Tumors of the brachial plexus

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Tumors of the brachial plexus are relatively rare and present a clinical challenge for the neurosurgeon. The management of these tumors therefore requires not only an understanding of the complex anatomy of the brachial plexus but also an appreciation of the appropriate surgical approach to the various tumors that may be encountered. Over a 30-year period (1969–1999), 226 patients with brachial plexus tumors were evaluated and surgically treated by the senior authors (R.L.T., D.G.K.). In the present paper they review the most common benign and malignant brachial plexus tumors and discuss management and surgical principles established through their experience at the Louisiana State University Health Sciences Center.

KEY WORDS • brachial plexus • nerve sheath tumor • neurofibroma • schwannoma

Tumors of the brachial plexus are relatively rare and present a clinical challenge for the neurosurgeon. These entities may represent unusual disease and involve unfamiliar surgical territory for clinicians. Patients often present with evidence of an expanding mass or local or radicular pain; unlike patients with peripheral nerve injury or entrapment, those with tumors typically present without an objective neurological deficit. As these lesions are structurally intrinsic to the nerves from or around which they arise, the normal neurovascular anatomy may be greatly distorted. Tumor removal or even biopsy is accompanied by the risk of producing neurological deficit; the challenge for the neurosurgeon is to perform tumor removal as completely as possible while maintaining normal neural function. The management of these tumors therefore requires not only an understanding of the complex anatomy of the brachial plexus but also an appreciation of the appropriate surgical approach to the various tumors that may be encountered. In the following sections, we will review the most common benign and malignant brachial plexus tumors and discuss management strategies and surgical principles as garnered over a 30-year experience at LSUHSC.

SUMMARY OF CASES

Over a 30-year period (1969–1999), 226 patients with tumors involving the brachial plexus were evaluated and surgically treated at the LSUHSC. Of these, 144 patients (64%) presented with benign PNSTs such as neurofibroma, schwannoma, and localized hypertrophic neuropathy of the peripheral nerve (LHN). Thirty benign PNNSNTs (13%), including lipomas, hemangiopericytomas, desmoid tumors, and osteochondroma, were also encountered. Fifty-two (23%) of these tumors were malignant, including 21 primary sarcomas and 31 non–neural sheath malignancies. Most patients presented with evidence of a local mass, local pain or paresthesias. Variables assessed and recorded included tumor size, location, mobility, tenderness on palpation, and the presence/absence of a Tinel sign. Neurological deficits were documented by applying the muscle strength and sensory grading systems used at LSUHSC. Chest x-ray films were evaluated for their depiction of lower plexal tumors; plain cervical radiographs were assessed for evidence of foraminal enlargement or vertebral erosion. Computed tomography or magnetic resonance imaging was conducted to delineate tumor location, margins, and relationship to adjacent structures. In cases of malignant tumors, the metastatic workup included chest and abdominal computed tomography scans and Tc-labeled scans of the liver, spleen, and bone. Angiography was used to identify feeding vessels to vascular tumors. Myelography was performed in cases in which the tumors involved the spinal canal. Electromyography was undertaken in each patient. The histological diagnosis was based...
on the results of light microscopy and, occasionally, electron microscopy.

**Summary of Tumors and Surgical and Therapeutic Management**

**Surgery for Benign PNSTs of the Brachial Plexus**

An anterior supraclavicular approach was used to treat most tumors involving the roots and trunks. The infraclavicular approach was used for lesions involving the cords and distal plexal elements. A posterior approach was used for tumor involvement at the following sites: 1) spinal nerves at the intraforaminal level, 2) the C8–T1 roots, and 3) the lower trunk. The posterior approach was also used in patients who presented with residual or recurrent tumor or who had undergone radiotherapy.

**Surgery for Schwannomas**

Schwannomas were the second most frequent benign PNST involving the brachial plexus surgically managed at LSUHSC (54 of 141 lesions). A recommendation of surgery was made if the tumor caused intractable pain or weakness. Baseline function was preserved or improved in 89% of cases, with near-complete resolution of pain.

Schwannomas are thought to arise from an intraneural Schwann cell. For this reason, interfascicular dissection may be required to distinguish between the tumor and the affected nerve, although the two typically are distinct and separated by a fibrous capsule.

Histologically, schwannomas are composed of irregular Schwann cells admixed in an irregular connective tissue stroma. They are architecturally heterogeneous tumors, characterized by the presence of Antoni Type A and Type B neurilemma. Type A tissue is made up of elongated spindle cells arranged in irregular streams and is compact in nature. Type B tissue has a looser organization, often with cystic spaces intermixed within the tissue. The cystic spaces can result in high signal intensity on T2-weighted magnetic resonance imaging. Staining for the S100 antigen is positive in both schwannomas and neurofibromas, but the staining tends to be more intensely present in the former. Additionally Leu-7, epithelial membrane antigen, vimentin, collagen, and neurofilament protein are also valuable antigenic markers in the identification of schwannomas.

Interestingly, schwannoma development appears to be linked to the loss of tumor suppressor genes encoded on chromosomes 22, 17, and 19, whereas activation of protooncogenes is more commonly associated with the development of malignant PNSTs.

Patients with brachial plexus schwannomas tend to complain of local pain or radiculopathy that is typically exacerbated by tumor manipulation. The tumor is often a readily palpable mass, mobile in the transverse but not rostrocaudal plane. Review of the experience at LSUHSC and other major centers reveals that these patients tend to be neurologically intact on initial presentation.

Surgical management of these lesions is facilitated by the knowledge that a fibrous capsule envelops and separates the tumor from the nerve fascicles. Intraoperative NAP monitoring is used but should serve as an adjunct to direct visualization of nerve tissue. Surgical exposure is extended to include neurovascular structures both proximal and distal to the mass. The surrounding nerves and vascular structures are bluntly dissected away, thereby isolating the tumor and affected nerve. The proximal and distal aspects of the affected nerve are identified; our practice has been to encircle each end with a Penrose drain; this maneuver also facilitates gentle retraction of the neural elements. These proximal and distal elements are traced back to the tumor; interfascicular dissection at the poles of the tumor is used to distinguish traversing from displaced fascicles. In schwannomas, there are usually only one or two entering and exiting fascicles; intraoperative stimulation and recording often demonstrate the traversing fascicles to be nonfunctional, permitting their sectioning. The tumor is then removed as a single mass.

In the early interfascicular growth phase, small schwannomas displace nerve fibers without forming a capsule. Larger tumors increase the size of the parent nerve and become separated from surrounding fascicles by a capsule derived from peri- and epi-neurium. In larger tumors, the tumor capsule is opened longitudinally and the tumor is enucleated piecemeal so as to avoid placing adherent fascicles under tension. The tumor is gradually dissected away from the adherent but displaced fascicles, and it is then lifted away from the residual nerve. Finally, the capsule is sharply trimmed away from the remaining fascicles.

**Surgery for Neurofibromas**

Neurofibromas were the second most frequent benign PNST involving the brachial plexus surgically managed at LSUHSC (87 of 141 lesions). Resection of non-NF1 neurofibromas was indicated for tumors causing pain or neurological deficits, as well as for those lesions with an uncertain diagnosis or concern for malignancy. In patients with NF1, a lower clinical threshold was used with regard to resection due to the 15% risk of malignant degeneration associated with these tumors.

Neurofibromas are benign, heterogeneous tumors that arise from the connective tissue of peripheral nerve sheaths; it is hypothesized that the cell of origin may be a Schwann cell progenitor cell at a more primitive stage than one giving rise to a schwannoma. Unlike schwannomas, which tend to displace the surrounding neural structures, in neurofibromas, nerve fascicles are intimately involved in the tumor. In addition, there is a tendency for neurofibromas to arise from the motor portion of the nerve whereas most schwannomas arise from the sensory portion of the nerve. Histologically, neurofibromas are composed of Schwann cells and fibroblasts with perineurial cells, axons, and mast cells embedded in an extracellular matrix. Plexiform neurofibromas, commonly encountered in patients with NF1, are composed of the same cell types as cutaneous neurofibromas, but, in contrast, have an expanded extracellular matrix and often a rich vascular network. Solitary neurofibromas are more likely to be fusiform than plexiform. In past clinical practice, the major distinction between a schwannoma and a solitary neurofibroma was that a schwannoma can be resected while sparing the underlying nerve whereas resection of a neurofibroma requires sacrifice of the underlying nerve.
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The surgical principles utilized in the resection of these tumors are the same as those followed in the resection of schwannomas. Key steps include wide exposure, isolation of the tumor from adjacent neurovascular structures, and dissection of the tumor poles. Fascicular dissection is again performed to distinguish between fascicles abutting and those traversing through the tumor. The goal of surgery with fusiform neurofibromas remains the same: complete resection of the tumor, including removal of some of the tumor capsule, with preservation of function.

Using an interfascicular approach supplemented by NAP testing, 85% of patients with solitary neurofibromas underwent complete resection that allowed preservation or improvement of preoperative function. Although a similar proportion (83%) of patients with NF1-associated neurofibromas experienced preservation or improvement of preoperative function, this success often came at the cost of subtotal resection. Stated another way, the incidence of total resection in patients with NF1-associated neurofibromas was 76% compared with complete resection in all patients with solitary neurofibromas. Incidence of neurological deficit as well as new pain is increased if there had been prior open or closed biopsy or attempts at removal of the tumor.

Surgery for Peripheral Nerve LHN

Localized hypertrophic neuropathy of the peripheral nerve is also referred to in the literature as intraneural perineurinoma. Whether it represents a metaplastic or neoplastic lesion remains a matter of debate.5,13,15,24 Regardless, LHN is an exceedingly rare entity, representing less than 1% of PNSTs. It consists of proliferative perineurial cells infiltrating endoneurium, forming concentric layers around nerve fibers in a characteristic pseudoonion bulb pattern. Although this lesion is believed by some to be hypertrophic, other investigators have proposed a neoplastic identity based on its substantial proliferative activity, frequent expression of the p53 antigen, and clonal cytogenetic abnormalities associated with chromosome 22.8 All reported cases of LHN have been benign without recurrence or metastasis.

Microscopically, LHN is composed of enlarged nerve fascicles separated by abundant fibrous tissue. Septae of thickened perineurium extend inward to compartmentalize sectors of the nerve fascicles. The nerve fascicles display onion bulb–like structures consisting of concentrically arranged proliferating perineurial cells surrounding a central core of residual Schwann cells and nerve fibers. The Schwann cells retain S100 immunoreactivity, and strong epithelial membrane antigen immunoreactivity is seen in the perineurium, septae, and outer layers of the whorls.

Three patients with LHN of the brachial plexus underwent surgery at LHUHSC. External neurolysis alone or with internal neurolysis was performed unless intraoperative NAP monitoring demonstrated a minimal or low amplitude NAP; in these cases the lesion was resected. Manipulation of the lesion, particularly by internal neurolysis, was associated with worsening or complete loss of neurological function despite the fact that only neurolysis was performed.

Surgery for Benign PNNSNTs of the Brachial Plexus

During the 30-year period between 1969 and 1999, 111 patients at LSUHSC underwent operations to have benign PNNSNTs removed.17 In these cases, 33 lesions were found to involve the brachial plexus. Benign PNNSNTs of the brachial plexus included lipoma (two cases), hemangiopericytoma (one case), desmoid tumor (six cases), myositis ossificans (two cases), osteochondroma (one case), ganglioneuroma (three cases), meningioma (two cases), myoblastoma/ granular cell tumor (two cases), triton tumor (two cases), and lymphangioma (one case).

Most benign PNNSNTs involve the brachial plexus secondarily and produce symptoms due to nerve compression; others may actually arise within a nerve itself. Desmoids, myoblastomas, lymphangiomas, or extra- spinal meningiomas arise extrinsic to the neural elements of the brachial plexus, but they can adhere to or even invade the epineurium, making them difficult to remove. Hemangiopericytomas can envelop elements of the brachial plexus. In contrast, triton tumors arise from a nerve itself.

The surgical approach to benign PNNSNTs, excluding myositis ossificans, was similar to that undertaken for benign neural sheath tumors. Complete resection of these masses, although sometimes possible, was usually not indicated. Mobilization of the nerve away from the mass and neurolysis often dramatically improved the patient’s symptoms. Intraoperative NAP recording was performed, with sacrifice of nerve fascicles demonstrating absent or low amplitude NAPs. In the case of desmoid tumors, complete resection was often unachievable and recurrence was likely.

Surgery for Malignant PNSTs

Malignant PNSTs, also known as neurogenic sarcomas, include malignant schwannomas and neurofibrosarcomas. These lesions are rapidly growing, firm, and fixed; patients with malignant PNST may present with rapidly progressive loss of function or severe pain. In rare cases a patient may present with evidence of metastasis to lung, bone, liver, or spleen. Between 1969 and 1999, 21 patients with malignant PNSTs, eight of whom had NF1, underwent surgery at LSUHSC.17

Despite some differentiating features on physical examination, most malignant PNSTs were not identified as such until the time of biopsy or attempted removal. Once identified, malignant PNSTs are best treated with limb-sparing surgery involving wide local resection of tumor and adjacent soft tissues. Ideally, the pathological specimen contains a several-centimeter tumor-free margin of soft tissue traversing a nerve. Surgery is followed by local soft-tissue irradiation, accomplished either by brachytherapy or external beam radiotherapy. Although total resection is the goal, resection of malignant brachial plexus PNSTs is often impossible without risking severe vascular or neurological injury. In these cases treatment options include amputation or subtotal resection followed by radio- and chemotherapy.

Of the 21 patients with malignant PNSTs seen at LSUHSC, 15 underwent local resection; in six of these cases local resection was achieved with margins. The
remaining six patients underwent amputation in which the forequarter of the shoulder and arm was removed. At a mean follow-up interval of 52 months, 14 of 17 patients with neurogenic sarcomas of the brachial plexus had died; the mean postoperative survival duration was 25 months. At a mean follow-up interval of 47 months, two of four patients with noneurogenic sarcomas of the brachial plexus had died of their disease (mean postoperative survival 40 months).

Surgery for Malignant PNSSNTs

Malignant tumors with a non–neural sheath origin may involve nerves of the brachial plexus by direct extension from a primary site or metastasis to a nerve or adjacent tissues. Metastatic disease involving a nerve may be seen with lymphoma, bladder cancer, or melanoma; it may also occur in thymoma, breast, lung, pancreatic, and prostate cancer. Lesions at an intracavitral level often represent direct extension (for example, Pancoast tumor), whereas spread of disease from local lymph nodes is more commonly supracavicular. Management of these tumors must be individualized to account for the severity of symptoms, extent of systemic disease, and medical comorbidities. Indications for surgery include pain, paresthesias, and progressive neurological deficit with otherwise controlled systemic disease.

At LSUHSC, we treated seven patients with Pancoast syndrome secondary to direct extension of an apical pulmonary tumor to the lower brachial plexus.17 These patients presented with shoulder pain radiating in the ulnar distribution of the arm, often with radiographic evidence of destruction of the first and second ribs. In some of these cases, a palliative approach, consisting of posterior subcapular resection of the first rib and subtotal resection of the apical tumor to decompress the lower plexal elements, was undertaken. A high contralateral open cervical cordotomy may also be used to palliate pain associated with Pancoast syndrome.

Discussion

A diverse group of tumors, both intrinsic and extrinsic to the neural elements, and benign or malignant in nature, may affect the brachial plexus. Benign tumors affecting the brachial plexus offer the surgeon not only the challenge of intervening while maintaining nerve function but often also the reward of achieving tumor control or cure. Even in those with malignant lesions, the neurosurgeon plays a role in establishing tumor control or in the palliation of associated symptoms.

Over a 30-year period (1969–1999), 226 patients with tumors involving the brachial plexus were evaluated and surgically treated at LSUHSC.17,18 Of these, nearly two thirds presented with benign PNSTs. Of the benign PNSTs, the majority (62%) were neurofibromas and the minority comprised schwannomas (37%) and LHN of the peripheral nerve (1%). A smaller number of benign PNSSNTs, including lipomas, hemangiopericytoma, desmoid tumor, and osteochondroma, were also encountered. These lesions, although defined by their location extrinsic to the plexal neural elements, were often closely invested in the neurovascular structures and soft tissues of the brachial plexus region. Finally, about one third of the patients in this series presented with malignant tumors such as primary sarcomas (21 of 52) and non–neural sheath malignancies (31 of 52).

An anterior supra- or infracavicular approach to the brachial plexus was used for the majority of the surgically treated tumors. A smaller population of patients underwent surgery performed via a posterior subcapular approach. Both of these approaches have been described extensively in previous reports.5–7,20 The posterior approach was chosen under the following conditions: 1) the proximal spinal nerves, especially those at the intraforaminal level, were involved; 2) the lower plexus root (C8–T1) or trunk were involved by tumor; or 3) the patients had a history of radiotherapy or resection and, consequently, had severe scarring anterior to the plexus.

Regardless of the approach selected, the operative steps for resection of most neural sheath tumors are similar. Briefly, the proximal and distal aspects of the tumor are identified, and the tumor is isolated from the surrounding neurovascular structures. Involved and uninvolved fascicles at both the proximal and distal poles are identified by interfascicular dissection; intraoperative stimulation and recording are used to distinguish functional from dysfunctional fascicles with sacrifice of nonfunctional fascicles. The tumor is gradually dissected away from adherent but displaced fascicles and then lifted away from the residual nerve. Finally, the capsule is sharply trimmed away from the remaining fascicles.

During the resection of schwannomas, one finds that almost all nerve fascicles run along the outside of the tumor capsule. Fascicles traversing through the tumor, if tested with stimulation and recording techniques, are usually nonfunctional and can be sectioned. This permits the surgeon to remove the tumor as a solitary mass or piece-meal amid the fascicles. In contrast, neurofibromas are often characterized by the presence of multiple traversing nerve fascicles. Nonetheless, careful intraoperative stimulation and recording aid the surgeon in teasing the tumor away from the peripheral, functional fascicles. In some cases, tumor resection may require sectioning of a functional fascicle; in these instances, an interpositional autologous nerve graft may be placed to mitigate the expected functional deficit. In some cases of large NF1-associated neurofibromas, whether fusiform or plexiform, total resection was not always the goal of surgery. Rather, surgery with the goal of adequate neural decompression was considered palliative.

The therapeutic approach to malignant tumors depends on the origin and location of the lesion. Although total resection is the goal of surgery, this is often impossible with plexal malignancies because of the risk of severe neurovascular injury and functional loss. Conversely, simple biopsy sampling of malignant tumors without excision or substantial decompression is usually not indicated. Amputation is seldom indicated at the time of the initial operation; rather, permanent specimen sections from multiple sites are obtained and examined, not only to confirm the diagnosis of malignancy but to assess the extent of invasion of adjacent structures.

The modern approach to peripheral nerve tumor surgery began after Virchow20 described the distinction between nerve sheath tumors and neuromas resulting from trauma.
or amputation. Schwannomas were first described as a discrete pathological entity in 1910 by Verocay, who called them “neurinomas,” although an 1886 paper by Courvoisier of a tumor resected from the C-5 nerve root (resulting in paralysis of the deltoid and biceps muscles) was most likely the first report of a tumor arising from the brachial plexus. In 1970, Dart et al. reported 27 cases of plexus tumors. That same year, Fisher and Tate conducted a review of all brachial plexus neoplasms reported in the literature, including four of their own patients who harbored schwannomas. Since 1970, numerous groups have described their experience in caring for patients with tumors of the brachial plexus.

More recently, Kehoe et al. reported on 104 patients who presented with a solitary benign peripheral nerve tumor, 15 of which involved the brachial plexus. The majority of their patients presented with the primary complaint of a palpable mass; less than half complained of local pain or paresthesias. Of note, the authors found that the incidence of neurological symptoms doubled after surgical exploration, underscoring the need for vigilance, accurate preoperative diagnosis, and careful surgery.

Artico et al. reported on cases involving 119 PNSTs, 11 of which involved the brachial plexus. In 93% of their patients with schwannomas and 81% of their patients with neurofibromas motor function stabilized or improved postoperatively. At the 6-year follow-up, the best surgical results were observed in the patients with schwannoma, whereas the worst results were demonstrated in those with plexiform neurofibroma.

Huang et al. reported their experience with 42 patients with brachial plexus tumors treated at the University of Pennsylvania between 1990 and 2001. The most common presenting symptom was pain (70%), followed by sensory loss (61%) and weakness (52%). About half of their patients harbored benign nerve sheath tumors; of these, 55% presented with a neurofibroma whereas 45% had a schwannoma. Six of the 11 patients with a neurofibroma had NF1. Of the patients presenting with malignant tumors of the brachial plexus (38%), nearly half were found to have a metastatic lesion, most commonly from a lung or breast primary tumor. The remainder presented with primary malignancies, including neurogenic sarcoma, chondrosarcoma, Ewing sarcoma, and chordoma. Sixteen percent of patients presented with benign non–neural sheath nerve tumors. Eighty-two percent of their patients with neurofibromas experienced improvement or stabilization of pain following surgery; 73% of these same patients experienced stabilization or improvement of their motor function. Of patients presenting with schwannomas, 89% had improved or unchanged pain, and 78% had improved or unchanged motor function following surgical resection. Of the 17 patients who underwent surgery for malignant brachial plexus tumors, 59% reported improvement or stabilization of pain postoperatively and 35% reported improvement or stabilization of motor function. For patients with malignant brachial plexus nerve sheath tumors, the mean duration of survival was 3.7 years. For patients with metastatic tumors of the brachial plexus region, the mean duration of survival was 2.3 years.

In their paper, Binder et al. described the treatment of 25 consecutive patients with primary brachial plexus tumors at the University of California, San Francisco seen between 1992 and 2003. The most common presenting symptoms were a palpable mass, paresthesias, local pain, and weakness. Tumor types included schwannomas (15 cases), neurofibromas (five cases), malignant PNSTs (four cases), and desmoid tumors (one case). Gross-total resection was achieved in all cases of schwannoma and in one of the five with neurofibroma.

The experiences of surgeons at these institutions highlight many of the conclusions drawn from our experience at LSUHSC. With the exception of plexiform tumors, benign nerve sheath tumors should be considered curable lesions with an acceptable surgical risk of injury to neuromuscular structures. Even in patients with malignant tumors of the brachial plexus, palliation of pain and preservation or improvement of neurological function should be considered a goal, with tumor control a reality for some.

References


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