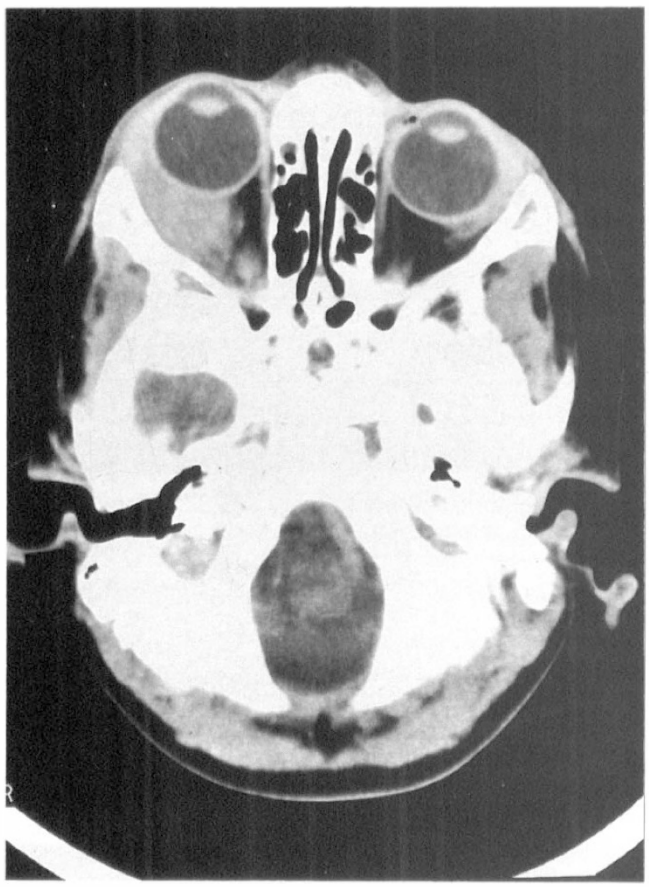

Fig. 2. *Orbital CT scan demonstrating a soft tissue density mass posterior and lateral to the right globe.*

indicated shadowing in the right superior perihilar region. Orbital CT scan demonstrated a soft tissue density mass posterior and lateral to the globe, which was displaced anteromedially (Fig. 2). There was no evidence of bone destruction and contrast failed to elicit significant enhancement. Extension into the cranial cavity was absent, and sections through the brain were normal.

Rhabdomyosarcoma was suspected, and a biopsy was performed. Bone marrow aspiration was undertaken at the same time. The orbital biopsy demonstrated an inflammatory granulomatous lesion with caseation. As an infective lesion had not been suspected, no material was sent for microbiological examination. A decision was made to commence triple anti-tuberculous therapy (rifampicin, isoniazid, pyrazinamide + pyridoxine). Tuberculin skin testing produced a 10 mm erythematous reaction without induration, and investigation of family members has failed to identify a source of infection to date.

Discussion

Intraorbital extraocular tuberculous disease is very rare. The predominant route by which tubercle bacilli reach the eye or orbit is haematogenous, after infection of the lungs. The pulmonary loci may not be evident clinically or radiologically. Both ocular and orbital tuberculosis are usually unilateral.[1] Orbital involvement may cause proptosis, dacryoadenitis, sinus formation, keratitis and ectropion.[2] The globe and orbital tissues may be involved simultaneously.[3]

In most cases reported, tuberculin tests were positive, and there was usually evidence of widespread tuberculosis.[4–6] Non-mycobacterial infections, neoplasms and developmental abnormalities are much commoner causes of proptosis than tuberculosis. However, the recent dramatic increase in the prevalence of this infection – in the United Kingdom and worldwide – warrants the inclusion of tuberculin testing in the investigation of childhood proptosis.

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Sir,

Cutaneous Malignant Melanoma Metastatic to the Choroid: A Clinicopathological Case Report

Metastases to the eye and ocular adnexa are relatively rare compared with other secondary sites; however, they are not infrequent, and are the most common malignancy to affect the eye.[1] The distinction between metastases and primary uveal melanoma is important because of the disparate methods of management, the importance of prompt diagnosis of the primary tumour and the prognostic implications. We report an interesting case of cutaneous malignant melanoma metastatic to the choroid. The pigmented appearance of the tumour initially mimicked a choroidal melanoma; however, the clinical features gave clues to the diagnosis, which was confirmed on pathological examination.

Case Report

A 26-year-old woman first noticed a change in a mole behind her left knee in October 1985. She had had a

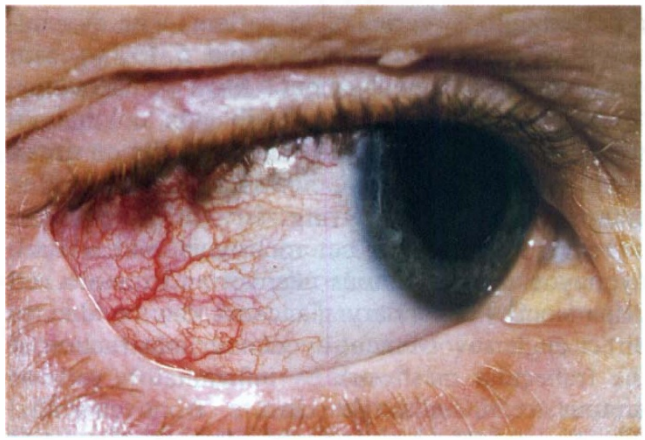

Fig. 1. *Sentinel vessels on the lateral aspect of the globe.*

lesion there all her life, but this had started to get larger and she sought medical advice in April 1986. A pigmented warty lesion 1.5 cm in diameter was removed from the left popliteal fossa, which proved to be a nodular malignant melanoma, Clarke level 4, Breslow thickness 11.6 mm. Due to the depth of invasion of the tumour, she underwent a further wide excision of the area with skin graft, and the histology on this was negative for malignant melanoma.

Systemic examination was unremarkable, with no hepatomegaly or palpable lymphadenopathy in the groin; chest radiograph and liver function tests were normal. After discussion, she agreed to undergo a course of adjuvant chemotherapy with intravenous vindesine to reduce the risk of metastatic spread. However, she developed severe neutropenia, peripheral neuropathy and alopecia after two 5 mg doses, and further treatment was abandoned.

She remained well with no evidence of recurrence for 8 years until November 1994, when she presented to the eye department with a 2 month history of blurred vision in the right eye associated with a field defect. In addition the eye had become red over the previous 2–3 days. On examination the corrected

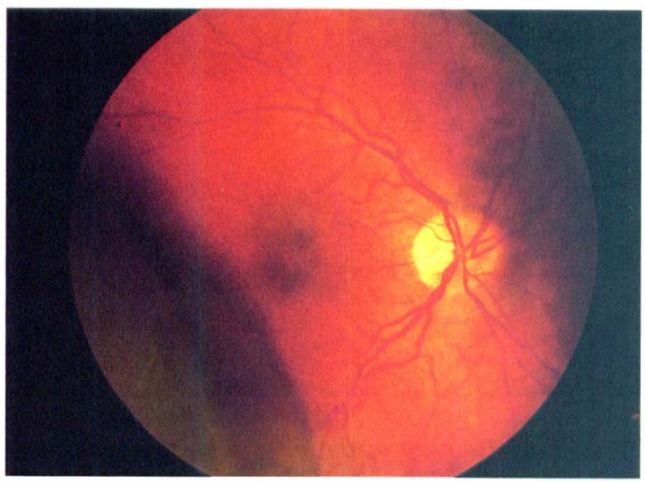

Fig. 2. *Large pigmented choroidal mass extending from the temporal ora serrata to within 1 disc diameter of the fovea.*

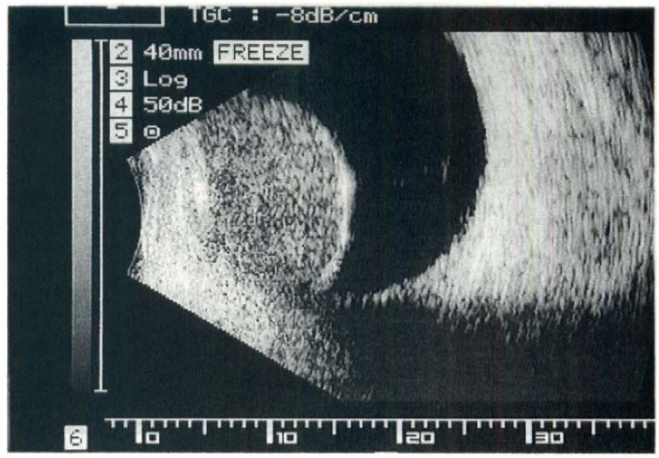

Fig. 3. *B-mode ultrasound scan showing large intraocular tumour.*

visual acuity in the right eye was 6/12 compared with 6/5 in the left eye. There was an area of injected scleral vessels on the lateral aspect of the globe (Fig. 1); the anterior chamber was deep and quiet. Fundus examination after dilatation revealed a large, heavily pigmented nodular mass arising from the choroid, extending from the temporal ora serrata to within 1 disc diameter of the fovea (Fig. 2). There was no overlying retinal detachment and the tumour dimensions on ultrasound scan (Fig. 3) were a base of 17 mm and a height of 12 mm. General systemic examination was unremarkable; however, a chest radiograph revealed two opacities in the left lung compatible with secondary deposits.

The ocular tumour increased in size rapidly over the course of the following 3 weeks and two pigmented abdominal subcutaneous nodules subsequently developed. The aggressive nature of the lesion in the presence of metastases at other sites, strongly favoured a choroidal secondary deposit rather than a primary melanoma of the choroid. The patient underwent a course of external beam radiotherapy to the right eye and was commenced on intravenous vindesine given in three divided doses of 3 mg each at 2 weekly intervals. Despite this, the vision dropped to counting fingers in the temporal field only, with shallowing of the temporal anterior chamber and an increase in the intraocular pressure to 30 mmHg. The eye was becoming increasingly painful, with pain radiating to the upper teeth, and therefore the decision was taken to enucleate the globe.

Pathology

The enucleated right globe measured 25 × 23 × 24 mm. The optic nerve stump was 1 mm in length and appeared externally unremarkable. The globe was irregularly distorted with a prominent bulge on the temporal aspect of the scleral surface. Horizontal section revealed a large choroidal mass of heterogeneous composition measuring up to 14 × 17 mm in

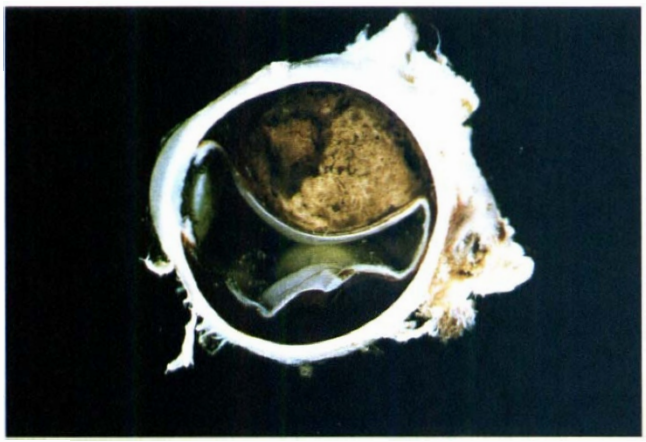

Fig. 4. *Cross-section of the enucleated globe showing an extensive choroidal mass of heterogeneous composition (top) and subretinal haemorrhage (bottom).*

cross-section (Fig. 4). The retina was circumferentially detached, with extensive subretinal haemorrhage. Histological examination of the intraocular tumour showed the appearances of a malignant melanoma composed of large polygonal cells with abundant eosinophilic cytoplasm (Fig. 5a). Some cells exhibited a granular cytoplasmic appearance, with an eccentric nucleus and a prominent nucleolus. A variable quantity of melanin pigment was present throughout the tumour. Multifocal necrosis was evident and numerous mitotic figures were readily identified. The presence of retinal detachment and subretinal haemorrhage was confirmed. The tumour invaded the underlying choroid and sclera, but complete scleral penetration was not identified. The vortex veins appeared free from tumour. The anterior chamber was unremarkable.

Immunocytochemistry showed a strong positive reaction for S100 protein, neuron-specific enolase and HMB45, all of which are characteristic of malignant melanoma. Comparison of the intraocular tumour with the cutaneous malignant melanoma removed in 1986 showed closely similar histological features, with numerous large polygonal cells containing abundant eosinophilic cytoplasm (Fig. 5b). Immunocytochemistry on the original cutaneous tumour showed a pattern of results identical to those for the intraocular tumour.

Discussion

Prior to the routine use of indirect ophthalmoscopy and ultrasonography, metastatic uveal disease and primary melanoma of the choroid were frequently confused. In this case the past history of malignancy, and most significantly the aggressive nature of the lesion, which demonstrated rapid growth over a short period of observation, were important indicators of the diagnosis.

Metastatic cutaneous melanoma to the eye is considered to be a rare clinical entity; however, a reported autopsy series of 15 patients with disseminated cutaneous melanoma found 5 (33%) with ocular or orbital involvement.[2] Most ocular metastases form distinct tumours visible on ophthalmoscopy, the uveal tract being the most common site of involvement.[3] There have, however, been reports of cutaneous melanoma giving rise to vitreous and aqueous seeding, iris heterochromia and a dark hypopyon due to tumour necrosis and tumour cell dispersion.[4,5] Secondary glaucoma can be due to direct angle involvement by tumour, obstruction of the trabecular meshwork by inflammatory cells or tumour cells, or angle closure from choroidal detachment.[6] The retina is normally a very rare site of metastatic involvement; however, interestingly a literature review in 1982[7] found that of 43 cases of cutaneous melanoma metastatic to the eye and adnexa, 9 (21%) involved the retina.

The distinction between primary and metastatic disease is important in terms of determining the course of treatment and the prognostic implications. The common natural course of ocular metastatic disease in malignant melanoma is a pre-existing

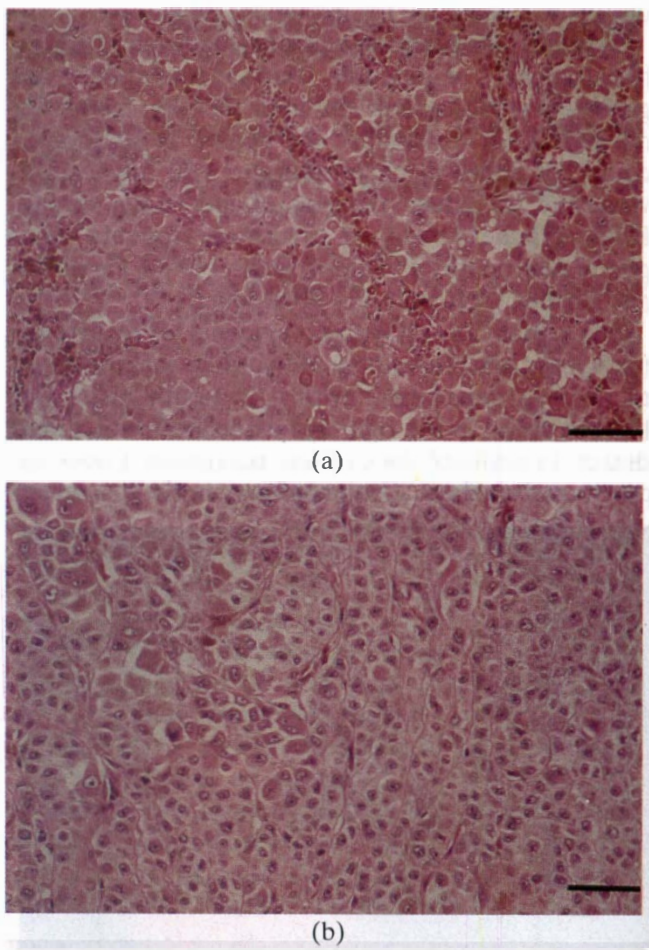

Fig. 5. *(a) Histology of the intraocular tumour (H&E stain) showing large polygonal cells with abundant eosinophilic cytoplasm, pleomorphic nuclei and prominent nucleoli. (b) The appearances in the original cutaneous melanoma are similar. Scale bar represents 50 μm.*

primary cutaneous lesion and several known visceral metastatic sites that precede diagnosis of the ocular metastasis. In contrast, visceral metastases are rare at the time of diagnosis of primary choroidal melanoma. In this case the ocular tumour was the first indication of any metastatic spread and prompted the discovery of other visceral secondaries. This report therefore emphasises the fact that the eye can be the initial site of a clinically identifiable recurrence of cutaneous malignant melanoma[6,8] and that ocular symptoms can develop up to 10 years after the excision of the primary tumour.[8]

Treatment of cutaneous malignant melanoma metastatic to the viscera and eye is usually palliative, and consists of a combination of external beam radiotherapy and chemotherapy. Enucleation was required in this case as the tumour had become extensive, resulting in a blind painful eye. External beam radiation therapy may relieve ocular pain and can be considered in painful eyes with visual potential. The response rate of metastatic melanoma to conventional forms of external beam irradiation is approximately 30–50%.[9] Radioactive plaque treatment can also be considered in patients with an isolated choroidal metastasis.[6]

The survival rate of patients with cutaneous malignant melanoma is partly related to the depth of dermal invasion,[10] which was deep in this reported case. The prognosis with ocular metastases is poor, due to the presence of disseminated disease and the fact that current chemotherapeutic regimes are of limited potential against this malignancy. Studies have shown a median survival of 72 days[6] and fewer than 10% of patients survive more than 8 months.[2]

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Sir,

Bilateral Orbital Metastases from Breast Carcinoma Masquerading as Thyroid Eye Disease

Carcinoma of the breast is the most frequent cause of death due to malignant disease in women[1] and is the most common cause of ocular and orbital metastases.[2,3] Despite this, misdiagnosis of orbital metastases commonly occurs.[4] There are several reasons cited for this in the literature: lack of suspicion, diverse clinical manifestations[4] and difficulty in obtaining an accurate history with regard to previous cancer. Metastatic tumours to the orbit usually result in a focal mass. With breast metastases, however, the growth pattern may be diffuse and can simulate an orbital inflammatory process clinically.[5] We present a case of orbital breast metastases which proved diagnostically challenging because of bilateral, almost completely symmetrical signs and symptoms, which were entirely consistent with a clinical diagnosis of thyroid eye disease.

Case Report

A 64-year-old Caucasian woman was referred from the local radiotherapy department for an urgent ophthalmic opinion. She had been referred for radiotherapy by her local ophthalmologist for treatment of compressive optic neuropathy secondary to thyroid eye disease. The diagnosis of thyroid eye disease had been made 4 months previously on the basis of a history of primary hypothyroidism managed with thyroxine, and the presence of