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Metastatic pleural mesothelioma initially masquerading as chalazion

Metastases confined to the eyelid are rare. They usually derive from breast, skin, gastrointestinal, and urogenital tracts.¹ Malignant pleural mesothelioma is an uncommon malignancy presenting a steady rise in its incidence over the past 25 years.² It usually gives local metastases, although distant metastases are also reported.²

To our knowledge, an eyelid metastasis from pleural mesothelioma has never been reported. We describe a patient with pleural mesothelioma who developed a solitary eyelid metastasis. The lesion initially manifested as a recurrent chalazion. Histological confirmation has been obtained antemortem. Histopathology was consistent with the primary tumour.

Case report

A 57 year old man presented with unilateral painful swelling of the left upper eyelid

Figure 1 Diffuse thickening of the left upper eyelid corresponding to the metastatic lesion. The multifocal pattern of the infiltration is apparent. There was some loss of eyelashes. The lesion had a deep reddish, non-nodular appearance.

followed by high fever and weight loss. During the previous 6 weeks, he had been treated with local and systemic antibiotics for recurrent chalazia without any improvement. His medical history included pleural malignant mesothelioma for which he had undergone surgery combined with chemotherapy. Eighteen months elapsed between the diagnosis of mesothelioma and the presentation of the eyelid lesion. During that time he remained asymptomatic without any local recurrences or metastases to any of the common sites at the regular follow up.

On examination, a diffuse thickening of the eyelid with ill defined margins was noted (fig 1). The lesion seemed multifocal. The overlying skin was not movable but there were no surface irregularities or hyperkeratoses. The eyelid was too sensitive to invert. Examination of the right eye was unremarkable. There was no double vision. Visual acuity was 20/20. Slit lamp and fundus examination, and intraocular pressures were

normal. The tumour did not extend into the orbital cavity, as seen on the magnetic resonance image.

A biopsy was taken from the eyelid. Examination of the specimen showed a malignant epithelioid neoplasm with histological and immunohistochemical features similar to those of the primary pleural tumour, and consistent with malignant mesothelioma (fig 2). The patient was referred to the oncology department. Metastatic investigation revealed no other metastatic sites. Chemotherapy was initiated but without any response. The patient died 3 months later of lung metastasis.

Comment

Malignant mesothelioma is an aggressive tumour with a dismal prognosis.² This is consistent with the short lifespan of our patient after the detection of the eyelid lesion. There have been few reports of orbital metastasis of malignant mesothelioma but we are unaware of any previous report of an eyelid metastasis.³

Misdiagnosis of eyelid metastases is not uncommon. In a clinicopathological study of 31 patients with metastatic disease to the eyelid, metastasis was suspected in only 32% of the cases.¹ Chalazia can simulate other lesions. In a series of 1060 cases with the clinical diagnosis of chalazion, 6.4% were clinically misdiagnosed.⁴ In an otherwise healthy man the persistent eyelid infiltration of the present case, besides chalazion, would also recall a sebaceous carcinoma. The associated loss of lashes makes it suspicious of such a tumour. In the reported case pathological evaluation of the recurrent, atypical “chalazion” proved critical. Thus, any recurrent chalazion should be evaluated histopathologically. Accumulation of tumour cells in a multifocal pattern is indicative of a “field effect” at the level of the eyelid.⁵

Figure 2 (A, B) Histopathological examination demonstrates a population of large, epithelioid cells with severe pleomorphism, atypia, and abundant cytoplasm, infiltrating striated muscle (A) and skin adnexae (B). A hair follicle, sweat glands, and part of a sebaceous gland can be seen on the left of (B) (haematoxylin and eosin; original magnification $\times 400$). (C, D) Immunoreactivity of neoplastic cells for both vimentin (A) and pankeratin AE1/AE3 (B) (amplified avidin-biotin method with Ventana’s “NexES” automatic immunostainer; original magnification $\times 400$). The cells were negative to antibodies against calretinin, CD141 (thrombomodulin), TTF1, cytokeratin 5/6, CEA (polyclonal) BerEP4, HMB 45, MART1, EMA, and CD30 (Ki 1).

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.

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Does intravitreal injection of bevacizumab have an effect on the blood-aqueous 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-aqueous 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.

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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