We conclude that metastatic disease should be considered in the differential diagnosis of eyelid lesions. The present case emphasises the need for a good medical history in cases of persistent eyelid swelling. Even in the case of a history of an atypical primary tumour, like pleural mesothelioma, histopathological examination is necessary if those lesions fail to respond to treatment.

E K Tsina

Department of Ophthalmology, Hygeia Hospital, Athens, Greece

D Papaioannou

Histopathology Department, Hygeia Hospital, Athens, Greece

F O Matsouka, P A Kosmidis

2nd Medical Oncology Department, Hygeia Hospital, Athens, Greece

Correspondence to: Efthymia K Tsina, MD, PhD, Department of Ophthalmology, Hygeia Hospital, 35 Kifisias Street, Athens, 11523, Greece; etsina@hotmail.com

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References

- 1 **Mansour AM, Hidayat AA.** Metastatic eyelid disease. *Ophthalmology* 1987;**94**:667-70.
- 2 **Mah E, Bittar RG, Davis GA.** Cerebral metastases in malignant mesothelioma: case report and literature review. *J Clin Neurosci* 2004;**11**:917-18.
- 3 **Gibson A, Musa F, Pearson A, et al.** Metastatic mesothelioma presenting with proptosis. *Am J Ophthalmol* 2004;**137**:968-9.
- 4 **Ozdamar PC, Codere F, Callejo S, et al.** Accuracy of the clinical diagnosis of chalazion. *Eye* 2004;**18**:135-8.
- 5 **Cavanagh HD, Green WR, Goldberg HD.** Multicentric sebaceous adenocarcinoma of the meibomian gland. *Am J Ophthalmol* 1974;**77**:326-32.

Does intravitreal injection of bevacizumab have an effect on the blood-ocular barrier function?

Bevacizumab (Avastin), a humanised monoclonal anti-VEGF antibody originally developed for intravenous therapy of metastatic cancer, is now being used as off-label therapy in age related macular degeneration.¹ The cost effective drug promises not only anti-angiogenic capabilities in neovascular eye disease, but has also anti-exudative effects by lowering transendothelial permeability of blood vessels.²

Blood-ocular barrier (BAB) breakdown has been reported after intraocular application of lyophilised rhuFab formulations.³ Anterior chamber inflammation is one of the most frequently reported adverse events (19%) after pegaptanib injections.⁴ We wanted to post these safety issues for bevacizumab by objective detection of aqueous protein concentration.

Methods

The anterior chamber reaction was analysed in 60 patients receiving 1.25 mg of bevacizumab for age related macular degeneration. All patients opted for treatment after being given detailed information about the limited

Figure 1 Aqueous flare as photon counts per millisecond at baseline and after 1 day, 1 week, and 1 month for patients after intravitreal bevacizumab injection. The bar within the box plots represents the median, the edges the 25th/75th percentiles and the whiskers extend from the ends of the box to the outermost data point within quartile-1.5 (interquartile range).

experience of the drug, its side effects and off-label character. Mean age was 73 years. 38.3% were male. Postoperatively, gentamicin/dexamethasone ointment was applied once. Aqueous humour flare was measured with the laser flare meter (FC-2000, Kowa Co Ltd, Tokyo, Japan) 30 minutes after pupil dilatation. Routine testing was performed at baseline, on the first postoperative day, after 1 week, and after 1 month. Flare values were expressed as photon counts per millisecond (ph/ms). Descriptive statistics were used to detect the difference in flare values (JMP 5.0.1.2; $\alpha = 0.05$).

Results

The mean flare values were 9.71 ph/ms (95% CI 8.41 to 11.03) at baseline and 9.87 ph/ms (95% CI 8.41 to 11.03) on the first postoperative day, declining to 8.39 ph/ms (95% CI 7.57 to 9.22) after 1 week and 8.25 ph/ms (95% CI 7.40 to 9.09) after 1 month (fig 1).

An increase in anterior flare on the first postoperative day was seen in 51.7% (31 of 60) of cases (mean change +0.14 ph/ms, 95% CI -0.91 to 1.21, $p = 0.84$). The decrease of flare after 1 month was significant (each pair, Student's t , $p < 0.05$). Presence (seven of 60) and quantity of cells in the anterior chamber did not change during the observation period.

Comment

Measurements by flaresmeter have been shown to be accurate and reproducible and more sensitive in quantifying BAB damage than anterior chamber fluorophotometry.⁵ Flare values are known to significantly increase with age. The values at baseline in this study showed a similar distribution as in age matched control groups.⁶

A single injection of bevacizumab caused only slight flare increase on the first day. Incidence of cells did not differ from occasional findings in normal eyes.⁷ The injection itself or non-specific inflammation could explain the temporary BAB reduction. In our experience even repeated injections of the potentially immunogenic full length antibody bevacizumab have not caused inflammatory or allergic reactions.

The reduction of flare in the course of time might be related to direct pharmacodynamic

effects of the drug lowering the permeability of intraocular blood vessels.² Further investigation is necessary to assess whether flare could be used as a non-invasive indicator of bevacizumab concentration or drug efficiency. Stabilisation of BAB over 28 days is consistent with the assumed half life, longer than that of ranibizumab or pegaptanib.

Further studies with longer follow up should be undertaken to assess tolerability and safety, also in respect of repeated application.

F Ziemssen, M Wurga, I M Neuhann, M Leitritz, S Biester, S Grisanti, K U Bartz-Schmidt, Tuebingen Bevacizumab Study Group
University Eye Hospital, Tuebingen, Germany

Correspondence to: Dr Focke Ziemssen, University Eye Hospital, Schleierstrasse 12, D-72076 Tuebingen, Germany; focke.ziemssen@med.uni-tuebingen.de

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References

- 1 **Rosenfeld PJ, Moshfeghi AA, Puliafito CA.** Optical coherence tomography findings after an intravitreal injection of bevacizumab (Avastin) for neovascular age-related macular degeneration. *Ophthalmic Surg Lasers Imaging* 2005;**36**:331-5.
- 2 **Bates DO, Harper SJ.** Regulation of vascular permeability by vascular endothelial growth factors. *Vasc Pharmacol* 2002;**39**:225-37.
- 3 **Heier JS for the FOCUS Study Group.** Intravitreal ranibizumab (Lucentis) with verteporfin photodynamic therapy for neovascular age-related macular degeneration: year one results. ASRS scientific paper presentation 2005, Montreal, Quebec, Canada.
- 4 www.maccugen.com/safety.asp.
- 5 **Kuehle M.** Laser lyndallometry in anterior segment diseases. *Curr Opin Ophthalmol* 1994;**5**:110-16.
- 6 **Sirwardena D, Kotecha A, Minassian D, et al.** Anterior chamber flare after trabeculectomy and after phacemulsification. *Br J Ophthalmol* 2000;**84**:1056-7.
- 7 **Shah SM, Spalton DJ, Smith SE.** Measurements of aqueous cells and flare in normal eyes. *Br J Ophthalmol* 1991;**75**:348-52.

Bilateral ocular metastasis from an occult primary melanoma

The simultaneous occurrence of bilateral uveal and conjunctival melanocytic tumours is rare, and in the absence of any apparent cutaneous primary melanoma is a difficult diagnostic problem, with the differential diagnosis including multiple primary ocular tumours, metastases, and a paraneoplastic syndrome.¹⁻⁴

We report the clinical picture and management of a patient with bilateral ocular melanomas, highlighting the value of magnetic resonance imaging (MRI).

Case report

A 44 year old man with a scotoma in his left visual field was found to have tumours superior to the left macula and in the inferior conjunctival fornix of the right eye. Histopathology showed a malignant melanoma with high mitotic rate. The right fundus showed three pigmented choroidal tumours and in the left eye there was one choroidal tumour (fig 1A). Fluorescein angiography of the left eye is shown (fig 1B, C).

Brain MRI showed bilateral diffuse uveal lesions with low signal on spin echo T2