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Editorial: Early diagnosis of choroidal melanoma

Malignant melanoma of the choroid is the most elusive intraocular tumour. It is notoriously unpredictable and does not follow set rules. In some cases a large tumour may remain localised for a few decades and even undergo spontaneous regression, whereas in others a small lesion of relatively innocent appearance may shower lethal metastases. The latter characteristic is further highlighted in the case study this month of Char *et al.*[1] They report that diffuse choroidal melanomas are particularly treacherous; not only are they difficult to diagnose but they also undergo early extraocular extension. Since the patient's life as well as his sight may be at stake, early detection of such tumours is of paramount importance. It is imperative, however, to differentiate lesions simulating malignant melanoma so that unnecessary enucleation may be avoided. Mistakes in the diagnosis of melanotic lesions are not uncommon. Depending on the experience of the surgeon, the nature of the growth, the availability of reliable diagnostic aids, awareness of simulating lesions, and prevalent attitude towards intraocular malignancy, the incidence of unwarranted enucleation may vary from 3 to 24%.[2–5]

Although malignant melanomas of the choroid need to be differentiated mainly from spindle cell naevus, metastatic carcinoma, choroidal haemangioma, and massive subretinal haemorrhage, they may occasionally be confused with posterior scleritis, postoperative choroidal detachment, disciform retinal degeneration, retinal angioma, osseous choristoma of the choroid, and hyperplasia of retinal pigment epithelium. The clinical features and the ophthalmological appearance of such lesions are insufficient for a definitive diagnosis, and therefore several noninvasive diagnostic techniques have been described with intent to avoid unnecessary enucleation as well as to prevent any undue risk to the life of the patient. The following is a short account of the most popular diagnostic methods.

Fluorescein angiography is valuable in detecting acute and chronic changes in the pigment epithelium and the sensory retina overlying a suspected neoplasm. The presence of drusen, choroidal neovascularisation, and cystoid retinal degeneration are suggestive of a slowly growing and probably 'benign' tumour. Malignant melanomas show wide variation in their growth pattern and degree of pigmentation. The angiographic picture is thus a reflection of these variables. In general, however, evidence of widespread destruction or reactive proliferation of the pigment epithelium with multiple pin-point leakage of dye from the surface of the lesion is indicative of a rapidly growing tumour.[6] The finding of an irregular pattern of moderate-size blood vessels within a raised choroidal mass suggests a malignant neoplasm. Since benign choroidal naevi are often confined to outer layers of the choroid, they do not usually produce changes in the pigment epithelium and present with hypofluorescent filling defect within a normal pattern of background fluorescence. Angiography alone will not differentiate a metastatic carcinoma from a melanoma, especially if it is amelanotic.

The *radioactive phosphorus* (^{32}P) *test* for intraocular melanoma was introduced 28 years ago and has since evoked both staunch opposition and blind faith. The dust of stormy debates has yet to settle, mainly because of the test's unreliability in the diagnosis of small lesions in the posterior pole. Furthermore there does not appear to be a significant correlation between ^{32}P uptake and the size of the tumour, the cell type, and frequency of mitosis and hence degree of malignancy.

Since recent improvements to the probe and its application after conjunctival incision for posteriorly placed tumours, the reliability of the ^{32}P test has much improved and appears to be positive in over 90% of patients with malignant melanoma of the choroid.[7–9] The test may be negative, however, for small tumours and may be falsely positive for large naevi, haemangioma, leiomyoma of the ciliary body, granulomatous uveitis, hyperplasia of retinal pigment epithelium, and osseous choristoma of the choroid.[3 6 10] Furthermore the ^{32}P test cannot differentiate malignant melanoma from metastatic carcinoma of the choroid.

In a study reported in this issue of the journal Moseley and Foulds[11] have re-evaluated the ^{32}P test in the diagnosis of intraocular malignancy. They have carried out this test using a newly developed solid state detector consisting of a beta-sensitive conductor and have found that an 80% increase in radioactive uptake over the control value is strongly indicative of malignancy.

Ultrasonic evaluations in ophthalmology currently use frequencies of 5 to 25 MHz to provide echoes from the physical interfaces between tissues and cells having sufficient acoustic discontinuities to reflect sound. Three display modes are in use; the A mode, B scan, and the M mode. Of these the B scan is the most popular and easy to interpret,

because the 2-dimensional display corresponds to the histological cross-section of the lesion. In combination with the A mode it is of utmost importance in the differential diagnosis of posterior pole lesions, especially when ophthalmoscopic examination cannot be carried out because of opaque or hazy media.[12] A malignant melanoma on the B scan appears as a solid mass with a smooth and generally convex surface, but when it breaks through the Bruch's membrane it gives rise to a collar-stud appearance, which is rare in metastatic carcinoma and is not seen in haemangioma. The measurement of increase in size of a tumour over a period of time will differentiate rapidly growing metastatic carcinoma from a usually slow growing spindle cell melanoma. Ultrasonic evaluations when carried out in conjunction with ^{32}P test appear to provide the most reliable data for differential diagnosis of a choroidal lesion, and several studies at various centres indicate a 95% reliability for differentiating neoplasms from non-neoplastic lesions.[8 12 13]

Immunological tests for the diagnosis of intraocular melanoma are in their infancy. Although it has been shown that choroidal melanoma cells contain both surface membrane and cytoplasmic tumour-associated antigens,[14] the current methods of detection of cellular and humoral immunity to these antigens suffer from several drawbacks, mainly because the true nature of the tumour antigens is unknown and therefore the interpretations of false positive or negative results are extremely difficult. In an indirect immunofluorescent study of tumour antigenicity[15] cells from malignant melanoma of the choroid were exposed to sera from patients with a variety of non-neoplastic disorders, and it was found that an appreciable proportion of the sera were associated with positive cytoplasmic fluorescence. Further immunological studies,[16] however, showed that a proportion of these antibodies were directed against a contractile element present in a variety of mammalian tissues. In this issue of the journal Malaty *et al.*[17] show conclusively that the cytoplasm of melanoma cells contain actin filaments which are the main source of cross-reactivity and error in immunodiagnosis. Until sensitive methods are developed to remove successfully all the cross-reacting antibodies, the results of serological tests for the diagnosis of choroidal melanoma need to be interpreted with circumspection. Sunba, Rahi and Morgan, in a study (to be reported) of cellular immunity against such tumours, have found a positive correlation between lymphocyte transformation and extraocular extension of the lesion. Again the technique appears to be unreliable in the early diagnosis of choroidal melanoma, but it promises to be another useful test for determining the prognosis of this elusive and unpredictable tumour.

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