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Sir,

Intravitreal bevacizumab for macular edema secondary to retinal macroaneurysm

Bevacizumab, a humanised monoclonal antibody to vascular endothelial growth factor, has been given as an intravitreal injection for age-related macular degeneration,[1] macular oedema due to retinal vein occlusion,[2,3] and diabetic macular oedema.[4] Here, we present a case of macular oedema secondary to retinal macroaneurysm, which resolved with intravitreal Bevacizumab.

Case report

A 42-year-old female presented with diminution of vision in her right eye for 1-month duration. The patient was a known hypertensive and diabetic.

The best corrected visual acuity (BCVA) was 20/400 OD and 20/20 OS. Anterior segment examination was normal bilaterally. The intraocular pressure was 18 mmHg bilaterally. Ophthalmoscopic examination revealed mild nonproliferative diabetic retinopathy in both eyes and intraretinal haemorrhages along the superotemporal arcade with severe macular oedema and lipid exudation involving the fovea in the right eye (Figure 1b). Based on fluorescein angiography a diagnosis of retinal arteriolar macroaneurysm was made (Figure 1a). The central macular thickness (CMT) measured on optical coherence tomography (OCT) was 607 μ OD and 179 μ OS.

The patient's blood pressure was controlled on oral medication. Fasting blood sugar was 5 mmol/l on oral hypoglycaemic. Lipid profile was within normal limits.

After a written consent was signed by the patient, an off-label intravitreal bevacizumab injection (1.25 mg) was given in the right eye. At 4 weeks, BCVA improved to 20/100, retinal haemorrhages resolved and exudation also reduced (Figure 1b). The CMT decreased to 271 μ, although some macular oedema persisted. Intravitreal bevacizumab was repeated and within 2 weeks, there was complete resolution of macular oedema, with CMT of 173 μ and BCVA of 20/50 (Figure 1c).

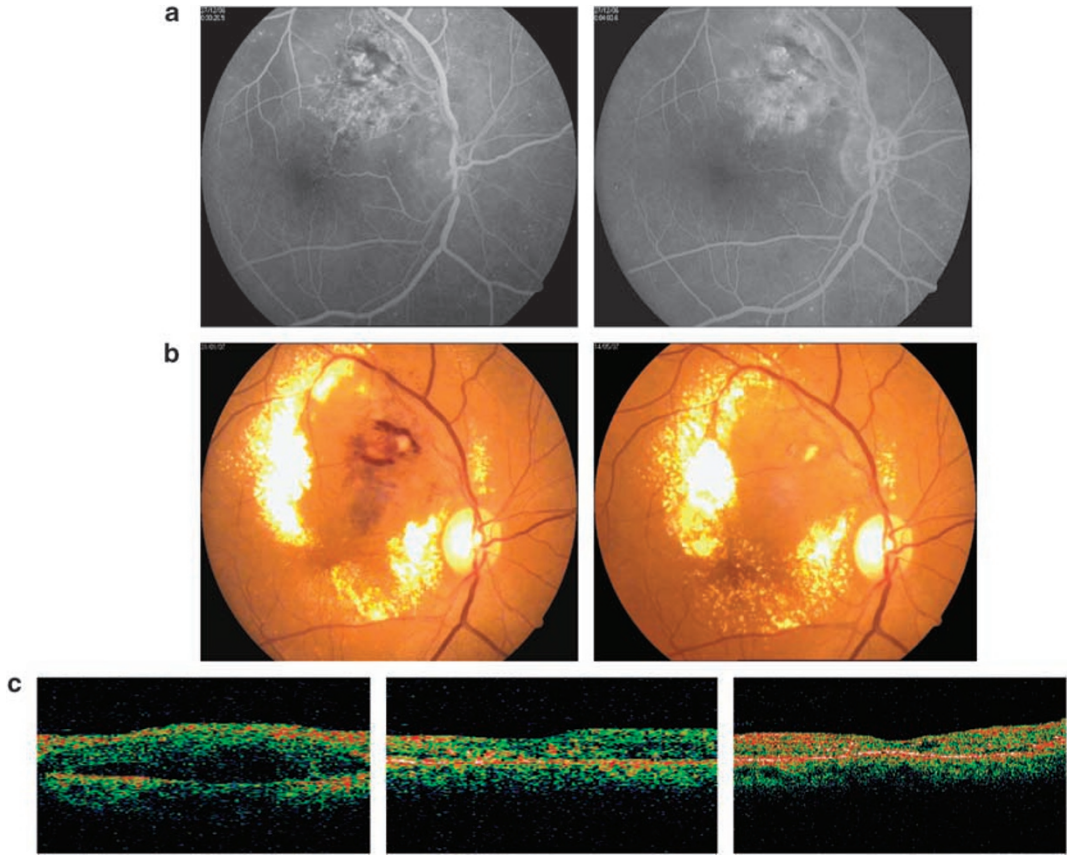

Figure 1 (a) Fluorescein angiogram showing hypofluorescence from blockage due to retinal haemorrhages and a hyperfluorescent retinal macroaneurysm with leakage of dye in late phase. (b) Fundus photograph showing retinal macroaneurysm along superotemporal retinal arteriole associated with retinal hemorrhages, lipid exudation and macular edema (left). Post bevacizumab injection fundus picture showing resolved retinal hemorrhages and decrease in lipid exudation and macular edema (right). (c) Retinal thickness measured by optical coherence tomography at baseline (607 μ; left), after 4 weeks (271 μ; middle), and after 6 weeks (173 μ; right).

Comment
Retinal macroaneurysm are localised dilatations of retinal arterioles. Hypertensive women in the sixth or seventh decade have a predilection. The most common clinical symptom is decline in central visual acuity due to retinal oedema, exudation or haemorrhage.[5] Direct laser photocoagulation of the macroaneurysm may be considered if the lipid exudates coming from it threaten the fovea. Treatment when haemorrhage is present is fraught with difficulties.

The present case would not have benefited from laser photocoagulation due to the severity of macular oedema and presence of retinal haemorrhages. Although spontaneous resolution is known occur, in the present case, bevacizumab might not only have hastened the decrease in retinal thickness but also provided superior visual outcome. Intravitreal bevacizumab is also well tolerated and no adverse effects were observed. The results observed in this case are provocative and require additional investigation.

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Sir,

Plasma metalloproteinase-9 in age-related macular degeneration

Chau *et al*[1] described raised plasma metalloproteinase-9 (MMP-9) in age-related macular degeneration (ARMD), hypothesising that if atherosclerosis and ARMD share a common mechanism, then systemic MMP-9 and MMP-2 may be increased in patients with ARMD. While it is a plausible hypothesis, it is unclear why they have not tested it in a simple cross-sectional analysis of two groups—one with ARMD but no atherosclerosis and another group with atherosclerosis but no ARMD. Instead, each of their three sample groups includes patients with or without a history of symptomatic atherosclerosis (eg, myocardial infarction) as well as risk factors (eg, hypertension). This is pertinent as cardiovascular disease and its risk factors substantially affects MMP levels.[2,3]

The authors state 'no statistically significant differences in clinical data related to atherosclerosis were observed between subjects in the three groups included in the study'. As they offer no statistical test or data in support of this statement, it is unclear to us how they can make this assertion. The authors provide no power calculation to assure the reader that the risks of statistical error types 1 and 2 have been addressed and minimised, given the small numbers in each subject group. We wonder whether in fact the failure to find a difference between data sets is because of a small number error (ie, false negative).

Chau *et al*[1] choose to present their data as SEM, which denies the reader a simple estimate to the distribution of the data—many would argue that the correct measure of variance is SD.[4] One of their results is a mean of 740 ng/ml with SE 494 ng/ml. We submit that these data are likely to have a strong non-normal distribution and so convention states that it should be presented as median and interquartile range. We wonder which other indices also have a non-normal distribution, which could be determined by a test of statistical normality (eg, the Anderson–Darling test). The importance of distribution is that it governs the method of analysis. Differences in three or more data sets with a normal distribution should be sought using analysis of variance (ANOVA), as the authors have used. However, if their data contain at least one data set with a non-normal distribution, then the correct analysis would be a test such as the Kruskall–Wallis test. In addition, neither ANOVA nor the Kruskall–Wallis test tell us of differences between individual groups. A *post hoc* test is necessary to probe for such intergroup differences should have been performed; student's *t*-test is inappropriate. We will appreciate it if the authors can provide these analyses, as well as a power calculation.

While we do not doubt the accuracy of the raw data derived from the plasma, we have difficulty with their analysis and presentation of the results. They may find a different story with their data, the findings of which could be important.

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