Eye (2018) 32:1411–1420
https://doi.org/10.1038/s41433-018-0069-4

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CORRESPONDENCE

Association of *Chlamydia trachomatis ompA* genovar with trachoma phenotypes

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Received: 16 July 2017 / Revised: 9 November 2017 / Accepted: 9 January 2018 / Published online: 5 March 2018

Introduction

The chlamydial *ompA* gene encodes the major outer membrane protein (MOMP) [1]. The importance of *ompA* genovar on the severity of trachoma phenotypes is unclear, but the MOMP may influence the host immune response, and hence the clinical signs of trachoma. In the present study, we genotyped chlamydia from a series of children with trachoma in order to assess this hypothesis.

Methods

This is a secondary analysis from a cluster-randomized clinical trial conducted in Ethiopia starting in March 2003 [1]. As part of the trial, we examined and collected swabs of the upper right tarsal conjunctival from all children aged 1–5 years in each of 40 Ethiopian communities before any intervention, and then at 2 and 6 months after a single mass azithromycin distribution [2, 3]. We assessed for the presence or absence of follicular trachoma (TF) and intense inflammatory trachoma (TI) using the World Health Organization simplified grading system (Fig. 1) and processed conjunctival swabs for chlamydial DNA using Roche AMPLICOR [4].

For the present study, we chose a random sample of chlamydia-positive swabs from 21 communities at the pretreatment, 2-month, and 6-month visits, with swabs matched by community. From each swab, we extracted DNA and amplified a region of the *ompA* gene with previously published primers [5]. The *ompA* PCR products were sequenced in both directions, edited, aligned to reference sequences (A/HAR-13; NC_007429 for A genovar and

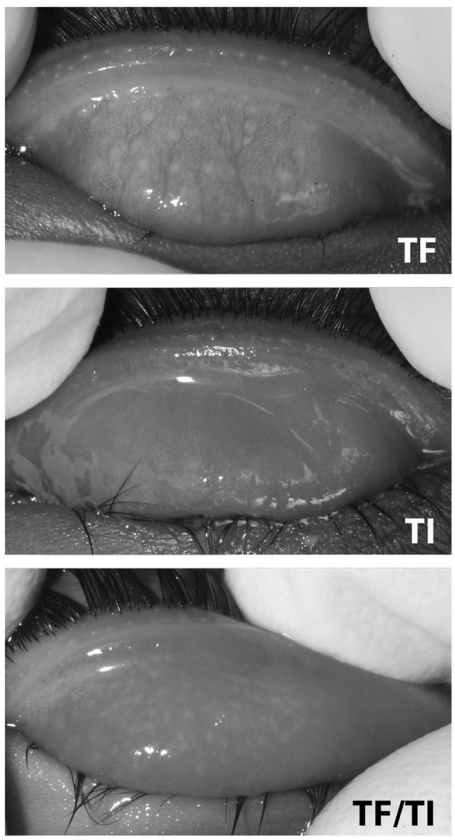

Fig. 1 Superior tarsal conjunctival photographs demonstrating the World Health Organization simplified trachoma grading system. The top panel shows follicular trachomatous inflammation (TF), characterized by ≥5 follicles measuring ≥0.5 mm in diameter in the upper tarsal conjunctiva. The middle panel shows the intense trachomatous inflammation (TI), characterized by inflammatory thickening that obscures more than half of the deep underling superior tarsal conjunctival blood vessels. The bottom panel shows both TF and TI. Photographs do not correspond to the individuals in the present study; they were taken at a later study visit and are shown for illustrative purposes only.

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Table 1 Distribution of trachoma grades according to *ompA* status

Explanatory variable	Trachoma grade				
	No TF or TI ($N = 17$)	TF ($N = 144$)	TI ($N = 30$)	TF and TI ($N = 160$)	Odds ratio (95% CI)[a]
B *ompA* genovar, %	3 (17.7%)	33 (22.9%)	4 (13.3%)	53 (33.1%)	1.78 (1.06–2.97)[b]
Age, years; mean (SD)	3.5 (1.3)	3.2 (1.5)	2.7 (1.5)	3.0 (1.4)	0.98 (0.64–1.49)
Female, %	7 (41.2%)	66 (45.8%)	16 (53.3%)	72 (45.0%)	0.98 (0.64–1.49)

[a]Ordinal logistic regression, with response variable coded in four categories, listed in increasing order of severity: No TF or TI, TF, TI, TF and TI

[b]Relative to *ompA* genovar type A

B/Tunis-864; DQ064280 for B genovar), and then assigned a genotype. Laboratory personnel were masked to the conjunctival examination findings. We used mixed effects ordinal logistic regression to determine whether genovar was a significant predictor of TF and/or TI, with age and sex as covariates and community and child as nested random effects. We coded the response variable in the following ascending order: neither TF nor TI (0), TF (1), TI (2), TF and TI (3).

Results

We identified 359 chlamydia-positive swabs for this ancillary study. Of these, we could extract DNA and determine the *ompA* sequence from 351 (97.8%) swabs from 274 distinct children. Within genovars, we identified 11 different A genotypes ($N = 258$) and 4 different B genotypes ($N = 93$). Type B genovars were more likely than type A genovars to have TF and TI (OR 1.74, 95% CI 1.03–2.94, $P = 0.04$, Table 1).

Discussion

We found that the chlamydial B genovar was more likely than the A genovar to have more intense trachomatous inflammation. Few previous studies have commented on the relationship between *ompA* type and clinical trachoma, although a Gambian study with very few B genovars found differing amounts of clinical trachoma in different genotypes of the A genovar [6]. An association between *ompA* type and host phenotype is plausible since many believe the MOMP is an important target of immunity and *ompA* variants could therefore elicit differential host immune responses. Limitations of this study include its relatively small-sample size and its unclear generalizability to areas with less prevalent trachoma. Nonetheless, we provide evidence suggesting that chlamydial MOMPs may play a role in the host inflammatory response in trachoma.

Role of the funder/sponsor The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Funding This study was supported by the International Trachoma Initiative, the National Institutes of Health (grants U10EY016214 and R21AI55752), the Bernard Osher Foundation, That Man May See, the Harper Inglis Trust, the South Asia Research Fund, and the Research to Prevent Blindness.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Eye (2018) 32:1413–1414
https://doi.org/10.1038/s41433-018-0067-6

Optimisation of intravitreal injection technique using a Barraquer speculum with solid flat blade and finger stabilisation

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Received: 3 January 2018 / Accepted: 11 January 2018 / Published online: 9 March 2018

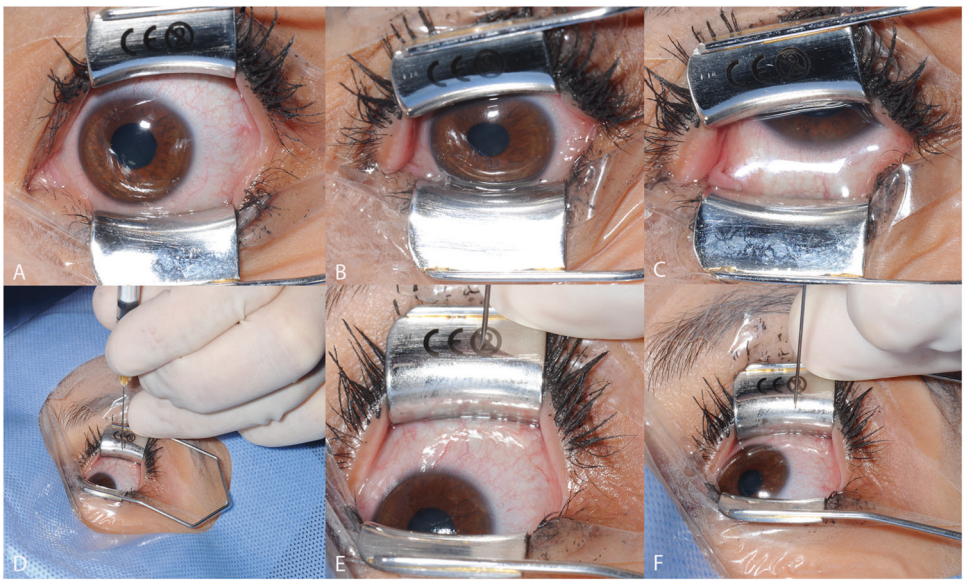

Fig. 1 Series of colour photographs illustrating a modified technique for IVT. **a** Placement of a Barraquer speculum with solid flat blade, with inferonasal gaze and no eye squeezing. **b** Purposeful eye squeezing with visible narrowing of the PA. **c** Maximum severe eye squeeze with upward movement of globe. **d**, **e** Demonstration of modified injection technique, with firm downward pressure being applied to the solid flat blade of the speculum with the ring finger of the left hand to stabilise the globe position and reduce severity of sudden eye movements. **e**, **f** Inferonasal gaze with and without eye squeezing, demonstrating reduced severity of narrowing of the PA and reduced Bell's phenomenon. (Full informed consent obtained)

Intravitreal injections (IVTs) are common ophthalmic interventions and core competency for ophthalmologists. Although simple and relatively safe, complications do occur, including cataract and retinal detachment. It is common to encounter subjects who squeeze their eyes excessively during injections. Others move unexpectedly, particularly if pain is felt or if patients suffer dementia. Such situations add additional risk and may alarm the injector.

Hard eye squeezing causes several problems. It narrows the palpebral aperture (PA), reducing the distance between injection site and eyelid margin, increasing risk of eyelash touch. Squeezing can elicit a Bell's phenomenon, with upward gaze of the globe. If pain is felt, squeezing and movement can be marked and sudden, being particularly problematic with the needle in the eye. If movement is deemed too risky, injection treatment may be discontinued temporarily or permanently. No literature exists on optimal management of these situations. Often injectors do not adapt the IVT technique in these patients.

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We describe a simple and effective IVT technique which reduces severity and impact of these problems, and could be adopted as the default technique. It improves control of the injection process offering additional risk reduction in patients with the aforementioned difficulties. The technique has been adopted in real injection clinics. A series of photographs (Fig. 1a–f) were taken using a volunteer (Mary Awad) for demonstration of the technique without delivering an IVT, illustrating the advantages in a superotemporal IVT.

The injector places a Barraquer speculum with solid flat blade (Fig. 1a). Figure 1a further shows inferonasal gaze without squeezing, demonstrating a large area of superotemporal sclera for injection. Figure 1b illustrates inferonasal gaze, with purposeful hard eye squeezing. The PA is significantly narrowed, limiting available injection sites. Figure 1c was taken after eliciting a sudden severe squeeze (with upward globe movement) secondary to unexpected instillation of G. Proxymetacaine onto the ocular surface and exposed eyelashes by the injector in an attempt to alleviate the problem.

Figure 1d illustrates hand positioning for the modified IVT technique. The injector instructs the patient to look inferonasally, holding the syringe in their non-dominant hand between thumb and index finger. The point of injection is marked superotemporally with a calliper. The ring finger is placed on the upper solid part of the speculum and firm downward pressure applied, stabilising the globe in its downward gaze position, offering increased resistance to sudden ocular movements, securing the globe in a more stable position. The authors find it reduced narrowing of the PA during squeezing, maintaining a more constant distance between the upper speculum/eyelid margin and injection site. The dominant hand is free to inject the drug.

This technique offers significant advantages over alternative methods of globe stabilisation, including utilisation of forceps, which results in a one-handed injection technique. A right-handed injector, if desired, can use this technique with their nondominant hand to stabilise the speculum either standing superiorly for left eyes or indeed standing on the right side of the patient for right eye injections, making the technique easy to learn and perform.

Acknowledgements We would like to acknowledge Andrew Martin from the photography department at the Royal Derby Hospital for taking time to acquire the images.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Eye (2018) 32:1414–1415
https://doi.org/10.1038/s41433-018-0082-7

Do patients only remember who performed their cataract surgery if complications occur?

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Received: 12 February 2018 / Accepted: 18 February 2018 / Published online: 27 March 2018

Introduction

It is well recognised that patients have poor memory of clinical encounters and are surprisingly bad at recalling information discussed during consultations [1]. It has been variously hypothesised that patient literacy levels play an important role in patient recall of clinical information, and there have been suggestions that leaflets and other means of conveying information may be beneficial in aiding patient understanding [2]. With regard to cataract surgery, this has been extended to advocating a multimedia-assisted informed consent process, even in older patients, in order to assist patient recall and understanding of all the risks and benefits.

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There is a saying among cataract surgeons in Wales that patients only ever remember their surgeon if they suffered a complication. To our knowledge, there is no study that has officially examined this issue, and in light of the poor memory of patients in general and patients undergoing cataract surgery in particular we aimed to assess whether there was truth in this old Welsh adage [3].

Methods

Post-operative cataract extraction and intraocular lens implant patients seen in outpatient ophthalmology clinics or the Day Surgery Unit at Singleton Hospital, Swansea, were asked whether they recalled the name of the surgeon who performed their cataract operation. They were then asked whether the operation had gone well and their result compared with the information contained within the clinical record. Patients were included if they had undergone cataract surgery within the preceding 3 months and if they had both eyes operated on within this period, only the most recent operation was included in this study. If the patient had been operated on by a registrar or specialty doctor but named their responsible consultant this was determined to be positive recall. If the patient determined a complication had taken place, even though the operation note did not indicate that this was the case, the patient was included in the complication group. This study was conducted from November 2016 to January 2018.

Results

In total, 409 patients were included in this study, of whom 29 claimed to have suffered a 'complication'. There were 13 true intraoperative complications in this group, with the remaining 16 patients suffering from conditions such as post-operative uveitis or a dry eye after the procedure. True complications included posterior capsule rupture, dropped nucleus, anterior capsule tear and zonular dehiscence.

Of the 380 patients who had not suffered a perceived complication, 61 recalled the identity of their surgeon (16.1%). Of the 29 patients who had suffered a perceived complication, 5 patients recalled the identity of their surgeon (17.2%). Chi-square analysis of these figures did not reveal a statistically significant difference between the two groups.

Discussion

In the brave new world of informed consent, much emphasis is placed on involving the patient in the process and on weighing up the best means of conveying information, so that it can be recalled and used in a meaningful manner for a valid consenting process to take place. Perhaps, it is taken for granted that if a patient is expected to remember complicated information about the operation they are to undergo, they will also remember the name of their surgeon. An extrapolation of this, and perhaps the origin of the saying that 'patients remember bad surgeons', is that the more eventful the procedure, the more memorable the surgeon. This is the first study to demonstrate that not only do patients not in fact remember their surgeon's name with greater clarity if the procedure is not perceived to have gone as planned, but they do not tend to remember their names very much at all.

In both groups, less than a fifth of patients successfully recalled the name of their surgeon. This information can either suggest that yet more information may need to be provided to the patient, including perhaps the name of their surgeon and their complication rate; or indeed that the studies which demonstrate abysmal patient recall of important clinical facts coupled with this study demonstrate that the entire process of a valid clinical consent needs to be rethought. It may be cold comfort to the surgeon suffering an intraoperative complication that the patient will not recall their name, if the consenting process leading up to that point may not be entirely valid.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Eye (2018) 32:1416–1417
https://doi.org/10.1038/s41433-018-0085-4

A 10-year analysis of microbiological profiles of microbial keratitis: the North East England Study

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Received: 27 February 2018 / Accepted: 13 March 2018 / Published online: 3 April 2018

Tan et al. [1] recently reported a 12-year analysis of microbial keratitis in a tertiary eye centre (Manchester) in which they found a significant decreasing trend in Gram-positive keratitis along with an increasing trend in Moraxella keratitis. According to the literature and our experience, Moraxella keratitis is known for its chronicity and slow response to treatment [2, 3]. In view of their findings, we performed a 10-year retrospective analysis (January 2008–December 2017) on the microbiological profiles of microbial keratitis in Sunderland Eye Infirmary (one of the three main eye centres in the North East of England) to determine if the changing trend of microbial keratitis was similar across the UK.

During our study period, a total of 407 positive corneal scrapes (out of 914 scrapes) were identified, giving a yield rate of 44.5%. Of 407 cases, 212 (52.1%) were female and mean age was 55.9 (SD 21.0) years; 57 (14.0%) cases were polymicrobial. A total of 478 organisms were isolated; these included 308 (64.9%) Gram-positive and 127 (26.2%) Gram-negative organisms, 20 (4.2%) fungal, and 23 (4.8%) acanthamoeba. For descriptive and analytic purposes, the study was divided into two time periods, namely 2008–2012 and 2013–2017. We observed a similar increasing trend in Moraxella keratitis, although statistical significance was not achieved. However, there was an increasing trend in Gram-positive organisms, particularly coagulase-negative staphylococci, and a decreasing trend in Gram-negative organisms, particularly pseudomonas, in our region (Table 1). Reassuringly we only identified two (0.5%) cases of methicillin-resistant staphylococcus aureus (MRSA) over the past 10 years. This was in contrast to the considerably high prevalence of MRSA-related ocular infection reported in other countries [4]. In addition, acanthamoeba keratitis was more commonly associated with patients of younger age group as compared to those with Gram-positive, Gram-negative and fungal keratitis (Table 2). This was most likely related to the use of contact lens in younger patients.

Our study supports the inherent nature of geographical and temporal variations of microbiological profiles of

Table 1 Summary of microbiological profiles of microbial keratitis in Sunderland Eye Infirmary between 2008–2012 and 2013–2017

Organisms	2008–2012 $N = 209$; N (%)	2013–2017 $N = 269$; N (%)	P-value
Gram-positive	125 (59.8)	183 (68.0)	0.063
Streptococcus	32 (25.6)	26 (14.2)	0.012
S. *aureus*	33 (26.4)	32 (17.5)	0.060
CoNS	40 (32.0)	84 (45.9)	0.015
Bacillus	11 (8.8)	21 (11.5)	0.450
Others[a]	9 (7.2)	10 (5.5)	0.534
Gram-negative	65 (31.1)	62 (23.0)	0.048
Pseudomonas	31 (47.7)	19 (30.6)	0.049
Moraxella	19 (29.2)	26 (41.9)	0.135
Others[b]	15 (23.1)	17 (27.4)	0.573
Fungi	12 (5.7)	8 (3.0)	0.134
Yeast	5 (41.7)	5 (62.5)	0.361
Filamentous	7 (58.3)	3 (37.5)	0.361
Acanthamoeba	7 (3.4)	16 (6.0)	0.188

Chi-square test was used to detect any significant changing trend of the microbiological profiles between the two time periods. Significant P-values (0.05) are underlined. The calculation of the proportions of organisms was performed at two levels; the first level comprised Gram-positive and Gram-negative organisms, fungi and acanthamoeba; and the second level comprised the subtypes of the organisms within the four groups

CoNS coagulase-negative staphylococcus

[a]Other Gram-positive organisms included Aerococcus, Enterococcus, Kocuria, Micrococcus, Mycobacterium and Rothia

[b]Other Gram-negative organisms included Acinetobacter, Aeromonas, Burkholderia, Haemophilus, Klebsiella, Neisseria, Ochrobactrum, Raoultella, Serratia, Sphingomonas and Stenotrophomonas

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Table 2 Association of age and gender with the microbiological profiles of microbial keratitis

	Gram-positive ($N = 309$)	Gram-negative ($N = 126$)	Fungi ($N = 20$)	Acanthamoeba ($N = 23$)	P-value
Age, years	56.3 (21.1)	57.6 (20.4)	55.3 (21.8)	34.4 (12.9)	<u><0.001</u>
Gender, N (%)					0.404
Female	151 (48.9)	60 (47.6)	7 (35.0)	14 (60.9)	
Male	158 (51.1)	66 (52.4)	13 (65.0)	9 (39.1)	

Age is presented in mean (SD). One-way ANOVA test was used to analyse the mean differences and χ^2 test was used to analyse the categorical variables between the four groups. Significant P-value (<0.05) is underlined

microbial keratitis in different regions, including the UK [5]. This highlights the importance of up-to-date examination of microbial keratitis in a particular region.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Eye (2018) 32:1417–1418
https://doi.org/10.1038/s41433-018-0086-3

Response to: A 10-year analysis of microbiological profiles of microbial keratitis: the North East England study

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Received: 13 March 2018 / Accepted: 13 March 2018 / Published online: 3 April 2018

Many thanks for alerting us to the microbiological profiles of microbial keratitis from our colleagues in the North East of England study. As our article had urged other authors to analyse their own local microbial data, we are delighted to see this work being undertaken in other areas of the UK.

This data highlights the need for individual local analysis in order to tailor appropriate antibiotic therapy. Similar rates of bacteria, fungi, and acanthamoeba are seen across the two centres. Indeed the increasing trend in gram positive pathogens, less than 150 miles from our centre is interesting. A similar but not statistically significant trend was seen

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in Moraxella keratitis infections, which chimes with our findings.

It would be interesting to know if our colleagues intend on analysing antimicrobial sensitivities for this data, and what specific statistical analysis was performed to produce these findings. It is possible that if shorter time intervals are used for the data, subtler trends may be detected.

Our colleagues report a higher ratio of positive scrape results than our series; 44.6% from over the 10 year period. It would be interesting to know under which conditions our colleagues perform corneal scraping in the context of suspected microbial keratitis.

We commend our colleagues in the North-East for their hard work, and hope that other centres are able to find the time to join in!

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Eye (2018) 32:1418–1419
https://doi.org/10.1038/s41433-018-0090-7

Letter to the Editor

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Received: 8 November 2017 / Accepted: 14 March 2018 / Published online: 13 April 2018

We read with interest the article by Cui et al. [1]. In the article, the efficacy and safety of conbercept and ranibizumab for neovascular age-related macular degeneration were compared in a retrospective case-controlled non-inferiority study. However, the authors made some mistakes in describing the study design.

First, a case-control study is often used to identify potential risk factors for a disease by comparing the frequencies of the risk factors of an illness group to one or more control groups [2]. The researchers first group the participants in a case-control study according to their outcome status and then looks backward to compare the levels of exposure between groups. In Cui's study, however, 180 patients were divided by the status of intervention/exposure and then were followed longitudinally for the outcomes, which was essentially a forward-looking study instead of a backward-looking case-control study.

Second, the retrospective design mentioned in the article was also doubtful. By definition, a retrospective study is always an observational study, which is more subject to bias and confoundings [3]. Missing data is also the Achille's heel of a retrospective study. But what we saw in the article was a well-controlled multicentre study. The interventions were chosen by the participants after only been informed with the names of the drugs. The baseline characteristics were balanced. And the attrition proportion was merely 6.7% with no documented treatment switching. However in a similar study in California, 14.4% of the 452 participants were either lost to follow-up or died, and another 17.3% had changed their treatments [4].

Finally, a non-inferiority design is almost always used in randomized control trials [5].

We believe quasi-experiment should be a more appropriate term for Cui's study. A quasi-experiment prospectively enrolls participants and assigns them to different arms according to a pre-specified non-random allocation strategy [3, 6]. The study in question had a so-called weak quasi-experimental design as the participants chose to receive either conbercept or ranibizumab treatment all by themselves [6]. Thus, the groups would have been different in a number of ways.

To carefully design a study and transparently report it are important, not only for minimizing the risks of bias and controlling for potential confounders but for properly interpreting the results of studies and correctly ranking the evidence.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Eye (2018) 32:1419–1420
https://doi.org/10.1038/s41433-018-0091-6

Optic disc pit maculopathy

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Received: 18 December 2017 / Accepted: 14 March 2018 / Published online: 13 April 2018

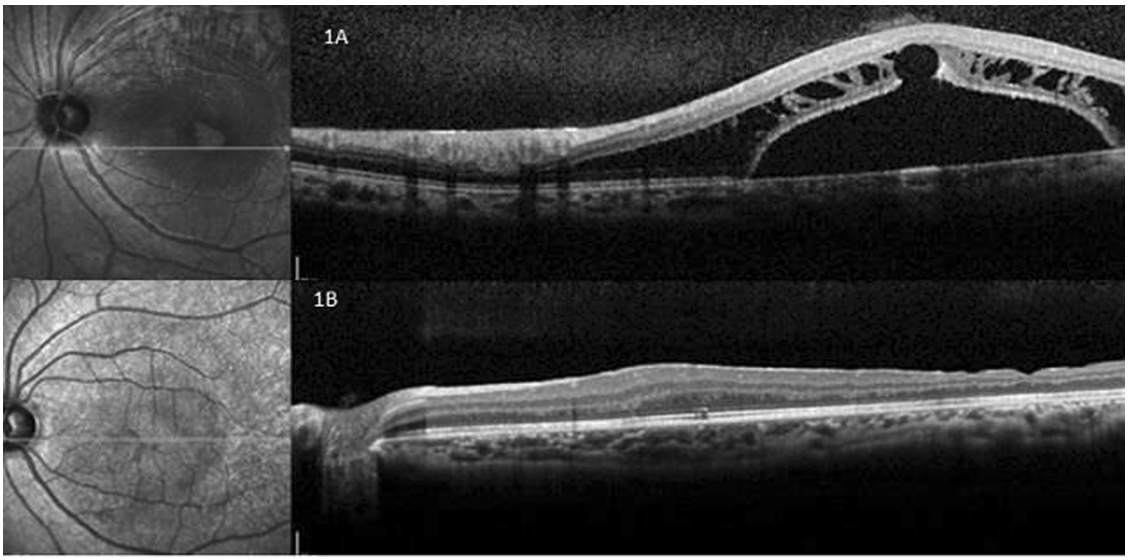

Fig. 1 Optic disc pit maculopathy in a 9-year-old boy before surgery (1A) and 22 months after surgery (1B)

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We read with interest the recent article by Avci et al. [1] reviewing the 51 cases of optic disc pit maculopathy (OPD-M) treated with pars plana vitrectomy. We would like to share our experience of OPD-M in a child with follow-up for 3 years and emphasize few learning points.

We performed a 23G vitrectomy with internal limiting membrane peel and SF6(20%) in a 9-year-old boy with

ODP-M, who presented with incidental finding of unilateral visual loss. His visual acuity at presentation was counting finger in the affected eye and had been recorded 6/6 2 years earlier by his optician. The subretinal fluid took 22 months to completely disappear (Fig. 1). Vision recovered to 6/6 unaided.

We would like to emphasize two important learning points in managing OPD-M. First, there may be a significant delay in complete retinal reattachment in OPD-M after surgery, i.e., 22 months in our case. Hence, the clinician should monitor it for an extended period before performing a second intervention, as suggested by Avci et al. [1]. Second, young patients may have surprisingly good visual outcome after surgery despite poor visual acuity at presentation.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Avci R, Kapran Z, Ozdek S, Teke MY, Oz O, Guven D, et al. Multicenter study of pars plana vitrectomy for optic disc pit maculopathy: MACPIT study. Eye. 2017;31:1266–73.