Case 1 shows a well-defined circular smooth area of fluorescence consistent with a serous PED next to an area of retinal pigment epithelial mottling. This may represent an adjacent area of occult, and or atrophy, judging from the colour photograph and optical coherence tomography (OCT). It is most likely that this is a retinal angiomatous proliferation (RAP) lesion that can respond well to conventional dose anti-VEGF treatment. Case 2 also appears to show serous PED. With Case 3 it is reported that there is a retinochoroidal anastomosis at the margin of the vPEDs. The colour photograph and OCT suggest that the lesion is a serous PED associated with RAP. Again in our experience this would settle well with conventional dose anti-VEGF treatment.[2]

Vascularised PEDs have been defined as areas of irregular elevation of the pigment epithelium and consist of a stippled hyper fluorescent appearance on angiography. These are not usually as bright or discrete as serous RPE detachments in the early phase of angiography.[3,4] Furthermore, they gradually brighten and the vascular network might be visible on ICG.

Serous PEDs can occur without a vascular component in the context of lots of drusen and do not respond to ranibizumab. They also can occur with RAP, with polypoidal choroidal vasculopathy and as part of a mixed 'wet' AMD picture. Indocyanide green angiography (ICG) can be useful to identify the lesion type but is best performed with high-resolution ICG with early video, such as is possible with the Heidelberg systems. As no ICG is shown, it is hard to comment on the quality of what was seen.

It is pleasing to see that the cases reported all did well but we would be interested to know whether the authors had any other cases of suspected vPED that did not respond or indeed the outcome of other types of choroidal neovascularisation that were also treated with high-dose ranibizumab. We agree that further analysis of a larger cohort is required but would require strict inclusion criteria on what constitutes a vPED before recommending monthly high-dose ranibizumab.

Conflict of interest

J Talks has received travel expenses and or attended advisory boards for Allergan, Novartis, Bayer, Alamera Sciences. The remaining authors declare no conflict of interest.

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SJ Talks, R Gupta and A Browning

Department of Eye, Royal Victoria Infirmary, Newcastle upon Tyne, UK
E-mail: james.talks@nuth.nhs.uk

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Sir,

Response to Talks *et al*

We would like to thank Talks *et al*[1] for their interest in our article entitled 'High-dose ranibizumab therapy for vascularized pigment epithelial detachment'[2] and their letter to the editor that questions the presence of vascularized retinal pigment epithelial detachment (PED) in the three published cases. Although we understand their concern, we stand by our classification of PED in these three cases. Our study has incorporated strict inclusion and exclusion criteria as well as multi-modal imaging for patient enrollment and assessment of the fundus lesions throughout the study.

The classification of PED is complicated and requires a historical overview. Serous PEDs are well circumscribed lesions that fill rapidly and homogeneously on fluorescein angiography (FA) and that fail to show any overt signs of CNV.[3] Gass[4] defined a vascularized serous PED as a serous PED with overt signs of CNV such as a hot spot or a notch. In Figures 1 and 2, a large serous PED component is certainly present but there is high suspicion for a CNV focus by virtue of the irregular fluorescence (which shows focal leakage and a hot spot in the late phase of the FA) present at the nasal edge of the PED in Figure 1 and the presence of a hot spot at the temporal edge of the serous PED in Figure 2. Moreover, the serous PED is large and irregular in each case and cystoid macular edema and subretinal fluid (SRF) are present with optical coherence tomography (OCT) imaging, consistent with the presence of an underlying CNV focus. The presence of a cluster of hard exudates along the temporal margin of the PED in Figure 2 further supports the presence of CNV underlying the PED in case 2. Thus, the findings of multi-modal imaging are consistent with the diagnosis of a vascularized serous PED for both cases 1 and 2.

We further make the distinction of a vascularized serous PED *vs* a fibrovascular PED in which an RPE detachment is present but a distinct serous PED is not identified. A fibrovascular PED was defined during the course of the Macular Photocoagulation Study[5] and the subsequent Treatment of Age-Related Macular Degeneration With Photodynamic Therapy Investigation and Verteporfin in Photodynamic Therapy Trial[6] as an area of RPE elevation with stippled hyperfluorescence and late staining on FA.[5] Indeed, in case 3 the authors were able to identify stippled filling of the PED with an obvious leaking 'hot spot' on the

FA (that likely represents a RAP lesion), and SRF was noted with the PED on OCT, all leading to the diagnosis of a fibrovascular PED associated with a RAP lesion for case 3.

Please note that all PEDs were classified by the lead author. Each of these readings was then confirmed, independent of the original grade, by one of our co-authors (DS), who reanalyzed all FP, FA, indocyanine-green, and OCT images to ensure consistency. Any lesions with discordant readings were disqualified. Owing to the space limitation, we could only include a few selected images for the cases in our publication. In response to the letter by Talk *et al*, we have also obtained an independent review of our three cases by Dr Michael Ip at the Fundus Photograph Reading Center at the University of Wisconsin, who agreed with our classification and assessment of all three cases.

Although these three cases of PED responded well to a high dose of ranibizumab, we do not wish to make any conclusions regarding the efficacy and safety of high-dose ranibizumab therapy until the results of our prospective study are released.

Conflict of interest

The authors declare no conflict of interest.

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CK Chan[1,2], P Abraham[3] and D Sarraf[4,5]

[1]Southern California Desert Retina Consultants, Medical Group, Palm Desert, CA, USA
[2]Department of Ophthalmology, Loma Linda University, Loma Linda, CA, USA
[3]Black Hills Regional Eye Institute, Rapid City, SD,USA
[4]Retinal Disorders and Ophthalmic Genetics Division, Jules Stein Eye Institute, University of California, Los Angeles, Los Angeles, CA, USA
[5]Greater LA VA Healthcare System, Los Angeles, CA, USA
E-mail: cchan@desertretina.com

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