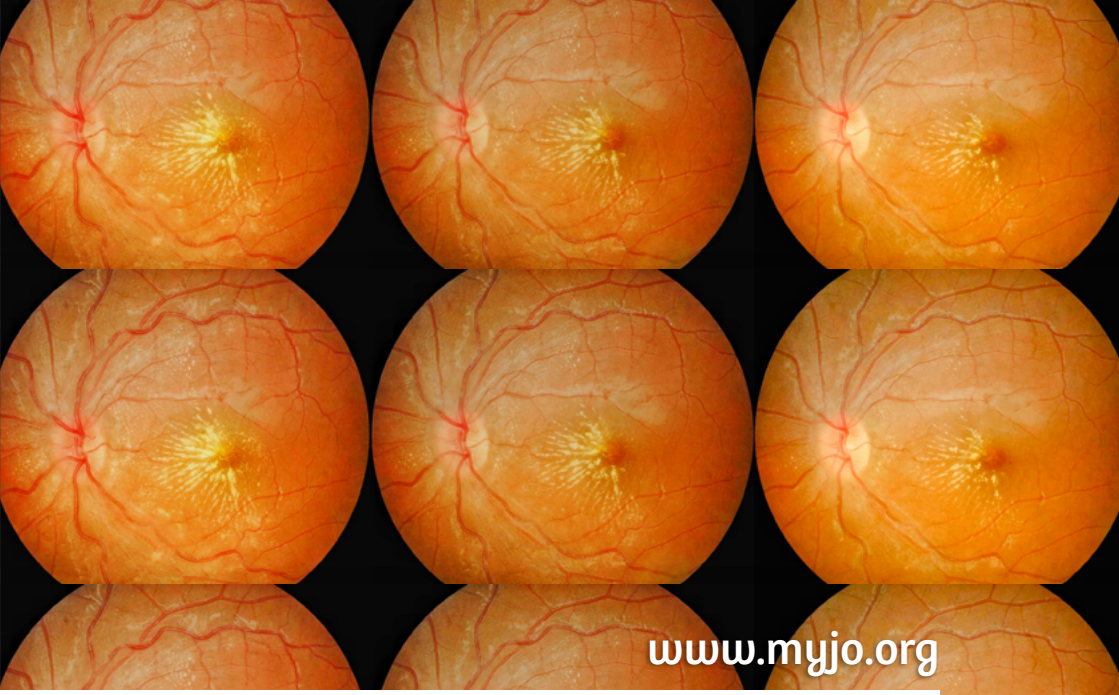

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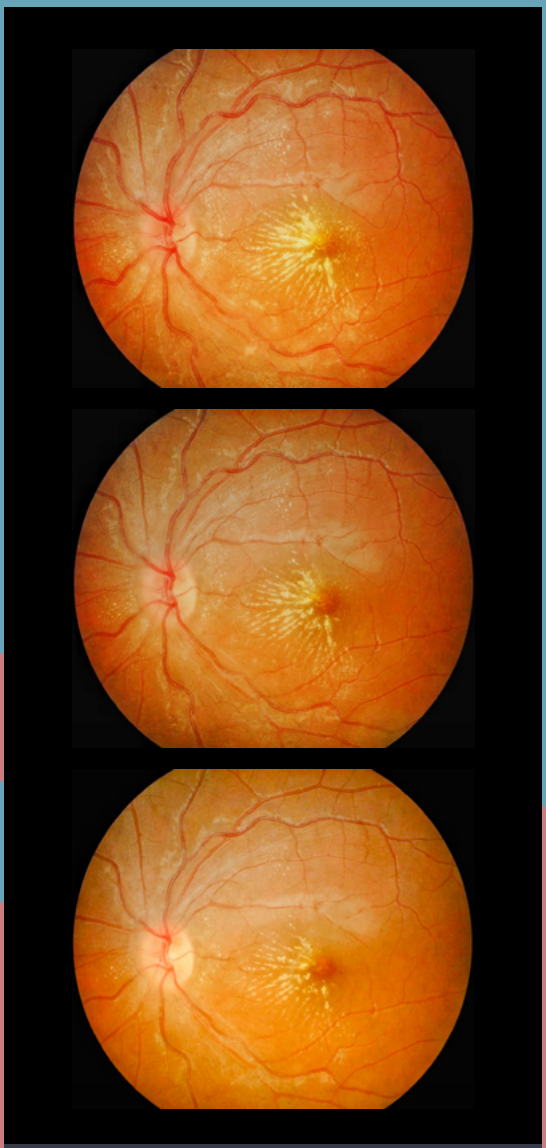

ABOUT THE COVER IMAGE

Meow, the scratchy star features a case of ocular bartonellosis. The image belongs to the personal collection of Dr. Wan Hazabbah Wan Hitam, Universiti Sains Malaysia.

Malaysian Journal of Ophthalmology

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Table of contents

Case reports

Eye-quiz

Malaysian Journal of Ophthalmology

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Editorial
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The association of platelet indices with diabetic retinopathy: what's next?

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Continuous discoveries in the knowledge of diabetic retinopathy have led to a better understanding of this complex disease that has been dominating the ophthalmology fraternity for several decades. Generally, the concepts of micro-occlusion and micro-infarction have been seen to be of primary concern. Nevertheless, there are other important angles or pathological processes that must be emphasized to manage the condition optimally. Although some countries have progressed rapidly in the management of diabetic retinopathy, most countries still consider this disease an uphill challenge to battle against. Changing the approach from treating the end stage of the disease to proactive care could therefore help the health care system to approach the problem from a different angle.

The availability of various intravitreal anti-VGEF treatments have currently given us much hope in the treatment of diabetic macular oedema. Imagine the impact of a paradigm shift in health care if we were able to objectively measure the severity of a disease before it progresses and becomes more difficult to treat. In other words, even if we are not extremely successful with our comprehensive prevention efforts, we could potentially be able to address the increasing problems of diabetic retinopathy in our society with proactive management measures.

The association between ischemic heart disease and mean platelet volume as an important clinical biomarker has been well studied. The fact that platelet parameters are potentially associated with increased thrombotic phenomena has provided a sound basis for ophthalmic researchers to investigate potential similar associations with ocular microthrombi.[1] Identifying the most appropriate indicators and levels of corresponding biomarkers could prove ground-breaking for the clinical management of diabetic eye disease.

Mean platelet volume (MPV) is one of the platelet indices positively related to platelet adhesion and aggregation.[2] A higher MPV value means a higher adhesion and aggregation rate. This plays a very important role in the damaged microcirculatory system in diabetic eyes. Therefore, it is not surprising that we see a consistent relationship between platelet indices and severe diabetic retinopathy.[2,3] Furthermore,

adhesion and aggregation could accelerate thrombosis formation in the presence of persistent vascular endothelial damage in diabetic patients. Ongoing research into the relationship between sorbitol metabolism and platelet indices may also change our perspective in the management of diabetic retinopathy in the future.[4-6] Hopefully, as more relevant indices are identified in the future, this will help to increase the likelihood of predictors of severe diabetic retinopathy.

The research article by Pradipta *et al.* in this current issue is one of the long-awaited findings from our region that further support the strong correlation between platelet indices and severity of retinopathy.[7] It is interesting that the correlation becomes much clearer when it reclassifies groups of retinopathy. It is easy to understand that our clinical classification is based on the apparent signs. The final correspondence between laboratory values and clinical findings will be better defined with similar research in the future. We look forward to further publications on relevant topics from this part of the region, as diabetic complications are much more common in our population than in other parts of the world.

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Editorial
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From my laptop

A year of challenges and turbulence is finally coming to an end. Covid-19 is still here to stay and remains a significant part of our life. With the fear and anxiety of Covid-19, the wave of 'new normal' set in. The internet of things and everything virtual is now a big chunk of the new normal, including scientific conferences. The 10th Conjoint Ophthalmology Scientific Conference (COSC) 2020 turned virtual on 18–19 September 2021. This conference is a collaborative effort of Universiti Sains Malaysia, Universiti Malaya, Universiti Kebangsaan Malaysia, and Ministry of Health since 2011. The long history of COSC is available in the supplement accompanying this issue of the Malaysian Journal of Ophthalmology (MyJO). Do check out this interesting history!

MyJO marked another first with the publication of this supplement, which comprises abstracts accepted in the successful virtual 10th COSC. Kudos to Hospital Selayang team (Ministry of Health) for an informative, well organized, and interesting conference.

To all Malaysian ophthalmologists and the young trainees, please continue to work together toward the greater success of our fraternity in Malaysia and abroad. I wish you all a happy new year and a restful and well-deserved end of the year break. See you next year energized with new resolutions and new dreams. Let us dream for indexation of MyJO!

Till we meet again.

Professor Dr. Liza Sharmini Ahmad Tajudin
Chief Editor

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Mean platelet component in non-proliferative and proliferative diabetic retinopathy

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Abstract

Introduction: Diabetic retinopathy (DR) remains a visually debilitating disease and is commonly classified according to its severity as non-proliferative DR (NPDR) or proliferative DR (PDR). Those suffering from PDR tend to have worse vascular complications and prognosis. Platelets exposed by vasculopathy caused by DR may be activated to try to maintain haemostasis. This activity can be illustrated by the mean platelet component (MPC). Therefore, by MPC monitoring we may be able to predict the progression from NPDR into PDR.
Purpose: To investigate the difference of MPC in patients with NPDR and PDR.
Study design: Cross-sectional.
Materials and methods: This study involved 71 DR patients. Preliminary data regarding the patients' demographic characteristics, diabetes history, related diseases, medication history, and general eye examination were recorded. Fundus photographs were taken after dilating eyedrops and DR was graded by an ophthalmologist. The patients were grouped into NPDR and PDR. Mean platelet component was analyzed using the automatic hematology analyzer ADVIA 120.
Results: Mean platelet component (MPC) was 26.69 g/dl (± 1.79) and 25.52 g/dl (± 1.20) in the NPDR and PDR group, respectively (p = 0.002), but was not clinically significant. In depth analysis into the DR grades differed significantly between mild NPDR and high-risk PDR (p = 0.015), and moderate NPDR and high-risk PDR (p = 0.024). Using our definition of mild DR (mild and moderate NPDR) and severe DR

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(high-risk and advanced PDR), there was a significant difference with mean MPC of 27.01 g/dl (± 1.64) and 25.31 g/dl (± 1.22), respectively (p = 0.001). The proportion of activated platelets was also higher in severe DR. Negative correlations were found between MPC with duration of DM (r = -0.333; p = 0.004) and MPC with systolic blood pressure (r = -0.241; p = 0.043).
Conclusion: There was a significant difference in MPC between NPDR and PDR, but the results should be interpreted carefully. Further analysis between the mild and severe form of DR strengthened this finding.

Keywords: ADVIA 120, diabetic retinopathy, mean platelet component, non-proliferative diabetic retinopathy, platelet activation, proliferative diabetic retinopathy

Purata komponen platelet diabetik retinopati bukan proliferatif dan proliferatif

Abstrak

Pengenalan: Diabetik retinopati (DR) merupakan penyakit yang menyebabkan penurunan penglihatan dan sering diklasifikasi mengikut keterukan sebagai bukan proliferatif (NPDR) dan proliferatif (PDR). Pesakit PDR cenderung mengalami komplikasi vaskular dan prognosis yang lebih teruk. Platelet yang terdedah akibat vaskulopati yang disebabkan oleh DR boleh diaktifkan untuk pengekalan haemostasis dan ianya boleh dilihat dari nilai purata komponen platelet (MPC). Oleh itu, perkembangan NPDR ke PDR boleh diramal dengan pemantauan MPC.
Tujuan: Untuk mengkaji perbezaan MPC dikalangan pesakit NPDR dan PDR.
Rekabentuk kajian: Keratan rentas.
Material dan metodologi: Kajian ini melibatkan 71 orang pesakit DR. Data preliminari meliputi ciri demografi, sejarah diabetis, penyakit berkaitan, sejarah perubatan dan pemeriksaan umum okular direkodkan. Gambar fundus diambil selepas penggunaan ubat titis pengembangan mata dan ianya di gredkan kepada NPDR dan PDR oleh seorang Oftalmologis. Analisa MPC dilakukan menggunakan 'automatic hematology analyzer ADVIA 120'.
Keputusan: Nilai MPC adalah 26.69 g/dl (±1.79) untuk NDPR dan 25.52 g/dl (± 1.20) untuk PDR (p = 0.002), tetapi tidak signifikan secara klinikal. Analisa selanjutnya terhadap gred DR menunjukkan perbezaan signifikan antara NDPR ringan dan PDR risiko-tinggi (p = 0.015) dan antara NDPR sederhana dan PDR risiko-tinggi (p=0.024). Perbezaan yang signifikan (p = 0.001) turut didapati apabila pesakit diklasifikasikan kepada DR ringan (NDPR ringan dan sederhana) dan DR teruk (PDR risiko-tinggi dan teruk). Nilai MPC untuk DR ringan adalah 27.01 g/dl (±

1.64) dan untuk DR teruk adalah 25.31 g/dl (± 1.22). Kadar pengaktifan platelet juga didapati lebih tinggi dalam DR teruk. Korelasi negatif diperolehi antara MPC dan tempoh DM (r = -0.333; p = 0.004) dan antara MPC dan tekanan darah sistolik (r = -0.241; p = 0.043).
Kesimpulan: Terdapat perbezaan MPC yang signifikan antara NPDR dan PDR. Walaubagaimana pun keputusan ini perlu di interpretasi dengan teliti. Analisa selanjutnya antara DR ringan dan teruk mengukuhkan hasil kajian ini.

Katakunci: ADVIA 120, diabetik retinopati, diabetik retinopati bukan proliferatif, pengkatifan platelet, diabetik retinopati proliferatif, purata komponen platelet

Introduction

Diabetic retinopathy (DR) is a significant microvascular complication of diabetes mellitus (DM), which has a debilitating impact on vision and is the most frequent cause of blindness among adults aged 20–74 years.[1] Globally, the number of DR cases is expected to rise from 126.6 million in 2010 to 191.1 million in 2030.[2] The prevalence of DR among DM patients was reported to be from 27.8%[3] to 34.08%.[4] Patients with DR carry the risk of progressing into vision-threatening diabetic retinopathy (VTDR) and approximately 56.3 million will suffer in 2030 if no proper management is undertaken. Those with VTDR have lower quality of life and are burdened with higher cost of treatment.

DR is mainly classified into two large groups: non-proliferative diabetic retinopathy group (NPDR) and proliferative diabetic retinopathy (PDR). Between these two groups, the latter is more severe and tends to cause more visual complications. Several known complications related to PDR are retinal detachment, vitreous hemorrhage, and glaucoma, which are rarely found on NPDR. Therefore, PDR warrants early detection and thorough management.[5]

Increase in platelet reactivity has been stated to be a risk factor for progression to PDR. For example, one parameter of the platelet activation index, mean platelet volume (MPV), was increased in PDR subjects in China.[5] Another study also mentioned the role of platelet activation in inflammation, which worsened the state of DR.[6] Platelets are anuclear discoid cells that circulate in the bloodstream and contribute to hemostasis by mainly plugging damaged blood vessels. When activated, such as by endothelial dysfunction caused by chronic hyperglycemia in DM, they will change shape, adhere to the subendothelial surface, form thrombi, and secrete aggregation factors.[7,8] In another study, platelet aggregation was reported to be higher in PDR subjects compared with NPDR and normal subjects, further showing the difference in platelet activation between these groups.[9]

Platelet activation can be measured with a practical and relatively inexpensive method using an automatic hematology analyzer. Compared to traditional platelet

parameters such as MPV or platelet distribution width, mean platelet component (MPC) is considered the newer addition.[8] The MPC value represents platelet density, and upon activation, it will decrease due to the release of platelet granule contents.[10] Currently, there in no clinical guideline for using MPC in DM subjects with DR; therefore, evidence-based research is needed.

Materials and methods

Subjects

This study used a cross-sectional design, involving 71 subjects with DR during the study period at Dr. Sardjito General Hospital Yogyakarta from January to June 2018. The subjects were examined and their blood sampled to check for MPC density. The inclusion criteria were patients aged 30 years old or above, diagnosed with type 2 DM previously, with DR, willing to having their blood sampled, and who provided informed consent. Exclusion criteria for this study were subjects on antiplatelet therapy, subjects with coronary or congestive heart disease, subjects with deep vein thrombosis, rheumatoid arthritis, and chronic obstructive pulmonary disease, and subjects with 20 years of smoking history.

Data collection

Demographic and clinical data were taken prior to fundus photograph, including age, gender, DM history, related diseases, medication history, previous eye surgery, previous eye trauma, history of allergies, and general eye examination including visual acuity and anterior segment. From the fundus photographs, the subjects were classified as having NPDR or PDR and grouped accordingly. Blood sampling was performed and parameters such as HbA1c, CBC, MPC, and other platelet parameters were examined at the Laboratory of Clinical Pathology, Faculty of Medicine, Universitas Gadjah Mada. The study followed the tenets of the Declaration of Helsinki. The Ethics Committee of the Faculty of Medicine, Universitas Gadjah Mada-Dr. Sardjito General Hospital approved the study protocol. After detailed explanation, informed consent was obtained from each patient prior to examination.

Statistical analysis

Statistical analysis was performed using the SPSS 23.0 for Windows software. Data were expressed as the mean ± SD. Normality of all data samples was first confirmed by the Kolmogorov-Smirnov test. Differences in research subject characteristics were analyzed using the chi-square test for categorical data and unpaired t-test for numerical data if the distribution was normal or Mann-Whitney test if the distribution was abnormal. The mean MPC values was analyzed using the unpaired t-test, and the proportion between groups was analyzed using the chi-square test. To compare mean MPC between more than two groups, ANOVA test was performed.

Pearson correlation test was used for analyzing relationships between MPC and other parameters.

Results

Demographic characteristics are listed in Table 1. There were mostly female subjects in both groups; mean age was 58.96 ± 7.66 years and 55.65 ± 9.10 years for the NPDR and PDR groups, respectively. There was a significantly higher mean systolic blood pressure in the PDR group.

Table 1. Characteristics of the study subjects

Variable	**NPDR**	**PDR**	***p***
N (%)	51 (71.83%)	20 (28.17%)	< 0.001*
Gender, n (%) Male Female	 14 (27.5%) 37 (72.5%)	 6 (30%) 14 (70%)	0.830
Age, yr (± SD)	58.96 (± 7.66)	55.65 (± 9.10)	0.125
BMI (kg/m2)	24.73 (± 4.17)	23.82 (± 2.94)	0.378
DM duration, yr (± SD)	7.66 (± 8.12)	10.3 (± 6.37)	0.196
Visual acuity (logMar)	0.82 (± 0.52)	1.09 (± 0.67)	0.088
DR grade: Mild NPDR Moderate NPDR Severe NPDR Very severe NPDR Early PDR High-risk PDR Advanced PDR	 13 (18.31%) 20 (28.17%) 17 (23.94%) 1 (1.41%)	 4 (5.63%) 11 (15.49%) 5 (7.04%)	
HbA1c, % (± SD)	9.14 (± 2.38)	8.37 (± 2.30)	0.239
SBP (mmHg)	139.24 (± 21.37)	151.80 (± 20.59)	0.028*

NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy: N (%): numbers (percentage); BMI: body mass index; DM: diabetes mellitus, SBP: systolic blood presssure

Table 2 provides an overview of total MPC values in subjects with DR and betweeen genders. It also shows the differences in mean MPC between NPDR and PDR. Although the results were statistically significant, they were not clinically significant, as the difference between them was under 1.65 g/dl. Furthermore, 1.65 g/dl is the difference in mean MPC between normal subjects and those with heart failure, since we did not discover any that correspond to NPDR and PDR at the time. This number was determined at the beginning of the sample calculation by using another MPC study on vasculopathy.[11]

Table 2. MPC values in subjects with diabetic retinopathy

Variable	n	Mean (g/dl)	SD	MPC (g/dl)		*p*
				Minimum	Maximum	
Male	20	25.92	± 1.67			0.176
Female	51	26.53	± 1.70			
Total †	71	26.36	± 1.71	22.70	29.70	
NPDR	51	26.69	± 1.79			0.002*
PDR	20	25.52	± 1.20			

MPC: mean platelet component; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; MPC: mean platelet component; †Total: MPC of NPDR and PDR subjects

*$p < 0.05$: was considered statistically significant

Figure 1 further analyzes the relationship between DR severity and MPC values. There were significant differences in MPC values between mild NPDR groups and high-risk PDR ($p = 0.015$), and between moderate NPDR and high-risk PDR ($p = 0.024$).

Table 3 shows the proportion of MPC values under 26.7 g/dl, which is the MPC value on activated platelets.[8] In this study, it was found that the PDR group had a significantly greater proportion of MPC values below 26.7 g/dl.

Table 4 displays the mean MPC for subjects with mild DR (mild and moderate NPDR) and severe DR (high-risk and advanced PDR); the difference was statistically and clinically significant ($p = 0.001$, difference >1.65 g/dl). It also presents the proportion test between those groups by using MPC value limit of 26.7 g/dl. The results showed that in the severe DR group (high-risk and advanced PDR) the proportion of MPC values below 26.7 g/dl was significantly greater than in the mild DR group (mild and moderate NPDR).

This study also analyzed the correlations of MPC with age, DM duration, and systolic blood pressure using the Pearson method. A significant correlation was found between MPC levels and duration of DM ($r = -0338$; $p = 0.004$), and between MPC and systolic blood pressure ($r = -0.241$; $p = 0.043$). There was no significant relationship between MPC and age ($r = -0.410$; $p = 0.735$).

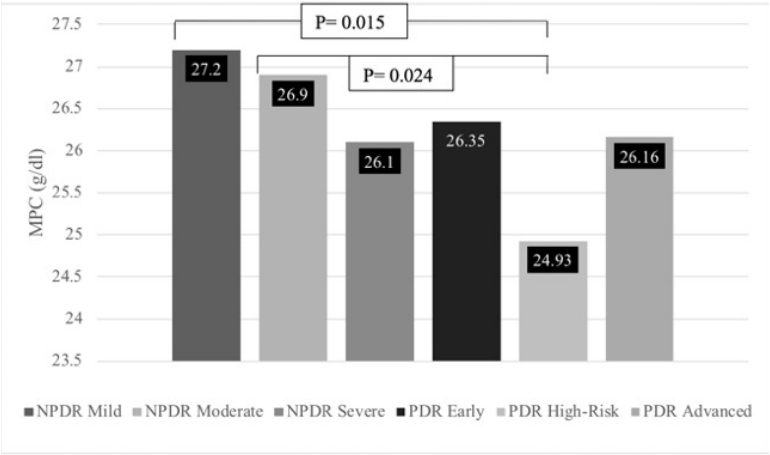

Fig. 1. The mean MPC values for each diabetic retinopathy severity.

Table 3. Proportion of MPC values < 26.7 g/dl between NPDR and PDR

Variable	NPDR (n = 51)	PDR (n = 20)	*p*
MPC < 26.7 g/dl	20 (39.2%)	18 (90%)	< 0.001*
MPC > 26.7 g/dl	31 (60.8%)	2 (10%)	

NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; MPC: mean platelet component
*$p < 0.05$ was considered statistically significant

Table 4. Difference in mean MPC between mild DR (mild and moderate NPDR) and severe DR (high-risk and advanced PDR)

Variable	Mild and moderate NPDR (n = 33)	High-risk and advanced PDR (n = 16)	*p*
MPC (g/dl), (mean ± SD)	27.01 (± 1.64)	25.31 (± 1.22)	0.001*
MPC < 26.7 g/dl	10 (30.3%)	15 (93.8%)	< 0.001*
MPC > 26.7 g/dl	23 (69.7%)	1 (6.2%)	

NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; MPC: mean platelet component
*p < 0.05 was considered statistically significant

Discussion

In this study, there were more women than men in both groups. This has been supported by several prior studies showing that more women suffer from DM and greater DR severity.[12-14] The mean age was higher in the NPDR group; this may be due to our sample size, which is smaller than that of previous studies. The mean age in the PDR group was similar to that in prior studies, with a range of 50–64 years.[15] The BMI between the two groups was not statistically significant. This result may reflect the conflicting findings between high BMI as a risk factor[16] or even protective[17] for DR.

The average duration of DM was higher in the PDR group, similar to Kajiwara *et al.*[14] This is explained by the fact that greater DM duration tends to cause greater microvascular damage. Visual acuity between the two groups was not statistically significant, but a lower average was obtained in the PDR group, which was similar to previous studies.[18] HbA1c level was not statistically significant, which may be due to more strict sugar control in severe DR groups. The examination of systolic blood pressure shows a significantly higher result in the PDR group, in accordance with the theory that increase in pressure triggers deterioration of DR.[19]

This study evaluated the characteristics of MPC in all subjects to provide more data regarding MPC in DR patients. The mean obtained was 26.36 g/dl, illustrating that most subjects experience platelet activation, represented by MPC values below 26.7 g/dl.[8] Activated platelets release granules, causing their density to lessen, which results in decreasing MPC value.[10] The mean MPC between NPDR and PDR was found to be statistically significant, but not clinically significant because the difference was less than 1.65 g/dl. This limit was determined in the sample calculation by using other vasculopathic abnormalities[11] as a reference since there is no MPC-related research with DR that can represent it. Considering those results, this study further examined the difference in MPC values between DR severity (Fig. 1) and obtained statistically and clinically significant results between mild NPDR and high-risk PDR, and between moderate NPDR and high-risk PDR. This shows there is higher platelet activation in high-risk PDR. This can be caused by neovascularization triggered by retinal ischemia.[20] In these conditions, abnormal blood vessels grow and are easily damaged, leading to more platelets being activated. Activated platelets release intracellular substances stored in alpha and dense granules to begin the process of hemostasis.[21] One component contained within the granule is vascular endothelial growth factor (VEGF), which spurs neovascularisation, thus worsening DR.[22,23] On the other hand, in the advanced PDR group there was no significant difference from mild or moderate NPDR; this could be due to the complete neovascularisation process and regression.[24] Another possibility is the use of long-acting antidiabetic drugs in advanced PDR subjects that are likely to affect the platelet activation index.[25] However, there is no evidence to prove a relationship with MPC. When compared with the NPDR group, the number of activated platelets in the PDR group

had a greater proportion (Table 3), in agreement with the previous theory.[20,26]

Based on the results, this study also conducted a comparison of MPC values in mild DR (defined as mild and moderate NPDR) with severe DR (defined as high-risk and advanced PDR). The results are listed in Table 4, which shows significant difference on the mean MPC and the proportion of activated platelets. The mean MPC value is significantly lower in severe DR, which is consistent with the theory that worse DR has more activated platelets.[27,28]

In addition to MPC values between NPDR and PDR, this study also analyzed MPC based on gender, as well as the association of MPC with age, DM duration, and systolic blood pressure. The findings in Table 2 showed that there was no statistically significant difference in MPC between men and women, which is in accordance with previous studies on platelet parameters.[29] In the correlation test with age, no statistically significant results were obtained, although a negative correlation was found, similar to a previous study on the Korean population.[30] As for the duration of DM and systolic blood pressure, there was a significantly negative correlation with MPC; this indicates that the longer a person has DM or the higher the systolic blood pressure, the lower the MPC value. This is because the duration of prolonged DM will exacerbate vasculopathy in DR[31] and high systolic blood pressure will result in endothelial dysfunction.[32]

The main limitation of the present study is its retrospective nature, which cannot establish a causal relationship between MPC and PDR development. Furthermore, the grouping of subjects into NPDR or PDR was based only on the assessment of neovascularization through fundus photographs. Although fundus photographs have a sensitivity between 88.9% and 97.7%, and a specificity between 98.9% and 100% to detect DR,[33] we did not use a seven-field stereo fundus, which could have led to underestimation of the number of PDR subjects.[34]

In summary, PDR subjects have lower MPC values compared with NPDR. This distinction grew when a comparison was made between the lower and higher end of the disease spectrum. These data suggest that MPC has a role in disease progression on subjects with NPDR. The authors suggest that further studies are needed to observe whether MPC values can be used to predict the progression of NPDR into PDR, thus allowing earlier management.

Declarations

Ethics approval and informed consent

The study followed the tenets of the Declaration of Helsinki. The Ethics Committee of the Faculty of Medicine, Universitas Gadjah Mada-Dr. Sardjito General Hospital approved the study protocol. After detailed explanation, informed consent was obtained from each patient prior to examination.

Competing interests
None to declare.

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Refractive outcomes of laser-treated and non-laser-treated retinopathy of prematurity at Hospital Selayang: a 2-year retrospective review

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Abstract

Objective: To compare the refractive outcomes of laser-treated and non-laser-treated retinopathy of prematurity (ROP) infant, at 2 years of age in Hospital Selayang.
Methods: Retrospective review involving patients born between 2016 and 2018. They were divided into those who were treated with laser photocoagulation, and those who were observed. Laser treatment was given to infants with threshold and high-risk, pre-threshold disease. Refractive error was identified by cycloplegic refraction at 2 years of age.
Results: There were 22 eyes from 11 infants in the laser-treated group, all of which had zone II ROP with plus disease; of these, four had stage 2 ROP and 18 had stage 3 ROP. There were 53 eyes from 28 patients in the non-laser-treated group. The mean birth weight for the laser-treated and non-laser-treated groups was 966.9 ± 92.6 g and 1019.3 ± 282.0 g, respectively ($P = 0.398$). Mean gestational age for the laser-treated and non-laser-treated groups was 28.2 ± 2.2 weeks and 27.7 ± 2.2 weeks, respectively ($P = 0.390$). At 2 years, the mean spherical equivalence for the laser-treated and non-laser treated groups was -0.55 ± 2.49 D and +0.17 ± 1.43 D, respectively, although the difference was not statistically significant ($P = 0.120$). Myopia was

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commoner in the laser-treated group (six eyes [27%] *vs* five eyes [9%], *P* = 0.047), and two eyes from two different infants (10%) from this group also developed high myopia (> -6.00 D). For hypermetropia and astigmatism, there were no statistically significant differences between the groups (all *P* > 0.05). High myopia was strongly related to the post-conceptual age when receiving laser therapy (*P* = 0.025). In the laser-treated group, two infants (9%) had amblyopia and one (5%) had exotropia at 2 years of age. None of the eyes developed structural retinal sequelae.
Conclusion: Despite successful treatment of ROP, a significant number of laser-treated eyes developed myopia. This highlights the need for long-term refractive screening in these patients.

Keywords: laser, Malaysia, myopia, refractive error, retinopathy of prematurity

Hasil refraksi bayi retinopati pra-matang yang dirawat dan tidak dirawat dengan laser di Hospital Selayang: Kajian retrospektif 2 tahun

Abstrak

Objektif: Membandingkan hasil refraksi bayi pra-matang yang mempunyai masalah retinopati pra-matang (ROP) yang dirawat dengan laser dengan yang tidak diberikan rawatan laser di Hospital Selayang.
Metodologi: Reviu retrospektif melibatkan bayi yang dilahirkan diantara 2016 dan 2018. Bayi pra-matang dengan ROP dibahagikan kepada 2 kumpulan iaitu yang dirawat dan yang tidak dirawat menggunakan laser. Rawatan laser diberikan untuk kes ambang dan pra-ambang yang berisiko tinggi. Nilai refraksi diukur pada umur 2 tahun.
Keputusan: Sebanyak 22 biji mata dari 11 bayi yang mendapat rawatan laser, dan 53 biji mata dari 28 bayi yang tidak mendapat rawatan laser digunakan dalam kajian ini. Kesemua 22 biji mata yang mendapat rawatan laser mempunyai ZON II ROP dengan penyakit plus. Dari jumlah tersebut, 4 mempunyai ROP peringkat 2 manakala 18 mempunyai ROP peringkat 3. Purata berat lahir bagi kumpulan yang dirawat laser dan tidak dirawat laser adalah 966.9 ± 92.6 g dan 1019.3 ± 282.0 g (*P* = 0.398) secara berturut. Purata umur kehamilan bagi kumpulan yang dirawat laser adalah 28.2 ± 2.2 minggu dan yang tidak menerima rawatan laser adalah 27.7 ± 2.2 minggu (*P* = 0.390). Pada rawatan susulan 2 tahun, purata sfera setara bagi kumpulan yang dirawat laser dan tidak dirawat laser adalah -0.55 ± 2.49 D dan 0.17 ± 1.43 D, namun perbezaannya tidak signifikan (*P* = 0.120). Peratusan miopia adalah lebih tinggi untuk kumpulan yang menerima rawatan (6 mata [27%]

berbanding 5 mata [9%], $P = 0.047$) dimana 2 biji mata dari 2 bayi yang berbeza (10%) didapati mempunyai miop tinggi (> -6.00 D). Tidak ada perbezaan statistik yang signifikan untuk hipermetropía dan astigmatisma (semua $P > 0.05$). Miopia tinggi berkait dengan umur bayi ketika mula menerima rawatan laser ($P = 0.025$). Dalam kumpulan yang dirawat laser, dua bayi (9%) mempunyai ambliopia dan seorang (5%) mempunyai eksotropia pada usia 2 tahun. Tiada mata yang mempunyai komplikasi pada struktur retina.

Kesimpulan: Kebanyakan mata bayi ROP yang berjaya dirawat dengan laser mengalami masalah miopia. Ini menunjukkan kepentingan pemeriksaan refraktif susulan untuk kumpulan pesakit ini.

Kata kunci: laser, Malaysia, miopía, kesalahan refraksi, retinopati pramatang

Introduction

Retinopathy of prematurity (ROP) is a proliferative vascular retinopathy affecting mainly low birth weight and premature infants. It is caused by the abnormal development of retinal blood vessels in premature infants, and may be either mild with no subsequent complications, or aggressive with neovascularisation and even retinal detachment. The prevalence of severe ROP varies from 5% to 26% of premature births and is strongly associated with lower birth weight and lower gestational age infants.[1] Comparison between different population-based studies is difficult because of variability in study designs, gestational ages of included infants, survival rates, and treatments used. In 2017, the Malaysian National Neonatal Registry (MNNR) reported that from a total of 16,449 babies in the NICU of 44 participating hospitals, 20.2% of babies were born below 32 weeks' gestation and 22.9% had birth weights of 1,500 g and below.[2] Of the 1,899 premature infants who underwent ROP screening, 13.3% had ROP stages 1 and 2, and 2.2% had ROP stage 3.[2] With advances in neonatology allowing better survival of infants with extremely low gestational age and birth weight, it is anticipated that there will be an increase in the number of ROP cases in the future.

Globally, ROP is the leading cause of vision-threatening conditions in infants, ranging from 33% to 73%.[3] Myopia is the most common sequelae, accounting for up to 80% of infants with ROP. Even in successful anatomical outcomes, severe myopia remains an important cause of visual impairment, especially in eyes that have received laser treatment. The Early Treatment for Retinopathy of Prematurity (ETROP) study revealed an increased prevalence of myopia and high myopia in eyes with laser-treated ROP than in eyes with spontaneously regressed ROP without laser treatment.[4] Other complications of ROP include strabismus (23% to 47%),[3] amblyopia (19% to 53%),[5,6] retinal detachment (22%),[7] and acute angle-closure glaucoma, which can occur in cicatricial ROP.[8]

There is limited data on refractive outcomes of laser-treated ROP eyes in the Malaysian population. In this study, we set out to report the refractive outcome at the 2-year follow-up among laser-treated and non-laser treated (observed) ROP infants in Hospital Selayang.

Methods

This was a retrospective study of the medical records of pre-term infants with ROP born in Hospital Selayang between 2016 and 2018. This study adhered to the tenets of the Declaration of Helsinki and ethical approval was obtained from the Ethical Committee for Medical Research in Hospital Selayang (research ID: 61604). Infants were included in the study if they were born at or less than 32 weeks of gestation, had a birth weight of 1,500 g or below, were diagnosed with ROP, and completed 2 years of eye clinic follow-up. Infants were excluded if they were treated with intravitreal anti-VEGF, given cryotherapy, or had incomplete medical records. ROP was classified based on the International Classification of Retinopathy of Prematurity (Table 1).[9] This classification reported ROP by retinal zone involvement, severity, extension in clock hours, and the presence or absence of plus disease. The infants were divided into two groups: ROP treated with laser and ROP which was observed. Laser treatment was given to infants with threshold and high-risk, pre-threshold ROP (indications as in Table 2, based on the 2005 Malaysian Clinical Practice Guidelines on ROP).[10-12]

When indicated, laser treatment was administered within 72 hours of diagnosis. Panretinal photocoagulation was applied to the avascular retina from the ridge to the ora serrata in a near-confluent manner, via laser indirect ophthalmoscopy with indentation by two trained ophthalmologists in the neonatal care unit. Once ROP had regressed and the retina had completed vascularization, the infants were followed up for cycloplegic refraction, fundus examination, and strabismus or other ROP sequelae. Refractive errors were documented at 1 and 2 years of age. Myopia was defined as an eye condition in which the spherical equivalent (SE) refractive error is ≥ -0.5 D when ocular accommodation is relaxed. Myopia was divided into two categories: low myopia (-0.50 D to < -6.00 D) and high myopia (≥ -6.00 D).[13] Hypermetropia was divided into low (< +5.00 D) and high (> +5.00 D). Astigmatism was classified as high if ≥ -2.00 D.[14] Data were analysed using SPSS version 26 (IBM Corporation, Armonk, NY, USA). Independent t-tests were used for comparison of continuous variables, and chi-square tests for categorical variables. Pearson correlation analysis was used to assess the correlation of myopic progression in the laser-treated ROP group, with gestational age, birth weight, stage of disease, total number of laser shots received, and post-conceptual age when receiving laser therapy.

Table 1. The International Classification of Retinopathy of Prematurity[9]

Location	
Zone I	Posterior retina within a 60° circle centred on the optic nerve
Zone II	Extends from the edge of zone I centrifugally to the nasal ora serrata
Zone III	Residual crescent of retina anterior to zone II
Extent	Number of clock-hours involved
Severity	
Stage 0	Immature retinal vasculature with no ROP
Stage 1	Demarcation line between vascularized and avascular retina
Stage 2	Ridge (demarcation line with height, width, and volume) ± small tufts of neovascular tissues
Stage 3	Ridge with extraretinal fibrovascular proliferation
Stage 4	Partial retinal detachment
4A	Extrafoveal detachment
4B	Retinal detachment includes fovea
Stage 5	Total retinal detachment
Plus disease	Vascular dilatation (venous) and tortuosity (arteriolar) of posterior retinal vessels in at least 2 quadrants of the retina

Table 2. Criteria for laser treatment in ROP (based on Malaysian Clinical Practice Guidelines on ROP, 2005)[10-12]

Threshold disease	**High-risk, pre-threshold disease**
Defined as having **all** the following: Stage 3 ROP in zone I or zone II Involving 5 or more contiguous clock hours; or 8 or more cumulative clock hours Presence of plus disease	Defined as **any** of the following: Zone I, any stage ROP with plus disease Zone I, stage 3 ROP without plus disease Zone II, stage 2 or 3 ROP with plus disease

Results

There were 56 premature infants with ROP of various stages born at Hospital Selayang between 2016 and 2018. Of these, 13 infants received laser treatment while 43 were observed. This study included 22 eyes of 11 infants that received laser treatment for ROP and 53 eyes of 28 infants that were only observed (two infants in the laser-treated ROP group and 15 in the non-laser-treated ROP group were lost to follow-up at the 2-year stage). Among the laser-treated infants, all had bilateral ROP involving zone II and thus received bilateral laser treatment. Of the total, four eyes had stage 2 ROP with plus disease, and the remaining 18 eyes had stage 3 ROP with plus disease. Four eyes had threshold disease and 18 eyes had pre-threshold disease. No infants had aggressive posterior ROP (APROP). As for the observed group, three infants had unilateral disease and two infants had pre-plus disease. Thirty eyes had zone II ROP, and 23 eyes had zone III ROP. There were 32 eyes with stage 1 ROP and 21 eyes with stage 2 ROP. There were no infants with stage 3 ROP, or ROP involving zone I in the observed group. Table 3 summarises the characteristics of the study population and laser parameters. Retreatment with laser was not required by any of the study infants.

Table 3. Characteristics of the study population

Parameters	**Mean ± SD (range)**		***p*-value* (95% CI)**
	Laser-treated ROP	**Non-laser-treated ROP**	
Mean gestational age (weeks)	28.2 ± 2.2 (26–32)	27.7 ± 2.2 (25–35)	0.390 (-0.6 to 1.6)
Mean birth weight (grams)	966.9 ± 92.6 (790–1075)	1019.3 ± 282.0 (586–1750)	0.398 (-175.3 to 70.5)
Post-conceptual age when receiving laser treatment (weeks)	40w 5d ± 2w 5d (36w–44w)	-	-
Total number of laser shots	2738.9 ± 708.4 (1707–4682)	-	-
Laser energy (mw)	238.2 ± 42.8 (180–340)	-	-

*t-test

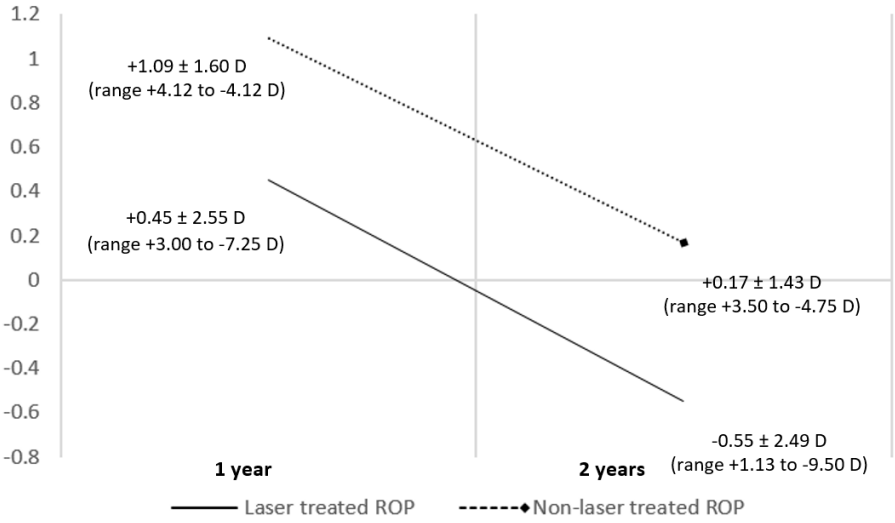

Fig. 1. Spherical equivalence outcomes at 1 and 2 years of age (mean ± SD). Note that differences between the groups at both 1 and 2 years were not statistically significant (P = 0.194 and P = 0.120, respectively).

Both groups of ROP eyes showed gradual increase in myopia at 2 years (Fig. 1). At 2 years, the mean SE for the laser-treated and non-laser treated groups was -0.55 ± 2.49 D and +0.17 ± 1.43 D, respectively, although the difference was not statistically significant (P = 0.120). Table 4 summarises the refractive outcome at 2 years. Two eyes (9%) from two different infants had high myopia, with SE of -9.50 D and -6.25 D, and both developed amblyopia needing treatment with contact lenses and eye patching. These eyes with high myopia received laser treatment at earlier post-conceptual ages of 36 weeks (for stage 3, zone II with plus and threshold disease) and 38 weeks (for stage 3, zone II with plus disease and pre-threshold disease), respectively. One infant (5%) had exotropia. All eyes had a favourable anatomical outcome and none of the eyes showed structural posterior pole sequelae such as narrowing of arcades, disc or macular dragging, vitreous membranes, or peripheral tractional retinal detachment. Pearson correlation analysis of myopic progression in the laser-treated ROP group with gestational age, birth weight, stage of disease, and total number of laser shots received showed non-statistically significant correlations (all $p > 0.05$). However, there was a statistically significant correlation between development of myopia and post-conceptual age when receiving laser therapy (r = 0.49, p = 0.025).

Table 4. Refractive error at 2 years of age

Refractive error	**Laser-treated ROP** ***n*** **(%)**	**Non-laser-treated ROP** ***n*** **(%)**	***p*-value*** **(*X*² value)**
Myopia Low myopia High myopia	6 (27%, range -0.50 to -9.00 D) 4 (18%) 2 (9%)	5 (9%, range -0.50 to -3.00 D) 3 (6%) -	0.047 (3.9) 0.090 (2.9) -
Hypermetropia	15 (68%, range +1.75 to +0.25 D)	36 (68%, range +3.50 to +0.50 D)	0.983 (0.0)
Emmetropia	1 (5%)	12 (23%)	0.059 (3.6)
Astigmatism High astigmatism	16 (73%, range -0.50 to -2.50 D) 1 (5%)	43 (81%, range -0.50 to -3.50 D) 3 (6%)	0.419 (0.7) 0.845 (0.0)

*Pearson chi-square test (X^2)

Discussion

In our study population, the mean birth weight and gestational age for laser-treated ROP infants was 966.9 g and 28.2 weeks, respectively. These are consistent with data from other Asian countries that report higher birth weights and gestational ages compared to Western studies.[14-18] For example, the ETROP study from the United States reported mean birth weight and gestational age as 703 g and 25 weeks, respectively.[18] These differences may be attributed to ethnic variations, and increased survivability of lower birth weight and younger infants in Western or more developed countries.

In our study, although not statistically significant, the SE at 2 years was more myopic for the laser-treated group than for the non-laser treated group (-0.55 ± 2.49 D *versus* +0.17 ± 1.43 D, respectively). The mean change of SE in 1 year duration for the laser-treated and non-laser treated groups was -1.00 ± 1.10 D and -0.94 ± 0.96 D, respectively (p = 0.813). We wonder if statistical significance would have been reached with a larger sample size. The myopia rate for our laser-treated patients was 27%, with presence of high myopia in 9%. This compares to only 9% with myopia and no cases of high myopia in the observed group. Our rates are similar to those reported by Katoch *et al.*, where from a total of 69 laser-treated ROP eyes, 24.7% of eyes had low myopia and 1% had high myopia.[19] In general, this pattern of higher prevalence and greater severity of myopia among laser-treated ROP was also

seen in other studies with onset as early as 6 months to 3 years.[4,14,16,20] A literature review on refractive errors in laser-treated ROP eyes (Table 5) shows a difference in prevalence of myopia ranging from 26% to 93%. Again, we believe this large range in myopia rates is due to the variability in study design, study population in terms of cultural diversity and access to health care, gestational ages of included infants, survival rates, and treatment used. It is postulated that tissue destruction from the laser-treated avascular peripheral retina may cause alterations in the development and maturation of the zonules, ciliary body, and lens.[5] While premature infants without ROP or those with spontaneous resolution of ROP may also develop myopia, the magnitude is lower compared with treated ROP.[21,22]

Most studies have reported that the prevalence of myopia is positively correlated with lower birth weight and greater severity of ROP.[3,19,23] Few studies have also found that progression to myopia is associated with a greater number of clock hours of ROP, a greater number of laser spots, and a longer time for disease regression.[16,24] In this study, there was no statistically significant correlation between myopic progression and either gestational age, birth weight, stage of ROP, or total number of laser shots received. However, we report a statistically significant association of myopia with younger post-conceptual age when laser treatment was first given. This finding is similar to that of Lok *et al.,* where it was suggested to be related to increased susceptibility of eyes towards laser therapy and more aggressive ROP presented at an earlier age of life.[25]

Currently, the recommended treatment for ROP is laser ablation to the peripheral avascular retina for eyes with threshold disease and high-risk, pre-threshold disease. Unfortunately, this laser therapy may destroy the peripheral retina, leading to peripheral vision loss. Recently, intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF), especially bevacizumab and ranibizumab, has been used as an alternative treatment and has offered benefit for disease stages previously not responsive or unsuitable for the standard laser therapy.[26] The use of anti-VEGF agents for the treatment of ROP is increasing worldwide. However, several aspects of anti-VEGF remain controversial, including its ocular efficacy, appropriate drugs and dosage, need for retreatment, and possibility of long-term systemic effects.[27,28] Anti-VEGF treatment has been speculated to provide better refractive outcomes.[29] However, it is still early to conclude the visual outcomes and confirm the long-term systemic safety. Both treatments of ROP, be it laser or intravitreal anti-VEGF, carry their own risks and benefits. Nevertheless, the risk of complications due to untreated ROP outweigh the risk of complications from laser or anti-VEGF treatment. The treatment choice also depends on the parents' decisions and medication costs. In Hospital Selayang, intravitreal anti-VEGF treatment for ROP was only started in 2019 and has involved relatively few infants so far.

A few limitations of this study include the retrospective nature of data collection, a relatively small number of eyes analysed, and short duration of follow-up. There was also limited information pertaining the extent of the laser treatment given in

Table 5. Refractive error prevalence in other studies.

Author (country, year)	MFU (years)	MBW (g)	MGA (weeks)	Eyes (*n*)	TM	HM	H	Others
Axer-Siegel *et al.*[30] (Israel, 2008)	3	834 ± 250	26 ± 2	194	55.2%	23.9%	*	Strabismus 29%, retinal detachment 3.8%
Katoch *et al.*[19] (India, 2011)	1	1121 ± 254	29 ± 2	69	26%	1%	59%	Strabismus 8%
Al-Otaibi *et al.*[16] (Saudi Arabia, 2012)	5	897 ± 34	27 ± 3	114	64%	29%	29%	Macular dragging 11%, retinal detachment 4%, exotropia 54%, esotropia 44%
Yang *et al.*[20] (China, 2012)	9	1256 ± 315	29 ± 2	60	93%	*	*	*
ETROP [4] (USA, 2013)	6	703 ± 148	25 ± 1	372	64.8%	35.5%	*	*
Ruan *et al.*[31] (China, 2014)	2	1410 ± 316	30 ± 2	115	45%	7%	*	*
Nguyen *et al.*[14] (Vietnam, 2015)	5	1426	30	100	59%	32%	21%	Strabismus 14%
Present study (Malaysia, 2021)	2	966 ± 93	28 ± 2	22	27%	9%	68%	Strabismus 5%, amblyopia 9%

MFU: mean follow-up; MBW: mean birth weight; MGA: mean gestational age; TM: total myopia; HM: high myopia; H: hypermetropia
Data presented as either mean ± standard deviation, or *n* (%). *Data not available.

the medical records. Our study, however, is still very relevant as there is limited data from Malaysia on the refractive outcomes of laser-treated ROP. We recommend further research into this less known topic for the Malaysian population to improve treatment regimens for sight-threatening ROP.

Conclusion

Despite achieving favourable anatomical outcomes, a significant proportion (27%) of laser-treated ROP eyes developed myopia at 2 years of age. This earlier emmetropisation may lead to the development of high myopia as the child grows, which may in turn lead to amblyopia or other complications from high myopia. This highlights the need for regular refractive screening and follow-up after laser treatment of ROP and treatment where appropriate to optimise the visual potential and outcomes in children.

Declarations

Ethics approval and consent to participate
This was a retrospective study of the medical records of pre-term infants with ROP born in Hospital Selayang between 2016 and 2018. This study adhered to the tenets of the Declaration of Helsinki and ethical approval was obtained from the Ethical Committee for Medical Research in Hospital Selayang (research ID: 61604).

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

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Cosmetic contact lenses: beauty can be blinding

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Abstract

Background: Although cosmetic contact lenses are ideally indicated for patients with corneal and iris abnormalities, they are currently fashionable among the younger generation of emmetropes to enhance their physical appearance. Cosmetic contact lens wearers carry a greater risk of microbial keratitis, even more so with counterfeit ones.
Case presentation: Here, we report two cases of counterfeit cosmetic contact lens wearers with *Acanthamoeba* keratitis (AK) who were misdiagnosed as herpes simplex virus (HSV) keratitis.
Conclusion: AK is a sight-threatening complication among contact lens wearers. Since clinically AK may masquerade as HSV, early diagnosis of AK is often delayed. As both microorganisms can mimic each other, determining the co-existence of both infections can be challenging. Delay in initiating proper treatment can lead to blinding complications.

Keywords: Acanthamoeba keratitis, cosmetic contact lens, herpes simplex masquerade syndrome, radial keratoneuritis

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Kanta sentuh kosmetik: kecantikan yang boleh menbutakan

Abstrak

Latar belakang: Secara idealnya, indikasi pemakaian kanta sentuh kosmetik adalah untuk pesakit yang mempunyai kornea atau iris mata abnormal. Namun, ianya kerap dipakai oleh generasi remaja emetrop untuk mempertingkatkan keterampilan diri. Pengguna kanta sentuh kosmetik berisiko tertinggi untuk jangkitan keratitis, dimana kesannya lebih teruk jika menggunakan kanta sentuh kosmetik tiruan.
Pembentangan kes: Dua (2) kes pemakai kanta sentuh kosmetik tiruan dengan Acanthamoeba keratitis (AK) yang telah di salah diagnos sebagai HSV keratitis di peringkat awal, dilaporkan.
Kesimpulan: Acanthamoeba keratitis adalah kompikasi yang mengancam penglihatan di kalangan pengguna kanta sentuh. AK selalunya sukar dikesan diperingkat awal kerana mudah menyamar sebagai herpes simplex virus, secara klinikal. Oleh itu, pengenalpastian keujudan mikroorganisma tersebut adalah mencabar. Kelewatan dalam memulakan rawatan boleh menyebabkan komplikasi terhadap penglihatan.

Kata kunci: Acanthamoeba keratitis, kanta sentuh kosmetik, keratoneuritis radial, sindrom penyamar herpes simplex

Introduction

Contact lenses are often used to replace spectacles, which are perceived as unattractive, particularly among younger age groups and females with refractive errors.[1] However, with the influence of social media, cosmetic contact lenses have lately gained popularity among emmetropes. Cosmetic contact lenses are often used to change the colour of the iris as well as the shape and size of the cornea without any surgical intervention. Despite regulation in many countries, counterfeit cosmetic contact lenses are widespread, especially in Southeast Asia including Malaysia.[2] The complications of cosmetic contact lenses are similar to those for refractive correction.[1]

Corneal infection is the greatest sight-threatening complication related to contact lenses. Contact lenses have been identified as a risk factor for *Acanthamoeba* keratitis (AK) in 95% of reported cases.[3] However, diagnosis of AK is often delayed and challenging. Here, we report two case cases of counterfeit cosmetic contact lens wearers who were misdiagnosed with herpes simplex masquerade syndrome.

Case presentation

Case 1

An emmetropic 19-year-old woman who regularly wore cosmetic contact lenses, presented with painful bilateral red eye, photophobia, tearing, and decreased visual acuity for a week. She bought her cosmetic contact lenses and lens solutions from various unauthorized sellers including through online shopping for the past 4 years. She also occasionally bought the extended wear contact lenses. She claimed to practice good contact lens hygiene techniques, but occasionally slept while wearing the contact lenses.

On examination, her visual acuity was 6/36 bilaterally. Anterior segment examination showed multiple epithelial pseudodendrites and epithelial erosion in both eyes. Bilateral corneal sensation was intact. Based on the clinical findings, she was treated as herpes simplex virus (HSV) keratitis and prescribed ointment acyclovir with oral analgesia. However, after a week of treatment, there was no improvement in her visual acuity. Subsequently, she developed bilateral keratoneuritis with multifocal stromal infiltrates and ring infiltrates. There was also the early formation of stromal abscess measuring 2 mm (vertical) x 1.6 mm (height) in the left eye but without the presence of cells. Bilateral corneal sensation was reduced. Both fundi were unremarkable. Corneal scraping found double wall *Acanthamoeba* cysts on haematoxylin and eosin (H&E) staining.

The diagnosis was revised as bilateral AK based on clinical findings and microbiological evidence. She was treated with topical chlorhexidine 0.02% and brolene 0.1% hourly for both eyes. A week after initiation of intensive treatment, pseudodendrite and ring infiltrate density lessened; visual acuity in the right eye improved to 6/24 but remained 6/36 in the left eye. After 3 months of treatment, visual acuity for both eyes improved to 6/18. The patient is, at the time of writing, still undergoing treatment with gradual tapering of medication.

Case 2

A 35-year-old schoolteacher and regular cosmetic contact lens wearer presented with reduced vision and painless bilateral red eye for a week. She was emmetropic but had been wearing cosmetic contact lenses for the past 5 years. She preferred extended wear contact lenses and often slept without removing them. She also often washed her face with tap water while wearing her contact lenses. She stopped wearing her contact lenses for a week after having eye redness related to her complaint.

On examination, visual acuity was 6/24 bilaterally. Anterior segment examination showed a peripheral dendritic lesion with stromal infiltrates in both eyes. There was diminished corneal sensation on both eyes. She was treated for HSV keratitis and started on ointment acyclovir and fluorometholone eye drops. One week later during her follow-up visit, her symptoms improved but there was

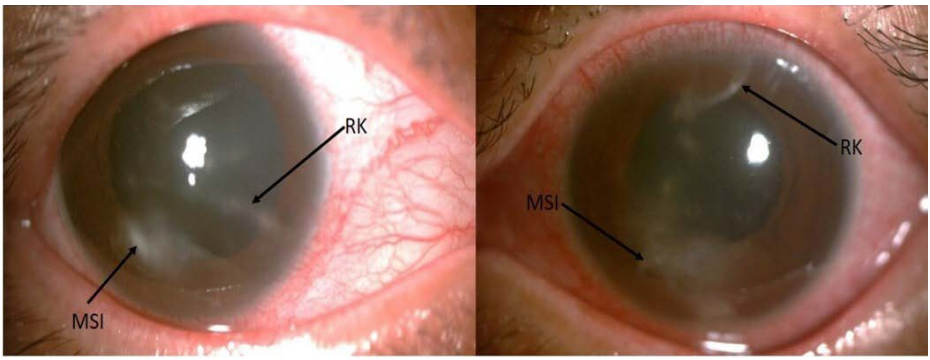

Fig. 1. Anterior segment photograph of Case 2 showing the presence of radial keratoneuritis (labelled RK) and stromal infiltrates (labelled MSI).

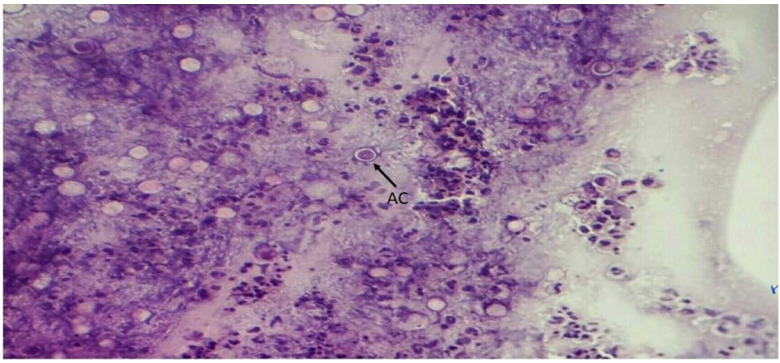

Fig. 2. Histopathological examination slide showing the presence of Acanthamoeba cyst (labelled AC) from the corneal scraping.

perineural infiltrates in both eyes (Fig. 1). Corneal scraping found double wall *Acanthamoeba* cysts on H&E staining (Fig. 2).

Diagnosis was revised as bilateral AK and the patient was started on topical chlorhexidine 0.02% and brolene 0.1% hourly for both eyes. There was clinical improvement with reduced density of perineural infiltrates after a week of intensive treatment. Visual acuity in the right eye improved to 6/12 and to 6/18 in the left eye. After 3 months of initial treatment, the perineural infiltrates resolved but her vision did not improve further. At the time of writing, the patient is still on treatment and long-term follow-up.

Discussion

Emmetropic cosmetic contact lens wearers may perceive they do not need specialist fitting or advice on adequate use and care of the lenses due to aesthetic and often infrequent usage. This perhaps increases the risk of microbial keratitis, a sight-threatening complication.[2] Increased roughness and the presence of dye in these cosmetic contact lenses increase the risk of trauma and infection.[1] Due to infrequent use, long exposure in contact lens solution may incubate microorganisms. AK has been reported in cosmetic contact lens wearers more often than in conservative contact lens wearers.[9]

Epithelial manifestations of AK include pseudodendrites, epithelial microerosions, and subepithelial microcysts. Pseudodendritic lesions in AK differ from those of HSV keratitis, where these do not have round spot-like widenings at the ending of the epithelial erosions.[4] The stromal manifestations include multifocal stromal infiltrates, Wessely immune rings, and radial keratoneuritis.

Both cases in this report demonstrated the presence of dendritic lesions with epithelial involvement (Case 1) and stromal involvement (Case 2). Epithelial involvement is usually suggestive of active replication of the virus, while stromal infiltration is associated with immune-mediated response to a non-replicating virus.[6] Ring infiltrates may be present in AK and HSV keratitis. Stromal oedema and infiltrates can occur in AK, which masquerade as a disciform lesion in HSV keratitis (Case 2). Decreased corneal sensitivity is another common sign for both corneal infections.[7] Thus, they can both mimic each other, which further delays management.[8]

HSV may reduce the healing ability and defence mechanism of the cornea, leading to an immunocompromised state. Thus, potential coexisting infections of *Acanthamoeba* and other organisms is possible.[5] Corneal sensitivity to mechanical stimuli is associated with the number of recurrences in HSV keratitis and part of the presenting signs of AK.[4] The absence of corneal sensation in Case 2 may further predispose to secondary infection and impaired healing process. However, no viral culture or polymerase chain reaction were done to confirm HSV. In addition, confocal microscopy has the potential to aid in differentiating HSV keratitis from AK.[7]

Both cases were treated initially as HSV keratitis based solely on clinical findings. Even though both cases appeared to improve, the pathognomonic sign of AK, a radial pattern of perineural infiltrates developed subsequently.[8] The cases were then treated as AK based on the clinical and microbiological evidence. General practitioners are advised to regard with a high index of suspicion corneal infections in patients with reduced vision and a history of contact lens use, particularly cosmetic ones. Although there was a slight delay in management, the infection was contained in both cases. However, both patients unfortunately developed visual impairment as the sequelae. It is thus important to raise awareness among the public of the danger of beauty to vision. Indeed, beauty is in the eye of the beholder.

Declarations

Consent for publication

The corresponding author declares to have received informed, sufficient, and express consent from the patients for the use of their clinical data and images in this article.

Competing interests

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Scedosporium scleritis following pterygium excision with conjunctival autograft

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Abstract

A 67-year-old female presented 6 months following left pterygium surgery with autoconjunctival graft with presumed episcleritis. Following a trial of topical dexamethasone, she returned with pain, reduced vision, and a donor-site scleral nodule. MRI orbits demonstrated scleritis, and oral prednisolone was commenced for presumed immune-mediated scleritis. Ten days later, vision reduced to light-perception with significant vitritis overlying a subretinal lesion associated with the donor site. A vitreous tap cultured *Scedosporium aurantiacum*. Treatment consisted of vitrectomy, scleral debridement with corneal patch graft, with both systemic and intravitreal voriconazole. Further scleral debridement was attempted but unable to be completed due to its posterior extent. As repeat MRI orbits showed persistent active scleritis in proximity to the optic nerve which posed a risk of meningitis, a decision was made for enucleation. This case highlights the difficulties in distinguishing between infectious and autoimmune scleritis, and the importance of excluding infection, particularly in eyes with prior surgery.

Keywords: conjunctival autograft, fungal scleritis, pterygium

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Skleritis scedosporium selepas pengasingan pterygium menggunakan cantuman auto konjuntiva

Abstrak

Seorang wanita berusia 67 tahun yang telah menjalani surgeri pterygium mata kiri dengan cantuman autokonjuntiva, disangka mengalami episkleritis 6 bulan selepas surgeri. Selepas menggunakan dexamethasone secara topikal, pesakit mengalami penurunan penglihatan, sakit mata dan kehadiran nodul sklera di tapak-penderma. MRI orbit menunjukkan skleritis dan prednisolone secara oral dimulakan untuk yang disangka skleritis 'immune-mediated'. Sepuluh hari kemudian, penglihatan pesakit menurun ke persepsi cahaya dengan vitritis meliputi lesi subretina yang berkait dengan tapak-penderma. *Scedosporium aurantiacum* telah dikultur menggunakan 'vitreous tap'. Rawatan yang diberi merangkumi 'vitrectomy', 'scleral debridement' dengan cantuman tampalan kornea serta voriconazole secara sistemik dan intravitreal. Cubaan untuk melakukan 'surgical debridement' lebih mendalam tidak berjaya kerana kedudukannya ditakat posterior. MRI orbit ulangan menunjukkan skleritis aktif berterusan berhampiran dengan saraf optik, yang menjadi risiko kepada meningitis. Oleh itu, enukleasi telah dilakukan. Kes ini menonjolkan kesukaran untuk membezakan antara skleritis autoimun dan berjangkit serta kepentingan untuk mengenalpasti jangkitan, terutama pada mata yang telah menjalani surgeri.

Keywords: cantuman auto konjuntiva, pterygium, skleritis fungus

Introduction

Infectious scleritis is a rare but potentially devastating complication of pterygium surgery. While infectious scleritis comprises only 5–10% of scleritis overall,[1] infection is the most common cause of scleritis following pterygium surgery with poorer outcomes compared to non-infectious scleritis.[2,3] Distinguishing between infectious and non-infectious scleritis poses a complex clinical challenge and incorrect diagnosis can result in significant ocular morbidity.

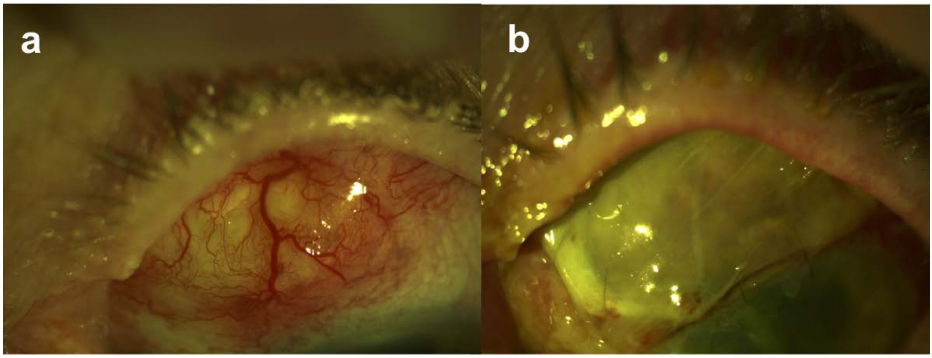

Fig. 1. The patient's left eye. (*a*) Slit-lamp image showing conjunctival injection and a scleral nodule. (*b*) Slit-lamp photo following scleral debridement, corneal patch graft, and amniotic membrane transplant.

Case report

A 67-year-old female presented with mild left eye discomfort 6 months following recurrent pterygium excision with autoconjunctival graft. Twenty-five years' prior, she underwent bilateral pterygium excision with beta-radiation. Her medical history included Graves' disease without thyroid eye disease, with no personal or family history of other autoimmune disease.

Examination was normal except for mild conjunctival injection at the donor site (Fig. 1). Dexamethasone 0.1% drops QID were started for presumed episcleritis. One month later, she re-presented with worsening pain and reduced corrected vision from 6/6 to 6/15. The donor site showed marked conjunctival injection and a non-necrotic scleral nodule without epithelial defect. Fundus examination showed a superonasal subretinal nodule with no overlying subretinal fluid. A serological infectious and autoimmune screen was unremarkable. MRI orbits showed superior scleral thickening (Fig. 2).

Oral prednisolone 50 mg daily was commenced for presumed autoimmune scleritis. Symptoms transiently improved, but the pain recurred following dose reduction to 12.5 mg 6 days later. Assuming the symptoms were secondary to the somewhat rapid taper, prednisolone was increased to 50 mg.

Four days later, she presented with light perception vision and dense vitritis overlying the subretinal nodule. A vitreous tap was performed alongside intravitreal voriconazole 100 mcg/0.1 ml, vancomycin 1 mg/0.1 ml, and ceftazidime 2.25 mg/0.1 ml. Hourly topical 1.5% gentamicin, 5% vancomycin, and 1% voriconazole were commenced. Prednisolone was ceased on a rapid taper. *Scedosporium aurantiacum* was isolated from intravitreal fluid and oral voriconazole 200 mg daily was commenced. A pars plana vitrectomy followed by scleral debridement with

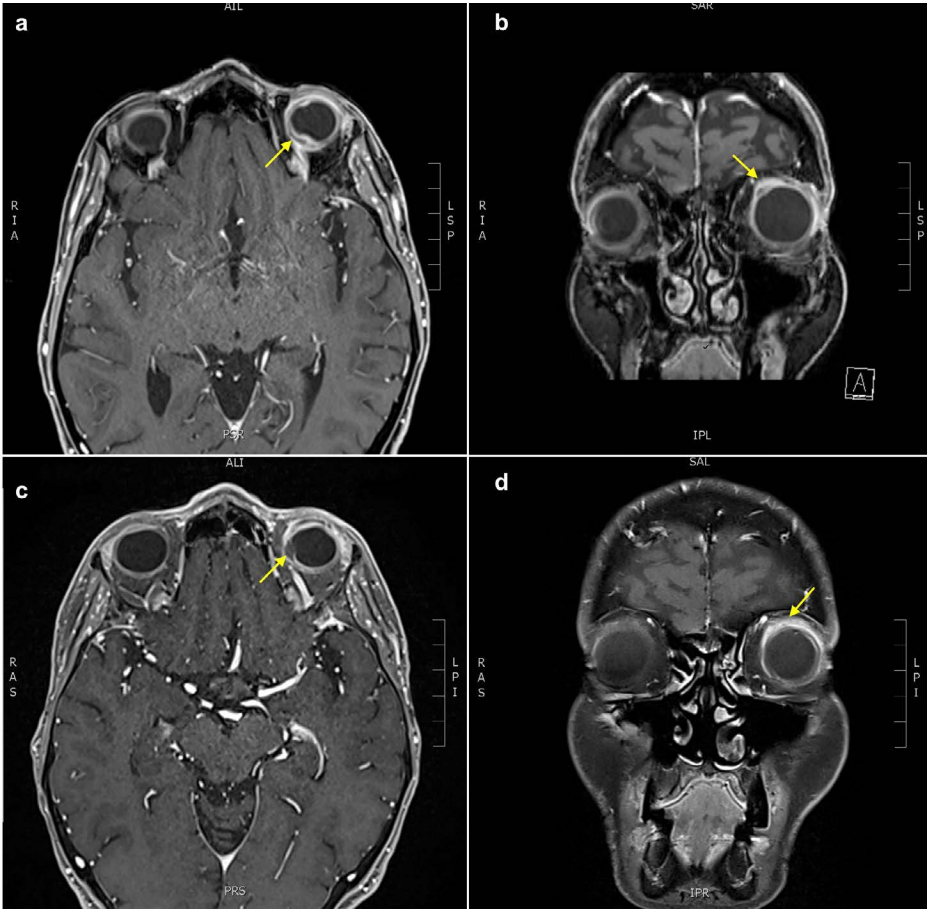

Fig. 2. MRI brain with T1-weighted imaging. (*a, b*) At presentation, thickening and enhancement of the left sclera with superomedial contour deformity consistent with scleritis and subchoroidal effusion. There was enhancement of the orbital optic nerve. (*c, d*) Following surgical excision with local and systemic antifungal treatment, there were improved but persistent inflammatory changes, as demonstrated by the hyperintense signal around the left globe and the residual superomedial subchoroidal collection.

corneal patch graft and amniotic membrane transplant was performed to promote corneal epithelialisation. Subsequently, the pain and vitritis resolved with reduction of the subretinal nodule.

One month later, severe pain recurred despite maximal medical therapy. Further scleral debridement up to 18 mm posterior to the limbus was performed, but the posterior extent could not be reached. Repeat MRI orbits demonstrated persistent

active scleritis adjacent to the optic nerve. Due to an inability to adequately debride the involved sclera and its proximity to the optic nerve, which the infectious disease specialists deemed to pose a risk of life-threatening meningitis, a decision was made for enucleation.

Discussion

Scleritis following pterygium surgery may be infectious or, less commonly, non-infectious. Amongst a wide range of bacterial and fungal microorganisms, *Pseudomonas aeruginosa* is the most common pathogen.[4-6] It is hypothesized that surgical destruction of conjunctival and episcleral vasculature predisposes the sclera to microorganism invasion.[5] The timing of onset of symptoms of infectious scleritis following pterygium surgery varies considerably, with several two large series reporting a mean interval of approximately 4 years.[4,7]

This case highlights the difficulty in differentiating between infectious and non-infectious scleritis, which have similar presentations and initially respond to immunosuppression. While the treatment for non-infectious scleritis involves steroid therapy, the treatment of infectious scleritis is antimicrobial therapy. Treating infectious scleritis as autoimmune scleritis can result in poorer outcomes.[3] As it can be very difficult to distinguish between the two entities, Doshi *et al.* suggest that, due to the devastating consequences of infectious scleritis, empirical treatment broad-spectrum topical antibiotics and antifungals is prudent.[2]

This case is unusual in two ways. Firstly, it is unusual for postoperative infectious scleritis to be non-necrotising, as the vast majority (93–95%) present with scleral necrosis.[4,7] Diagnosis can be particularly difficult in non-necrotising cases where a scrape cannot be taken. In patients without scleral necrosis, Jain *et al.* recommend performing a scleral scrape after the nodule is "de-roofed".[5] This case is also unusual in that the scleritis involved the donor site; the authors are not aware of this being described previously.

In summary, this case highlights the difficulties in distinguishing between infectious and autoimmune scleritis. In eyes with a history of prior surgery, infectious aetiologies are important to consider.

Declarations

Consent for publication

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

Competing interests
None to declare.

Funding
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None to declare.

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Case report
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Intravitreal moxifloxacin in acute post-phacoemulsification endophthalmitis: a case report

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Abstract

Background: Vancomycin and ceftazidime are commonly used intravitreal antibiotics to treat acute post-phacoemulsification endophthalmitis. However, they are not commercially available in appropriate therapeutic dose for intravitreal injection. Moxifloxacin is a broad-spectrum antibiotic that is commercially available in appropriate therapeutic dose for intravitreal injection, thus providing a rationale for its use in acute post-phacoemulsification endophthalmitis.
Case presentation: A 46-year-old female presented with blurred vision, redness, and pain in the right eye 5 days after phacoemulsification. Visual acuity was hand movement and conjunctival and circumcorneal injection, corneal oedema, anterior chamber reaction, and vitreous opacities were observed. The patient was treated with intravitreal moxifloxacin 500 µg/0.1 ml, vitrectomy, and topical and oral antibiotics. Visual acuity improved to 6/15 and follow-up at 5 weeks did not reveal any signs of intraocular inflammation.
Conclusion: Intravitreal moxifloxacin is an alternative in the treatment of acute post-phacoemulsification endophthalmitis.

Keywords: acute post-phacoemulsification endophthalmitis, intravitreal moxifloxacin

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Penggunaan moxifloxacin secara intravitreal untuk 'post-phacoemulsification endophthalmitis' akut

Abstrak

Latarbelakang: Vancomycin dan ceftazidime adalah antibiotik intravitreal yang kerap digunakan untuk rawatan 'post-phacoemulsification endophthalmitis' akut. Namun, dos terapeutik yang sesuai untuk suntikan intravitreal tidak terdapat secara komersial. Moxifloxacin adalah antibiotik spektrum lebar yang terdapat secara komersial dalam dos sesuai untuk suntikan intravitreal dan oleh itu menjadi rasional untuk rawatan 'post-phacoemulsification endophthalmitis' akut.
Pembentangan kes: Seorang wanita berusia 46 tahun hadir dengan kabur penglihatan, mata merah dan sakit pada mata kanan, 5 hari selepas 'phacoemulsification'. Hasil pemeriksaan mendapati akuiti visual adalah pergerakan tangan, injeksi konjuntiva dan 'circumcornea', oedema kornea, reaksi kamar anterior dan opasiti vitreous. Pesakit dirawat menggunakan intravitreal moxifloxacin 500 µg/0.1 ml, vitrectomy dan antibiotik topikal dan oral. Akuiti visual meningkat ke 6/15 dan pemeriksan susulan selepas 5 minggu tidak menunjukkan sebarang inflamasi intra okular.
Kesimpulan: Moxifloxacin intravitreal merupakan alternatif rawatan 'phacoemulsification endophthalmitis' akut.

Kata kunci: moxifloxacin intravitreal, 'phacoemulsification endophthalmitis' akut

Introduction

Endophthalmitis is an inflammation involving intraocular tissue and fluid that can be caused by microorganisms from exogenous (postoperative and post-traumatic) or endogenous (septicaemia) origins which occupy the anterior and posterior segments of the eye. Endophthalmitis is an ophthalmological emergency and may lead to permanent visual deterioration or even blindness if not dealt with prompt therapy.[1]

The incidence of postoperative endophthalmitis at Cipto Mangunkusumo-Kirana Hospital, Jakarta, Indonesia between January 2007 and July 2010 was 0.45% and 74.7% of those cases were found after cataract surgery.[2] The causative microorganisms were *Pseudomonas* species, *Staphylococcus epidermidis*, *Acinetobacter* species, haemolitic Streptococcus, *Klebsiella* species, *Streptococcus viridians*, *Bacillus* species, *Enterobacter* species, and *Serratia liquefaciens*.[2] Among of them, the most common causative microorganisms were *Pseudomonas* species (17%) followed by

S. epidermidis (11%), and *Acinetobacter* species (11%).[2]

Commonly used intravitreal antibiotics to cover gram-positive and gram-negative bacteria in acute post-phacoemulsification endophthalmitis are vancomycin and ceftazidime. However, vancomycin and ceftazidime are not commercially available in appropriate therapeutic dose for intravitreal injection, thus requiring manual dilution. This may increase the risk of contamination and dilution errors, which may further cause intraocular toxicity.

One of the newest fourth-generation fluoroquinolones is moxifloxacin, which targets both DNA gyrase and type IV topoisomerase. Moxifloxacin has superior coverage for gram-positive bacteria in comparison to second and third-generation fluoroquinolones and also sustains exceptional exposure for gram-negative bacteria with low minimum inhibitory concentration. We found two case reports where commercially available, undiluted moxifloxacin ophthalmic solution was administered intravitreally and found effective and safe in the treatment of post-traumatic endophthalmitis in humans.[3,4] These case reports provided the rationale for intravitreal administration of a single antibiotic with broad spectrum coverage in the case of acute post-phacoemulsification endophthalmitis we herewith present.

Case presentation

A 46-year-old non-diabetic female presented with sudden blurred vision, redness, photophobia, and pain in the right eye 5 days after phacoemulsification in the right eye. Visual acuity was hand movement. Blepharospasm, conjunctival and circumcorneal injection, chemosis, mild corneal oedema, +4 flare and +4 cells in the anterior chamber with 1 mm hypopyon, pupillary membrane occluding the pupil (Fig. 1A), intraocular lens (IOL) in the capsular bag, and intraocular pressure (IOP) of 20 mmHg were noted. B-scan ultrasonography showed vitreous opacities (Fig. 1B) and flat retina. We diagnosed the patient as acute post-phacoemulsification endophthalmitis. We started treatment with 0.5% moxifloxacin eye drops (Molcin HCl 5 mg/ml ophthalmic solution, Bekasi, Indonesia) hourly, combination of tobramycin 3 mg and dexamethasone 1 mg eye drops (Cendo Tobroson, Bandung, Indonesia) hourly, ciprofloxacin tablets 500 mg twice daily, atropine sulfate 1% eye drops (Cendo Tropin, Bandung, Indonesia) twice daily, timolol 0.5% eye drops (Cendo Timol, Bandung, Indonesia) twice daily, and emergency intravitreal injection of moxifloxacin 0.1 ml of 500 µg/0.1 ml (Molcin HCl 5 mg/ml ophthalmic solution, Bekasi, Indonesia) because we could not perform pars plana vitrectomy at the time.

Intravitreal injection of moxifloxacin was given under topical anaesthesia with tetracaine hydrochloride 0.5% (Cendo Pantocain, Bandung, Indonesia) using a 1 mL tuberculin syringe with a 30-gauge needle and inserted 3.5 mm posterior from the limbus in the inferotemporal quadrant. Previously, we performed anterior chamber paracentesis (0.1 ml) to take a specimen for culture and avoid IOP elevation.

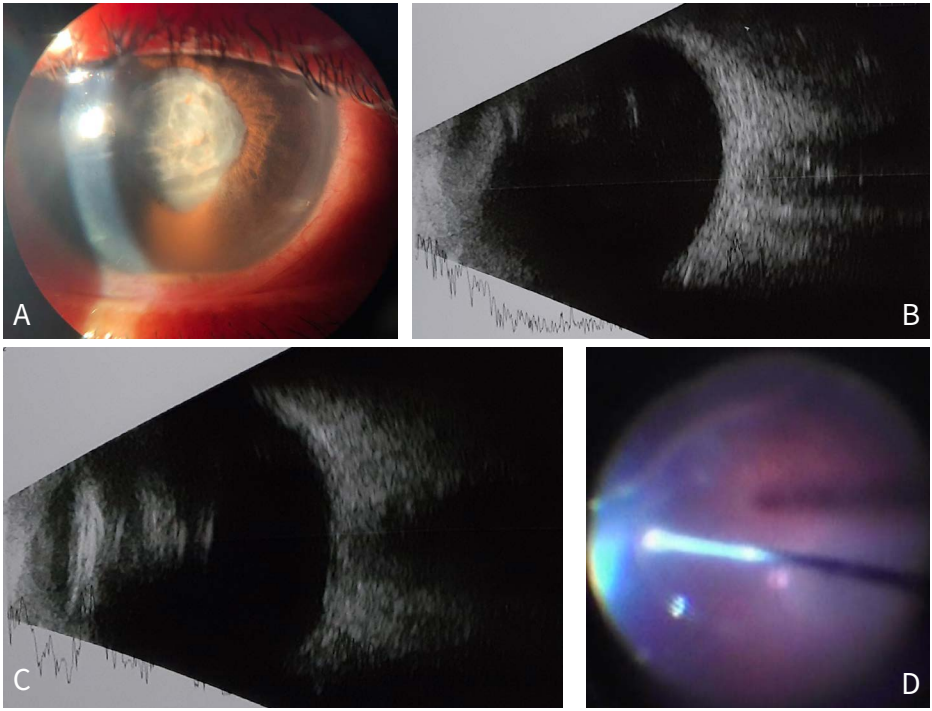

Fig. 1. Clinical features of the right eye on presentation: (*A*) chemosis, mild corneal oedema, +4 flare, +4 cells, 1 mm hypopyon, and pupillary membrane on the slit lamp examination, as well as (*B*) vitreous opacities on B-scan ultrasonography. (*C*) B-scan ultrasonography of the right eye after 24 hours of emergency moxifloxacin intravitreal injection showing no improvement of vitreous opacities. (*D*) Pars plana vitrectomy after 24 hours of emergency moxifloxacin intravitreal injection showing no improvement of clinical features and B-scan ultrasonography.

Twenty-four hours after the moxifloxacin injection, the clinical features and the B-scan ultrasonography did not improve (Fig. 1C), so we performed an elective pars plana vitrectomy under general anaesthesia (Fig. 1D). Previously, we took a vitreous sample (0.2 ml) through the vitreous cutter for culture and sensitivity. We repeated intravitreal moxifloxacin at the end of pars plana vitrectomy.

Postoperative treatment included moxifloxacin 0.5% eye drops (Molcin HCl 5 mg/ml ophthalmic solution, Bekasi, Indonesia) hourly, combination of tobramycin 3 mg and dexamethasone 1 mg eye drops (Cendo Tobroson, Bandung, Indonesia) hourly, atropine sulphate 1% (Cendo Tropin, Bandung, Indonesia) twice daily, timolol 0.5% eye drops (Cendo Timol, Bandung, Indonesia) twice daily, and ciprofloxacin tablets 500 mg twice daily.

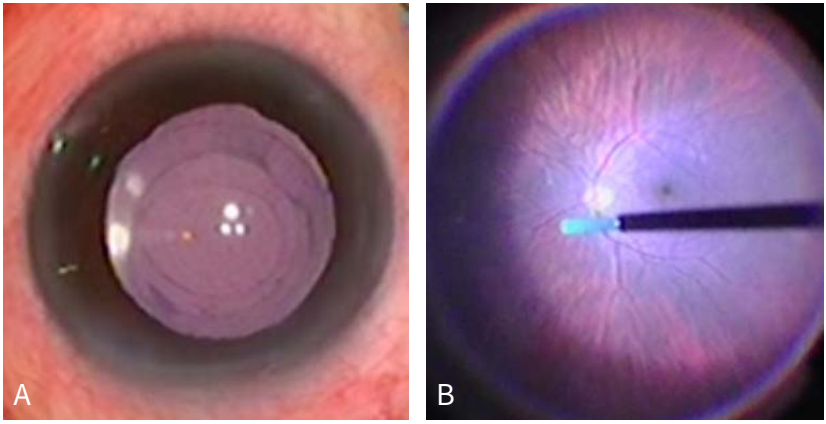

Fig. 2. Clinical features at 5-week of follow-up: (*A*) no signs of intraocular inflammation and (*B*) no signs of retinal toxicity.

We discharged the patient after 5 days of hospitalization with visual acuity of 3/60 and significantly improved clinical features. The aqueous and vitreous culture revealed no growth of microorganisms. At the 5-week follow-up (Fig. 2), visual acuity was 6/30, best-corrected visual acuity was 6/15, and the patient did not show any signs of intraocular inflammation or retinal toxicity such as retinal oedema, cotton wool spots, and retinal haemorrhages.

Discussion

The gold-standard treatment of endophthalmitis is vitrectomy.[5] However, if it cannot be performed immediately, intravitreal antibiotics may be used as an alternative therapy.[5] Intravitreal antibiotics without pars plana vitrectomy can also be administered if the retina cannot be visualized or there is fundus reflex.[6] The patient should be monitored very closely, especially in the first 24 hours.[6] Pars plana vitrectomy can be performed if the clinical condition does not improve.[6]

Moxifloxacin is a fourth-generation fluoroquinolone that can rapidly inhibit DNA synthesis by promoting cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase and type IV topoisomerase, resulting in rapid bacterial death.[7] It has improved the coverage of gram-positive, gram-negative, and anaerobic bacteria.[8] Moxifloxacin also exceeded the known minimum inhibitory concentration values for most pathogens that cause endophthalmitis in infected rabbit eyes.[8] Several bacteriological, histopathological, and clinical outcome studies in experimental animal and cell culture models have explored the role of intravitreal moxifloxacin in the treatment of endophthalmitis. Intravitreal moxifloxacin did not cause electroretinographic or retinal histologic abnormalities in rabbit eyes at a concentration up to

150 µg/mL (0.1 ml of 200 µg moxifloxacin injected intravitreal into 1.2 ml of rabbit vitreous volume).[9] If proven safe and efficacious by further study in humans, intravitreal moxifloxacin injections could be considered as an alternative to currently used antibiotics.[9] Another study reported that intravitreal use of moxifloxacin at concentrations of up to 150 µg/mL did not show significant toxicity in primary human retinal pigment epithelium cells and primary optic nerve head astrocyte cells.[10]

Two case reports reported that intravitreal moxifloxacin was effective and safe in the treatment of post-traumatic endophthalmitis in humans.[3,4] In an era of increasing multidrug resistance, intravitreal moxifloxacin may play a role in the management of endophthalmitis. The vitreous volume of an adult emmetropic human eye is approximately 4 mL, giving an empiric concentration of 125 µg/mL when 500 µg/0.1 mL moxifloxacin is injected intravitreally.

Keeping the aforementioned studies in mind, we performed intravitreal injection of moxifloxacin 0.1 ml of 500 µg/0.1 ml in our case. We used undiluted, unpreserved, ready-to-use, and commercially available moxifloxacin ophthalmic solution to avoid the cumbersome procedure of intravitreal injection preparation, risk of contamination, and dilution error, which might further cause intraocular toxicity.

Intraocular purulent material accumulation in endophthalmitis comprises endotoxins, exotoxins, bacterial cell walls, enzymes, inflammatory cells, and humoral agents representing the body's immune response.[6] The retina may continue to be damaged by the remaining inflammatory response even when the intravitreal antibiotic has successfully destroyed the bacteria.[6] Vitrectomy can maximize the removal of the infectious and inflammatory load in the eye.[6] It appears rational to remove all harmful agents from the vitreous cavity before visual acuity deteriorates to light perception and irreversible damage occurs.[6] We performed vitrectomy as there was no clinical improvement after 24-hours of intravitreal antibiotics. The clinical result in our case was good with improved visual acuity, complete reduction of intraocular inflammation, and no signs of retinal toxicity.

Conclusion

As demonstrated by previous case reports and this report, intravitreal injection of moxifloxacin is a potentially safe and effective alternative to intravitreal injection of vancomycin and ceftazidime in the treatment of acute post-phacoemulsification endophthalmitis. However, further studies may be required to assess the long-term effectivity and safety of this drug compared to intravitreal injection of vancomycin and ceftazidime as the standard intravitreal antibiotic treatment for endophthalmitis.

Declarations

Consent for publication
The patient has provided informed consent for the use of their clinical data and images in this case report.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgments
None to declare.

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Visual disturbance as primary symptom of pituitary apoplexy in pregnancy

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Abstract

Pituitary apoplexy in pregnancy is a potentially fatal condition caused by acute ischaemic infarction or haemorrhage of pre-existing pituitary adenoma or within a physiologically enlarged pituitary gland. It has a wide spectrum of clinical presentations ranging from a mild headache to sudden collapsed. Here, we report a life-threatening case of pituitary apoplexy in a non-functioning pituitary macroadenoma occurring during pregnancy that presented with bilateral blurring of vision. Visual field showed bitemporal superior quadrantanopia. Urgent non-contrast brain MRI revealed an acute expansion of a hemorrhagic pituitary lesion complicated with local compression to the optic chiasm. The patient underwent an uneventful right supraorbital craniotomy and excision of the tumour under general anaesthesia with no foetal loss. The repeated visual field at 2 weeks after surgery showed recovering visual field defect. Hence, early neurosurgical intervention is advisable to prevent mortality and morbidity due to permanent visual field loss.

Keywords: pituitary apoplexy, pregnancy, visual field defect

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Gangguan penglihatan sebagai simtom primer pituitary apoplexy semasa hamil

Abstrak

Apoplexy pituitari semasa hamil merupakan keadaan yang berpotensi membawa maut. Ia terjadi akibat infarksi iskemia akut atau pendarahan sama ada di adenoma pituitari sedia ada atau di dalam kelenjar pituitari yang besar secara fisiologi. Apoplexy pituitari mempunyai spektrum klinikal yang luas; dari sakit kepala ringan hingga tidak sedarkan diri secara tiba-tiba. Satu kes apoplexy pituitari dalam makroadenoma pituitari yang tidak berfungsi (non-functioning pituitary macroadenoma) semasa hamil, dilaporkan disini. Pesakit mengalami kabur penglihatan secara bilateral dan hasil ujian medan penglihatan menunjukkan superior kuadrantanopia bitemporal. MRI otak tanpa kontras menunjukkan peningkatan saiz adenoma pituitari dengan pendarahan yang menghimpit kiasma optik. Pesakit telah menjalani surgeri 'supraorbital craniotomy' pada sebelah kanan dan pembuangan tumor di bawah bius am, tanpa kehilangan foetal. Ujian medan penglihatan yang dijalankan 2 minggu selepas surgeri menunjukkan defek medan penglihatan beransur pulih. Oleh itu, intervensi awal surgeri neuro adalah dicadangkan untuk menghalang kehilangan medan penglihatan kekal bagi kes sebegini.

Kata kekunci: apoplexy pituitari, gangguan medan penglihatan, kehamilan

Introduction

Pituitary apoplexy in pregnancy is an uncommon but life-threatening medical condition. It requires a multidisciplinary approach to reduce the morbidity and mortality rate. Visual disturbance is one of the most common presentations and bitemporal superior quadrantanopia is the typical visual field defect. Another ocular clinical feature is ophthalmoplegia, which is caused by local compression to the cavernous sinus.

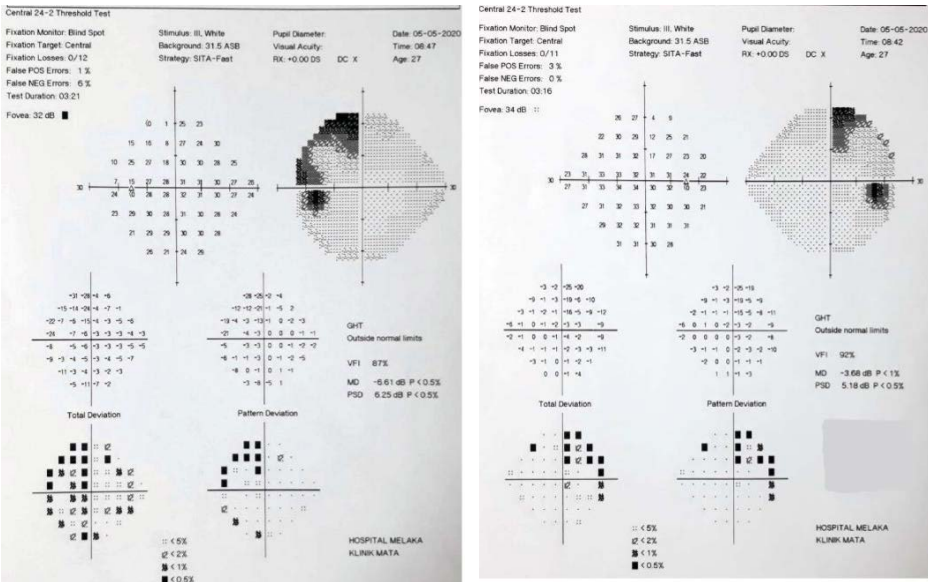

Fig. 1. Left (*a*) and right (*b*) visual fields at presentation.

Case presentation

A 27-year-old woman at 24 weeks of pregnancy with underlying non-functioning pituitary macroadenoma presented with generalized and progressively worsening bilateral blurring of vision for 1 month. There were no other neurological symptoms. On examination, vision was 6/9 OU. Visual field showed bitemporal superior quadrantanopia with no relative afferent pupillary defect (Fig. 1). No papilledema was seen on fundus examination. Other neurological examinations were unremarkable. The vital signs were stable. Urgent non-contrast brain MRI revealed an acute expansion of a hemorrhagic pituitary lesion complicated with local compression to the optic chiasm (Fig. 2). Urgent neurological, endocrine, and obstetric referrals were made. She was started on intravenous hydrocortisone 50 mg every 8 hours and regular monitoring of haemodynamic status. She underwent an uneventful right supraorbital craniotomy and tumour excision under general anaesthesia with no foetal loss. Repeated visual field 2 weeks after surgery showed recovery in the visual field defect with no further deterioration in vision (Fig. 3).

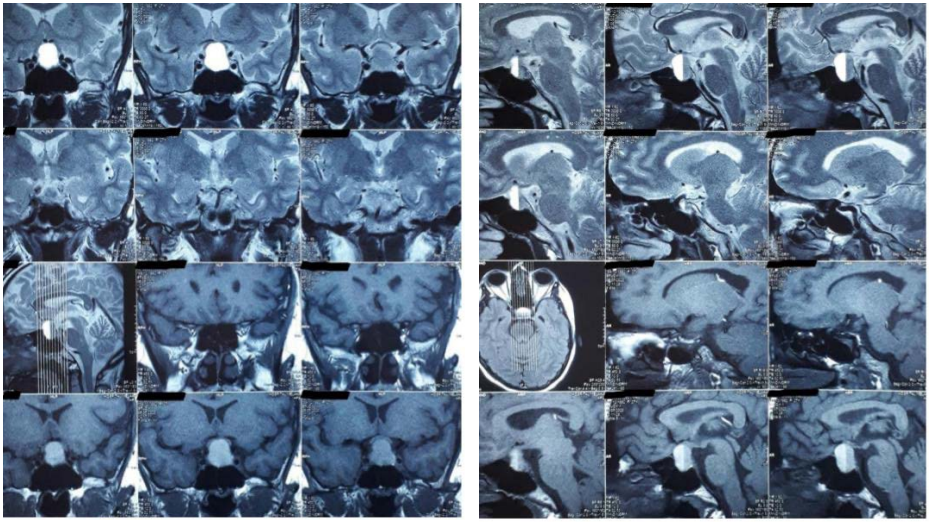

Fig. 2. Coronal (*a*) and sagittal (*b*) views of brain MRI.

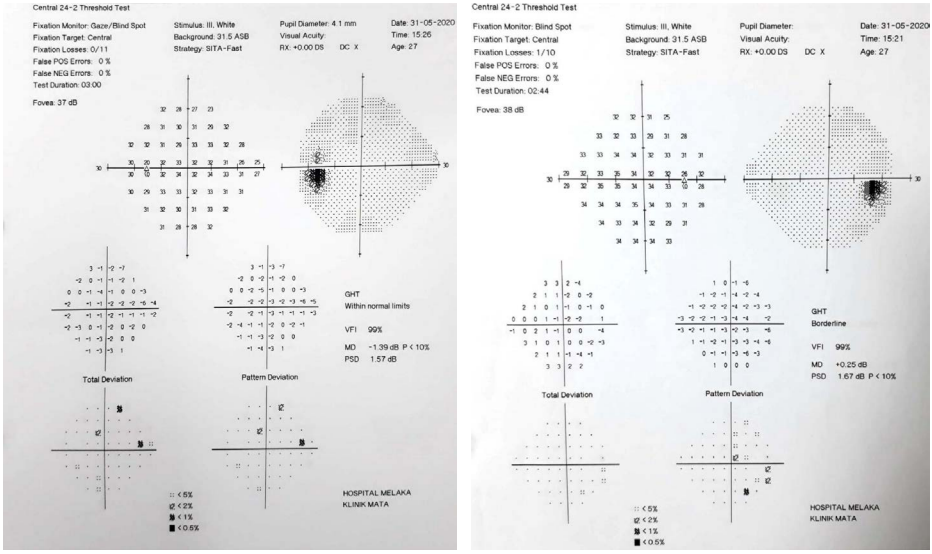

Fig. 3. Left (*a*) and right (*b*) visual fields 2 weeks after surgery.

Discussion

Pregnancy is one of the known risk factors for developing pituitary apoplexy. Other risk factors include oestrogen replacement therapy, coagulopathies, diabetes mellitus, hypertension, and head trauma.[1,2] The pituitary gland undergoes remarkable physiological adaptations and haemodynamic changes to meet the increased metabolic demands of pregnancy and foetal development, as evidenced by an MRI study showing an increment of up to 45% in pituitary volume during the first trimester.[3] Increased number of lactotroph cells and physiological elevation of serum prolactin also contribute to pituitary enlargement.[1] Despite having higher energy requirements, it has a limited expression of angiogenic factors, therefore a limited blood supply. Hence, pituitary adenomas have a greater likelihood to bleed and undergo infarction.[4]

The presenting symptoms of pituitary apoplexy in pregnancy include sudden and severe headache (97%), visual disturbances (61%), and nausea (33%), with 24 weeks' gestation as median time of presentation.[1] The more severe clinical features associated with pituitary apoplexy include altered level of consciousness (22%) and autonomic dysfunction due to adrenal insufficiency, which can be life threatening.[1] In this case, the patient presented with visual complaints as the primary symptom as evidenced by bitemporal superior quadrantanopia defect in visual field examination. Another common ocular clinical feature of pituitary apoplexy is ophthalmoplegia.

Early surgical intervention is indicated in patients with persistent and deteriorating visual field defects.[5] Compression to the optic chiasm may lead to reversible or irreversible injury. Reversible mechanisms include impedance of axoplasmic flow, conduction blockage, and demyelination. Persistent and severe compression may lead to irreversible axonal fibre degeneration.[6] In this case, the patient underwent supraorbital craniotomy and tumour excision 1 week after presentation. Repeated visual field 2 weeks after surgery showed visual field defect recovery, suggesting reversible injury due to local compression of the optic chiasm. In some cases, ongoing recovery of visual field defects over the years may be explained by the likelihood of neural plasticity.[6]

Conclusion

Early symptom recognition and a multidisciplinary approach are crucial in managing pituitary apoplexy in pregnancy prevent mortality and morbidity due to permanent visual field loss.

Declarations

Consent for publication
The patient provided informed consent for the use of the clinical images and information contained in this case report.

Competing interests
None to declare.

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Iron at the angle

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Fig. 1.

Clinical context

An incidental finding of a 55-years-old who man presented to eye clinic for conjunctivitis. Further assessment revealed history of ocular trauma 10 years ago while cutting grass. Vision in the right eye was 6/9; the anterior chamber was quiet with normal fundus.

Question 1

Describe the findings in Figure 1.

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Question 2

What are the potential complications of a retained intraocular metallic foreign body?

Answer 1

A triangular shape of metallic foreign body seen at the inferior angle of the eye with localized metallic rust deposition on the adjacent endothelium.

Answer 2

The potential complications of ocular siderosis[1] are the following:

- Cornea: Haziness and granular appearance of the corneal stroma with endothelium.
- Trabecular meshwork: Secondary open-angle glaucoma.
- Iris and pupil: Iris heterochromia, anisocoria, and accommodation failure.
- Lens: Focal rusty-brown nodules of subcapsular cataract and siderosis lentis.
- Retina: Degeneration of the inner retina and retinal pigment epithelium.

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