Anterior uveal neurilemmoma—a rare neoplasm simulating malignant melanoma

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SUMMARY A 30-year-old woman presented with dilated episcleral vessels in the right eye which were found to be associated with an underlying ciliary body tumour. Contact lens examination, transpupillary transillumination, ultrasonography, computerised tomography, magnetic resonance imaging, and fine needle aspiration biopsy produced apparently conflicting and inconclusive results, and the eye was enucleated. Light and electron microscopy showed the lesion to be a neurilemmoma (schwannoma), of which very few cases have been reported. The clinical and pathological features are described and discussed.

Intraocular, benign, peripheral nerve neoplasms are rare. Shields *et al.*¹ listed 18 tumours occurring in 17 patients, only two of whom had associated neurofibromatosis. Only four of these tumours were in the ciliary body; three were described as neurilemmomas, the other as a neurofibroma. More recently Rosso *et al.*² have added a further case. We describe an additional case which caused diagnostic difficulties despite the use of modern ancillary investigations. The correct diagnosis became apparent only after examination of the enucleated eye.

Clinical history

A 30-year-old Caucasian woman presented in September 1985 with a two months' history of gradual deterioration of vision in the right eye. She also had prominent episcleral vessels which she had first noticed five years previously in the same eye. Her general health was good and there was no relevant family history of ocular or systemic disease.

On examination the vision in the right eye was found to be reduced to 6/12, with correction, as a result of localised lens opacification, subluxation, and indentation by a large inferonasal ciliary body tumour (Fig. 1a). The tumour appeared pigmented and solid on ophthalmoscopic examination and was related to the overlying dilated episcleral blood vessels. Gonioscopy showed narrowing of the angle

inferonasally but the appearance was otherwise normal. The intraocular pressure, pupillary reactions, and remainder of the anterior and posterior segments of the eye were normal. The left eye was healthy, with an uncorrected visual acuity of 6/5. No abnormalities were found on general physical examination.

The tumour transilluminated brightly. Ultrasonography suggested that it was cystic in nature. Computerised tomography, however, suggested that the lesion was solid (Fig. 1b); there was no response to intravenous contrast medium. Fine needle aspiration biopsy was performed on 19 September 1985

Fig. 1a External photograph, right eye. The circumferential extent of the inferonasal ciliary body tumour is visible against the red reflex.

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Fig. 1b High resolution CT scan. The consistency of the tumour tissue was described as being identical to that of brain.

Fig. 1c Oblique sector ultrasound scan performed with a 10 MHz contact probe, showing solid nature and posterior extent of tumour, as well as posterior indentation of lens. Because of the anterior location of the lesion, the base is poorly defined.

beneath an inferonasal lamellar scleral flap, but the findings were equivocal (see below).

Subsequently the patient was referred to the Tennent Institute for further investigation and treatment. The above findings were confirmed except that ultrasound examination was suggestive of a solid lesion (Fig. 1c) of approximate dimensions 17 mm anteroposteriorly $\times$ 11 mm wide. Magnetic resonance imaging suggested a lesion of similar dimensions, but whether it was a solid tumour or a cyst containing proteinaceous fluid could not be determined (Fig. 1d). On angiography the lesion was completely non-fluorescent. The ^{32}P test was not performed. Excision biopsy was considered inappropriate, mainly because of the large size of the tumour, which involved more than one-third of the ciliary body. The eye was enucleated on 11 October 1985 because the tumour was increasing in size and because malignant melanoma could not be excluded.

Materials and methods

An air dried smear of the material obtained by fine needle aspiration biopsy was prepared and stained by the Giemsa technique.

After enucleation the globe was fixed in cacodylate buffered 3% glutaraldehyde for 24 hours, then sectioned obliquely (45°) and examined under saline with a dissecting microscope. A block including the

pupil and optic nerve was prepared, embedded in paraffin wax, and sectioned by routine techniques. Sections were stained with haematoxylin and eosin (H and E) and by the diastase/periodic acid-Schiff, Loyez, Bodian, and Perls' techniques.

For transmission electron microscopy small pieces of tumour were postfixed in 1% osmium tetroxide in cacodylate buffer, dehydrated through graded

Fig. 1d Magnetic resonance imaging. Axial view. SE40 sequence with TR:570MS; TE80MS performed on 0.15 T resistive magnet (Picker International) using a surface coil prototype. This demonstrates a well defined lesion giving a high signal.

Fig. 2 Fine needle aspirate, Giemsa stain. Loosely adherent tumour cells, in a fibrillary background, showing only minor nuclear abnormalities. No pigment is present.

alcohols, and embedded in epoxy resin (Araldite). Ultrathin sections were cut, stained with uranyl acetate and lead citrate, and examined with a Philips 301 electron microscope.

Results

FINE NEEDLE ASPIRATION BIOPSY

The smear showed a fibrillary background containing

Fig. 3 Enucleation specimen. Macroscopic photograph.

loosely adhering cells of monomorphic appearance with ill defined cytoplasm and cell borders, mild nuclear pleomorphism, and some irregularity of chromatin distribution (Fig. 2). Nucleoli were inconspicuous, and no mitoses were seen. No pigment was noted.

No definite diagnosis was made in either centre where the smears were examined. It was thought that the lesion was a solid tumour and that malignant melanoma could not be excluded.

ENUCLEATED EYE

Macroscopic findings. The globe measured 23×24×23 mm. Transillumination revealed a shadow in the inferonasal region. On oblique sectioning there was a rounded tumour mass measuring 15 mm anteroposteriorly × 11 mm high × approximately 15 mm wide, in the inferonasal region extending from the ciliary body to behind the equator (Fig. 3). It was white in colour and soft and homogeneous in texture. On transillumination at this stage the tumour showed unusual hyperlucency. The remainder of the eye appeared normal.

Light microscopy. The tumour formed a rounded mass distorting the ciliary body. It consisted of spindle cells with pale eosinophilic cytoplasm, in a finely fibrillary background. The nuclei showed finely dispersed chromatin and inconspicuous nucleoli, though there was some (generally mild) variation in nuclear size and shape. Groups of cells formed bundles and whorls, with some areas showing ill defined nuclear palisading, though this feature was not prominent (Fig. 4). Other areas showed loosely arranged cells and appeared microcystic (Fig. 5). The appearances were consistent with Antoni A and B areas of a neurilemmoma. Occasional bundles of myelinated nerve fibres were identified at the periphery of the tumour (Fig. 6). No features suggesting malignancy were present; mitotic figures were very rare and no areas of tumour necrosis or haemorrhage were seen. Occasional small foci within the tumour were rich in fine vascular channels.

Electron microscopy. The tumour cells from the cellular areas showed ovoid, sometimes multiple nuclei with clumping of the nuclear chromatin. The cells were surrounded by uninterrupted basement membrane material including collagen fibres (Fig. 7). Long-spacing collagen was noted in the basement membrane with a periodicity of 100–120 nm ('Luse bodies') (Fig. 7). Cytoplasmic processes showed intercytoplasmic interdigitations with pseudomesaxon formation (Fig. 8). A few poorly developed intercellular junctions were present. The cytoplasm of the tumour cells contained scattered mitochondria as well as Golgi complexes, short segments of rough endoplasmic reticulum, free ribosomes, and

Fig. 4 'Antoni A' area. Tumour cells in a fibrillary background. Ill defined nuclear palisades are arrowed. (H and E).

Fig. 5 'Antoni B' area. Tumour cells are more widely spaced and the tissue appears microcystic. (H and E).

Fig. 6 A myelinated peripheral nerve bundle (arrowed) is present at the edge of the tumour. Scleral connective tissue is also seen (top right of field). (H and E).

Fig. 7 Electron micrograph. Tumour cells are covered by uninterrupted basement membrane and scattered collagen fibres. Long spacing collagen in the basement membrane is shown in the inset. ($\times 1900$; inset $\times 19\ 000$).

lysosome-like dense bodies. A few cells contained membrane bound vesicles, some of which contained electron dense material, possibly melanosomes and melanophagosomes.

In the less cellular areas there were occasionally lipid vacuoles within the cells, which were also surrounded by the basement membrane material. One cell showed a cilium which was seen lying in a vacuole. Pinocytotic vesicles and intracytoplasmic filaments were frequently found in the cytoplasmic processes.

Discussion

We have established the diagnosis of neurilemmoma (schwannoma) in this case by both light and electron microscopy.^{3,4} No unusual features were seen by light microscopy, and the ultrastructural features of extensive basement membrane formation and pseudomesaxons are characteristic of neurilemmoma and not melanoma. Further, the presence of pre-melanosomes would not be diagnostic of melanoma, as they may be seen in pigmented neurilemmoma.⁴

The interest of the tumour, therefore, lies in its rare occurrence in the anterior uvea.

While the term ciliary body neurilemmoma reasonably describes the clinical presentation of this and other reported cases, it is unsatisfactory as a pathological description. The presumptive structure of origin of the tumour is a ciliary nerve. On the basis of published descriptions the tumour described by Callender and Thigpen⁵ appears the most likely actually to have arisen in the ciliary body. Two of the descriptions^{2,6} do not include an illustration of the gross specimen or a low power photomicrograph. In our case, and that of Hogan and Zimmerman⁷ and that of Donovan,⁸ the tumour could have arisen from a ciliary nerve in the uveal tract anywhere from around the equator posteriorly to the ciliary body anteriorly. We have therefore used the term anterior uveal neurilemmoma in recognition of our uncertainty of its exact site of origin.

We also consider that the tumours in four of the cases^{5,9-11} listed as neurofibromas in the review of Shields *et al.*¹ would now be termed neurilemmomas. It appears, then, that the majority of uveal nerve

Fig. 8 Electron micrograph. Cytoplasmic processes of the tumour cells entrap extracellular material to form pseudomesaxons. ($\times 15\,000$).

sheath neoplasms are neurilemmomas rather than neurofibromas.

The clinical features of this case illustrate some of the diagnostic problems of lesions presenting as ciliary body tumours.

On ophthalmoscopy the lesion appeared to be a cyst with a pigmented lining. This impression was supported by the highly translucent quality of the tumour and by its total lack of fluorescence on angiography. Ultrasonography was strongly suggestive of a solid lesion; computerised tomography was non-contributory; magnetic resonance imaging did not differentiate between a solid lesion and a cyst filled with highly proteinaceous fluid. In retrospect these apparent contradictions could be accounted for by the physical consistency of the neurilemmoma and its lack of pigmentation in the presence of an intact overlying pigment epithelium. The failure of magnetic resonance imaging to differentiate between a solid and a cystic lesion is presumably attributable to a high water content of the tumour.

It is worth emphasising that solid tumours, as well as cysts, may transilluminate if they are non-

pigmented, as was reported with a similar case.⁸ Further, the occurrence of a cystic appearance clinically does not necessarily indicate a benign lesion, as melanomas may occasionally be cystic.¹² Even melanin pigmentation, whether observed clinically or by light or electron microscopy, is not of absolute diagnostic value, since, as noted above, nerve sheath tumours may synthesise melanin. Heavy pigmentation of nerve sheath tumours is rare, however.

The lack of fluorescence by this tumour on angiography contrasts with the findings in previously reported cases.^{1,2,13,14} This phenomenon was probably due to the fact that the overlying pigment epithelium was intact.

Episcleral 'sentinel' vessels are often present with ciliary body melanoma. Their presence in this patient, as in a previous case,² therefore, is not a reliable indicator of malignancy. Also it should be noted that the rate of growth of neurilemmomas, despite their benign behaviour, may surpass that of melanomas.¹ The ³²P test, an indicator of tumour growth rate, was not performed in this case. A previous report¹ suggests that a borderline result was likely.

Thorough assessment of the fellow eye as well as the rest of the patient is essential.¹⁵ Cysts tend to be bilateral. The presence of extraocular malignancy or von Recklinghausen's disease may suggest the diagnosis, though a possible association between von Recklinghausen's disease and choroidal melanoma has also been recorded.¹⁴

In view of the clinical problem, fine needle aspiration biopsy might have yielded a definitive diagnosis; in general melanomas may readily be diagnosed by this method.¹⁶ However, none of the several pathologists who saw the material was experienced in aspiration cytology of ocular lesions. Even had the diagnosis of neurilemmoma been made by aspiration cytology, the assessment of the malignant potential of nerve sheath tumours is usually based on mitotic counts rather than nuclear pleomorphism. This requires examination of histological sections. Thus the technique may have been of less value in this particular case.

Excision biopsy would seem to be the ideal way of reaching a definitive diagnosis, because, as well as providing suitable tissue for histology, it could itself be effective therapy, while preserving the eye. In this case, however, retention of a useful eye was considered unlikely, because excision of more than one-third of the ciliary body would have been required. Enucleation was therefore unavoidable, not only because (in the absence of a definite diagnosis) the tumour posed a possible threat to life, but also because it would inevitably have resulted in a blind, painful eye, whatever the diagnosis.

In conclusion, this case history is instructive because it demonstrates that the differential diagnosis of ciliary body tumours remains a difficult clinical problem, despite the availability of a wide range of modern diagnostic techniques. Excision biopsy, if technically feasible, may offer a reasonable alternative to enucleation in specialist centres.

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References

- 1 Shields JA, Sanborn GE, Kunz GH, Augsberger JJ. Benign peripheral nerve tumour of the choroid. *Ophthalmology (Rochester)* 1981; **88**: 1322-9.
- 2 Rosso R, Colombo R, Ricevuti G. Neurilemmoma of the ciliary body: report of a case. *Br J Ophthalmol* 1983; **67**: 585-7.
- 3 Erlandson RA, Woodruff JM. Peripheral nerve sheath tumours: an electron microscopic study of 43 cases. *Cancer* 1982; **49**: 273-87.
- 4 Burns HK, Silva FG, Forde KA, Mount PM, Clarke HB. Primary melanocytic schwannoma of the stomach. *Cancer* 1983; **52**: 1432-41.
- 5 Callender GR, Thigpen CA. Two neurofibromas in one eye. *Am J Ophthalmol* 1930; **13**: 121-4.
- 6 Ferry A. Lesions mistaken for malignant melanoma of the posterior uvea. *Arch Ophthalmol* 1964; **72**: 463-9.
- 7 Hogan MJ, Zimmerman LE. *Ophthalmic pathology, a textbook and atlas*. 2nd ed. Philadelphia: Saunders, 1962: 443-5.
- 8 Donovan BF. Neurilemmoma of the ciliary body. *Arch Ophthalmol* 1956; **55**: 672-5.
- 9 Moorhouse JH. Case of neurofibroma of the choroid of acoustic nerve type. *Trans Ophthalmol Soc UK* 1939; **59**: 416-20.
- 10 Stough JT. Intra-ocular neurofibroma. *Arch Ophthalmol* 1937; **18**: 540-6.
- 11 Trevor-Roper PD. Case of neurofibroma of the choroid. *Br J Ophthalmol* 1944; **28**: 177-80.
- 12 Zakka KA, Foos RY, Spencer WH, Kerman BM, Newman NM, Pettit TM. Cavitation in intraocular malignant melanoma. *Arch Ophthalmol* 1982; **100**: 112-4.
- 13 Packard RBS, Harry J. Choroidal neurilemmoma—an unusual clinical misdiagnosis. *Br J Ophthalmol* 1981; **65**: 189-91.
- 14 Vannas S, Raitta C, Tarkanen A. Neurilemmoma of the choroid in Recklinghausen's disease. *Acta Ophthalmol (Kbh)* 1974; suppl 123: 126-33.
- 15 Damato BE, Foulds WS. Ciliary body tumours and their management. *Trans Ophthalmol Soc UK* in press.
- 16 Augsberger JJ, Shields JA. Fine needle aspiration biopsy of solid intraocular tumours: indications, instrumentation and techniques. *Ophthalmic Surg* 1984; **15**: 34-60.

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