Peripheral nerve tumours
— diagnostic and therapeutical basics

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In this review of international literature, we have described recent opinions on diagnostics and therapy of peripheral nerve tumours. We have emphasised the use of differential diagnostics on certain stages of therapeutic procedures. The importance of proper surgical technique choice and its influence on final results have been especially underlined. Other important factors influencing final therapeutical results have also been considered and discussed.

**key words:** peripheral nerve tumours, peripheral nerve neoplasms, neurilemmoma, neurofibroma, malignant neurilemmoma, von Recklinghausen’s neurofibromatosis, microsurgical techniques

Peripheral nerve tumours are divided into the following groups:

a) neoplasms of neural trunks and branches;
b) paraganglionic neoplasms (pheochromocytoma, chemodectoma);
c) ganglionic neoplasms (neuroblastoma, ganglion-neuroma) [12].

Peripheral nerve tumours have rather rare appearance among soft tissue tumours [39, 44]. They consist about 1.0–4.9% of all hand and arm tumours [8, 43]. Table 1 illustrates systematisation of peripheral nerve tumours [39].

In clinical practice, benign neural trunks tumours are the most frequently diagnosed, whereas malignant tumours are the less frequent and tumours of consistency of hamartoma, choristoma or granulocellular tumour [2, 4, 9, 19–21, 25, 39] are only occasional.

It is known that the so called neuroma in continuity, which is the partial nerve laceration (side neuroma), long term irritation (fusiform neuroma) or unsuccessful microsurgical reconstruction, causes the deformation of the neural trunk [14]. Other non neoplasmatic pathologies of tumours are intraneural thecal cysts [39].

Peripheral nerve tumours are difficult to differentiate from other soft tissue tumours during initial physical examination. They and can be mistaken for lipomas or

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<th>Table 1. Classification of peripheral nerve tumours</th>
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<td>1. Benign tumours:</td>
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<tr>
<td>a) neurofibroma (solitary, diffuse, plexiform, epithelioid, pa-cinian, storiform)</td>
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<td>b) schwannoma, neurilemmoma, neurinoma (cellular, plexi-form, melanocytic, epithelioid, ancient)</td>
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<td>c) neurothekeoma</td>
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<td>d) granular cell tumour</td>
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<td>2. Malignant tumours:</td>
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<td>a) malignant peripheral nerve sheath tumour — MPNST — schwannoma malignum</td>
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<td>b) primitive neuroectodermal tumour PNET</td>
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<td>3. Hamartoma (lipofibromatous h.)</td>
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<td>4. Choristoma (neuromuscular ch.)</td>
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<td>5. Neurinoma in continuity</td>
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synovial cysts [2, 32, 43], especially, when a growing tumour causes only slight paresthesias and small neurological deficit, which is characteristic for neurilemmoma [2, 39]. This benign tumour from Schwann cells is usually small, round or oval with well defined nodule on forearm or palm [2, 9]. It is rarely found on fingers [32]. It can be moved aside or rotated by 90° forearm or palm [2, 9].

Neurilemmoma is usually a small tumour less than 5 cm in diameter. Nevertheless, big growing neurilemmomas (about 20 cm) have also been reported [3, 26, 27, 43]. Rather slight neurological deficits can be explained by slow, eccentric ingrowth of the tumour due to the elasticity of the epineurium and perineurium.

In spite of some characteristic features neurilemmoma is difficult to differentiate from neurofibroma both in clinical [36] and preoperative imaging examinations [2, 33].

Neurofibroma is a benign tumour from Schwann cells, perineurial cells and fibroblasts. Usually, it occurs as a single tumour localised superficially (when arises from the superficial cutaneous branches) or deeply (when from bigger neural trunks) [39]. Neurilemmoma is often located on fingers [28] and makes up 1–3% of all hand’s tumours [20]. Multiple neurofibromas and diffuse form occur in over 10% cases of Recklinghausen disease type 1 [9]. Pathognomic of the Recklinghausen disease type 1 is a plexiform neurofibroma [39], which in 10% cases becomes malignant [2, 7, 42]. Clinical signs of the neurofibroma are similar to those found in neurilemmoma [2, 39]. Differential diagnostics is more sufficient after surgical exposure. In case of appearance of small, encapsulated, round or oval, smooth and shining superficially, eccentrically located inside the nerve and easily removable tumour, it is diagnosed as neurilemmoma [2, 36, 43]. Incidentally there is only a necessity of resection of a part of the nerve trunk. It is usually possible to remove the nodule without touching the nerve fascicles, which are not a part of the tumour. In case of neurofibroma, which is located inside the nerve trunk, excision is much more difficult because the structure of the tumour is often mixed with fascicles of the nerve trunk. This makes it necessary to cut both “entering” and “leaving” the tumour fascicles. It is necessary to cut off the involved part of the nerve trunk [2, 36] and perform the microsurgical reconstruction with nerve grafting (usually from the sural nerve). Because of this situation, neurological deficit is more significant after neurofibroma removal [2] than after resection of neurilemmoma. Excision of a single neurofibroma tumour (histopathologically confirmed) located in the subcutaneous tissue requires ruling out the patient’s Recklinghausen disease. If this is not the case, treatment can be judged as completed [39]. Removing these types of tumours leads to the removal of cutaneous nerve, which is the base of the growing tumour. When the nerve is important for the hand or foot function, it is necessary to perform the microsurgical reconstruction directly or with grafts. However, the nerve of growing tumour very often remains unidentified [39].

Careful decision about surgical treatment should be made in cases of classic, generalised form of Recklinghausen disease. It is not indicated to excise many small asymptomatic tumours; surgical treatment should be reserved for fast growing and progressive, symptomatic tumours [2, 6]. This applies to both superficially and deeply located tumours.

Special attention and carefully designed procedure should be applied to cases when intraoperatively irregular, relatively big, connected to the surrounding tissue and penetrating the nerve trunk structure tumour has been spotted [39]. All these characteristics suggest malignant process. The most frequent malignant neoplasm of the peripheral nerves is neurilemmoma malignum (schwannoma malignum), which constitutes 10% of all soft tissue malignant tumours [9]. Ethiopathogenesis of this malignant tumour is not definitely clear. A genetic mechanism has been suggested after clinical data that 40–50% of neurilemmoma malignum cases occur in patient with diagnosed Recklinghausen disease [7, 13, 35]. Researchers at Mayo Hospital have been proven that neurilemmoma malignum appearance risk is 4600 times bigger in patients with Recklinghausen disease than in patients without this diagnosis [5]. Other authors suggest that risk of appearance of neurilemmoma malignum in patients with Recklinghausen disease is between 4–5% usually after 10–20 years of disease duration [7, 13, 35]. The influence of radiation on neurilemmoma malignum development has been proved in about 11% of cases [10]. Neurilemmoma malignum develops the most frequently inside the nerve trunk or on the basis of existing neurofibroma [7]. Rather rarely the basis can be neurilemmoma [30, 37].

During the preoperative clinical examination, the patient feels pain because of the growing tumour, which causes neurological deficit [7, 24]. The symptoms can be present for many months or even years, but this long
period does not determine benign character of the tumour [7, 34].

Intraoperatively neurilemmoma malignum is presented as big, fusiform or egg-shaped tumour of hard consistency and coloured brown. Advancing necrosis can lead to the point where the tumour turns soft, yellow with haemorrhagic focuses. As the tumour grows it can be surrounded by pseudo capsules, which can give illusion of sharp contours of the tumour [39]. It is not advised to dissect or transect the tumour in sites of junction with the surrounding soft tissue [39]. The final treatment should be performed after full diagnostics has been made. In the treatment one must consider “en block” excision of the tumour or amputation [2, 39]. The choice of method depends on: tumour localisation — including the distance from the chest and pelvis, its diameter, malignancy and the fact if the tumour is a primary change or recurrence. Application of radiotherapy and chemotherapy has only palliative importance and is focused on pain level decreasing and local recurrences or micrometastases prophylaxy [2, 39].

Relatively rare but very aggressive are primitive neuroectodermal tumours, which involve among others also nerve trunks [16, 18, 22]. They usually occur as big, often of diameter more than 9 cm, fast growing tumours, which cause pain and impairment of the nerve function. At the time of diagnostics, about 25–50% of patients develop metastases in other organs [16, 22], and the tumours themselves are big and difficult to remove. Intraoperatively there is solid brown tumour with haemorrhagic focuses and infiltrated margins. After decisive diagnosis based on biopsy results, treatment similar to that of schwannoma malignum has to comprehensively include surgical „en block” excision or amputation with chemotherapy and radiotherapy.

A lot of controversies about treatment methods are connected with another peripheral nerve tumour; lipofibromatous hamartoma. This non-malignant tumour grows slowly and is usually located inside the median nerve, less frequently in the ulnar and radial nerves in young patients [2, 15, 29, 39]. During tumour growth in the epineurium and perineurium, it is stretched by the mature fatty tissue and fibrous tissue, which also infiltrates between nerve fascicles [29] and makes surgical dissection more difficult. At the beginning, the tumour grows at the forearm region without symptoms, but later on nerve compression symptoms occur in the symptomatology remaining carpal tunnel syndrome or Guyon’s syndrome; this case only occurs in children and teenagers [29, 31]. Intraoperatively big, more than 5 cm in diameter, fusiform inflation of the nerve is spotted. It is yellow or orange-yellow without strait connection to the surrounding tissue [39]. Most authors suggest in these cases nerve trunk decompression with biopsy of fibromatous and fatty tissue [39] or with biopsy of the cutaneous branch of the median nerve if it is involved [20, 31]. They represent opinions that an attempt to excise the tumour by interfascicular dissection often leads to loss of motor and sensory nerve functions, among others by impairing the blood supply [15, 31, 39]. In many cases, improvement in nerve function and decrease of tumour diameter were observed after only nerve decompression [2]. In cases where this type of surgical procedure symptoms remain or return (pain, systematic tumour growth), it is suggested to excise the tumour saving fascicles [40]. Repeated nerve decompression and the accompanying opening of the carpal tunnel, in cases of recurrence, do not bring any positive results [1, 20]. There are reports about surgical removal of the lipofibromatous hamartoma with immediate reconstruction by sural nerve grafting [29]. It is not however the method of choice because most authors do not accept [15, 20, 31, 39, 40]. In cases of digital nerve involvement, treatment includes nerve decompression, tumour excision or partial nerve resection with its reconstruction depending on specificity of the nerve involved and extent of the ingrowth [39]. Similar procedures like in hamartoma treatment are indicated in cases of choristoma. They are however so rare that they don’t cause problems in everyday clinical practice [4, 25, 39]. Among other tumours of nerve trunks and branches worth to mention are granulocellular tumour [9, 21] and neurothekeoma [11]. They are rather small not exceeding 1 cm in diameter (neurothekeoma) or 2 cm (granulocellular tumour). They are located in the subcutaneous tissue and exist for many years before they can be diagnosed. They grow from the small cutaneous nerves, which remain unnoticed at the time of tumour resection [11, 39].

The final clinical diagnosis of peripheral nerve tumours after surgical treatment is based on the histopathological examination. Sometimes however it has to be confirmed by electron microscopic and immunohistochemical essays [30] and cytogenetic investigation [23].

Results of treatment of benign tumours are generally good. Nodules coming from cutaneous branches are treated by the simple excision, usually with sacrifice of the thin nerve, excluding situation when the basis for tumour is a nerve of great importance for the sensory function of the hand. Recurrence rate is rather low [2, 11, 39]. Good results are obtained also after surgical removal of the neurilemmoma from major nerve
trunks [17, 26, 36, 43]. Commonly the remission of symptoms is observed after surgery and the risk of postoperative neurological deficit is about 4% [6]. Neurological deficit symptoms usually disappear [2, 32]. However, in cases of big growing tumours, deficit symptoms can be noticed for a longer period [17, 26]. More significant neurological deficit can be observed after neurofibroma excision. Such a deficit is caused by involvement of the nerve fascicles in the tumour structure [36]. Precise dissection and microsurgical reconstruction of the nerve continuity enables gradual the recovery of nerve functions [2, 39].

Prognosis in malignant tumours of peripheral nerves is poor, especially for the primitive neuroectodermal tumours. Recurrence rate in these tumours is rather high — about 15–45% cases [22] and longer period of survival of patients is less than 40% [39]. In cases of neurilemmoma malignum, better prognosis is reserved for patients without Recklinghausen disease diagnosed (5-year survival rate 16–23%) in comparison with patients with symptoms of this disease (5-year survival rate 47–53%) [5, 41]. This tumour is characterised by constant growth, tendency to spread by blood flow (metastases to the lungs in 20% of cases) and by continuity along the nerve trunk, reaching the spinal cord [9, 39]. Total tumour resection “en bloc” or by amputation is the only chance for complete cure.

Results of treatment are of course connected with the character of the tumour, but depend also on proper qualification for treatment and optimal operative technique choice. Qualification for the treatment should be based on detailed anamnesis and careful clinical electromyographic study of the nerve conductivity. In selected cases, treatment also depends on imaging diagnostics [33, 38]. An experienced team should carry out the surgical procedures with good microsurgical instruments and devices (loupes and microscopes). Both the patient and the surgeon should be prepared for different modes of intraoperative decisions (tumour excision, nerve resection with microsurgical reconstruction, biopsy following longitudinal incision, nerve decompression).

REFERENCES