SOLITARY TUMOURS OF PERIPHERAL NERVE TRUNKS

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Primary solitary tumours of the peripheral nerve trunks are relatively infrequent. Three such tumours have been treated at Hammersmith Hospital during the last four years, but a search of the hospital records for the period 1939–1950 has not shown any similar cases. (Solitary tumours of the auditory nerve and spinal nerve roots are not included in this report.) In these three patients the tumour involved the radial, lateral popliteal and ulnar nerves respectively. In only one of them was the diagnosis made before operation.

A swelling arising from a main nerve trunk may be a traumatic false neuroma, a neurofibroma, a neurilemroma or, more seldom, a neurofibrosarcoma. There are only two benign tumours which arise from nerve trunks. One of these is the neurilemroma, which develops from the cells of Schwann, and with which this paper is mainly concerned; the other is the neurofibroma, which is derived from fibroblasts and will be discussed only in relation to the true neurilemroma.

Nerve axons cannot give rise to tumours independently of their parent cells, but if damaged or divided they coil up into a mass of connective tissue and give rise to a false neuroma. Peripheral tumours of nerve cells can occur only in situations where there are nerve ganglia, as in the sympathetic plexuses or the thoracic root ganglia. They are included in the group of ganglion-neuromas, comprising less than one per cent of nerve tumours outside the central nervous system, and will not be discussed here.

NOMENCLATURE AND CELL OF ORIGIN

The three tumours reported here are regarded as benign tumours of the nerve sheath. These tumours are called by many names—neurilemoma, Schwannoma, neurinoma, perineural fibroma or fibroblastoma, palisaded neuroma, peripheral glioma—and are frequently confused with the neurofibroma (Mayo and Barber 1934, Cutler and Gross 1936b) as indicated by Craig (1945). The term neurilemoma (from νεῦρον—nerve, λέμα—a closely adhering sheath, and οίκος—a tumour) will be employed here.

There are two views on the origin of tumours of nerve sheaths. Masson (1932) and Stout (1935a), basing their theory on histological investigations, believed that the tumours are derived from the sheath cells of Schwann (Schwann 1847). They maintain that Schwann cells of the nerve sheaths are also responsible for the large areas of collagen and reticulin fibres that are interspersed between the cells. This view is supported by Nageotte (1932) and by Stewart and Copeland (1931), by the tissue culture studies of Murray and Stout (1940), and by the examination of a large bulk of material carried out by Willis (1948). Skinner (1929), from a study of neurilemmomas of the acoustic nerve, suggests that though the Schwann cells are the “type cell” the intercellular connective tissue of the tumour is in the nature of a tissue reaction and derived from the adjacent tissues.

The opposite view, that these tumours arise from the connective tissue fibroblasts of the perineurium or endoneurium, is put forward by Mallory (1914, 1920) and by Penfield (1927, 1932), whose theory is based on the assumption that tissues derived from ectoderm are incapable of forming the collagen and reticulin fibres which are invariably present. They therefore apply the name perineural fibroblastoma to them. Tarlov (1940) has supported this by special staining techniques. Even in a normal nerve trunk it is difficult to distinguish...
between the endoneurium and the Schwann-cell syncytium and the difficulty is greater in the case of a nerve tumour.

Both schools admit that the Schwann cells of a normal nerve sheath are derived from the neural crest and are therefore ectodermal in origin, as demonstrated by Harrison (1908, 1924) and Harvey et al. (1926, 1933).

Patients with solitary neurilemmomas may show associated characteristics of von Recklinghausen's disease, and neurilemmal tissue is frequently found in true neurofibromata (Penfield 1927). There is therefore difficulty in deciding the origin of the neurofibromata and in determining the relationship between the neurofibromata and the true nerve sheath tumours. Foot (1945) has suggested that they may be a scirrhous form of neurilemmoma. In a neurofibroma, however, the parent nerve appears to be expanded by a diffuse increase of all the sheath tissues with separation of the nerve fibres and bundles as they traverse the swelling. This may not be a true tumour at all, but a "hamartoma"—a tumour-like malformation with the tissues in improper proportion or distribution and a prominent excess of one particular tissue (Albrecht 1904, Willis 1948). Trotter (1926) believed that the fibromatous formation of a neurofibroma was due to a deficiency of the normal nerve sheaths, as a result of which the non-insulated nerve fibres give rise to fibrosis by local irritation of the adjacent tissues—in much the same way as a foreign body would. Willis indicates that generalised neurofibromatosis predisposes to the development of a true tumour, either a neurilemmoma or a localised progressive fibroma or a malignant sarcoma, superimposed on the original lesion. Similar views are expressed by Worster-Drought et al. (1937) and by Bailey and Herrmann (1938).

INCIDENCE AND SITE

The incidence is about the same in both sexes and these tumours have been found from infancy to old age. It is difficult to assess the true incidence of neurilemmomas as they are often unrecognised; it is equally difficult to assess their incidence in different situations, as most of the cases have been reported in the literature of special groups.

Neurilemmomas usually arise as solitary tumours from the main nerve trunks. Stout (1935a) reviewed 194 previously published cases and added fifty additional ones; of these the majority of tumours were derived from main nerve trunks. More recently Money (1950) reported thirteen neurilemmomas amongst 360,672 patients over a period of thirty-eight years; of these seven were from major nerve trunks. Sjövall (1937) found seventy nerve tumours in 31,331 necropsies but failed to distinguish between neurilemmomas and neurofibromas.

Several authors (Mayo and Barber 1934, Cutler and Gross 1936b) record these tumours as "solitary neurofibromas not associated with von Recklinghausen's disease," but from the descriptions and photographs it is evident that at least some of them could have been neurilemmomas.

In addition to the peripheral nerves of the limbs, the cranial nerves also give rise to neurilemmomas. The auditory nerve is the most frequent site inside the skull; in the neck the facial nerve (Loeliger 1947), the glossopharyngeal nerve (Cedermark 1949), the vagus (Tarlov 1940, Murley 1948, Paul 1949) and the hypoglossal nerve (Friedman and Eisenberg 1935, Haase 1946) may be affected. Gordon-Taylor (1940) recorded a tumour probably arising from either the glossopharyngeal or the vagus nerve which exactly simulated a carotid body tumour clinically and at operation. The cervical sympathetic trunk also may give rise to a neurilemmoma (Callum 1949). Thirteen of Stout's (1935a) series of fifty tumours occurred in the head and neck, and Ehrlich and Martin (1943) found that 43 per cent were in this situation; but this high incidence may be due to the relatively large numbers of head and neck tumours treated at the Memorial Hospital, New York.

These tumours may also grow from the spinal nerve roots and give rise to symptoms of spinal cord compression (Elsberg 1925, Rogers 1948), or they may extend outwards through
the intervertebral foramen, which constricts the tumour to a "dumb-bell"  (Eden 1941). Occasionally a neurilemmoma may occur in the subcutaneous tissues, but they never develop in the dermis (Biggart 1949).

The stomach is a relatively common site for a neurilemmoma (Minnes and Geschickter 1936, Ransom and Kay 1940), and a peculiar epithelioid type of the tumour described by Willis (1948) grows in this situation but has not been reported as occurring elsewhere. Other less frequent sites are the tongue (Stout 1935a), the sympathetic nerves (presumably derived from the Remak sheath cells, which are the counterpart of Schwann cells of myelinated nerves) and the skeleton (de Santo and Burgess 1940). Only three of the tumours have been described in bone and one of these appears to have been due to secondary invasion of the sacrum by a neurilemmoma of a spinal nerve root. The osseous lesions present as simple, clearly defined defects in the affected bones and are wholly unlike the typical bone lesions of von Recklinghausen's disease of nerves.

CLINICAL FEATURES

The solitary neurilemmoma of a peripheral nerve trunk usually presents as a symptomless swelling discovered accidentally by the patient, which has been present for several years before he seeks treatment (Lewis and Hart 1930, Stout 1935b). Even with large tumours, interference with nerve conduction is unusual (Ewing 1940). If the affected nerve and its tumour are lying in a lax intermuscular plane, pressure-effects—paresis or analgesia—are less likely to occur (Case 1) than if the nerve is in contact with unyielding bone (Case 2) or enclosed in a restricted fascial compartment (Case 3). Motor or sensory disturbances alone do not indicate malignancy, as suggested by some authors. There is usually no discomfort except in response to external pressure.

In the limbs, neurilemmomas occur most often in the front of the arms and the back of the legs—that is, on the flexor aspects, which is to be expected from the anatomical distribution of the main nerve trunks. The swelling is usually movable from side to side but the nerve prevents its being moved in the long axis of the limb. If the tumour is near the surface and has undergone extensive cystic degeneration it may be transilluminated.

PATHOLOGY

Neurilemmomas are well circumscribed encapsulated tumours with the bundles of the parent nerve passing to one side or spread out over the surface of the tumour (Livingston and Hastings 1947). Neurofibromata are less well defined at the edges and may blend with the surrounding tissue; they often infiltrate the parent nerve, with thickening of its trunk for a variable distance beyond the main tumour mass. Nerve bundles traverse the centre of the neurofibroma instead of passing to one side (Willis 1948). A neurilemmoma may be firm and fibrous but it frequently undergoes cystic degeneration; a neurofibroma is always solid and never becomes completely cystic. The three tumours recorded here had undergone extensive cystic degeneration and their appearance at operation was identical, though the histological picture varied (Figs. 1, 6 and 8).

Most neurilemmomas are solitary (Stout 1946) but true neurofibromas are almost always multiple (Barnard and Robb-Smith 1945). However, neurilemmomas may occasionally develop in addition to neurofibromas in multiple neurofibromatosis. Conversely, though a solitary nerve tumour is nearly always a neurilemmoma, it may occasionally be a true neurofibroma (Willis 1948).

Histology—Neurilemmomas show a palisade arrangement of cells in parallel rows with intervening fasciculated bands of collagen or reticulin fibres which can be demonstrated by silver stains (Fig. 4). The cells may also be arranged in whorls. Both the palisading and the whorls are referred to as Verocay bodies (Verocay 1908, 1910), after the author who first described them and differentiated the specific neurilemmoma of the nerve sheath from the
neurofibroma. A neurilemmoma may be solid with a well defined orderly arrangement of cells and fibres (Fig. 2), or there may be many areas of myxomatous cystic degeneration with a looser texture and more haphazard reticulated arrangement of the fibres and the cells. These are known as Type A and Type B tissue respectively (Antoni 1920) and are frequently present in the same tumour (Fig. 3). The cystic areas in Antoni type B tissue may coalesce and form larger cysts (Fig. 3). Stout (1935b) and Cutler and Gross (1936a, 1936b) have described tumours which appear to be entirely cystic and in which the typical structure of the neurilemmoma has been replaced by a fibrous capsule. Other authors (Wadstein 1931, Ferguson 1937) refer to these cystic tumours as "ganglia" of the nerve trunks. All these cysts are probably degenerate nerve tumours; there seems no reason to suppose that either a normal or an injured nerve trunk will undergo cystic degeneration.

A similar cystic change had developed in the second and third cases of the series. It seems likely that the central cystic degeneration of a neurilemmoma with distension of the tumour will destroy the tumour cells but leave the more resistant intercellular fibrous tissue as a capsule. Injury appears to initiate or accelerate cystic degeneration (Case 3). Such a change would be more likely where the nerve is passing through a rigid compartment, like that surrounding the ulnar nerve at the wrist (Case 3), or where it lies in direct contact with unyielding bone (Case 2). The cellularity of the cyst wall in Case 2 (Fig. 7) suggests a transitional stage between the typical histological appearance of Case 1 and the simple cyst with a fibrous capsule where the cystic degeneration is complete (Case 3).

Malignant change—Tumours arising from Schwann cells are benign, and local enucleation does not appear to initiate malignant change (Stout 1946). Even if the tumour is incompletely removed in an effort to preserve the continuity of the nerve trunk, local recurrence is infrequent: there was only one local recurrence in Stout’s series of 144 cases and this tumour did not become malignant (Stout 1946). But the neurofibromata of von Recklinghausen’s disease are liable to malignant change and it appears that operative intervention increases this risk, especially if the tumour is incompletely removed (Speed 1942, Aird 1949). It is therefore of great importance that these two types of nerve tumour should be differentiated before any attempt is made at surgical treatment. It is better to avoid surgical intervention with a
Case 1—The excised tumour. Low magnification. Two compact whorls of cells and fibres (Verocay bodies) are seen surrounded by more loosely arranged tissues in which there are numerous minute cystic spaces (Antoni B tissue). In the centre there are large areas of myxomatous degeneration without cell nuclei and some of these are already converted into irregular cystic spaces. As degeneration progresses the cysts coalesce and will ultimately form a single large cyst.

Case 1. Figure 3—High power view, showing the typical palisaded arrangement of the nuclei with orderly collagen fibres between the rows of cells (Antoni type A tissue). Figure 4—Section stained with a silver stain to demonstrate the arrangement of the reticulin fibres.
neurofibroma, but if an operation is necessary it is safer to resect the affected nerve trunk with the tumour (Cutler and Gross 1936a, Aird 1949).

The failure to differentiate between neurofibromas and neurilemmomas in many of the reported cases of apparently benign nerve tumours becoming malignant (Geschickter 1935, Cutler and Gross 1936b) makes it difficult to assess the relative liability of these two types of nerve tumour to malignant change, though it is known that many patients with multiple neurofibromatosis develop malignant neurofibrosarcoma (Garrè 1892, Hosoi 1931, Geschickter 1935). The solitary neurilemmoma is essentially a benign tumour and there is no proof that it ever becomes malignant, though on rare occasions a locally malignant nerve tumour has been suspected of originating from a benign neurilemmoma (Cutler and Gross 1936b). Four out of five malignant neurofibrosarcomata arise from pre-existing benign neurofibromata (Stout 1935a, Stout et al. 1937), and they seldom show histological evidence of neurilemmomatous structure (Willis 1948). Their structure and behaviour are similar to that of other sarcomata of the connective tissues (Stewart and Copeland 1931, Quick and Cutler 1927). There is no evidence to suggest that they arise from neurilemmal tissue.

**TREATMENT**

Solitary nerve tumours are usually neurilemmomas and can be enucleated completely by careful dissection. The nerve bundles are spread out over the surface of the tumour and it may be necessary to split the nerve longitudinally to gain access to it (Cutler and Gross 1936a). The injury inflicted on the nerve by the operation is likely to cause temporary paresis and hypoaesthesia in the affected area (Case 1) or to increase any such disability which may have been present before operation (Case 2). Nerve conduction usually recovers rapidly and the operation should later lead to a full return of function by relieving the pressure on the nerve.

If the tumour cannot be enucleated it is probably not a neurilemmoma but a neurofibroma, the nerve fibres running through the centre of the tumour instead of round it. Such tumours can be removed only by excision of the affected nerve segment with suture of the divided ends (Cutler and Gross 1936a). Because of the liability of this type of tumour to undergo malignant change it is probably unwise to attempt a simple enucleation (Speed 1942) or even biopsy unless clinical features—such as pain or increased size of the tumour—suggest that malignant change may already have taken place. Under these circumstances the suspected tumour should be widely extirpated, with its parent nerve (Herrmann 1950). All tumours removed at operation, however benign their macroscopic appearance, should be examined histologically for evidence of malignant change.

**CASE REPORTS**

**Case 1**—A woman aged sixty-seven sought advice for a symptomless swelling of the right arm which had been present for several months. She did not think it was getting larger, but she was anxious to have it removed.

On examination there was no visible external swelling, but on palpation a firm and slightly tender mass could be felt in the soft tissues over the lateral aspect of the distal third of the right upper arm. It was not attached to the overlying skin or to the underlying bone. The swelling was oval in shape and approximately one inch long, with its long axis in the line of the limb. It could readily be moved from side to side but would not move in the long axis of the arm. It became fixed by resisted flexion of the elbow. Its position was not affected by movements of the elbow and it was thought to be embedded in the substance of the brachialis muscle or the lateral intermuscular septum. There were no palpable axillary glands, no muscle weakness and no alteration in skin sensation. At operation in June 1947, the swelling was found to lie between the outer margin of the brachialis and the upper limit of the brachio-radialis muscles and in front of the lateral aspect of the triceps. With further dissection it became evident that the tumour was intimately connected with the trunk of the radial nerve (Fig. 1). The nerve bundles were spread out over the surface of the tumour and it was found possible to enucleate the tumour completely from the nerve by careful dissection. The external appearance was similar to that of a simple ganglion, and during the
CASE 2. Figure 5—The swelling over the head and neck of the fibula. Note the extensor paresis of the first toe. Figure 6—The multilocular cystic tumour of the lateral popliteal nerve with the nerve bundles spread over the anterior and outer aspects of the tumour.

FIG. 7
Case 2—The collagenous wall of one of the large cystic spaces. Two small nerves can be seen in the adventitia at the opposite side of the field.

Operation the capsule was inadvertently torn with the escape of clear gelatinous fluid. The radial nerve was preserved and at the close of the operation lay in its normal intermuscular plane.

Progress—The operation was followed by an incomplete radial nerve palsy, which recovered completely within three months. On examination three years later there was no recurrence of the swelling and there were full power and movement and normal sensation in the arm.
Histology—The sections showed a typical neurilemmoma with the cell nuclei arranged in rows and whorls with bands of collagenous fibres between (Figs. 2 and 3). In other areas the cells and fibres were irregularly arranged, with myxomatous degeneration and numerous small cystic spaces coalescing in places to form larger cysts (Fig. 2). Silver impregnation demonstrated many reticulin fibres (Fig. 4).

Case 2—A man aged forty-five was admitted to hospital in December 1949 with intermittent pain over the outer and anterior aspect of the left leg below the knee, in the region supplied by the lateral popliteal nerve. Recently he had noticed cramp when kneeling which had become worse in the previous four months. During the same period he had noticed a lump in the region of the head of the fibula which when touched produced a tingling sensation in the leg.

On examination there was a firm rounded swelling, approximately one inch in diameter, behind the head of the left fibula (Fig. 5). Although its centre appeared to be subcutaneous, it was intimately attached to the deep structures. The swelling was mobile across the axis of the limb but could not be moved longitudinally. Skin sensation was diminished to touch and pin-prick in the distribution of the lateral popliteal nerve, and there was well marked impairment of power of all the anterior crural and peroneal group of muscles. The extensor hallucis longus was completely paralysed.

Operation—The lateral popliteal nerve was exposed proximal to the tumour and followed down behind the fibula. At this point a cystic swelling approximately one and a half inches long and half an inch across was found lying underneath the gastrocnemius and behind the peroneal muscles (Fig. 6). The cyst was multilocular, with the branches of the nerve spread out over its anterior and superficial surface, with the loculi of the cyst herniating between the branches. The cyst was dissected away from the nerve with some difficulty and was punctured, with the escape of glairy fluid similar to that seen in a ganglion. The branches of the nerve were directly stimulated by faradic current: the peroneal muscles contracted strongly but none of the anterior crural muscles responded to the stimulus.

Progress—On the day after the operation there was complete paralysis of the anterior crural muscles and weakness (M3) of the peronei. There was no further decrease in the skin sensation. A month later the patient was discharged; he walked with a hinged inside below-knee iron, an outside T-strap and a toe-lifting spring. The tibialis anterior muscle had already recovered weak voluntary contraction. The paralysed muscles slowly recovered, and seven months after operation there was full normal power in all of them except the extensor hallucis longus, of which the strength was only M3. The affected muscles were therefore much stronger than before the tumour was removed. When last examined a year after operation there was full power of all the muscles, with normal skin sensation and no evidence of any recurrence of the tumour.

Histology—The microscopic sections showed that the tumour had undergone extensive cystic degeneration and some of the cysts had coalesced to form relatively large cavities surrounded by collagenous scar tissue. The wall of one of these cysts is shown in Figure 7.

Comment—Ferguson (1937) and Cutler and Gross (1936b) reported similar cases and Wadstein (1931) reported two cases and reviewed five others. It appears that the lateral popliteal nerve at this level is particularly liable to the formation of these cystic tumours.

Case 3—A woman aged fifty-one injured her hand slightly at housework in February 1950. She had immediate intense pain in the ulnar side of the hand, which passed off after a few minutes. A week later paraesthesiae and aching developed in the fourth and fifth fingers, and later there was progressive weakness and flexion deformity of these fingers with shrinkage of the hypothenar eminence. She attended hospital two months later. On examination there was analgesia to light touch and pin-prick in the distribution of the ulnar nerve in the hand and fingers. The hypothenar muscles were grossly wasted and typical deformity of the fourth and fifth fingers was present—flexion of the interphalangeal and extension of the metacarpo-phalangeal joints. It was thought that the disability was due to a direct contusion of the ulnar nerve and its adjacent tissues, and the patient was treated conservatively.

The sensory disturbance gradually recovered but the paresis and deformity persisted. Eight months after the original injury there was a palpable tender swelling of the ulnar nerve at the level of the pisiform. This was thought to be a traumatic neuroma. The hypothenar and interosseous muscles were severely wasted and voluntary straight finger flexion of the fourth and fifth fingers was impossible. Electrical stimulation of the nerve above the lesion produced contraction of all the muscles with the exception of the interossei. The nerve lesion was evidently incomplete and involved the deep branch of the ulnar nerve. Because of the swelling and the failure to respond to conservative treatment it was decided to explore the ulnar nerve at the wrist.

Operation—A cystic tumour of the ulnar nerve was found arising mainly from the deep branch and burrowing between the abductor and flexor digiti minimi, with the nerve bundles spread out.
over its anterior and medial surface (Fig. 8). The superficial branch of the nerve also was in intimate contact with the tumour but was not compressed or distorted. The tumour was carefully dissected away from the nerve but it was found necessary to excise the pisiform to obtain access to the deepest part. During the dissection the cyst was punctured, with the escape of glairy mucinous fluid.

*Progress*—Immediately after the operation there was a transient hypoaesthesia of the fourth and fifth fingers which resolved within a week. Six months later the voluntary power of all the affected muscles had increased and their response to galvanism was much stronger. Some weakness still persisted, however, and, as in severe injuries of the ulnar nerve at a higher level (McGowan 1950), it appears unlikely that full recovery of motor function will be obtained.

*Histology*—The microscopic sections showed complete cystic degeneration with a collagenous wall but no lining cells. In this specimen no residual true tumour tissue could be found (Fig. 9). Although no neurilemmal tumour tissue was present, because of its anatomy and clinical behaviour it was regarded as a neurilemmoma that had undergone complete degeneration. Similar extensive and sometimes complete cystic degeneration has been demonstrated in many of the previously published cases already discussed.

**SUMMARY AND CONCLUSIONS**

1. Three solitary tumours of the peripheral nerve trunks are reported. None of the patients showed evidence of von Recklinghausen's disease.
2. The origin of these tumours is discussed; the evidence suggests that they develop from the Schwann cells of the nerve sheaths, and they should therefore be called neurilemmomas.
3. A solitary tumour of a peripheral nerve trunk is usually a neurilemmoma and not a neurofibroma.
4. These tumours are often mistaken for neurofibromas, from which they are wholly distinct. They are uncommon, but probably occur more often than is generally appreciated.
5. A neurilemmoma is a benign tumour which can be distinguished from a neurofibroma on clinical and operative grounds. It must be enucleated with preservation of its parent nerve. There is negligible risk of recurrence and no risk of malignant change after operation.

6. Neurilemmomas are liable to cystic degeneration, especially in situations where they are subjected to pressure or injury. This cystic change may later destroy the usual cellular structure of the tumour and convert it into a simple cyst.

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