to assess each sector's GCL and GC-IPL thickness SD-OCT. Our system has an optical resolution of 8 m and an A-scan velocity of 100,000 A-scan/second. It measures the macula and optic disc over a 6 x 6-mm area. The superior (S), superonasal (SN), inferonasal (IN), inferior (I), inferotemporal (IT), and superotemporal (ST) sectors are the six divisions of the retinal layer used for macular measurements. GCL thickness is denoted by GCL+, and GC-IPL layer thickness is denoted by GCL++. The generated images were then charted in circle diagrams in three distinct colours (green: within the normal range, yellow: marginal, and red: outside the normal range) after being examined and compared to a normative database.

Statistical analysis

SPSS statistical software for Windows, version 26.0 (SPSS, Chicago, Illinois, USA), was used for all statistical analyses. Only the right eye was examined. The demographic and clinical features of the research population were summarised into mean/median and percentages displayed in tabular form. Data normality was evaluated using Kolmogorov-Smirnov. This study compared the GCL and GC-IPL thickness of HD patients with ESRD according to their DM status using a comparison test. To ascertain whether these differences occurred between the two groups, the Mann-Whitney Test was employed if the data were not normally distributed, and the independent T-test was employed if they were. A statistical result was considered significant if p was less than 0.05.

Results

Patient characteristics

Only 110 eyes of 110 enrolled patients who satisfied the inclusion and exclusion criteria were analysed out of 218 willing participants. Table 1 displays the baseline characteristics of the study population. Two groups of participants were formed: ESRD patients with DM (27 ± 24.5%) and ESRD patients without DM (83 ± 75.5%). The duration of HD was 30.8 months for the DM group and 50.6 months for the non-DM group. When comparing the two groups, no significant differences were found in any of the variables.

Table 1. Clinical characteristics of the study population. Data are given as mean ± SD.

Variables	Total patients (*N* = 110)	DM group (*n* = 27)	Non-DM group (*n* = 83)	*P*
Age (years)	46 ± 10.9	48.2 ± 6.6	50.3 ± 11.2	**0.009**
Gender, n (%) Female Male	 49 (44.5 %) 61 (55.5 %)	 12 15	 37 46	 0.882 0.720
Duration of HD (months)	38.8	30.8	50.6	**0.021**
IOP (mmHg)	13.0 ± 2.1	12.5 ± 1.6	11 ± 2.2	0.276
SE	1.63 ± 1.4	2.06 ± 1.6	1.44 ± 1.4	**0.007**
BCVA	0.3 ± 0.4	0.4 ± 0.6	0.2 ± 0.2	**0.008**
History of HT+	90	24	66	**0.019**

DM: diabetes mellitus; IOP: intraocular pressure; SE: spherical equivalent; BCVA: best-corrected visual acuity; HT: hypertension
Bold: Statistically significant, $p < 0.05$

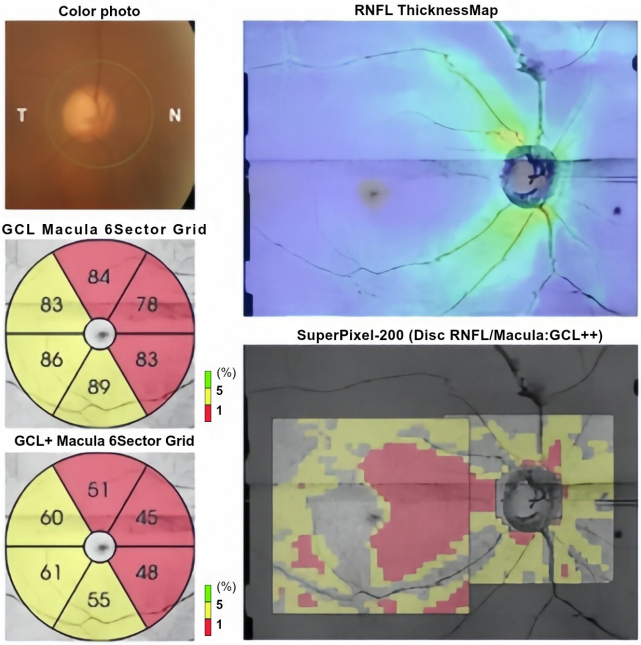

Fig. 1. GCL and GC-IPL thickness in haemodialysis ESRD patients with diabetes mellitus.

Table 2. Differences of ganglion cell layer thickness in haemodialysis patients based on diabetes mellitus status

Average GCL thickness (mm) per sector	**Total patients (*n* = 110)**	**DM group (*n* = 27)**	**Non-DM group (*n* = 83)**	***P***
Superior	69.4 ± 10.7	65.8 ± 15.2	70.7 ± 8.7	**0.014**
Superonasal	66.5 ± 11.4	60.8 ± 17.1	68.4 ± 8.7	**0.005**
Inferonasal	61.5 ± 11.5	54.8 ± 18.7	63.7 ± 7.0	**0.047**
Inferior	64.6 ± 10.3	58.5 ± 15.4	66.7 ± 6.8	**0.007**
Inferotemporal	65.4 ± 13.9	62.4 ± 21.2	66.4 ± 9.9	**0.004**
Supertemporal	104.5 ± 11.2	102.0 ± 16.1	105.3 ± 9.0	**0.009**

DM: diabetes mellitus; GCL: ganglion cell layer; DM: diabetes mellitus
Bold: Statistically significant, $p < 0.05$

Differences of GCL thickness in haemodialysis patients based on diabetes mellitus status

Figure 1 shows the six sectors that comprise the retinal layer: superior (S), superonasal (SN), inferonasal (IN), inferior (I), inferotemporal (IT), and superotemporal (ST). The inferonasal quadrant measured 54.8 ±18.7 µm in the DM group and 63.7 ± 7.0 µm in the non-DM group had the lowest average sectoral thickness values of GCL ($p = 0.047$). In contrast, the DM group's superotemporal sector had the highest average sectoral thickness values of 102.0 ± 16.1 µm, while the non-DM group was 105.3 ± 9.0 µm ($p = 0.009$). Table 2 shows the sectoral macular GCL thickness values in the DM and non-DM groups.

Differences of ganglion cell layer-inner plexiform layer thickness in haemodialysis patients based on diabetes mellitus status

The results of sectoral measurements of GCL thickness in both eyes between the two groups are displayed in Table 3. The inferotemporal sector measured 88.2 ± 31.5 µm for the DM group and 91.4 ± 12.1 µm for the non-DM group; the inferotemporal sector has the lowest average sectoral thickness values of GC-IPL ($p = 0.011$). The DM group had a maximum average sectoral thickness value of 107.2 ± 21.2 µm, while the non-DM group was 115.8 ±12.7 µm ($p = 0.137$). Significant variations were identified in the superonasal, inferonasal, inferotemporal, and superotemporal sectors ($p < 0.05$). There was no significant difference based on DM status ($p > 0.05$) in GC-IPL thickness in the superior and inferior sectors.

Table 3. Differences of ganglion cell layer-inner plexiform layer thickness in haemodialysis patients based on diabetes mellitus status

Average GC-IPL thickness (mm) per sector	Total patients (n = 110)	DM group (n = 27)	Non-DM group (n = 83)	*P*
Superior	113.7 ± 15.2	107.2 ± 21.2	115.8 ± 12.7	0.137
Superonasal	111.9 ± 15.9	102.3 ± 22.7	115.1 ± 12.5	**0.016**
Inferonasal	102.7 ± 17.8	96.4 ± 27.8	104.7 ± 11.7	**0.028**
Inferior	91.7 ± 19.3	86.6 ± 31.9	93.4 ± 12.4	0.194
Inferotemporal	90.6 ± 18.8	88.2 ± 31.5	91.4 ± 12.1	**0.011**
Supertemporal	105.3 ± 14.1	103.0 ± 21.8	108.4 ± 10.4	**0.016**

GC-IPL: ganglion cell-inner plexiform layer DM: diabetes mellitus

Sub-analysis on hypertension as confounding factor

One of the confounding factors is HT, which has been shown in earlier research to also reduce the thickness of the GCL and GCL-IPL. To examine the differences between groups with and without HT and DM, a sub-analysis was conducted. There was no discernible difference in the thickness of GCL and GC-IPL between the non-DM group with and without HT ($p = 0.30$). There was a significant difference in the thickness of GCL and GC-IPL between the DM(-) HT(+) and DM(+) HT(+) groups ($p = 0.006$).

Discussion

According to earlier research, ocular abnormalities are frequently observed in individuals with ESRD, particularly in those who also have concomitant conditions, including DM and HT. According to research by Widjaja *et al.*, hyperglycaemia and elevated diastolic blood pressure are the main predictors of cataracts and conjunctival and corneal calcification, which are the most common visual abnormalities in HD patients.[16] The GCL was assessed in our current study by comparing and analysing changes in GCL and GC-IPL thickness in ESRD patients with DM to ESRD patients without DM. In ESRD patients with DM, we found some notable reductions

in the GCL in every sector of the GCL circular scans. In contrast, we only observed a significant decrease in the superonasal, inferonasal, inferotemporal, and superotemporal sectors of the eye in the GCL-IPL circular scans, despite the fact that thinning was present in nearly every sector of the DM group. Additionally, this study demonstrates that samples with concomitant HT alone did not exhibit a reduction in GCL and GC-IPL thickness. In contrast to the sample with comorbid HT alone, the group with comorbid DM and HT displayed a considerable reduction in thickness.

As far as we are aware, there aren't many studies that compare the thickness of GCL and GCL-IPL in ESRD patients with and without DM. Few studies also demonstrate that ESRD patients have thinner IPL and GCL than healthy controls. However, there is notable thinning reported in a number of articles about RNFL assessment in ESRD patients. Gadelha *et al.* examined RNFL in the eyes of 22 ESRD patients in comparison to a healthy control group. Significant thinning was observed in the ESRD superior, nasal, and inferior sector RNFL.[17] Other studies also show the processes of retinal neurodegenerative indication in ESRD patients. In comparison to 38 healthy controls, Jung *et al.* assessed retinal alterations in 32 ESRD patients. With the exception of patients with DM, it showed a notable decrease in RNFL and GC-IPL thickness in ESRD patients.[9] Our results were comparable to those of Pekel *et al.*, who compared the average macular GCL-IPL thickness of healthy controls and patients with type 2 DM and found a statistically significant difference in the superonasal macular GCL-IPL thickness between the DM and control groups. Because GCL-IPL thickness was decreased in DM patients without retinopathy, the author also came to the conclusion that neuroretinal changes can occur before microvascular problems in DM.[18–20] Similar findings were reported by other researchers, who found that patients with and without diabetic retinopathy had variations in the thickness of the macular retina and each individual layer.[21–25] The RNFL may also narrow as a result of axonal loss.[26]

Our study, which found decreased macular GCL-IPL thickness in many sectors in both DM and ESRD patients, was consistent with all of these investigations. GCL was considerably lower in ESRD patients with DM in this study. Other studies have also observed similar changes. Van Dijk *et al.* assessed GCL thickness in type 1 DM patients with mild diabetic retinopathy and found GCL weakening in the pericentral region.[24] GCL and RNFL in type 2 DM patients did not significantly decline, according to another study. Reduced thickness of the inner retinal layer, including GCL and GC-IPL, is caused by the activation of metabolic pathways, such the polyol and hexosamine pathways, which are driven by hyperglycaemia and result in the production of free radicals and advanced glycation end products. Retinal microangiopathy and retinal neurodegeneration are the results of neural retina disorders brought on by the activation of these pathways.[27–29]

In contrast, a substantial decrease in GC-IPL thickness was observed in samples with a history of HT for more than 5 years in a previous study that compared 84 hypertensive patients with 117 healthy controls.[30] Retinal microcirculation problems

could be the cause of this decrease in retinal thickness. Ischemia in the retinal region is brought on by vasoconstriction and retinal vascular spasm to make up for the rise in systemic blood. Apoptosis can occur in the GCL, which is extremely vulnerable to hypoxic stress.[31] Another study assessed the thickness of the GC-IPL after splitting the HT group into those with a duration of less than 10 years and those with a duration of more than 10 years. Over a 10-year period, a notable reduction in GC-IPL thickness was observed in the HT group. Therefore, when assessing peripapillary microvasculature, the length of HT should be taken into account.[32] Furthermore, some earlier research also suggested a link between the incidence of ocular defects and elevated systolic blood pressure.[33]

According to our study, HD patients who have concomitant conditions experience retinal deterioration. As a result, early identification of neurodegenerative alterations as determined by SD-OCT is crucial and may eventually be incorporated into standard diagnostic screening procedures. The findings of this study may also serve as a guide for HD patients regarding the significance of a comprehensive ophthalmology examination. This study's cross-sectional design, limited sample size, and failure to account for certain confounding variables, such as HT, were among its weaknesses. This study did not provide any information on the control of blood flow velocity or quick of dialysate during HD to evaluate the removal of uremic toxins that may impact retinal neurodegenerative diseases. Future research should address each of those constraints.

Conclusion

This study's findings demonstrated a neurodegenerative process in the retinal layer associated with ESRD patients undergoing frequent HD. It may imply the significance of more regular ocular follow-up of ESRD patients with comorbidities, particularly DM and HT, in order to prevent further damage to the neural retina. Therefore, an integrated planned examination between the HD unit and the ophthalmology department must be improved.

Declarations

Ethics approval and informed consent

Written informed consent was obtained from patients who fulfilled the study's inclusion and exclusion requirements. The principles of good clinical practice standards and the Declaration of Helsinki's tenets were followed when conducting the investigations. The Dr. Soetomo General Academic Hospital Surabaya's Institutional Review Board approved the study protocol (Komisi Etik Peneliti Kesehatan Rumah Sakit Dr. Soetomo No.1155/KEPK/V/2019).

Competing interests
None to declare.

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Authors' contributions
SAW and IY conceived and designed the study. Research execution and data collection: DR, IY, ADP, RSD. Data analysis and interpretation include DR, ADP, and MF. DR, SAW, and YP prepared the manuscript and wrote the original text. Critically review and edit for essential intellectual content: SAW, YP, AT, MF, and WS. Final approval for the submitted version: SAW, YP, and AT.

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Exploring dedifferentiated orbital liposarcoma: a rare disease

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Abstract

Background: To report a rare case of dedifferentiated liposarcoma.
Case presentation: A 72-year-old man presented with worsening proptosis of the right eye for 2 months, accompanied by severe pain and redness. He had a three-year history of progressive upper eyelid swelling in the right eye. His vision in the right eye deteriorated in 1 year to no light perception. The right eye displayed severe non-axial proptosis, with inferomedial displacement and rupture of the globe caused by a 95 x 90 x 30 mm mass. Computed tomography of the orbit revealed a heterogeneous mass with calcification occupying intra- and extraconal space, with inferomedial displacement of the indented globe. Biopsy of the orbital mass in the right eye showed acute inflammation with squamous metaplasia. The patient underwent a lid-sparing modified exenteration procedure. Histopathological examination revealed dedifferentiated liposarcoma.
Conclusion: Dedifferentiated orbital liposarcoma can be debilitating, particularly when accompanied with displacement of the eyeball.

Keywords: dedifferentiated liposarcoma, proptosis, orbital mass

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Penerokaan dedifferentiated orbital liposarcoma: penyakit jarang berlaku

Abstrak

Latar belakang: Melaporkan satu kes jarang berlaku dedifferentiated liposarcoma.
Keputusan: Seorang lelaki berusia 72 tahun hadir dengan proptosis mata kanan yang semakin teruk selama dua bulan, disertai kesakitan dan kemerahan yang ketara. Pesakit mempunyai sejarah pembengkakan kelopak mata atas kanan yang semakin progresif selama tiga tahun. Penglihatan mata kanan merosot dalam tempoh satu tahun sehingga tiada persepsi cahaya. Mata kanan menunjukkan proptosis bukan aksial yang teruk, dengan bola mata teranjak dan pecah ke arah inferomedial akibat jisim berukuran 95 x 90 x 30 mm. Imbasan tomografi berkomputer orbit menunjukkan jisim heterogen dengan kalsifikasi yang melibatkan ruang intra- dan ekstrakonal, serta menyebabkan anjakan bola mata yang tertekan ke arah inferomedial. Biopsi jisim orbit pada mata kanan menunjukkan keradangan akut dengan metaplasia skuamus. Pesakit kemudiannya menjalani prosedur eksenterasi terubah suai dengan pemeliharaan kelopak mata. Pemeriksaan histopatologi seterusnya mengesahkan diagnosis dedifferentiated liposarcoma.
Kesimpulan: Dedifferentiated liposarcoma boleh menyebabkan morbiditi yang signifikan, terutamanya apabila disertai dengan anjakan bola mata.

Kata kunci: dedifferentiated liposarcoma, jisim orbital, proptosis

Introduction

Liposarcoma is a malignancy involving adipose tissue and are classified into well-differentiated, myxoid, pleomorphic, myxoid pleomorphic, and dedifferentiated.[1,2] Orbital liposarcoma is a rare entity as it predominantly manifests in the muscles of limbs and abdomen.[3] Through our literature search, we only found 6 reported cases of dedifferentiated liposarcoma; this is the first case reported in Malaysia.

Case report

A 72-year-old man presented with worsening proptosis in the right eye (OD) for 2 months, accompanied by severe pain, redness, and eye discharge. He had a 3-year history of progressive upper eyelid swelling in the OD. Vision in the OD deteriorated to no light perception in 1 year. The OD displayed severe non-axial proptosis, with a displaced and ruptured globe inferomedially, as shown in Figure 1. The mass

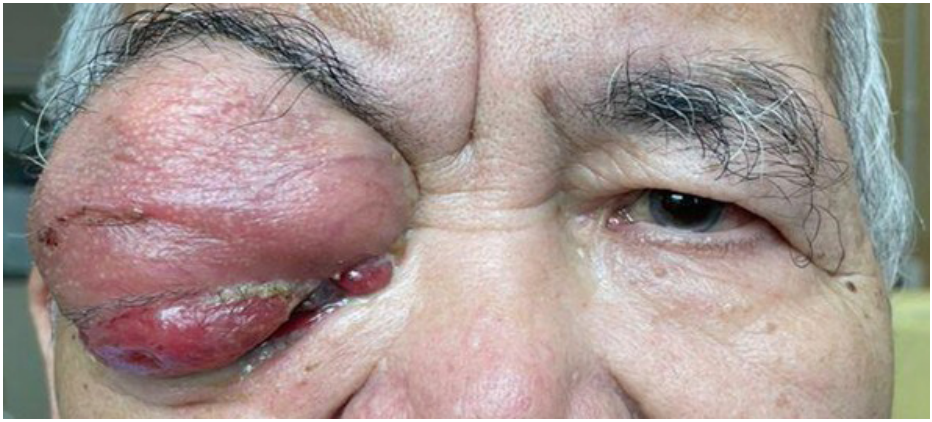

Fig. 1. Severe proptosis, redness and eye discharge.

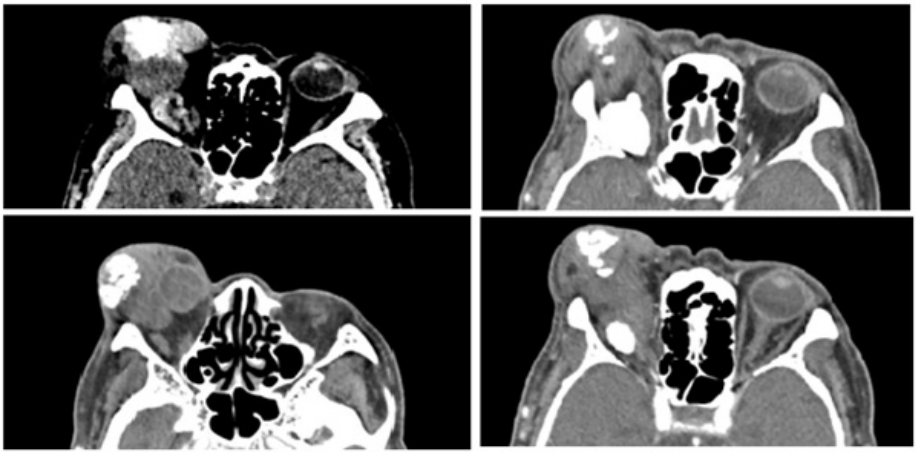

Fig. 2. Computed tomography shows a lobulated mass with dystrophic calcification at the lateral periorbital with extension to the intra- and extraconal spaces. The periorbital mass measured 4.3 x 5.0 x 4.4 cm; the intraorbital extension measured 4.0 x 2.4 x 2.1 cm. The intraorbital component is seen abutting the optic nerve.

measured 95 mm horizontally x 90 mm vertically x 30 mm in width, protruding anteriorly and causing superior displacement of the eyebrow. This mass pushed the right upper tarsus downward, leading to severe exposure and a thick layer of keratinization of the cornea. The surface of the mass appeared lobulated and exhibited a firm consistency. Visual acuity in the left eye was 6/9, with normal anterior and posterior segment ocular examination.

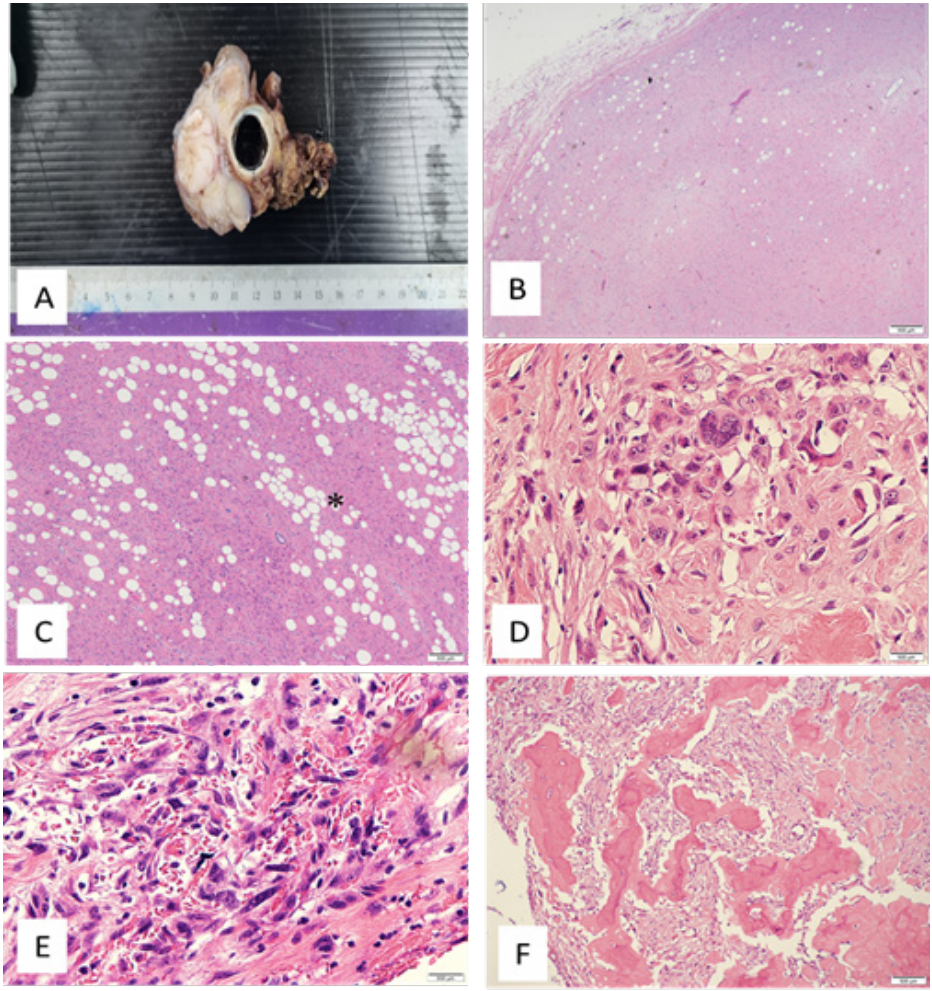

Fig. 3. Dedifferentiated liposarcoma. *(A)* Orbital tumour showing large firm mass with lobulated surface *(B, C)* Low-grade component (H&E x20, H&E x40). *(D)* Tumour cells showing pleomorphic bizzare nuclei; some show vacuolated cytoplasm (H&E x400). *(E)* Dedifferentiated component showing tumour-forming vascular channels forming angiosarcomatous elements (H&E x400) and *(F)* bone formation with lace appearance rimmed by pleomorphic bizarre tumour cells (H&E x200).

Computed tomography of the orbit revealed a heterogenous mass with dystrophic calcification occupying intra- and extraconal space with displacement of the indented globe inferomedially. The apical calcification was in continuation of the roof of the orbit with no intracranial extension, as seen in Figure 2. Incisional biopsy of the orbital mass in the OD showed acute inflammation with squamous metaplasia. The patient was counselled for exenteration in view of malignancy in the blind eye with ruptured globe. Consequently, the patient underwent a lid-sparing modified exenteration surgery under general anaesthesia. A skin incision was made 2 mm from the lid margin, extending to the subcutaneous tissue and carried to the level of the orbital rim. The periosteum was incised at the marcus marginalis. The orbital contents and periosteum were removed manually. The brow was anchored to the periosteum with 5-0 Prolene sutures. Reconstruction of the lateral and inferior socket was performed using 7-0 Vicryl sutures.

Histopathological examination (Fig. 3) revealed dedifferentiated liposarcoma. Histology showed a heterogenous pattern with areas of low- and high-grade transformation consisting of lipomatous area with lipoblasts, prominent osteod formation, pleomorphic spindle cells with bizarre nuclei and multinucleation, and tumour forming vascular-like channels with areas of destructive invasion and myxoid areas.

Immunohistochemical studies showed strong positivity for MDM2, p16, and S100, and patchy immunopositivity for CD34. Fluorescence in situ hybridization (FISH) analysis for MDM2 and CDK 4 gene amplification was positive, CDK4/CEP12 ratio > 2.0. Following surgery, the patient was referred to oncology for further management. The patient subsequently defaulted after the 1-month postoperative follow-up.

Discussion

Liposarcoma is a one of the most commonly diagnosed soft tissue sarcomas, comprising up to 12.8% of all soft tissue malignancies.[4] Liposarcoma in the head and neck region constitute a minority, representing less than 5% of all liposarcomas.[5] Liposarcomas occurring in the orbit are exceptionally uncommon, with approximately 40 documented cases in English literature, primarily in the form of case reports or small series.[5] In cases of orbital liposarcoma, presentation typically mirrors that of other slowly growing tumours in the orbit. Common signs include proptosis, eye displacement—with and without diplopia—as well as optic nerve compression resulting in pain and vision impairment, particularly if the tumour resides at the orbital apex.[6]

Based on Enzinger and Weiss, it has been categorized into five subtypes: well-differentiated, myxoid, round-cell, dedifferentiated, and pleomorphic.[7] Myxoid and well-differentiated subtypes are more common, as indicated by previous studies.[8] Well-differentiated liposarcomas typically exhibit increased mature adipocytes and

various lipoblasts in their pathology. Conversely, dedifferentiated liposarcomas present distinct histological features, characterised by fewer mature adipocytes and a prevalence of highly dysmorphic cells.[3]

Gene amplication of MDM2 and CDK4 proteins has been observed in well- differentiated and dedifferentiated liposarcomas.[9] According to Aleixo *et al.*, immunohistochemistry can be utilized to detect the overexpression of MDM2/CDK4 proteins, aiding in the diagnosis of well-differentiated liposarcomas and dedifferentiated liposarcomas. Similarly in this case, the exenterated eye was sent for FISH analysis for MDM2 & CDK 4 gene amplification and was found to be positive for both.

Diagnosing orbital liposarcoma clinically can be challenging due to the absence of specific diagnostic symptoms. When a tumour is suspected, imaging such orbital computerised tomography and magnetic resonance imaging are crucial for detecting any invasion into neighbouring structures. Histopathology remains the gold standard for diagnosis. Complete surgical resection is recommended once a confirmed diagnosis is obtained.[1] The efficacy of radiotherapy and chemotherapy in managing primary orbital liposarcoma remains uncertain, although radiotherapy has been reported for dedifferentiated liposarcoma.[3] Especially in this case, where we were unable to get clear margins, radiotherapy could have been considered an adjunct.

Conclusion

Dedifferentiated liposarcoma can be debilitating, particularly when accompanied with displacement of the eyeball. In such cases, the importance of a swift and precise management strategy plays a critical role in addressing the condition effectively.

Declarations

Informed consent for publication
The patient provided written informed consent for the inclusion of the clinical data and images presented in this report.

Competing interests
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The diagnostic puzzle of orbital myositis

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Abstract

Background: Idiopathic orbital inflammatory disease (IOID) is a diagnosis of exclusion that poses a diagnostic challenge as it may closely resemble other orbital pathologies.
Case report: A 69-year-old woman presented with progressive blurred vision in the left eye associated with eye pain, redness, proptosis and restricted extraocular movements for 3 weeks. Orbital imaging was suggestive of thyroid orbitopathy, but thyroid function tests were normal. After 8 weeks of medical decompression and oral prednisolone with a suboptimal response, an incisional biopsy of the left lateral rectus muscle revealed non-malignant skeletal muscle with inflammatory cell infiltration, consistent with IOID. Systemic corticosteroid therapy was continued for a total of 16 weeks, resulting in significant improvement in visual acuity, proptosis, and extraocular muscle function.
Conclusion: Given that IOID can mimic orbital pathologies, appropriate imaging and histopathological confirmation are essential for accurate diagnosis. Timely and adequate corticosteroid therapy can lead to favourable visual and functional outcomes.

Keywords: idiopathic orbital inflammatory disease, muscle biopsy, orbital myositis, orbital pseudotumor

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Cabaran diagnostik myositis orbital

Abstrak

Pengenalan: Penyakit radang orbital idiopatik (IOID) merupakan diagnosis pengecualian yang menimbulkan cabaran diagnostik kerana ia hampir menyerupai patologi orbital lain.
Laporan kes: Seorang wanita berusia 69 tahun hadir dengan penglihatan kabur progresif pada mata kiri, dikaitkan dengan sakit mata, kemerahan, bengkak dan pergerakan mata terhad selama 3 minggu. Imbasan orbital menunjukkan orbitopati tiroid, namun ujian fungsi adalah normal. Selepas 8 minggu rawatan dekompresi dan prednisolon oral dengan respons yang kurang memuaskan, biopsi pada otot 'lateral rectus' kiri menunjukkan tisu otot rangka tidak malignan dengan infiltrasi sel radang, selaras dengan IOID. Terapi kortikosteroid sistemik diteruskan selama 16 minggu, menghasilkan peningkatan ketara dalam ketajaman penglihatan, bengkak, dan fungsi otot ekstraokular.
Kesimpulan: Memandangkan IOID boleh menyerupai patologi orbital lain, pengimejan yang sesuai serta pengesahan histopatologi adalah penting untuk diagnosis yang tepat. Rawatan kortikosteroid yang tepat pada masanya dan mencukupi boleh membawa kepada hasil visual dan fungsi yang baik.

Kata kunci: biopsi otot, miositis orbital, penyakit radang orbital idiopatik, pseudotumor orbital

Introduction

Idiopathic orbital inflammatory disease (IOID), also known as pseudotumor, is a benign inflammatory disorder of unknown origin within the orbit.[1,2] IOID represents approximately 8–10% of orbital mass lesions and is the third most common orbital disease after thyroid orbitopathy and lymphoproliferative diseases.[1] It is commonly observed in middle-aged individuals, with no sex predilection.[1] IOID is classified based on the site of involvement, encompassing anterior, diffuse, apical, posterior, myositis, dacryoadenitis, periscleritis, perineuritis, and focal mass subtypes.[1]

Clinically, IOID presents with various ocular symptoms, with eye pain and periorbital swelling being common.[1] While most cases of orbital myositis can be diagnosed clinically without the need for a biopsy, certain atypical cases such as this case require a biopsy for accurate diagnosis. This article presents a case of orbital myositis mimicking thyroid ophthalmopathy and neoplasm, highlighting diagnostic challenges and the critical role of biopsy.

Case presentation

A 69-year-old woman with underlying hypertension and bilateral primary open-angle glaucoma presented with progressively worsening blurred vision in the left eye (OS) associated with binocular diplopia, eye redness, periorbital swelling, and restricted eye movement for 3 weeks. She denied photophobia, lacrimation, or headache. She also denied ocular trauma, connective tissue disease, thyrotoxicosis, fever, infective symptoms, or constitutional symptoms.

OS visual acuity (VA) was 6/60, (pinhole: 6/24) with a positive relative afferent pupillary defect. The OS was proptosed, hypotropic, and with periorbital swelling (Fig. 1, top). The conjunctiva was injected, chemosed inferiorly, the cornea was clear, and the anterior chamber was deep and quiet. Extraocular movement (EOM) was significantly limited in all gazes. Fundus showed tortuous vessels; otherwise, the optic disc was pink, not swollen, with a cup-to-disc ratio of 0.5, retina was flat, no choroidal folds, and no macular abnormalities. Intraocular pressure was normal. Hertel exophthalmometry measurement showed OS at 22 cm and OD at 20 cm. OD VA was 6/9 with no abnormalities seen. Systemic examination was unremarkable, including no palpable thyroid.

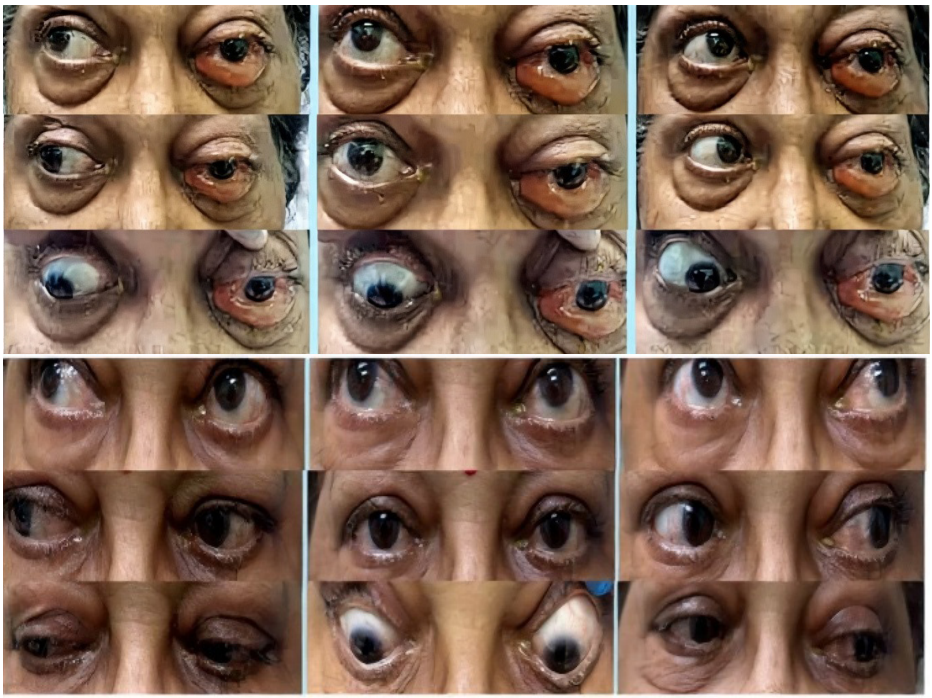

Fig. 1. (Top) Left eye proptosis with periorbital swelling and restricted EOM. *(Bottom)* Left eye post-treatment resolution of proptosis and improved EOM.

Blood investigations, including a full blood count, coagulation profile, inflammatory markers, such as erythrocyte sedimentation rate and C-reactive protein, antinuclear antibody, rheumatoid factor, tumour markers, thyroid hormone, thyroid peroxidase antibody, and syphilis and viral screenings were normal. The magnetic resonance imaging (MRI) scan showed a central, haemorrhaging, fusiform enlargement of the OS lateral rectus muscle measuring 3 cm (anteroposterior) x 2 cm (width) x 2 cm (craniocaudal), sparing the tendon and displacing the OS optic nerve (Fig. 2).

Intravenous 1 g methylprednisolone was administered daily for 3 days, followed by oral prednisolone with an initial dose of 1 mg/kg/day (a total of 60 mg/day), then tapered to 10 mg weekly for a total of 40 mg, and by 5 mg weekly for a total of 20 mg over the course of 8 weeks. A repeat scan showed no reduction in the lesion's size. The patient was co-managed with the oculoplastic team, and a left lateral rectus incisional biopsy demonstrated non-malignant skeletal muscle with inflammatory cells, discounting a diagnosis of neoplasm (Fig. 3). Oral prednisolone was furthered tapered to 2.5 mg weekly for a total of 5 mg for another 8 weeks. While on steroid therapy, patient was also on calcium supplements and gastric protection, with stable blood glucose levels and no obvious weight gain noted. The patient exhibited excellent recovery with a significant improvement in unaided VA to 6/9, optic nerve function, and EOM (Fig. 1b). At the latest monthly follow-up, the patient had been in remission for 10 months.

Discussion

Given that the MRI scan showed an EOM belly enlarged without tendon involvement, potential differential diagnosis for this case was thyroid orbitopathy. A similar finding was seen in a study where 6 patients with orbital myositis showed no tendon involvement.[3] However, our patient exhibited no other signs of thyroid eye disease and was euthyroid, making the diagnosis of thyroid orbitopathy unlikely. The absence of preceding infection and leucocytosis ruled out orbital cellulitis.[4] The biopsy clearly ruled out a tumour, which was initially suspected due to the presence of haemorrhage in the muscle seen on the MRI scan. The haemorrhage in our case could have been associated with inflammatory changes and mechanical stress induced by the enlarged muscle.[5] Haemorrhage can also occur in cases of orbital varices, which present with similar symptoms.[6]

Early intervention improves outcomes.[7] An early incisional biopsy was performed to guide the management as the patient showed a poor response to initial steroid therapy. Biopsy is generally recommended in cases with progressive neurologic deficits, lack of steroid responsiveness, persistent imaging abnormalities, and recurrence.[1]

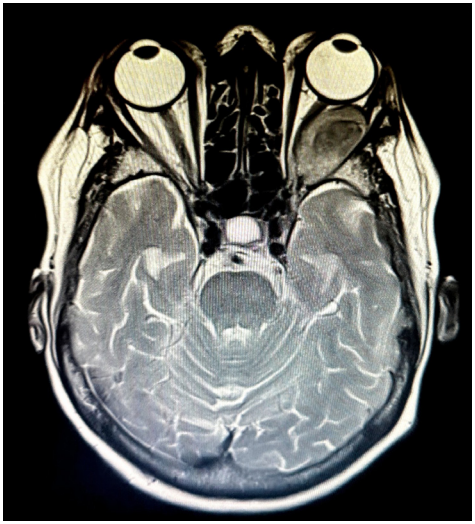

Fig. 2. MRI scan showing an enlarged left lateral rectus muscle.

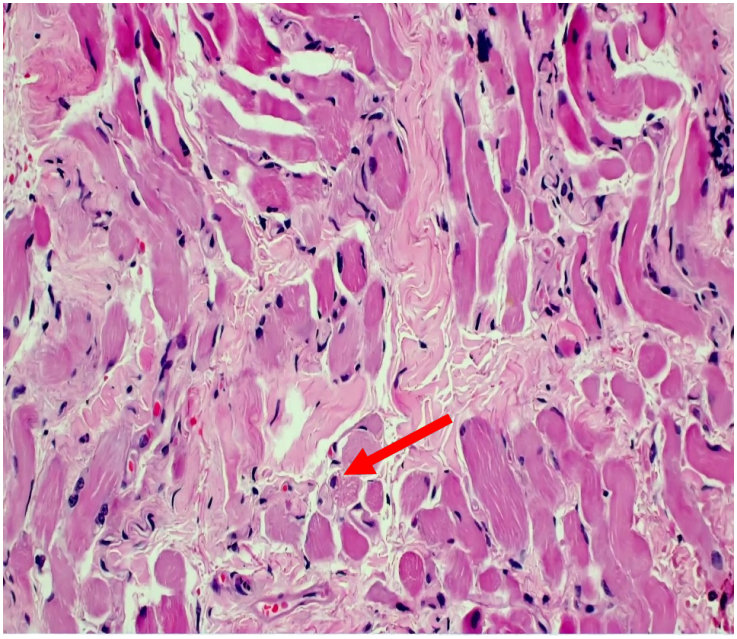

Fig. 3. Biopsy revealing benign skeletal muscle with inflammatory cells.

The primary aim of treatment is to reduce inflammation and improve vision. Corticosteroid therapy is the first-line treatment for orbital myositis. The typical initial dose is 1 mg/kg/day for a week, followed by a gradual tapering over 6–12 weeks.[8] In cases of severe presentation, intravenous methylprednisolone is prescribed for 3 days, followed by the previously described oral steroid regimen.[8] Since immunosuppressive therapy takes 6–8 weeks to manifest its full effect, maintenance of steroid therapy is necessary.[8] The primary mechanism of corticosteroids involves the inhibition of rapidly dividing cells, particularly leukocytes, thereby inducing an anti-inflammatory effect mediated by the inhibition of phospholipase A2 and cyclo-oxygenase pathways.[1]

Conclusion

This case highlights that prompt diagnosis, investigation, and management are crucial in achieving favourable outcomes in IOID.

Declarations

Informed consent for publication
The patient provided written informed consent for the publication of the clinical data and images provided in this article.

Competing interests
None to declare.

Funding
None to declare.

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Evidence of retrograde trans-synaptic degeneration: retinal ganglion cell atrophy following occipital stroke

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Abstract

Background: Trans-synaptic degeneration (TSD) is an uncommon phenomenon wherein the degeneration of one neuron leads to the subsequent degeneration of interconnected neurons.
Case report: A 50-year-old woman experienced sudden bilateral visual field loss for 10 days, accompanied by right-sided headache, numbness, tingling, and a sensation of tingling and heaviness in the tongue. The confrontation visual field indicated right homonymous hemianopia field loss, and automated static perimetry confirmed this finding. Magnetic resonance imaging showed recent acute infarcts on the left occipital lobe and optical coherence tomography of the ganglion cell layer revealed contralateral thinning, thus confirming retrograde TSD, as the post-synaptic damage in the occipital lobe was mirrored in the pre-synaptic neurons, *i.e.*, ganglion cells.
Conclusion: This case report demonstrated evidence of TSD in the retinal ganglion cell layer of a patient with acute occipital stroke.

Keywords: occipital stroke, retinal ganglion cells, trans-synaptic degeneration

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Bukti degenerasi trans-sinaptik retrograd: atrofi sel ganglion retina selepas strok oksiptal

Abstrak

Latar belakang: Degenerasi trans-sinaptik (trans-synaptic degeneration, TSD) merupakan fenomena yang jarang berlaku, di mana degenerasi satu neuron menyebabkan degenerasi seterusnya pada neuron-neuron yang saling berhubung.
Siri kes: Seorang wanita berusia 50 tahun mengalami kehilangan medan penglihatan bilateral secara tiba-tiba selama 10 hari, disertai sakit kepala di bahagian kanan, kebas, rasa mencucuk-cucuk, serta sensasi kesemutan dan berat pada lidah. Pemeriksaan medan penglihatan secara konfrontasi menunjukkan kehilangan medan penglihatan hemianopia homonim kanan, dan perimetri statik automatik mengesahkan dapatan tersebut. Pengimejan resonans magnetik menunjukkan infark akut terkini pada lobus oksipital kiri, manakala tomografi koheren optik lapisan sel ganglion menunjukkan penipisan pada bahagian kontralateral. Dapatan ini mengesahkan TSD retrograd, apabila kerosakan pascasinaptik pada lobus oksipital dicerminkan oleh perubahan pada neuron prasinaptik, iaitu sel ganglion retina.
Kesimpulan: Laporan kes ini menunjukkan bukti berlakunya TSD pada lapisan sel ganglion retina pada seorang pesakit yang mengalami strok oksipital akut.

Kata kunci: degenerasi trans-sinaptik, sel ganglion retina, strok oksipital

Introduction

Trans-synaptic atrophy, also referred to as trans-synaptic degeneration (TSD), is a condition in which the degeneration of one neuron causes the subsequent degeneration of connected neurons. This phenomenon is an uncommon condition with limited evidence, theoretically seen in neurodegenerative diseases such as multiple sclerosis, stroke, and optic neuritis.[1,2] The proposed mechanism of TSD is that synaptic dysfunction and pathology of synaptic adhesion molecule in the synaptic space leads to axonal and dendritic damage in postsynaptic neurons.

In theory, presynaptic to postsynaptic neuronal degeneration in the visual pathway is anterograde TSD, *i.e.*, degeneration in the posterior visual pathway, which results in changes in the lateral geniculate nucleus, optic radiation, and visual cortex. Postsynaptic to presynaptic degeneration is called retrograde TSD, *i.e.*, degeneration in the posterior visual pathway that results in changes or potential damage to the inner retina. This case report presents retrograde TSD.

Case presentation

A 50-year-old woman was referred to the ophthalmology clinic at Dr. Sardjito General Hospital, Yogyakarta, Indonesia with complaints of bilateral blurred vision, worse in the right eye and resembling white mist, for 10 days prior to her visit to the eye clinic. The incident occurred in the afternoon while the patient was sewing clothes, as this is her daily work. The blurred vision was accompanied by a right-sided headache, without dizziness, nausea, or vomiting. Other positive symptoms included numbness on the right side of her body, and a tingling and heavy feeling in the tongue. These symptoms started around the same time as the vision loss and worsened gradually.

The patient denied any history of head injuries or illnesses, and her past ocular history was unremarkable for any eye diseases or surgeries. She had a history of uncontrolled hypertension without medication. The patient's social history revealed that she was a passive smoker and denied any recent use of illicit drugs or any systemic diseases. She is the third of 4 siblings, all female, and 2 of which had a history of stroke. There was no family history of congenital anomalies.

Upon presentation at the clinic, the patient's peripheral pulse rate was measured at 78 beats per minute, respiratory rate was 18 cycles per minute, and blood pressure was 154 mmHg/75 mmHg. The patient was alert and oriented to person, place, and time, with no focal neurological deficits. Uncorrected distance visual acuity was 6/15 (20/50) bilaterally. With the pinhole test, the visual acuity improved to 6/12 (20/40) in the right eye and 6/9 (20/30) in the left eye. The best-corrected visual acuity with a +0.50 spherical lens improved to 6/6 E (20/20) in both eyes. Intraocular pressure was 15 mmHg in the right eye and 11 mmHg in the left eye.

On the slit lamp examination, the anterior segment was unremarkable, and no eyelid ptosis was present. The conjunctiva and anterior chamber were quiet. Pupils were equal, round, and reactive to light with no relative afferent pupillary defect. On posterior segment examination, both optic discs had well-defined borders, with a cup-to-disc ratio of 0.6 in the right eye and 0.5 in the left eye. The foveal reflex was present, and the arteriole-to-venule ratio was 2:3, with the presence of arteriolar copper wiring noted in both eyes. Extraocular muscles were intact with no restrictions. Upon contrast-sensitivity testing, the right eye had 19.2% and the left eye had 14.6%. There was red-green dyschromatopsia observed on colour vision testing with the Ishihara test. Confrontation visual fields revealed right homonymous hemianopia field loss.

The macular thickness measured by spectral-domain optical coherence tomography (OCT) revealed thinning of the superonasal [66 µm (normal mean: 81 ± 6 µm; range: 69–93 µm)] and inferonasal [62 µm (normal mean: 80 ± 6 µm; range: 68–92 µm)] regions of the circumferential sectors of the retinal ganglion cell layer (GCL) and plexiform layers in the right eye, and thinning of the superotemporal [65 µm (normal mean: 83 ± 7 µm; range: 70–96 µm)] and inferotemporal [64 µm (normal

mean: 84 ± 6 µm; range: 72–96 µm)] regions in the left eye (Fig. 1). The retinal nerve fibre layer (RNFL) thickness measurement showed no significant thinning in either eye. Automated static perimetry revealed right homonymous hemianopia (Fig. 1). Laboratory workup included a complete blood count and metabolic panel, but the results were unremarkable. Additional testing with magnetic resonance imaging (MRI) revealed recent acute infarcts, predominantly involving the left occipital lobe (Fig. 1). Based on the MRI findings, the patient was admitted to the neurology stroke service. The patient was prescribed 30 mg of aspirin daily, 5 mg of amlodipine daily, and 500 mcg of mecobalamin twice a day. The patient was regularly followed up every month at the eye clinic.

Discussion

The visual system is a good model for studying TSD because of its well-defined structure and strong connectivity between the retina and visual cortex.[3] These visual pathways can undergo neurodegenerative processes, which are bidirectional in nature. The defects might be detected through several techniques including OCT, advanced MRI techniques, electrophysiology, high- and low-contrast visual acuity tests, automated perimetry, and colour vision assessments.[4]

The degeneration process in the present case report is a retrograde TSD, in which the degeneration in the posterior visual pathway causes retinotopic changes in the anterior visual pathway (retinal ganglion cells), as shown in the OCT image (Fig. 1). Thinning of the homonymous hemimacula following damage to the optic radiation (a reduction in RNFL thickness was demonstrated in the nasal side of the contralateral eye and the temporal side of the ipsilateral eye in patients with cerebral infarction). The occipital stroke location is consistent with the thinning of the circumferential RNFL, GCL, and plexiform layers. It is hypothesized that the severity and location of RNFL thinning correlate with the site of damage and the region of infarcted arteries.5 When a neuron is damaged, its ability to transmit signals diminishes, leading to reduced synaptic inputs to connected neurons, causing apoptosis and degeneration process by releasing pro-inflammatory cytokines that can exacerbate neuronal injury and promote degeneration.[4,6,7] A prior study discussing homonymous visual field deficits in occipital lobe stroke patients mentioned varying rates of retrograde TSD manifestation. These patients had at least 10% of relative hemifield atrophy 2.5 years after experiencing a stroke. One case had the earliest onset, occurring 5.5 months post-stroke.[8]

Optic nerve atrophy can be evaluated using OCT measurements of the macular ganglion cell-inner plexiform layer (GC-IPL), optic nerve head, and peripapillary RNFL. This approach allows for non-invasive and repeatable evaluations. Upon understanding the TSD mechanism, GCL thickness can be used to analyse disease progression and help formulate treatment strategies.[8] OCT-detected TSD may

provide valuable information regarding the extent and chronicity of retrograde neuronal damage. Greater thinning generally indicates more extensive neuronal loss. Furthermore, reduced retinal layer thickness on OCT correlates with persistent visual field deficits and limited functional recovery, suggesting that the potential for neural regeneration is minimal once degeneration has stabilized.

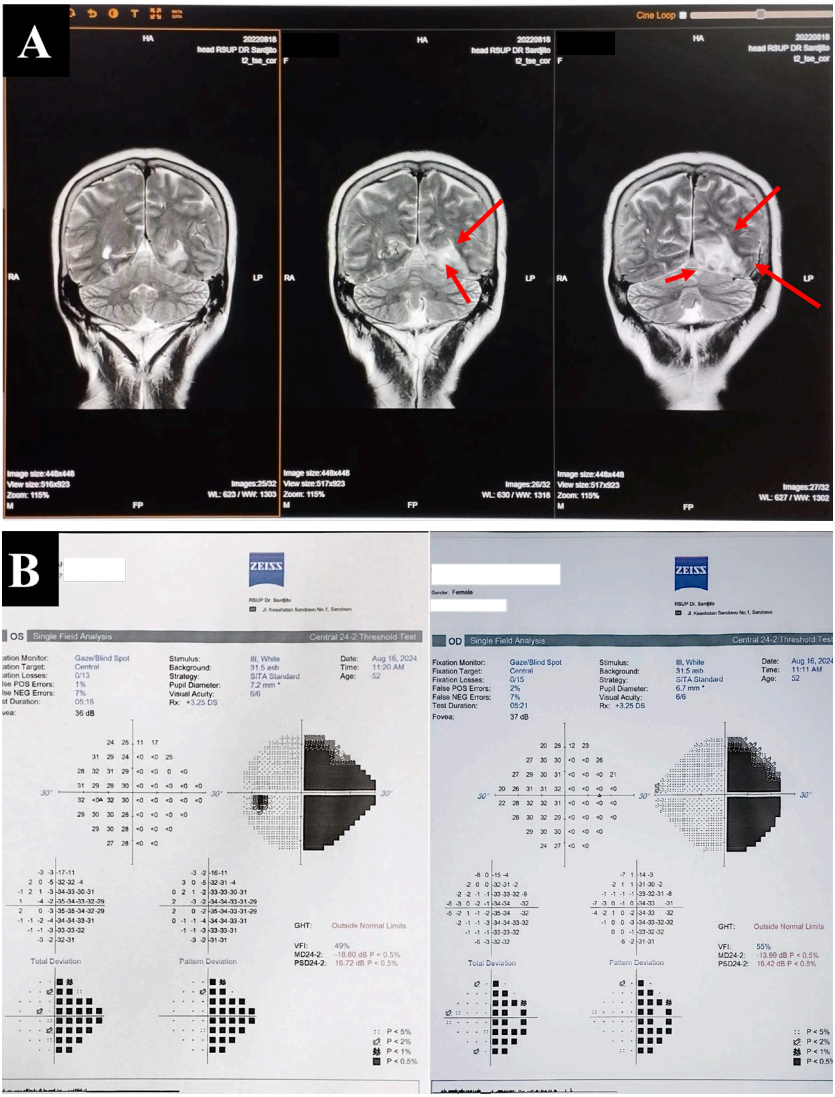

Fig. 1. (A) MRI shows acute infarcts on the left occipital lobe. *(B)* Automated static perimetry shows right homonymous hemianopia.

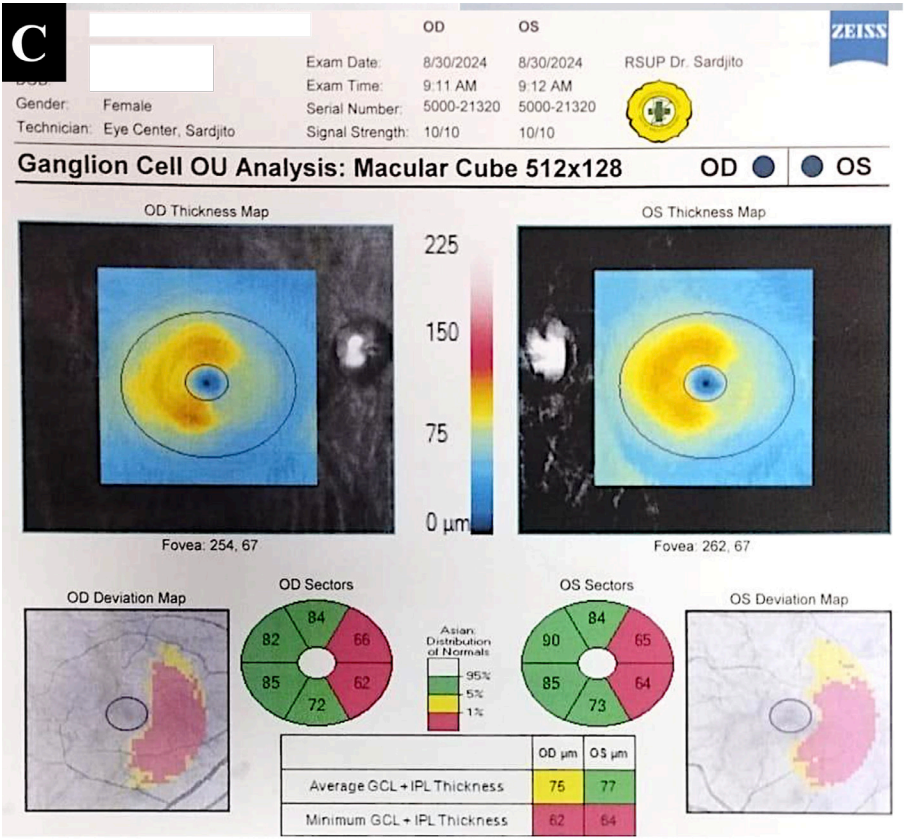

Fig. 1. (C) Superonasal and inferonasal regions of the circumferential ganglion cell layer.

Conclusion

Although TSD has been proposed theoretically, direct clinical evidence remains limited. This case provides supportive evidence of retrograde degeneration in the retinal ganglion cell layer following occipital stroke.

Declarations

Informed consent for publication
The patient provided informed consent for the publication of the clinical 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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A clinical diagnosis quandary: herpes zoster ophthalmicus versus paederus dermatitis

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Abstract

Background: Herpes zoster ophthalmicus (HZO) and *Paederus* dermatitis (PD) may present with overlapping dermatological features, leading to diagnostic challenges.
Case report: A 15-year-old boy presented with a one-week history of right eye pain, swelling, and fever, accompanied by vesicular lesions distributed along the right V1 and V2 dermatomes, respecting the midline. He reported a *Paederus fuscipes* bite in the right cheek two days before symptom onset. Examination revealed conjunctival chemosis, mechanical ptosis, restricted extraocular motility, and a grade 1 relative afferent pupillary defect. Imaging showed preseptal cellulitis with facial extension and lacrimal gland abscess. Treatment comprised oral acyclovir, intravenous ceftriaxone, intravenous metronidazole, and topical chloramphenicol ointment, with gradual improvement in systemic, ocular, and dermatological findings, and restoration of optic nerve function.
Conclusion: The clinical overlap between HZO and PD emphasizes the importance of a thorough clinical assessment—including dermatome pattern recognition, ocular examination, and systemic symptoms—to guide appropriate treatment.

Keywords: Herpes zoster ophthalmicus, orbital cellulitis, Paederus dermatitis

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Kebingungan diagnosis klinikal: herpes zoster ophthalmicus berbanding paederus dermatitis

Abstrak

Latar belakang: Herpes Zoster Oftalmikus (HZO) dan Dermatitis Paederus (PD) boleh memperlihatkan ciri dermatologi yang bertindih, menyebabkan cabaran dalam membuat diagnosis.
Laporan kes: Seorang remaja lelaki berumur 15 tahun hadir dengan sejarah sakit dan bengkak mata kanan selama seminggu, disertai demam dan lesi vesikel yang tersebar sepanjang dermatom V1 dan V2 kanan, tanpa melibatkan garis tengah. Beliau melaporkan gigitan serangga *Paederus fuscipes* (semut Charlie) di pipi kanan yang menjalar ke arah telinga, dua hari sebelum gejala bermula. Pemeriksaan menunjukkan kemosis konjunktiva, ptosis mekanikal, pergerakan mata yang terhad, dan kecacatan anak mata aferen relatif gred 1. Imbasan menunjukkan selulitis praseptal kanan dengan lanjutan ke muka dan abses kelenjar lakrimal. Rawatan terdiri daripada asiklovir oral, ceftriaxone dan metronidazole secara intravena, serta krim kloramfenicol topikal, dengan peningkatan beransur-ansur dari segi gejala sistemik, oftalmik, dermatologi serta pemulihan fungsi saraf optik.
Kesimpulan: Pertindihan klinikal antara HZO dan PD menekankan kepentingan penilaian klinikal yang teliti—termasuk pengecaman corak dermatom, pemeriksaan mata, dan gejala sistemik—bagi menentukan rawatan yang sesuai.

Keywords: Herpes zoster ophthalmicus, selulitis orbital, dermatitis Paederus

Introduction

Herpes zoster ophthalmicus (HZO) is a reactivation of the varicella zoster virus (VZV) within the ophthalmic division of the trigeminal nerve (V1). This reactivation occurs when the dormant VZV within the trigeminal nerve ganglion is triggered, leading to ocular symptoms.[1] Paederus dermatitis (PD) is an acute irritant contact dermatitis caused by the paederine toxin released by *Paederus fuscipes*, commonly known as Charlie ant2 in Malaysia. This condition manifests as a severe skin inflammatory reaction following exposure to toxin. Both conditions have similar dermatological features, which can create a diagnostic dilemma for clinicians who are unfamiliar with the less common PD, potentially resulting in delayed treatment.

Case presentation

A 15-year-old boy presented with a one-week history of right eye pain and swelling, accompanied by vesicular eruptions distributed along the right V1 and V2 trigeminal dermatomes, respecting the vertical midline (Fig. 1). Systemic symptoms included fever, chills, anorexia, vomiting, and headache. He had a history of childhood VZV infection and reported a recent *Paederus fuscipes* bite in the right cheek extending toward the ear, two days prior to symptom onset. Ocular examination revealed conjunctival chemosis, mechanical ptosis, limited ocular motility, and a grade 1 relative afferent pupillary defect, which was attributed to severe ocular inflammation and the presence of a lacrimal gland abscess. There was no corneal involvement, keratouveitis, or Hutchinson's sign (Fig. 2). The restricted ocular motility and ptosis were attributed to mechanical effects from significant periorbital oedema and conjunctival chemosis, rather than cranial nerve palsy. Contrasted computed tomography (CT) showed right preseptal cellulitis with facial extension and a lacrimal gland abscess, without evidence of orbital abscess (Fig. 3). Based on the clinical and radiological findings, the diagnosis HZO with lacrimal gland abscess was made, although PD remained a differential consideration. The patient received oral acyclovir (800 mg 5 times daily for 7 days), intravenous ceftriaxone (2 g daily for 5 days), followed by oral co-amoxiclav (625 mg 3 times daily for 5 days). He was also prescribed topical chloramphenicol ointment for skin lesions and preservative-free lubricants for ocular surface protection. Clinical improvement was observed by day 5, with resolution of fever, skin lesions, improvement in extraocular motility, and restoration of optic nerve function.

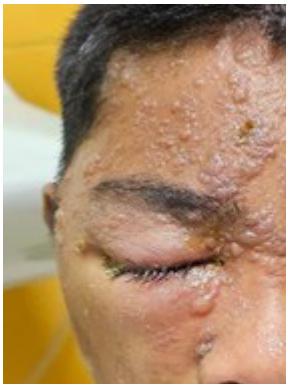

Fig. 1. Vesicular lesions along the V1 and V2 trigeminal dermatomes, respecting the vertical midline.

Fig. 2. Ocular examination revealed severe conjunctival chemosis with periocular vesicular lesions.

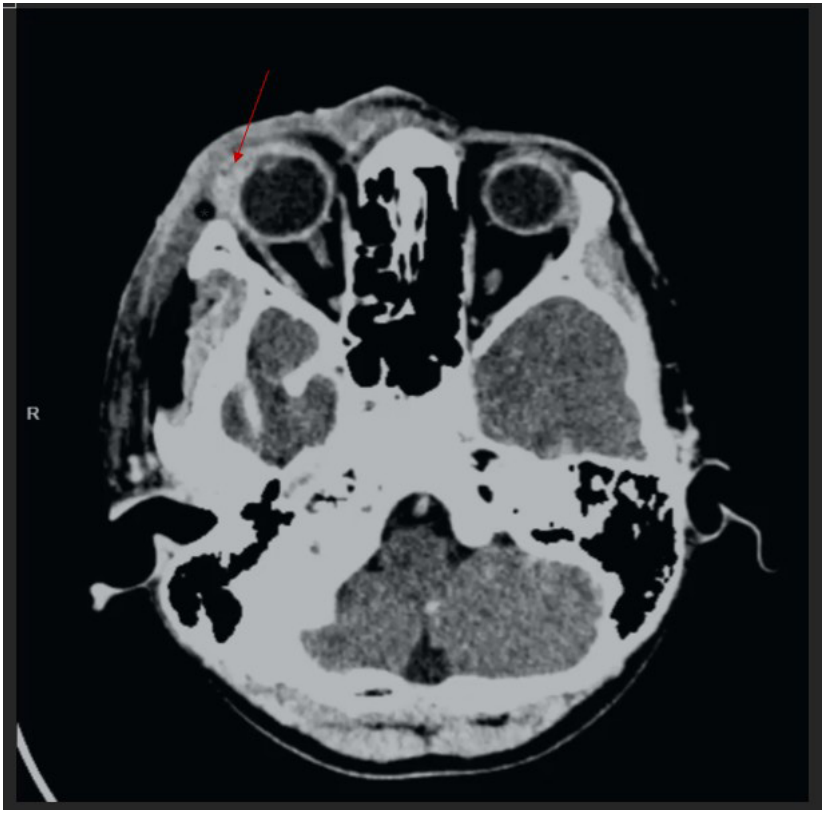

Fig. 3. Right lacrimal gland abscess (red arrow) with preseptal cellulitis.

Discussion

The diagnostic dilemma between HZO and PD arises from their similar clinical presentations, particularly the appearance of vesicular lesions, which can cause confusion for clinicians. In contrast, PD is caused by contact with the *Paederus* beetle toxin[2] often resulting in linear, vesicular lesions that evolve through stages of erythema, vesiculation, and squamous desquamation. The lesions typically appear within 24 to 48 hours of toxin exposure and are commonly localized to the face, neck, and arms, with occasional ocular involvement.[3] PD is characterized by linear skin lesions, often without a clear dermatome distribution, which can closely resemble the lesions seen in HZO. While most PD cases are mild, severe instances can involve systemic symptoms such as fever and joint pain.

Both conditions share overlapping clinical features, particularly the vesicular skin lesions. However, the key difference lies in the aetiology: HZO is viral, while PD is toxin-induced. In one case series, PD lesions were noted to resemble HZO but did not follow the dermatome distribution typical of HZO, which highlights the difficulty in distinguishing between the 2 conditions without a careful clinical assessment.[3] A skin biopsy in such cases can confirm the diagnosis, but this is rarely necessary when clinical presentation is characteristic.[4,5]

HZO management involves antiviral therapy, typically started within 72 hours of onset to reduce complications, whereas PD is treated as irritant contact dermatitis with measures such as cold compresses, antihistamines, and topical steroids.[1] The use of systemic corticosteroids is reserved for severe PD cases. Given the clinical overlap, it is crucial for clinicians to consider both conditions in the differential diagnosis of vesicular linear lesions,[2] especially when dermatome involvement is unclear or atypical.

Conclusion

This case underscores the importance of considering the lesion distribution and associated ocular or systemic findings when differentiating HZO from PD. While the patient had a recent *Paederus fuscipes* bite in the region of the affected dermatomes, the distribution of vesicular lesions strictly followed the right V1 and V2 dermatomes without crossing the midline, and was accompanied by ocular and systemic involvement, which are not typical in PD. The absence of Hutchinson's sign and keratouveitis does not exclude HZO but may suggest a milder ocular involvement. Ultimately, the classical dermatomal rash, coupled with optic nerve dysfunction and imaging findings of preseptal cellulitis with lacrimal gland abscess, favoured the diagnosis of HZO over PD.

Declarations

Informed consent for publication
Written informed consent was obtained from the patient and their guardian for publication of the details of their medical case and any accompanying images.

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Ocular melioidosis: a diagnostic challenge with devastating visual consequences

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Abstract

Background: Melioidosis is a multi-system infectious disease caused by *Burkholderia pseudomallei*. Ocular involvement in melioidosis is rare, with a reported prevalence of less than 2%. It frequently affects adults with diabetes. For severe melioidosis, ceftazidime remains the first-line treatment, followed by extended maintenance therapy to reduce the risk of relapse and recurrence.
Case presentation: A 58-year-old man, presented with a 4-day history of pain, redness and photophobia in the right eye. He had diabetes with a history of disseminated melioidosis. Ocular examination showed conjunctival injection, hypopyon in the anterior chamber, and elevated intraocular pressure in the right eye. A conjunctival culture and sensitivity swab found *Burkholderia pseudomallei*. He was treated with intravenous ceftazidime followed by oral trimethoprim-sulfamethoxazole and responded well to treatment.
Conclusion: Early diagnosis guided by a high index of clinical suspicion as well as prompt treatment are crucial for favorable outcomes.

Keywords: Burkholderia pseudomallei, endophthalmitis, ocular melioidosis

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Melioidosis okular: cabaran diagnostik dengan kesan buruk terhadap penglihatan

Abstrak

Latar belakang: Meliodosis merupakan penyakit berjangkit multisistem yang disebabkan oleh Burkholderia pseudomallei. Penglibatan mata dalam meliodosis jarang berlaku, dengan prevalens yang dilaporkan kurang daripada 2%. Ia sering menyerang golongan dewasa yang mempunyai penyakit kencing manis. Untuk penyakit meliodosis yang serius, ceftazidime kekal sebagai rawatan utama, diikuti dengan terapi jangka masa panjang bagi mengurangkan risiko penyakit berulang. *Laporan kes:* Seorang lelaki berumur 58 tahun hadir dengan sejarah sakit pada mata kanan, kemerahan dan fotofobia apabila melihat cahaya selama empat hari. Beliau merupakan pesakit kencing manis dengan sejarah meliodosis diseminata. Pemeriksaan mata kanan menunjukkan konjunktiva merah, hipopion di ruang hadapan mata dan tekanan mata yang tinggi. Kultur dan ujian sensitiviti swab konjunktiva mata kanan mengenal pasti Burkholderia pseudomallei. Pesakit telah dirawat dengan ceftazidime secara intravena, diikuti dengan trimetoprim-sulfametoksazol oral dan menunjukkan tindak balas yang baik terhadap rawatan. Kesimpulan: Diagnosis awal yang dipandu oleh tahap kecurigaan klinikal yang tinggi serta rawatan yang segera adalah penting untuk mencapai hasil rawatan yang baik.

Kata kunci: Burkholderia pseudomallei, endoftalmitis, melioidosis okular

Introduction

Melioidosis is an infectious disease caused by the gram-negative, motile, non-spore forming *Burkholderia pseudomallei* bacillus, which is found in soil and surface water and is widely distributed in tropical and subtropical regions. Although ocular involvement in melioidosis is rare, it may lead to devastating outcomes. The prevalence was estimated around 0.49 to 1.02%.[1] It is endemic in Southeast Asia (notably Thailand and Malaysia) and northern Australia.[2,3] Here, we report a case report of patient with melioidosis and ocular involvement.

Case report

A 58-year-old agricultural worker presented with a 4-day history of pain, redness, and photophobia in the right eye. Prior to this episode, he had poor baseline visual acuity, limited to counting fingers in both eyes, secondary to advanced diabetic eye disease with bilateral vitreous haemorrhage. His past medical history was significant for diabetes mellitus and disseminated melioidosis with splenic and left wrist abscess in 2023, microbiologically confirmed from blood and wrist pus cultures growing *Burkholderia pseudomallei*. He completed 6 weeks of intravenous ceftazidime followed by 3 months of oral doxycycline.

On initial examination, he was systemically stable with normal vital signs. Visual acuity was hand movement in the right eye and counting fingers in the left eye. Ocular examination revealed conjunctival injection, corneal oedema, fibrin, blood clot, and a nasal hypopyon in the anterior chamber, with elevated intraocular pressure in the right eye. Fundus examination was not possible due to vitreous haemorrhage. B-scan ultrasonography confirmed vitreous haemorrhage. A steroid challenge was performed and showed no worsening; thus, he was initially managed as neovascular glaucoma with severe anterior uveitis.

He was admitted for intraocular pressure control and further evaluation. Initial blood investigations, including full blood count, renal profile, liver function tests, and Mantoux test, were within normal limits. Endogenous endophthalmitis secondary to melioidosis was suspected in view of his diabetes mellitus, occupational exposure, prior history of melioidosis, and the appearance of vitreous loculations on follow-up B-scan imaging. He subsequently underwent intravitreal tap and injection of vancomycin and ceftazidime. Both vitreous and blood cultures yielded no growth. Conjunctival swab culture, however, grew *Burkholderia pseudomallei*. Abdominal ultrasonography revealed multiple splenic lesions, with the largest measuring approximately 0.9 × 1.2 cm, compared to a previous lesion measuring 1.5 × 2.0 cm during his prior episode of melioidosis in 2023.

One week later, a scleral abscess developed in the nasal aspect of the right eye (Fig. 1). Repeat B-scan showed improving vitreous loculations; however, a superior subretinal abscess was noted. He was referred for vitreoretinal intervention to reduce the intraocular infective load and improve antimicrobial penetration, but the patient declined the procedure.

He completed 8 weeks of intravenous ceftazidime, followed by eradication therapy with trimethoprim-sulfamethoxazole for 1 year. During follow-up, he remained well with no signs of disease recurrence, but he remained legally blind.

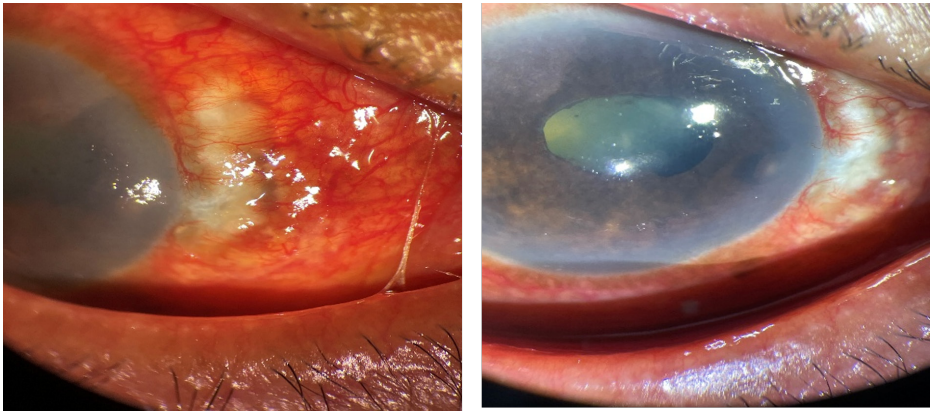

Fig. 1. Anterior segment photographs showing scleral abscess over nasal part of right eye.

Discussion

Melioidosis is a multiorgan infectious disease caused by *Burkholderia pseudomallei*. Based on previous reports, diabetes mellitus was the most frequently identified predisposing risk factor in Malaysia, with up to 60% of cases having pre-existing or newly diagnosed type 2 diabetes.[4] Recrudescence from latent infection may be triggered by impaired immunity, such as tuberculosis or acquired immunodeficiency syndrome.[5] These findings are consistent with our case report, which highlights disease recurrence in an older patient with diabetes and a prior history of disseminated melioidosis.

Melioidosis is widely recognized as “the great mimicker” because of its ability to affect any organ and present with a broad spectrum of clinical manifestations, ranging from benign skin and soft tissue lesions to a rapidly fulminant and fatal septicaemia. Ocular involvement can be either localized or as part of disseminated septicaemic melioidosis. Orbital cellulitis was the most common manifestation (44%) followed by endophthalmitis (25%), panophthalmitis (13%), preseptal cellulitis (13%), and panuveitis (6%).[6]

The gold standard for melioidosis diagnosis is isolation of *Burkholderia pseudomallei* from clinical specimens. Serological testing may aid presumptive diagnosis in severe septicaemic melioidosis cases or when infections are deep seated and tissue sampling is challenging.[7] This case emphasizes the diagnostic challenge posed by ocular melioidosis and the need for a high index suspicion in endemic regions, particularly among agricultural workers with relevant occupational exposure.

Treatment of fulminant melioidosis includes high-dose intravenous ceftazidime (100–120 mg/kg/day in divided doses), followed by an extended oral eradication phase to prevent relapse.[8,9] Despite initiation of systemic antibiotic, the occurrence

of endogenous endophthalmitis would still be unpreventable. Although antimicrobial therapy has shown to be effective, melioidosis is still highly associated with high mortality due to severe sepsis and its complications.

In most cases, the definitive management of ocular cases is surgery, including incision and drainage, debridement, pars plana vitrectomy, and/or enucleation. Despite appropriate systemic and intravitreal antimicrobial therapy, our patient declined surgical intervention and was left legally blind, underscoring the therapeutic challenges and poor visual outcomes associated with delayed or incomplete management.

Conclusion

In summary, ophthalmologists should maintain a high index of suspicion for ocular melioidosis in patients with ocular infections that fail to respond to conventional antibiotic therapy, particularly in endemic regions such as Malaysia. Although rare, ocular melioidosis can result in severe and irreversible visual impairment. Prompt recognition and timely initiation of appropriate systemic antimicrobial therapy, with or without surgical intervention, remain critical for optimizing visual outcomes and reducing mortality.

Declarations

Informed consent for publication
The patients provided informed consent for the publication of the clinical data and images contained in this case report.

Competing interests
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