Special Article

Neurosurgical Perspectives on Management of Peripheral Nerve Tumors

Bunpot Sitthinamsuwan MD, MSc*,
Sawanee Pumseenil RN**

** Division of Neurosurgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Neurosurgical Unit, Division of Perioperative Nursing, Department of Nursing, Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *Most of peripheral nerve tumors are benign. Surgical removal is still the standard treatment and should be considered in patients with symptoms.*
Objective: *The operation endeavors to excise tumors concomitant with preservation of neural function.*
Material and Method: *The authors reviewed medical literatures in terms of peripheral nerve tumor classification, clinical manifestation, diagnosis, intraoperative neurophysiological monitoring and surgical treatment.*
Results: *The most common peripheral nerve tumor is schwannoma. Malignant peripheral nerve sheath tumor (MPNST) is a rare entity and often associated with neurofibromatosis type 1. Patients with peripheral nerve tumors can present with palpable mass, pain, neurological deficits and pressure symptoms. Magnetic resonance imaging (MRI) is the gold standard method for diagnosis. Ultrasonography, diffusion tensor imaging (DTI) with tractography and electrophysiological studies are optional presurgical investigations. Operation complications can be avoided by using intraoperative neurophysiological monitoring. Surgery aims to remove the tumors totally. Functional nerve fascicles must be preserved. Radical resection is necessary in MPNST to improve survival outcomes.*
Conclusion: *Most of peripheral nerve tumors can be resected totally and have good prognosis. Diagnosis of the tumors is based on clinical examination and imaging studies. Malignant tumors must be treated aggressively to prolong survival rate.*

Keywords: *peripheral nerve tumor, schwannoma, neurofibroma, malignant peripheral nerve sheath tumor, surgical treatment*

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Peripheral nerve tumor is a large entity of neoplasm of the nervous system. The majority of the tumor has benign nature[1]; malignant neoplasm is found in a scant number of cases. The tumor can occur anywhere in the body, including the skin, head and neck region, extremities, thoracic, abdominal and pelvic cavities.

Because most of peripheral nerve tumor is benign and grows slowly, wait-and-see can be offered in asymptomatic patients with tumors encountered incidentally. In contrast, treatment should be performed in individuals with symptoms caused by the tumor, such as pressure symptom, pain or deformation of the organ. Also treatment should be promptly conducted in patients harboring tumors with suspicious malignant transformation e.g. tumor with rapid growth, hemorrhagic tumor or deeply located tumors[2].

Surgical resection is still the mainstay of treatment for peripheral nerve tumor. Advances in operative techniques and equipments are helpful for improving outcome and avoiding morbidity from surgical procedure. This article purposes neurosurgical perspective regarding operative management of peripheral nerve tumor in terms of tumor classification, clinical manifestation, diagnosis, intraoperative neurophysiological monitoring and surgical management.

Correspondence to:
Sitthinamsuwan B, Division of Neurosurgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: +66-2-4198003, Fax: +66-2-4113006
E-mail: bunpotsi@yahoo.com

Classification of peripheral nerve tumor

As aforementioned content, the majority of peripheral nerve tumor is benign. The most common type is schwannoma, followed by neurofibroma,

whereas malignant peripheral nerve tumor, such as malignant peripheral nerve sheath tumor (MPNST) is relatively uncommon[3]. Primary tumors of peripheral nerve arising from autonomic nerve ganglion cells, including neuroblastoma, paraganglioma, ganglioneuroma, are occasionally seen. Other rare neoplasms of the peripheral nervous system include metastatic tumor, perineurioma, lipoma or hemangioma[1]. Malignant tumors spreading from other organs to adjacent nerves are mentioned[3]; for example, Pancoast syndrome is characterized by a cancer of superior sulcus of the lung with involvement of the brachial plexus and cervical sympathetic nerves, resulting in brachial plexopathy and Horner's syndrome. Classification of peripheral nerve tumors is summarized in Table 1[1-5].

Clinical manifestation

A number of patients with peripheral nerve tumors remain asymptomatic. The tumors with various sizes can be encountered incidentally, usually by radiographic studies. Deeply situated tumors may not produce any symptom even though their sizes are relatively large, such as large schwannomas in the thoracic or abdominal cavity. On the other hand, small-sized tumor can result in obvious clinical complaints, for instance, severe radicular pain caused by spinal nerve root schwannoma.

Palpable lesion is a common clinical feature of peripheral nerve tumors[6-8]. Patients with brachial plexus schwannoma often present with palpable supraclavicular mass (Fig. 1A). Most cases usually have no pain or neurological deficit. Patients who have ulnar nerve schwannoma may present with palpable mass at the axilla.

Neuropathic pain is usually present in cases with tumors compressing or locating adjacent to sensory fascicles of nerves. Pain may be paroxysmal, continuous, or evoked by palpation, compression or

Table 1. Classification of peripheral nerve tumors[1-5]

Nerve sheath origin
Benign
Schwannoma (neurilemmoma)
Neurofibroma
Intraneural perineurioma
Malignant
Malignant peripheral nerve sheath tumor (MPNST)
Fibrosarcoma
Neuronal origin
Neuroblastoma
Ganglioneuroma
Ganglioneuroblastoma
Paraganglioma (chemodectoma)
Pheochromocytoma
Non-neuronal origin
Lipoma
Lipofibromatosis
Ganglion cyst
Hemangioma
Miscellaneous: endometriosis
Metastasis or invasion to peripheral nerve
Metastatic tumor
Pancoast tumor

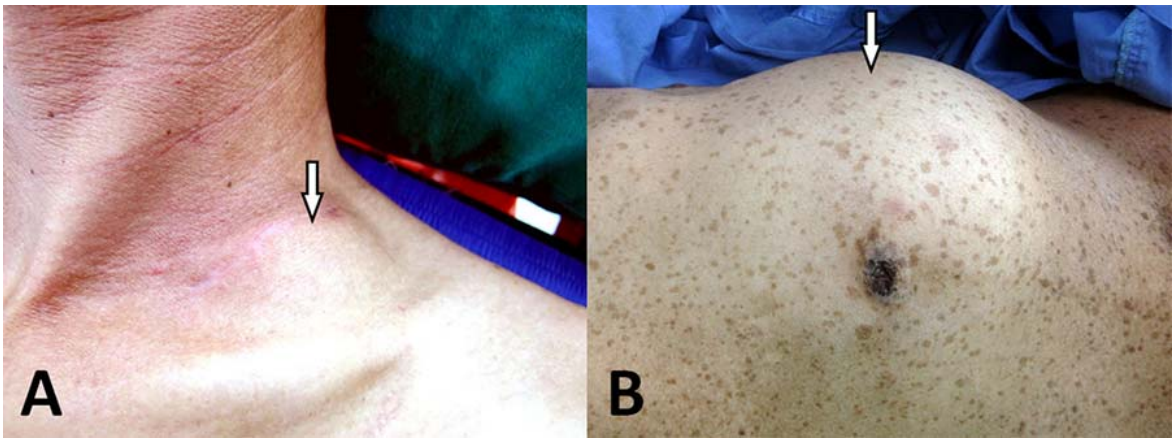

Fig. 1 Clinical presentation of peripheral nerve tumors: (A) palpable supraclavicular mass (arrow) in a patient with brachial plexus tumor; (B) a patient with neurofibromatosis type 1 and MPNST presenting with a huge intra-abdominal mass compressing the bowels.

stretching of tumors and associated nerves[2,8,9]. Sensory impairment may exist when nerve fascicles are chronically compressed by large tumors, particularly in areas with tight space. Motor deficit and atrophic changes of muscles innervated by compressed nerves are unusual unless motor axonopathy occurs. Rapidly progressive motor deficit is an important sign of malignant tumor[10-12]. Clinical presentation indicating malignancy of peripheral nerve is demonstrated in Table 2[13,14].

Pressure symptoms may be caused by tremendous tumors compressing contiguous organs. Large peripheral nerve tumors at the head and neck region may have pressure effect to the regional organs[15]. Intra-abdominal schwannomas can gradually grow and compress the intra-abdominal organs, producing abdominal pain and discomfort[16] (Fig. 1B). Urinary frequency, pelvic discomfort, gluteal pain, constipation, leg pain, weakness or paresthesia may occur as a result of large peripheral nerve tumors in the pelvic cavity compressing the urinary bladder, rectum and lumbosacral plexus[17,18].

Diagnosis

Most of peripheral nerve tumors can be diagnosed by history taking and physical examination. Imaging studies are useful to confirm the diagnosis, localize the tumors, define involvement of neurovascular structures, extent of the tumors and render information for operative planning[9]. Of them, magnetic resonance image (MRI) is the investigation of choice for peripheral nerve tumors[2,4,9]. Heterogeneous enhancement of tumors on contrast-enhanced MRI is typical character of schwannoma (Fig. 2). Magnetic resonance neurography ameliorates visualization of the regional nerves around the tumors.

Ultrasonography is also beneficial for diagnosis of peripheral nerve tumors[19,20]; it can be used to differentiate between schwannoma and neurofibroma[21,22]. In schwannoma, normal nerve fascicles are continuously seen but displaced by the tumor. On the contrary, continuity of nerve fascicles is obscure in neurofibroma and MPNST. Furthermore, MPNST has larger size and ill-defined margin[20,23]. Intra-operative ultrasonography is helpful for localizing small non-palpable tumors[24]. Utilization of intraoperative high-resolution and contrast-enhanced ultrasound has been proposed for differentiating peripheral nerve tumors from tumor-like lesions[25].

Recently, diffusion tensor imaging (DTI) with tractography has been incorporated in preoperative planning for peripheral nerve tumors. Peripheral nerve fascicles and anatomical relationship to the tumors can be visualized by using DTI with tractography and surgical risk of postoperative functional deficits can be predicted by the DTI findings[26-28].

Electrophysiological studies of nerve conduction study (NCS) and electromyography (EMG) are alternative in diagnostic investigation of peripheral nerve tumors. Neurophysiological characteristics are usually normal in most patients. Functional abnormalities may occur, such as increased distal

Table 2. Clinical predictors of malignant peripheral nerve tumor[13,14]

Clinical predictor	Positive predictive value (%)
Severe motor impairment (MRC grade <3/5)	100
Rapid growth of tumor	95
Pain at rest	75
Neurological deficit	73
Pain	20 to 30

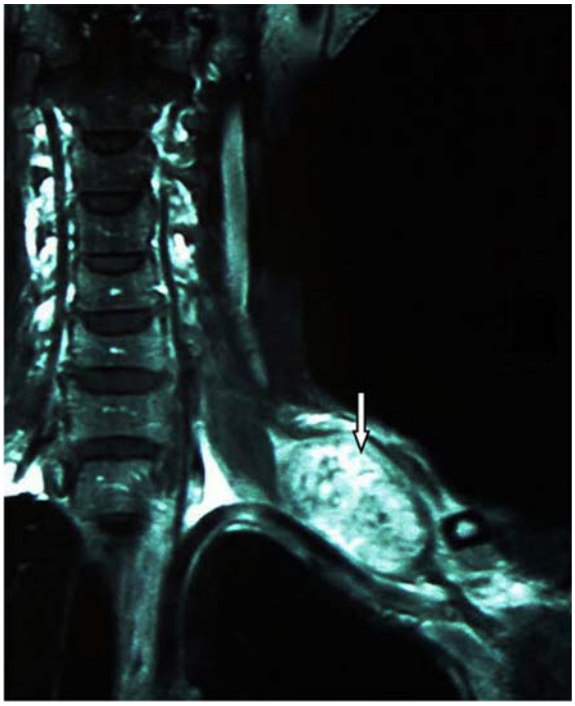

Fig. 2 Contrast-enhanced MRI of the brachial plexus showing well-demarcated heterogeneous enhancing mass at the left brachial plexus (arrow); this is typical features of schwannoma.

latency and delayed conduction velocity[1]. The studies also render baseline nerve function used for comparing with postoperative studies[29].

Intraoperative neurophysiologic monitoring

Neurophysiological monitoring during tumor resection is valuable in early detection of neural damage and avoidance of operative morbidity[1,2,29]. Intra-operative muscle relaxant is discontinued in cases requiring neurophysiological monitoring and electrical stimulation[2]. Nerve conduction studies can record motor, sensory and compound nerve action potentials across the tumor site. A decrement in amplitude of action potentials indicates axonal loss. In patients with tumors in proximal location, such as proximal segment of the brachial plexus, somatosensory evoked potentials (SSEP) is helpful for monitoring the integrity of sensory pathway[30], while motor evoked potentials (MEPs) can be used for detecting discontinuity of motor pathway[29]. Free running EMG is a popular physiological monitoring of nerve damage; appearance of neurotonic discharges indicates that the monitored nerve is being compressed, stretched or irritated[29]. Direct electrical stimulation of peripheral nerve tumors with recording of compound muscle action potentials (CMAPs) from target muscle is useful to evade nerve injuries during dissection and resection of the tumors. Direct nerve stimulation is also utilized to identify functioning nerve fascicles and tumors, particularly schwannoma can be dissected from the functioning fascicles without damage[2,29,30].

Surgical management

Good results are usually obtained after surgery of peripheral nerve tumors. Pain, pressure effect, motor and sensory deficits can be improved following tumor resection[31-33].

Presurgical consideration[2,34-37]

Surgical resection is the most effective treatment of peripheral nerve tumors for relieving presenting symptoms. Nevertheless, wait-and-see therapy is appropriate in asymptomatic patients or who with medical diseases unsuitable for surgery.

In neurofibromatosis patients with multiple neurofibromas, surgical removal should be considered for only lesions producing symptoms or those with doubtful malignant transformation.

The major propose of surgery is to achieve total excision without recurrence in the long-term period.

In some patients, for example, neurofibroma of the major functioning nerve or schwannoma which markedly adheres to neighboring functioning fascicles, total resection cannot be accomplished. Subtotal resection or surgical debulking for cytoreduction of the tumor is mandatory in such cases.

Biopsy is appropriate in cases with tumor infiltrating adjacent nerve without mass effect.

Intra-operative consideration[2,30,31,36,38-41]

Intra-operative neurophysiological monitoring, good microsurgical equipment and gentle microsurgical techniques are important in the improvement of surgical outcome and avoidance of complications.

Exposure of the distal portion of the limb is mandatory in surgical resection of peripheral nerve tumors of an extremity (Fig. 3A).

Operative exposure should be adequate to visualize the proximal and distal parts of the nerve from which the tumor originates (Fig. 3B).

In patients with peripheral nerve tumors located in vicinity to common sites of entrapment neuropathy, such as the carpal tunnel, cubital tunnel, fibular neck, prophylactic surgical decompression should be considered for preventing subsequent nerve compression in the future.

Major principle of peripheral nerve tumor resection is total excision of the tumors with preservation of nerve function (Fig. 4).

The vast majority of schwannoma can be removed totally without postoperative nerve dysfunction, whereas subtotal debulking with conserving nerve function is the aim of surgery in neurofibroma involving the major nerves.

Extracapsular total resection is possible, especially in small-sized tumors. In large-sized tumors or tumors located in a limited space, intracapsular debulking to reduce tumor size followed by removal of residual tumor and capsule is a common strategy.

When tumor capsule cannot be separated from functioning nerve fascicles, that part of the capsule should be left for preventing nerve injury.

Surgical consideration in MPNST[2,36,42-45]

MPNST is associated with neurofibromatosis type 1. It can be found in patients with schwannomatosis and neurofibromatosis type 2[44].

When MPNST is suspected, open biopsy is more appropriate than fine needle aspiration (FNA) because cytology obtained by FNA may mislead diagnosis. Overdiagnosis of MPNST may lead to

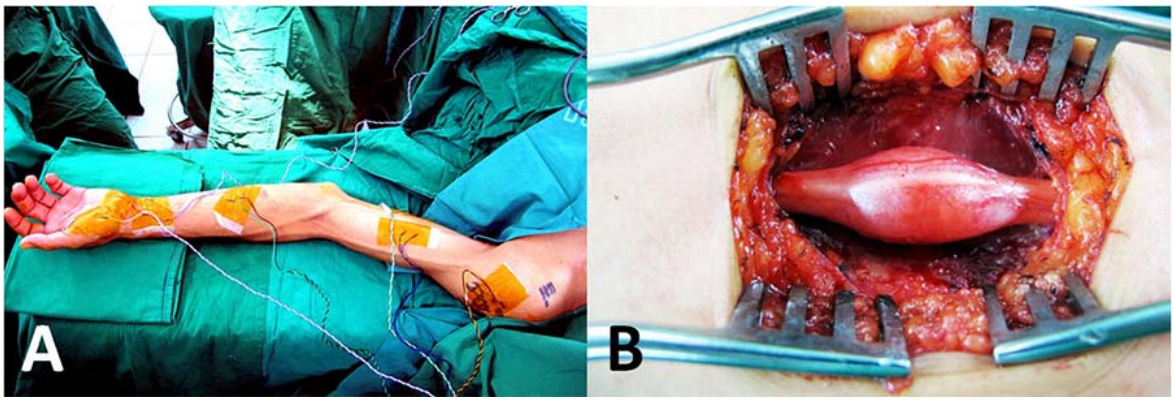

Fig. 3 Operative exposure in surgery for peripheral nerve tumors: (A) the distal limb should be exposed for observing movement during electrical stimulation of the nerve; intraoperative neurophysiologic monitoring, including SSEP, free running EMG and electrical nerve stimulation are used; (B) surgical exposure of the parent nerve proximal and distal to the tumor.

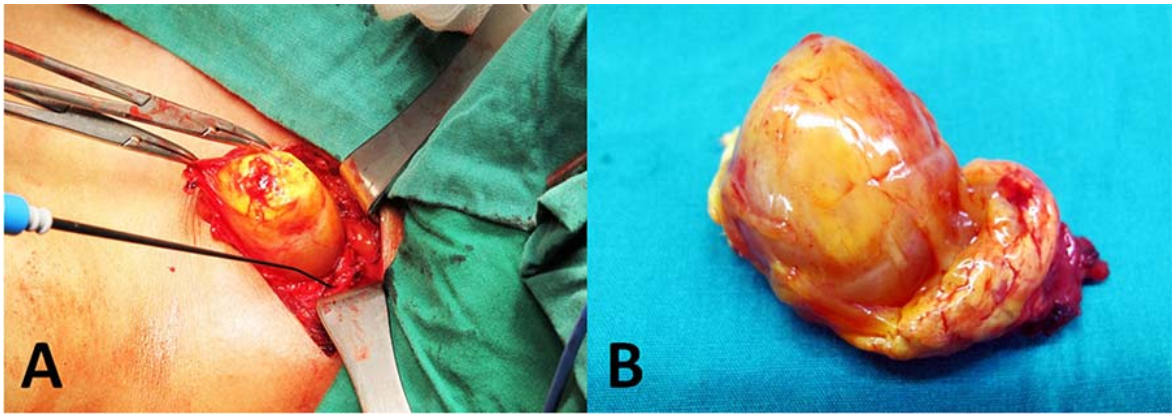

Fig. 4 Resection of peripheral nerve tumor: (A) circumferential extracapsular removal of schwannoma; (B) total excision of the tumor.

unnecessary extensive resection of tumor and surrounding tissue which significant postoperative neurological deficit and morbidity can occur.

The major goal of surgery for MPNST is excision of the entire tumor and surrounding structures (en-bloc resection) to achieve tumor-free margins. However, the parent nerve cannot be preserved in MPNST and postoperative neurological morbidity often ensues inevitably.

Nerve grafting is not popular in the treatment of MPNST because this kind of tumor carries grave prognosis.

A study of Evans et al showed 5-year survival from diagnosis was 21% for neurofibromatosis type 1 patients with MPNST and 42% for sporadic patients with MPNST[42]. Survival outcome is poorer in males[45].

Conclusion

Most of peripheral nerve tumors are benign and have good prognosis. Diagnosis is based on clinical examination and imaging studies. Total resection with preservation of neural function is the major goal of surgical treatment. Intraoperative monitoring is useful for avoiding neurological complications. MPNST should be treated aggressively to improve survival outcomes.

What is already known on this topic?

Patients with peripheral nerve tumors can present with diverse symptoms, including gradually growing palpable mass, compressive symptoms and

neuropathic pain. Surgical treatment should be considered in symptomatic lesions.

What is study adds?

Gross total resection with preservation of the parent nerve can be achieved in most cases of schwannoma. Cytoreductive surgery is considered in neurofibroma originating from the major functioning nerve. Radical resection of the lesion, parent nerve and surrounding connective tissue should be done in patients with MPNST. Intraoperative neurophysiological monitoring is valuable in reduction of operative morbidity.

Potential conflicts of interest

None.

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มุมมองทางประสาทศัลยศาสตร์ที่มีต่อการรักษาเนื้องอกเส้นประสาทส่วนปลาย

บรรพต สิทธินามสุวรรณ, สวนีย์ พุ่มสีนิล

ภูมิหลัง: *เนื้องอกเส้นประสาทส่วนปลายส่วนใหญ่เป็นเนื้องอกที่ไม่ใช่มะเร็ง การผ่าตัดยังคงเป็นการรักษามาตรฐาน ควรพิจารณาการผ่าตัดในผู้ป่วยที่มีอาการ*

วัตถุประสงค์: *การผ่าตัดมีวัตถุประสงค์เพื่อตัดเนื้องอกร่วมกับเก็บรักษาการทำงานของระบบประสาท*

วัสดุและวิธีการ: *ผู้นิพนธ์ได้ทบทวนบทความทางการแพทย์เกี่ยวกับเนื้องอกเส้นประสาทส่วนปลายในแง่ของการแบ่งชนิดของเนื้องอก อาการทางคลินิก การวินิจฉัย การตรวจการทำงานของระบบประสาทขณะผ่าตัดและการผ่าตัดเนื้องอก*

ผลการศึกษา: *เนื้องอกเยื่อหุ้มเส้นประสาทเป็นเนื้องอกของเส้นประสาทส่วนปลายที่พบบ่อยที่สุด มะเร็งของเยื่อหุ้มเส้นประสาทเป็นเนื้องอกที่พบได้ไม่บ่อย และมักเกี่ยวข้องกับโรคท้าวแสนปมชนิดที่ 1 ผู้ป่วยเนื้องอกเส้นประสาท ส่วนปลายสามารถมาพบแพทย์ด้วยเรื่องคลำก้อนได้ อาการปวด ความผิดปกติของระบบประสาท และอาการที่เกิดจากเนื้องอกกดเบียดอวัยวะ การตรวจภาพแม่เหล็กไฟฟ้าเป็นการตรวจที่เหมาะสมที่สุดสำหรับให้การวินิจฉัย การตรวจคลื่นความถี่สูง การตรวจภาพทางเดินของเส้นประสาท และการตรวจการทำงานของเส้นประสาทและกล้ามเนื้อเป็นทางเลือกในการตรวจเพิ่มเติมก่อนผ่าตัด การตรวจการทำงานของระบบประสาทขณะผ่าตัดช่วยลดภาวะแทรกซ้อนจากการผ่าตัดได้ การผ่าตัดมีเป้าหมายเพื่อนำเนื้องอกออกทั้งหมดร่วมกับเก็บรักษาการทำงานของใยเส้นประสาทที่สำคัญ สำหรับมะเร็งเยื่อหุ้มเส้นประสาทการตัดเนื้องอกร่วมกับเนื้อเยื่อรอบข้างมีความจำเป็นเพื่อเพิ่มการรอดชีวิตของผู้ป่วย*

สรุป: *เนื้องอกเส้นประสาทส่วนปลายส่วนใหญ่จะสามารถผ่าตัดออกได้หมดและมีการพยากรณ์โรคที่ดี การวินิจฉัยเนื้องอกอาศัยการตรวจทางคลินิกร่วมกับการตรวจทางรังสีวินิจฉัย เนื้องอกที่เป็นมะเร็งควรได้รับการรักษาที่เหมาะสมเพื่อเพิ่มอัตราการรอดชีวิต*