DEGENERATE NEURILEMMOMA : A DIAGNOSTIC PROBLEM

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SUMMARY: This is a review of our experience with degenerate neurilemmomas submitted to the Army Histopathology Registry (A.H.R.) from 1970-1975. The proliferation of vessels, bizarre spindle cells, and areas of degeneration were the principal features that led to errors in evaluation and diagnosis.

Introduction

In 1935 Stout delineated the clinical and pathological features of the nerve sheath tumour neurilemmoma (also known as schwannoma, lemmocytoma, neurinoma, acoustic neuroma and perineurial fibroblastoma). Although originally considered rare this is a lesion frequently encountered in surgical pathology and usually one which is recognised by its typical histological features. The neurilemmoma is a true neoplasm believed by most investigators to derive from nerve sheath cells of Schwann and thus to be of neuroectodermal origin (Murray and Stout 1940). A few workers still favour derivation from perineurial fibroblasts (Cravioto 1966, Santhaveerappa and Bourne 1966). The typical tumour is usually solitary, encapsulated or well circumscribed and adjacent to recognisable nerves. It shows Antoni A areas, the cellular regions; and Antoni B areas, the myxomatous regions, as well as so called Verocay bodies which are zones of collagen surrounded by palisading nuclei. The solitary type neurilemmoma gives no diagnostic problem usually, but the subvariety composed of thick vessels, hypercellular areas with nuclear atypism, and degenerative foci is apparently confusing to pathologists and prompted our investigation. This variant has been termed degenerate or "ancient" neurilemmoma (Ackerman and Taylor 1951).

Materials and methods

Clinical summaries and microscopic sections of 28 tumours coded as degenerate (ancient) neurilemmoma submitted to the Army Histopathology Registry from military hospitals in the United Kingdom and overseas and from civilian hospitals in Botswana, and Nepal over the period 1970-1975 were analysed.

Haematoxylin-eosin stains were studied in all cases. In selected cases Masson trichrome, Gordon and Sweet's silver impregnation for reticulin, the alcian blue stain for mucopolysaccharides and Perl's Prussian blue reaction for iron and Masson-Fontana for melanin were also performed.

Results

Age and sex

The ages of the 27 patients at the time of diagnosis ranged from 16 to 64 years, with 70 per cent of the cases occurring between the ages of 20 and 40 years (Table I). There

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Table I
Age distribution of 27 patients at the time of excision

Age group (years)	Number of cases	Contributing hospitals	
		Military	Civilian
10 to 19	2	1	1
20 to 29	10	7	3
30 to 39	10	5	5
40 to 49	1	1	—
50 to 59	3	2	1
60 to 69	1	—	1
Totals	27	16	11

were 25 male patients and 2 female patients. All the tumours submitted from overseas hospitals (Africa and Nepal) occurred in male patients (8 cases). There were 19 caucasian patients, 4 African negro patients and 4 Nepalese patients.

Anatomical location

The most common sites were the lower extremity (thigh, knee and ankle)—9 cases; the upper limbs (fingers, wrist and upper arm)—6 cases; head and neck region, including one intracranial acoustic nerve tumour—5 cases; chest wall and mediastinum—5 cases. Two tumours were removed from intraspinal nerve roots and one tumour arose in the retroperitoneum, presenting as an abdominal mass (Table II).

Table II
Distribution of 27 patients with 28 tumours

Anatomical site	Tumours	Anatomical site	Tumours
Head and neck, includes one intracranial acoustic nerve tumour	5	Chest wall and mediastinum	5
		Retroperitoneum	1
Upper extremity	6	Intraspinal nerve roots	2
Lower extremity	9	Total	28

Signs and symptoms

One degenerative acoustic neurilemmoma presented the classical signs and symptoms of this location. The intrathecal tumours were excised following spinal root compression syndromes. The retroperitoneal tumour presented as an abdominal mass which was thought to represent splenomegaly by a number of examining physicians. Of the remaining 24 cases only 4 summaries specifically mentioned localised pain,

tenderness or referred pain in relation to the tumour. The majority presented as a lump which tended to enlarge slowly. The clinical impression was some kind of neural tumour in only 12 cases and a variety of alternative tumourous conditions were suggested in 15 cases (Table III). An association with injury was not noted although specific enquiries

Table III
Initial clinical diagnosis of 27 patients

Diagnosis	Cases	Diagnosis	Cases
Neurilemmoma	4	Chemodectoma, carotid region	1
Neurofibroma	8	Hodgkin's lymph node	1
Ganglion	2	Thyroid nodule, mediastinum	1
Lipoma	3	Splenomegaly	1
Cyst	2	Branchial cleft cyst	1
"Nodule", "Lump" or "Tumour"	3	Total	27

were not made. None of the patients, including the patient with two separate tumours, showed any of the stigmata of von Recklinghausen's neurofibromatosis.

Gross observation

The tumours ranged in size from 1 to 7 cm in diameter with a mean of 2.5 cm. The tumour was always encapsulated or well circumscribed. The cut surfaces were yellow-tan or greyish-tan in colour, commonly with cystic, haemorrhagic and mucoid areas (Fig. 1). Thick walled vessels could sometimes be discerned. Nerve bundles were identified in many tumours entering the mass, either pushed to one side or adherent to it (Fig. 2).

Fig. 1. Encapsulated degenerate neurilemmoma with cystic change.

Fig. 2. Nerve bundles compressed by tumour (haematoxylin and eosin; x 40)

Microscopic findings

In addition to the Antoni type A and B tissue and Verocay bodies (Figs. 3 to 5), which are typical of any neurilemmoma, the characteristics common to degenerate

neurilemmomas were the focal areas of hypercellularity, nuclear hyperchromatism and pleomorphism together with proliferation of hyalinized vessels and sinusoidal blood spaces, some thrombosed (Fig. 6). The Verocay bodies and Antoni tissue types were

Fig. 3. Cellular, Antoni A type tissue (haematoxylin and eosin; $\times 40$).

Fig. 4. Myxoid, Antoni B type tissue (haematoxylin and eosin; $\times 40$).

Fig. 5. Verocay body formed by a double palisade of nuclei enclosing a space devoid of nuclei (haematoxylin and eosin; $\times 40$).

Fig. 6. Dilated vessels, one containing a thrombus surrounded by pleomorphic cells some having hyperchromatic nuclei (haematoxylin and eosin; $\times 40$).

sometimes difficult to identify and additional blocks had to be examined before the neurilemmomatous nature of the tumour was confirmed. These diagnostic areas were frequently best preserved near the capsule (Fig. 7). Some of the sinusoidal spaces showed reactive papillary proliferation of the lining endothelium of the type frequently encoun-

Fig. 7. Subcapsular recognizable neural tissue with Verocay bodies. The true nature of the tumour is often seen in this area (haematoxylin and eosin; x 40).

tered in thrombosed and obstructed vessels (reactive intravascular angiomatosis); this latter appearance is not to be confused with the intravascular papillations of an angiosarcoma (Salter and Salter 1975). Foci of extravasated red cells and deposits of haemosiderin pigment were seen indicating old haemorrhage. Collections of finely vacuolated lipid-filled macrophages were encountered in areas of degeneration and haemorrhage. Between the vascular spaces and residual neural tissue densely hyalinized connective tissue was frequently found. Calcification was not noted in any of our tumours although it has been reported (Harkin and Reed 1969). Cystic spaces lined by flattened cuboidal cells were sometimes bordered by hypercellular zones of closely packed, hyperchromatic elongated cells some with atypical enlarged nuclei and occasional giant cells. Moderate cellular pleomorphism was always present but mitotic figures were absent (Fig. 8). Interlacing bundles of closely packed cells sometimes mimicked a cellular leiomyoma or a fibrous histiocytoma. Scattered diffusely about the tumour, and occasionally forming dense aggregates, were numerous small dark cells (Fig. 9). These have been

Fig. 8. Moderate cellular pleomorphism with occasional giant cells but absence of mitotic figures (haematoxylin and eosin; x 100).

Fig. 9. "Lymphocytoid" cells in a small aggregate. The exact nature of these cells is uncertain (haematoxylin and eosin; x 100).

described as "lymphocytoid" cells and on light microscopy are indistinguishable from lymphocytes (Harkin and Reed 1969). Plasma cells and eosinophils were not prominent although occasional mast cells were present. Small amounts of acid mucopolysaccharide were demonstrated in the matrix in two tumours. Melanin pigment was not demonstrated but has been reported (Harkin and Reed 1969).

Treatment

Simple excision apparently cured all of the tumours in this series. No evidence of recurrence was detected in our cases and recurrence reported in the literature is extremely rare (Stout 1935, Ackerman and Taylor 1951).

Discussion

Only about half of the tumours were considered to be neural in origin on clinical examination. Neurilemmoma was suggested by the surgeon in 4 of the 27 cases. The remaining cases were called a variety of soft tissue tumours. The contributing pathologists did not always appreciate the neural origin and on 4 occasions misinterpreted the atypical features for a variety of sarcomas including synovial sarcoma, haemangiosarcoma, haemangiopericytoma, fibrosarcoma and malignant lymphoma. The smaller lesions, showing less marked degenerative change, were usually correctly diagnosed as some type of benign nerve tumour although neurilemmoma was not always recognised. A few were also confused with other benign conditions including haematoma, haemangioma, dermatofibroma and fibrous histiocytoma (Table IV). Usually the

Table IV
Contributing pathologists' diagnoses suggested for 28 degenerate neurilemmomas

Diagnosis	Cases	Diagnosis	Cases
<i>Benign</i> Degenerate Neurilemmoma	2	<i>Malignant</i> Synovial Sarcoma	1
Neurilemmoma (Schwannoma)	14	Angiosarcoma	1
Neurofibroma	3	Haemangiopericytoma	
Hamartoma	1	Lympho-reticular Malignancy	1
Haematoma/Haemangioma	1	Fibrosarcoma	1
Nodular Fasciitis	1		
Fibrous Histiocytoma	1		
Dermatofibroma	1		
Total	24	Total	4

obvious nerve attachment prompted the correct diagnosis. The extensive degenerate changes and cellular pleomorphism gave rise to the greatest confusion. A careful search of the entire lesion, often requiring examination of additional tissue blocks revealed the typical Antoni tissue types and the Verocay formations which are diagnostic of neurilemmoma. Having established the Schwannian origin of the lesion, the encapsulation or

circumscription together with the absence of mitoses, should indicate a benign neoplasm. Neurilemmomas are rarely a feature of von Recklinghausen's neurofibromatosis but none of our cases was so associated. Malignant transformation seems to be confined to neurofibromas and especially to neurofibromas occurring in von Recklinghausen's disease. A careful evaluation of all patients with solitary nerve tumours is essential to exclude neurofibromatosis. Histological examination alone will not resolve this. Clinical information, including past history and family history, together with X-rays on occasions, are required to exclude neural tumours in other sites. Malignant transformation of neurilemmomas, on the other hand, must be exceptional although denovo malignant schwannomas have been reported (Ghosh et al 1973). We found no examples of malignant transformation of degenerate neurilemmomas in our cases.

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