Eye (2003) 17, 420–452

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LETTERS TO THE JOURNAL

Sir,

A case of cutaneous melanoma metastatic to the right eye and left orbit

Eye (2003) **17,** 420–422. doi:10.1038/sj.eye.6700360

A 38-year-old man with a history of cutaneous melanoma excised 15 years previously presented with deteriorating vision in his left eye and was found to have a metastatic choroidal melanoma. After 2 months, he developed proptosis of the right eye and was found to have a metastatic extra global orbital lesion.

Various therapeutic regimens were used to obtain palliation and maintain visual acuity, including chemotherapy and radiotherapy. The left eye required enucleation for intractable glaucoma 6 months after presentation but the right eye maintained a visual acuity of 6/18 for 2 years, finally developing rubeotic glaucoma. The patient died shortly afterwards, $2\frac{1}{2}$ years after initial ophthalmological presentation, and 11 years after the first manifestation of metastatic disease.

Case report

A 38-year-old Caucasian male was referred to the Ophthalmic Oncology service at the Tennent Institute in June 1995. He complained of progressive deterioration of vision in his left eye, floaters and a nasal visual field defect. Fifteen years previously, he had had a malignant melanoma removed from his right arm, followed after 6 years by axillary lymph node clearance for local recurrence. After 6 years still, cutaneous metastases around his left mammary area were excised and just a week prior to his attendance, he had had six cutaneous secondary lesions removed.

Examination revealed corrected acuities of 6/9 in the right eye and 6/18 in the left. Anterior segments and intraocular pressures were normal. There was an isolated large elevated pigmented mass in the left temporal fundus extending from the ciliary body and an overlying serous retinal detachment. It measured $17 \times 17 \times 11$ mm on ultrasound and had high internal reflectivity, characteristic of metastases. Examination of the right eye was unremarkable. The patient received 20 Gy of radiotherapy in five fractions over 7 days to the left eye. Liver ultrasound did not show metastatic deposits.

After 2 months, the patient developed 3 mm of proptosis and inferior dystopia of the right eye. Visual acuity was 6/9 but choroidal folds were noted on fundoscopy. B-scan ultrasound and MRI revealed a lesion in the superior orbit measuring $25 \times 14 \times 24$ mm. The solitary lesion was consistent with a metastatic deposit (Figure 2). The patient received 20 Gy of radiotherapy to the right globe over 7 days with slight regression. After 3 months, however, a painful proptosis recurred. Systemic chemotherapy was the remaining option and three cycles of dacarbazine (DTIC) were prescribed.

Shortly after commencing the second cycle, visual acuity in the left eye deteriorated to perception of light. The intraocular pressure measured 64 mmHg with a flat anterior chamber, a fixed pupil, and a necrotic tumour obscuring the posterior segment. An enucleation was performed for painful intractable glaucoma.

Pathology (Prof. WR Lee, FRCPath, Tennent Institute of Ophthalmology) confirmed the presence of a large necrotic spindle cell melanoma measuring $20 \times 20 \times 15$ mm, with secondary effects of pupillary block, obliteration of the anterior segment, iris necrosis, and retinal detachment (Figure 1). Trans-scleral penetration was confirmed but the mass was confined to the globe. There was no evidence of a naevus or of retinal or vitreal spread, and tumour cells were not identified in the choroidal blood vessels. Review of the cutaneous melanoma also revealed a tumour of spindle cell type.

Tumour regression did not occur with DTIC and it was stopped. The patient was considered suitable for a trial agent, a thymidilate synthetase inhibitor (methotrexate analogue). Clinically, there was a partial response, but treatment was discontinued due to leucopenia and abnormal liver function. Interferon alpha was started at a

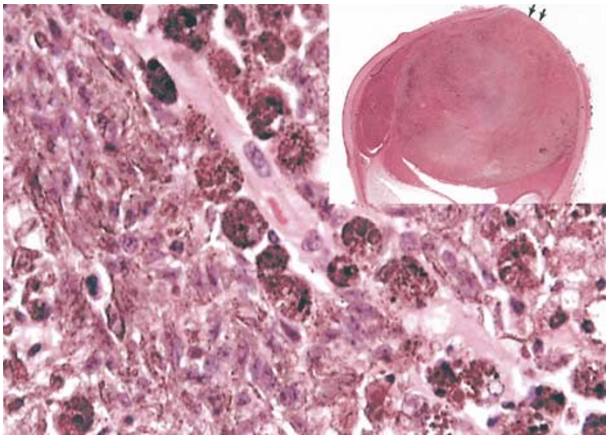

Figure 1 A high-power view of preserved spindle B melanoma cells and melanomacrophages around a blood vessel in the tumour (HE × 700). Inset: a low-power view of the globe containing a large necrotic pigmented tumour with scleral spread (arrows). The lens is subluxated and the anterior chamber is occluded. The iris and ciliary body are infarcted (HE × 5).

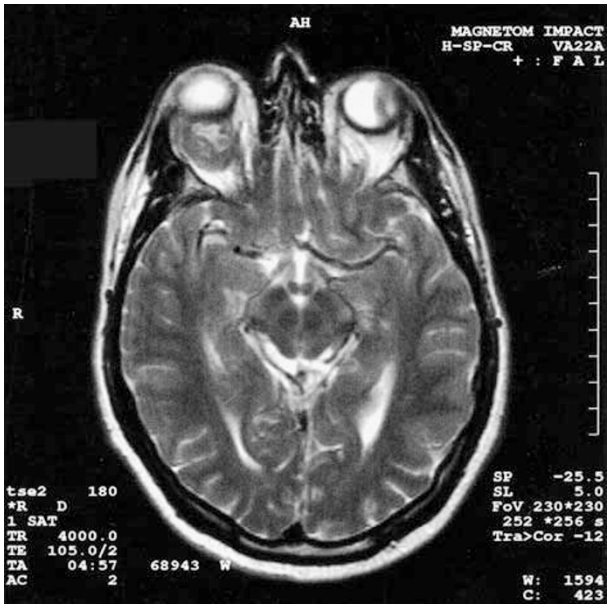

Figure 2 A T2-weighted axial MRI scan of the brain and orbits showing left intraocular mass and right retro-orbital mass.

dose of 3 mega units three times weekly, increasing to 10 mega units.

Despite chemotherapy, subcutaneous metastatic nodules developed in the right lid restricting ocular movements. Then 3 months later, the proptosis in the right eye increased to 7 mm. Palliative radiotherapy was repeated with dramatic regression of the proptosis.

The patient retained a visual acuity of 6/18 in the eye and was stable on systemic treatment for 18 months, despite the development of radiation retinopathy. Rubeotic glaucoma then developed in his right eye, requiring panretinal photocoagulation and topical beta blockers. The patient died shortly after in December 1997, $2\frac{1}{2}$ years after his initial presentation to the ophthalmology department.

Comment

This case is unusual in that there was bilateral presentation of metastases, one to the globe and the other to the orbit. The patient also survived for a long time after the first occurrence of metastatic disease, which involved regional lymph nodes. Metastasis to the eye is rare in cutaneous malignant melanoma, and it is estimated that only 0.5–1% of intraocular metastases originate from this primary tumour.[1] Intraorbital metastases occur even less frequently than those to the globe, and only two previous reports of simultaneous metastases to the eye and the orbit have been found in the literature.[2]

Differentiation between primary and metastatic melanoma can be problematic. DeBustros *et al*[3] used both the previous medical history and the presence of concurrent metastatic foci to establish their diagnosis of metastatic disease. This patient clearly had both of these features. Font *et al*[4] used a number of histological criteria to distinguish between the two. Some (lack of naevus cells at the base of the tumour), but not all, of these features were present in this case in the right eye. Nonetheless, Font *et al* acknowledge that histological differentiation between primary and metastatic melanoma may be difficult. Pathology of the left eye was not obtained at post mortem as metastasis was assumed due to the overwhelming clinical evidence.

Patients presenting with ocular metastases from cutaneous melanoma usually have widespread systemic disease at the time of ocular manifestation. Clinical presentation varies, depending on the site involved. Ramesh *et al*[5] reviewed the literature regarding intraocular sites of cutaneous melanoma metastases. In total, 75% involve the uvea, usually presenting with blurred vision or a visual field defect as in our case. Orbital involvement usually presents as a mass. Diplopia and extraocular muscle limitation are common as melanoma in the eye preferentially involves extraocular muscles.

Treatment of orbital metastases is palliative, using chemotherapy and radiotherapy. Current chemotherapeutic regimes are of limited potential. Dacarbazine is the most investigated agent and has partial response rates of 20%. Intravenous dicarbamazine, hydroxyurea, and BCG vaccination have resulted in intraocular tumour regression but not systemic regression.[6] Interferon alpha has shown a 30% partial response rate in tumour regression.[7] For symptomatic intraocular metastatic lesions, external beam or occasionally episcleral plaque radiation therapy (for isolated metastases) is the preferred treatment.[8] The response rate to external beam radiation is between 30 and 50%.[9]

One of the most commonly used palliative fractionation schedules is 20 Gy in five fractions, which seemed entirely appropriate in this case. Historically, melanoma responds better to a large dose per fractions, although more recently this has been considered to be of less significance. Therefore, 4 Gy fractions were used; a longer course of treatment was not prescribed in view of widespread metastatic disease and the likelihood of hepatic metastases. A similar dose was employed to the right eye with a slight response, which is considered a stable response (SD). Due to the failure of systemic chemotherapy, a further palliative radiotherapy course was given as a last resort with a surprisingly dramatic response.

The survival rate of cutaneous melanoma is related to the histological type of tumour and the depth of dermal invasion of the original lesion.[10] In this case, the primary cutaneous melanoma was spindle cell type with a depth of 10 mm. The prognosis is poor [11,12] due to disseminated disease and the poor response to chemotherapeutic regimes. However, the behaviour of melanoma is unpredictable and at times quiescent, resulting in long survival after initial diagnosis and even first onset of metastatic disease as demonstrated in this report.

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Sir,

Fluorescein angiography and patchy skin discoloration: a case report

Eye (2003) **17,** 422–424. doi:10.1038/sj.eye.6700361

Fundus fluorescein angiography is an invaluable and commonly used investigation for the management of various chorioretinal disorders. The complications occurring with this procedure are usually mild or rarely serious.[1] We present the unusual case of a patient who developed patchy yellow discoloration of the skin following intravenous administration of fluorescein sodium.

Case report

A 56-year-old male was referred to us with decreased vision in the right eye of 6 months duration. He had low-grade-B-lymphoma of the central nervous system, for which he underwent surgery combined with radiotherapy and chemotherapy 4 years ago. On examination, best-corrected visual acuities were 6/36 in the right eye and 6/5 in the left eye. He was noted to have macular oedema in the right eye and signs of exudative retinopathy in the left eye. A fundus fluorescein angiogram was arranged to investigate his clinical signs. As part of this procedure, a 22-gauge cannula was inserted into the right antecubital vein. A bolus of 5 ml of 10% sodium fluorescein (Martindale, Essex) was injected. No extravasation or leakage of the dye into the surrounding skin was seen. Fifteen minutes after the injection, multiple areas of patchy yellow skin discoloration were noted on the lateral aspect of the right arm and the right side of the anterior chest wall. The pattern of discoloration did not conform to any blood vessel distribution (Figures 1 and 2).

The patient did not develop any other adverse reactions to the fluorescein dye. He was observed for an hour and no further discoloration or allergic reactions were found to develop. The quality of the fluorescein angiography pictures was good. He was discharged home with the advice to seek medical attention should he develop any late reactions. The other patients who received the same batch of fluorescein sodium did not show any similar reactions. The patient was reviewed a week later, and he reported that the discoloration had faded gradually over the following 4 days without the development of any other adverse reactions. No fiuther cutaneous fluorescein staining was seen. A diagnosis of