Malignant Epithelioid Schwannoma with Melanocytic Differentiation: A Rare Tumour with an Unusual Feature

Sir,

Malignant epithelioid schwannoma (MES) is a rare variant of malignant peripheral nerve sheath tumour (i.e. malignant schwannoma), with a predominantly epithelioid pattern (1). The diagnosis is often confused because of the histopathological resemblance to undifferentiated carcinoma and malignant melanoma (2). We here present an MES with melanocytic differentiation based on the unusual clinical course of recurrences soon after surgery without development of metastases during a period of 10 years, and we report our histological, immunohistochemical and electron microscopical findings. A discussion of the differential diagnosis and the potential treatment of this tumour is presented.

CASE REPORT

A 31-year-old man was referred to our clinic in August 1995 with a painful tissue-fixed tumour, measuring $8 \times 8 \times 4$ cm and involving the left groin. Since 1986 twelve excisions had been performed, but the tumour had each time recurred soon after surgery at the same site. No signs of neurofibromatosis were seen. No evidence of distant metastases was detected in several examinations (skeletal scintigraphy, total body computertomography scan and nuclear magnetic resonance imaging). Neurological examination presented an incomplete failure of the N. femoralis sinister. Although extensive surgery was performed in September 1996, the tumour recurred again in April 1997.

Microscopically, we could observe a tumour with polygonal epitheloid cells with nuclei rich in chromatin, containing prominent nucleoli, arranged in rows and cords, atypical mitoses and necrosis (Fig. 1a). Parts of small nerves were seen, but no melanin pigment (Fig. 1b). The cytoplasm of the atypical epitheloid cells was strongly stained with PAS, but in Fontana-Masson staining no melanin pigment was observed in the tumour.

Immunohistochemical studies were performed using the APAAP-technique, the tumour cells showing a positive immunostaining for the following antigens: S-100, vimentin, neuron-specific enolase (NSE), gamma enolase, LEU7 and weakly for HMB-45 (Fig. 1b). We did not find a reaction for AE1/3 (pan-cytokeratin) or LCA.

By electron microscopy of paraffin-embedded sections we determined that there were numerous mitochondria, rough endoplasmatic reticula, and glycogen granules in the cytoplasm (Fig. 2a–d). Small granules with dense cores were often seen (Fig. 2b,d), but distinct cross-striation – suggesting immature melanosomes – was not observed.

DISCUSSION

We diagnosed this tumour as an MES with melanocytic differentiation, arising out of the N. femoralis sinister. The majority of MES reported in the literature originated in major nerves, including the sciatic, tibial, peroneal, facial, antebrachial cutaneous and digital. The tumours follow a distribution similar to ordinary malignant schwannomas, mostly occurring in patients 20 to 50 years of age (1).

The differential diagnosis includes neurotropic melanoma, atypical fibroxanthoma (AFX), epithelioid sarcoma, anaplastic carcinoma, large cell lymphoma and malignant melanoma. The neurotropic melanoma appeared to arise from the dermal connective tissue. The light microscopy is not typical of the two possible fibrohistiocytic neoplasms, AFX and epitheloid sarcoma (Fig. 2b).

By immunohistochemistry, carcinoma and lymphoma are excluded (no staining for AE 1/3 and LCA). Vimentin, S-100 and Leu7 are observed in melanomas and schwannomas. The positivity for NSE and gamma enolase is typical for a neuroendocrine cell differentiation of the tumour but has been previously described in malignant melanomas and MES. The tumour was weakly positive for HMB-45 (Fig. 1a). This antibody appears to be one of the most specific markers available for supporting a diagnosis of melanoma, but it is found in several other non-melanocytic tumours, for example adenocarcinomas and chordomas, and, recently for the first time reported, in a case of *MES of the skin with melanocytic differentiation* (3).

By electron microscopy no characteristic melanosomes are found. An abundance of glycogen, as seen in Fig. 2a*, may suggest that some tumour cells show both schwannian and melanocytic lines of differentiation. In melanoma it frequently occurs, but it is quite unusual in MES.

The distinction between amelanotic melanoma (see negative reaction for Fontana-Masson staining) and MES is very difficult. The previous diagnosis was "distant amelanotic meta-

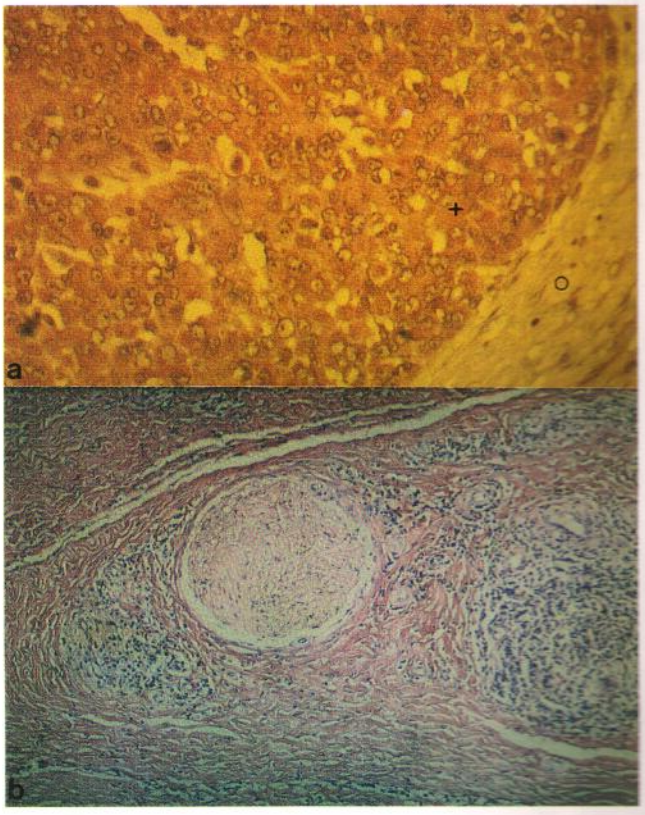

Fig. 1. Part of the epithelioid malignant schwannoma forming anastomosing cords and rows, sharply demarcated from a spindle cell area. (Positive immunostaining for HMB-45; *x*: tumour cells; *o*: stroma). Parts of a nerve are seen (*b*).

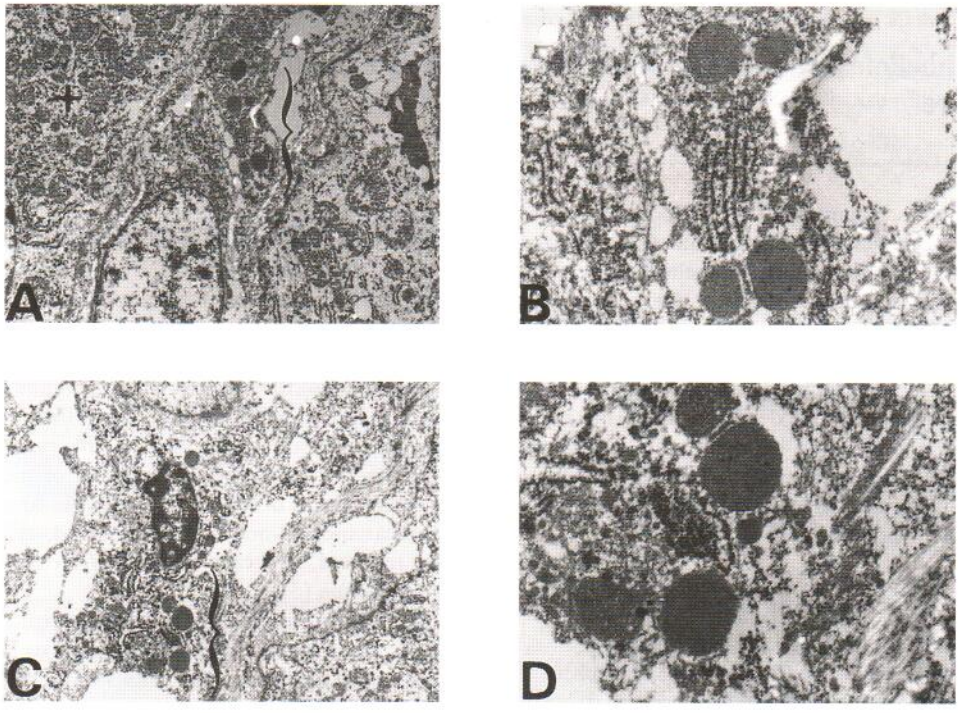

Fig. 2. (*a–d*). Electron micrographs of epithelioid cells (kindly performed by Prof. Dr. Luz, Institute of Pathology, GSF- München Neuherberg). Rough endoplasmic reticula, glycogen granules (+) and granules with dense cores (↕) are seen in the cytoplasm, but distinct cross-striation, suggesting immature melanosomes, could not be observed (*b* and *d* are magnifications of the marked area (↕) in *a* and *c*).

stasis of a malignant melanoma without a detectable tumor". However, MES looks like certain non-pigmented melanomas but does not run the clinical course of melanoma. The unusual clinical course of this case is that the tumour recurred soon after surgery without a development of metastases over a period of 10 years. The reason for the similarities between melanomas and MES, which are demonstrated in the reported case, may be that schwannian and melanocytic cells have a common embryological origin in the neural crest, suggesting that they derive from multipotential precursor cells. However, the knowledge of the correct diagnosis is important for the survival, prognosis and the treatment of the patient (4).

Radical surgery seems to be the best therapeutic choice. Only surgery can establish a final diagnosis and offers the best chance of survival. Chemotherapy (ephosphamid, carboplatin, VP16) or hyperfractionated radiation are also possible (4).

REFERENCES

1. Enzinger FM, Weiss SW. Soft tissue tumors. 2nd edn. St. Louis: CV Mosby; 1983. p. 781–815.
2. Stewart FW, Copeland MM. Neurogenic sarcoma. Am J Cancer 1931; 15: 1235–1320.
3. Shimizu S, Teraki Y, Ishiko A, Shimizu H, Harada T, Mukai M, et al. Malignant epithelioid schwannoma of the skin showing partial HMB-45 positivity. Am J Dermatopath 1993; 15: 378–384.
4. Ducatman BS, Scheithauer BW, Piepgras DG. Malignant peripheral nerve sheath tumors: a clinicopathologic study of 120 cases. Cancer 1986; 57: 2006.

Accepted May 29, 1997.

Matthias Thewes[1], Barbara Jungfer-Weber[1], Baldur Wiebecke[2], Reinhard Engst[1], and Johannes Ring[1]
[1]Department of Dermatology and Allergy, Biederstein, Technical University of Munich, Biedersteinerstraße 29, 80802 Munich, and [2]Institute of Pathology, Ludwig-Maximilians-University, Munich, Germany.