Peripheral non–neural sheath tumors are rare. A review of the literature over the last three decades demonstrates a paucity of case reports or small series of patients for each of these tumors, with the exception of the more common ganglion cysts of the peripheral nerve, about which many reports have been published.

Localized hypertrophic neuropathy of the peripheral nerve originates from hyperplasia of Schwann and/or perineurial cells. Localized hypertrophic neuropathy is thought by some to represent a hypertrophic lesion. Some investigators, however, have posited a tumor basis for these lesions because they have a clonal abnormality involving a loss of 22q11.2 with the NF2 tumor suppressor gene localized to 22q11.2-q12. If classified as a tumor, LHN is specified as a non–neural sheath tumor rather than a neural sheath tumor, and is, therefore, included in this review.

Benign non–neural sheath tumors also include lipomas and vascular tumors such as venous angiomas, hemangiopericytomas, glomus tumors, and hemangioblastomas. Myositis ossificans, osteochondromas, ganglioneuromas, meningiomas, cystic hygromas, myoblastomas or granular cell tumors, and epidermoid cysts are also benign PNNSTs.

Malignant PNNSTs arise from nonneural tissues and directly extend or metastasize to a nerve. Examples include breast or pulmonary cancers, which directly extend or metastasize to the perineurium or any potential space surrounding it. Osteogenic or soft-tissue sarcomas displace or adhere to the nerve or encase it and, in a few cases, actually invade the nerve. Lymphomas and melanomas can metastasize and secondarily involve a nerve by epineurial invasion or infiltration of the subperineurial zone, the interfascicular epineurium, and eventually the fascicle(s) themselves.

In this paper we report the results of a retrospective evaluation of the charts of 146 patients with benign or malignant PNNSTs that were located in the brachial and pelvic plexi and other major nerves and were surgically treated at the LSUHSC within a 30-year period. This is the first published report to address the issue of the incidence of benign and malignant PNNSTs with regard to their locations; a critical analysis was performed to determine if there is a correlation between tumor type and loca-
Peripheral non–neural sheath tumors at LSUHSC

tion. The frequency of tumors of each type and the surgical techniques performed to treat each type of tumor are presented. The results of a literature review of recent publications concerning the number of tumors reported for each type of tumor are included as well.

Clinical Material and Methods

In this retrospective study, charts were reviewed and findings documented for 146 patients who underwent surgery for benign and malignant PNNSTs between 1969 and 1999. Physical and neurological examinations were performed to assess the size and location of the tumor, localized tenderness on palpation of the mass, the presence or absence of a Tinel sign, and neurological deficits. Findings on CT and/or MR images were reviewed to document each tumor’s location, margins, and relationship to adjacent structures. For malignant PNNSTs, a metastasis evaluation included lung and abdominal CT scans and technetium liver, spleen, and bone scans. Angiograms were obtained for all tumors of vascular origin to delineate the feeding vessels and the tumor vascularity. Myelograms were evaluated when they had been obtained for tumors encompassing the spinal cord or nerve roots. Electromyography was also performed in each patient. Histological diagnoses based on light microscopy studies and at times electron microscopy studies and special staining in difficult-to-diagnose cases were reviewed. Tumors classified as benign or malignant and of non–neural sheath origin were included and the types of treatment for benign and malignant PNNSTs and the status of surgical margins of malignant PNNSTs were also assessed.

Operative Techniques Used for Benign Non–Neural Sheath Tumors

Ganglion and Epidermoid Cysts. For ganglia cysts extrinsic to the nerve and compressing it, the involved nerve was protected while the cyst was dissected away, and then dissection was performed around the lesion. The origin of the cystic lesion, which was usually the branch of the tibiofibular joint, was ligated close to the joint to reduce the risk of recurrence. Most ganglion cysts extrinsic to the nerve could be resected in this fashion with preservation of neurological function.

Localized Hypertrophic Neuropathy. External neurolysis alone or with additional internal neurolysis was usually performed on an LHN lesion. Manipulation of the lesion, particularly by internal neurolysis, at times produced additional or even complete loss of function, despite the fact that neurolysis was less invasive than resection. An alternative was to proceed with resection despite the attendant loss. The lost segment was replaced with an autologous graft in nine patients by using interposed sural or antebrachial cutaneous nerves and 7-0 or 8-0 monofilament sutures. Because the disease usually involved a significant segment of the nerve, the grafts were usually lengthy.

Intraneural ganglion cysts required a different, interfascicular approach. The ganglion cyst was usually dissected out and the nerve was subjected to internal neurolysis in the process. As was the case with extrinsic ganglion cysts, the entry point was isolated and ligated to reduce recurrence. For larger intraneural cysts the synovial-like contents of the cyst were evacuated and the capsule was dissected away from the decompressed and split fascicles. A larger lesion sometimes required several operations before obliteration.

In the one patient who was treated for an epidermoid cyst, after neurolysis of the involved nerve had been performed that nerve was gently retracted away from the mass and the cyst could be resected as a solitary mass.

Desmoid Tumors. Surgical treatment involved a wide exposure of the lesion and identification of the nerve(s) or plexus element(s) involved. A tumor was sharply dissected, as far as possible, away from the nerve or plexus elements. The involved epineurium required resection. The tumor was usually adherent to nerves as well as vessels and other structures, requiring an extensive and lengthy operation. Recurrence was likely.

Hemangiomas, Hemangiopericytomas, and Hemangioblastomas. The operative technique used to treat hemangiomas and hemangiopericytomas involved isolating and ligating vessels at the periphery of the lesion if they were not the major supply to an extremity. Nerves were dissected away from the lesion. Occasionally, a hemangioma or hemangioblastoma directly involved the nerve or appeared to originate within it; in this case a careful interfascicular dissection was necessary to remove each fascicle or group of fascicles containing abnormal vascular tissue.

Glomus Tumors. The two glomus tumors in this series required a wide local excision to minimize their recurrence. Despite such an approach, a peroneal glomus tumor recurred and required a repeated operation.

Intraoperative NAP recording was performed in all cases of LHN. Potentials were recorded proximal to the lesion, and the NAP was traced through and distal to the lesion. The lesion was resected if no NAP or one of poor amplitude, which required a large amount of amplification, was recorded across the lesion. Before resecting any portion of a nerve, a frozen-section analysis was obtained to confirm that the “onion whorls” of LHN were present. Uninvolved margins proximal and distal to the lesion were then obtained; that is, the structure of fascicles was observed at both ends of all resected segments.

Myositis Ossificans. 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.

Operative Techniques Used for Malignant Tumors of Non–Neural Sheath Origin

If a mass was palpable and/or visualized on an imaging study in a patient with a history of primary cancer, decompression of the involved neural elements was undertaken. Although indicated for malignant PNSTs, en bloc removal of tumor and adjacent tissues was not indicated for malignant PNNSTs involving the plexus. Unlike malignant PNSTs, nerves involved by metastasis from melanoma or another metastatic cancer could usually be treated with external neurolysis and careful removal of the tumor from the involved nerve. As much of the adjacent mass as possible was also removed. Usually this type of cancer did not invade the nerve beyond the epineural level, but exceptions existed, particularly in cases of breast cancer in which several patients with intraneural lesions required excision of
the neural element(s) with intraneural loci. If pain was a problem, resection of the involved neural element was palliative in some cases. This was especially so with pulmonary carcinoma, in which decompressive procedures sometimes involved the spinal canal as well as the nerve roots, spinal nerves, and plexal trunks.

**Results**

**Benign and Malignant PNNSTs: Histological Review and Incidence**

During the 30-year period between 1969 and 1999, 146 patients at LSUHSC underwent operations to remove benign or malignant non–neural sheath tumors of the brachial and pelvic plexi and the peripheral nerves (Table 1 and Fig. 1). Among these 146 cases, 111 benign PNNSTs (76%) were the most prevalent tumors followed by 35 malignant PNNSTs (24%). The locations of the benign tumors were relatively similar, with 39 tumors located in the upper extremities, 33 in the lower extremities, and 33 in the brachial plexus region. There was only one tumor located in the pelvic plexus.

The most frequently identified benign lesions were ganglion cysts (33 [30%] of 111 tumors), followed by LHN lesions (16 tumors [14%]), lipomas (12 tumors [11%]), tumors of vascular origin (12 tumors [11%]), and desmoid tumors (11 tumors [10%]). There were four (4%) each of lipofibrohamartomas, myositis ossificans, osteochondromas, and ganglioneuromas; two (2%) each of meningiomas, cystic hygromas, myoblastoma or granular cell tumors, triton tumors, and lymphangiomas; and one epidermoid cyst (1%).

Thirty-five patients underwent surgery to remove malignant PNNSTs (carcinomas; Table 2). Most of these tumors had their origins in the breast (15 tumors [43%]) or lung (nine tumors [26%]). Two melanomas (6%) had metastasized to a nerve, and one (3%) tumor each had metastasized from tumors of the bladder, rectum, skin, head and neck, and thyroid, and from a primary Ewing sarcoma. There was one lymphoma (3%) that had metastasized to the radial nerve and was reported in 1987 from this institution,70 and one chordoma (3%) and one osteosarcoma (3%) that had each metastasized to the brachial plexus.

**Locations of Benign Non–Neural Sheath Tumors**

**Ganglion Cysts and the Epidermoid Cyst.** There were 33 ganglion cysts excised in this series. Such cysts usually presented as a tender mass with pain and paresthesias in the distribution of the involved nerve or its branches. Most ganglion cysts arose from the lower extremity (20 tumors, 61% of the 33 ganglion cysts and 53% of the 38 lower-extremity tumors). There was one lymphoma (3%) that had metastasized to the radial nerve and was reported in 1987 from this institution,70 and one chordoma (3%) and one osteosarcoma (3%) that had each metastasized to the brachial plexus.

**Table 1**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Brachial Plexus Region</th>
<th>Upper-Extremity Nerve</th>
<th>Pelvic Plexus</th>
<th>Lower-Extremity Nerve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Location</td>
<td>No.</td>
<td>Location</td>
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<tr>
<td>ganglion cyst</td>
<td>suprascapular nerve</td>
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<td>median</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>radial–PIN</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ulnar–Guyon canal</td>
<td>2</td>
</tr>
<tr>
<td>LHN</td>
<td>brachial plexus</td>
<td>3</td>
<td>median</td>
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<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ulnar</td>
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</tr>
<tr>
<td>lipoma</td>
<td>brachial plexus</td>
<td>2</td>
<td>median</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>axillary nerve</td>
<td>1</td>
<td>PIN–radial</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ulnar</td>
<td>2</td>
</tr>
<tr>
<td>lipofibrohamartoma</td>
<td>venous angioma</td>
<td></td>
<td>median</td>
<td>4</td>
</tr>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>sciatic complex</td>
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<tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td>radial</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>cystic hygroma</td>
<td>accessory nerve</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>myoblastoma/granular cell tumor</td>
<td>brachial plexus</td>
<td>2</td>
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<td></td>
</tr>
<tr>
<td>triton tumor</td>
<td>brachial plexus</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lymphangioma</td>
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<td>1</td>
<td>median–ulnar</td>
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</tr>
<tr>
<td>epidermoid cyst</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total no. of cases</td>
<td></td>
<td>33</td>
<td>39</td>
<td>1</td>
</tr>
</tbody>
</table>

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(5%) each in the obturator, sciatic (near the sciatic notch), and ankle-level posterior tibial nerves.

The second place these tumors were commonly found was the upper extremity (nine tumors, 27% of the 33 ganglion cysts and 23% of the 39 upper-extremity tumors). Ganglion cysts arising from upper-extremity joints were extraneural and caused compression of the median nerve or the median nerve’s thenar sensory branch at the wrist (four [44%] of nine tumors) and the PIN (three [33%] of nine tumors). Cysts in this series were also found to compress the ulnar nerve or its superficial and deep branches in the Guyon canal at the wrist (two tumors [22%] of nine).

Of the 33 ganglion cysts, there were four cysts (12%) in the brachial plexus region, representing 12% of the 33 brachial plexus region tumors. These four cysts originated in the shoulder region in this series, although they did not appear to arise from the shoulder joint. These lesions occurred either in the region of the suprascapular notch or the scapular notch and involved the suprascapular nerve at that level. In both cases, the presentation was similar to that of a spontaneous suprascapular neuropathy.

One epidermoid cyst involving the sciatic nerve was removed.

Localized Hypertrophic Neuropathy. Sixteen LHN lesions were removed, six from the sciatic complex. These six lesions represented 38% of the 16 LHN tumors and 16% of the 38 lower-extremity tumors. Seven LHN lesions were resected from the upper extremity; these seven lesions represented 44% of the 16 LHN tumors and 18% of the 39 upper-extremity tumors. The median, radial, and ulnar nerves were the sites of four (57%), two (29%), and one (14%) of these seven lesions, respectively. The brachial plexus region was involved by three LHN tumors (19% of the 16 LHN tumors and 9% of the 33 brachial plexus region tumors).

Lipomas. In this series 12 lipomas found to compress a nerve were removed from various locations. In two cases the lipomas appeared to arise in the nerve. The upper extremity (seven tumors, 58% of the 12 lipomas and 18% of the 39 upper-extremity tumors) was the site of the majority of lipomas, with four (33%) of the 12 upper-extremity lesions arising from the median nerve, two (17%) of the 12

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**TABLE 2**

Thirty-five carcinomas involving nerve surgically treated at LSUHSC*

<table>
<thead>
<tr>
<th>Type of Tumor &amp; Area of Metastasis</th>
<th>No. of Cases</th>
<th>LR</th>
<th>LRM</th>
<th>Repair†</th>
<th>Improved Pain</th>
<th>Maintained Function</th>
<th>Mean FU (mos)</th>
<th>Deaths (MPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>breast brachial plexus</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11</td>
<td>10</td>
<td>17</td>
</tr>
<tr>
<td>radial nerve</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>lung brachial plexus</td>
<td>9</td>
<td>7</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>7</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>melanoma brachial plexus</td>
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<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>27</td>
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<tr>
<td>bladder brachial plexus rectum</td>
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<td>0</td>
</tr>
<tr>
<td>pelvic plexus skin (squamous)</td>
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<td>0</td>
<td>0</td>
<td>1</td>
<td>12</td>
<td>0</td>
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<tr>
<td>Ewing sarcoma brachial plexus</td>
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<td>1</td>
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<td>0</td>
<td>1</td>
<td>1</td>
<td>14</td>
<td>1 (18 mos)</td>
</tr>
<tr>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>lymphoma radial nerve</td>
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<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>60</td>
<td>1 (60 mos)</td>
</tr>
<tr>
<td>head &amp; neck brachial plexus</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>1 (4 mos)</td>
</tr>
<tr>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>42</td>
<td>0</td>
</tr>
<tr>
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<td>1</td>
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<td>31</td>
<td>2</td>
<td>3</td>
<td>7</td>
<td>30</td>
<td>24</td>
<td>20</td>
</tr>
</tbody>
</table>

* FU = follow up; LR = local resection of tumor; LRM = local resection with margins; MPS = mean postoperative survival; RT = radiation therapy.
† Repair was by grafts.
‡ Radiation therapy was applied using an external beam from a cobalt source.
from the ulnar, and one (8%) of the 12 from the radial nerve. Four (33%) of the 12 lipomas (or four [12%] of the 33 brachial plexus tumors) arose from the brachial plexus region; two (50%) of these were removed from the brachial plexus itself; one (25%) was removed from the musculocutaneous nerve; and another (25%) from the axillary nerve.

In addition to the 12 lipomas, there were four lipofibrohartomas, which arose from the upper extremity, specifically the median nerve.

**Vascular Tumors.** There were 12 tumors of vascular origin in this series. Subgroups of these 12 vascular tumors included four venous angiomas (33%), three hemangiomas (25%), two hemangiopericytomas (17%), two glomus tumors (17%), and one hemangioblastoma (8%). The majority of the venous angiomas (three [75%] of four tumors) were in the lower extremity and one was removed from the upper-extremity median nerve. Two (67%) of three hemangiomas (two [5%] of the 39 upper-extremity tumors) were removed from the upper extremity (the ulnar nerve) and one (33% of the three hemangiomas and 3% of the 38 lower-extremity tumors) from the lower extremity (the peroneal nerve). Hemangiopericytomas were removed from the brachial plexus tumor (one tumor, 50% of the two hemangiopericytomas and 3% of the 33 brachial plexus region tumors) and from the upper extremity at the median nerve (one tumor, 50% of the two hemangiopericytomas and 3% of the 39 upper-extremity tumors). There were two glomus tumors: one (50%) involving the digital nerve of the upper extremity and one (50%) involving the peroneal nerve of the lower extremity. One hemangioblastoma was removed from the median nerve of the upper extremity.

**Desmoid Tumors.** This lesion has its origin in the mesenchyma and usually arises in muscle or fascial structures connected to the muscle (Fig. 4). The majority of the 11 desmoid tumors removed at LSUHSC (six [55%] of 11) involved the brachial plexus. This number represents six (18%) of the 33 brachial plexus region tumors. The lower extremity had the next most frequent number (three lesions, 27% of the 11 desmoid tumors and 8% of the lower-extremity tumors), of which the sciatic complex was the site of two tumors (18%) followed by the peroneal nerve, which had one tumor (9%). The upper extremity (two tumors, 18% of the 11 desmoid tumors and 5% of the upper-extremity tumors) was the site of one tumor each (50%) of the median and radial nerves.

**Myositis Ossificans.** There were four cases of myositis ossificans in this series: two (50%) involving the brachial plexus (6% of the 33 brachial plexus region tumors) and the others involving the upper extremity with one tumor at the median nerve (25% of the four myositis ossificans lesions and 3% of the 39 upper-extremity tumors) and one at the radial nerve (25% of this type of tumor and 3% of the 39 upper-extremity tumors). One of the two patients with an ossified mass involving the brachial plexus underwent partial resection of a large area of axillary fibromyositis and a repeated operation for resection of residual tumor. The tumor involving the radial nerve, which appeared after the patient suffered a contusion to the lateral portion of the upper arm, presented as a large calcified mass and was removed. It had originated in the triceps muscle, had compressed the nerve as it came around the humerus in the radial groove, and was adherent to the nerve, although it had not invaded it.

**Osteochondroma.** In this series there were four osteochondromas, which are bony lesions. In the lower extremity, two (50%) of these tumors (5% of the 38 lower-extremity lesions) were removed from the peroneal nerve. There was one patient who had a large osteochondroma arising in the paraspinal region and extending to the brachial plexus. This lesion had arisen spontaneously and was associated with a thoracic outlet syndrome. A posterior subscapular approach was used for resection of both the tumor and the posterior portion of the rib followed by neurolysis of the brachial plexus. In the upper extremity, one tumor involved the hu-
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merus, resulting in a severe radial distribution deficit preoperatively. After removal of the tumor and neurolysis of the radial nerve the patient slowly regained function over a 2-year period.

Ganglioneuromas, Meningiomas, Cystic Hygromas, and Triton Tumors. These tumors were uncommon in the LSUHSC series. There were three brachial plexus and one pelvic plexus ganglioneuromas, two brachial plexus meningiomas, two accessory nerve cystic hygromas, and two triton tumors involving the brachial plexus.

Myoblastoma or Granular Cell Tumors. These tumors rarely involve nerve, but when they do, they are adherent and require careful dissection for their removal. The two myoblastomas or granular cell tumors in this series involved the brachial plexus. Both were firmly attached and involved the plexal trunks as well as the extraromoral portions of the spinal nerves.

Lymphangiomas. Of the two lymphangiomas in this series, one was found in an upper extremity. This lymphangioma, which involved the medial portion of the upper arm, enveloped the proximal median and ulnar nerves and these nerves required neurolysis. Another tumor was continuous with brachial plexus elements. This lesion was approached by a posterior subscapular approach. The first rib was resected and the tumor was successfully removed from the C-7, C-8, and T-1 spinal nerves as well as from the middle and lower trunks of the brachial plexus.

Malignant Tumors of Non–Neural Sheath Origin
(Metastatic Tumors)

Thirty-five patients presented with carcinomas involving a nerve and underwent operations for these metastatic tumors (Table 2). Breast carcinoma was the largest category of metastatic tumor involving a nerve (15 [43%] of 35 malignant tumors) and involved the brachial plexus or one of its outflows in the majority (14 [93%] of 15 tumors involving a nerve) of patients.

Discussion

Benign Non–Neural Sheath Tumors

Most benign non–neural sheath tumors secondarily involve a nerve and produce symptoms due to nerve compression rather than due to the lesion’s origin in the nerve, but there are important exceptions. Desmoid tumors, myoblastomas, lymphangiomas, or extraspinal meningiomas can be adherent to or even invade the epineurium, making them difficult to remove. Some ganglions are extraneural and can compress the nerve, and others either originate in or dissect to an intraneural level. Hemangiomas or hemangiopericytomas can envelop the nerve or elements of the brachial plexus, but the extremely rare hemangioblastomas can arise in the nerve, as can rare tumors of congenital origin such as triton tumors of the plexus.

Ganglion Cysts and Epidermoid Cysts. A ganglion cyst is thought to arise from an adjacent synovial joint and then track back along a small articular nerve branch to reach its final position within a major nerve trunk.61 The peroneal nerve was the most frequently involved nerve in this LSUHSC series of 33 ganglion cysts, with 15 of 20 tumors located in the lower extremity involving the peroneal nerve.

FIG. 4. Photomicrograph showing a desmoid tumor composed of pale eosinophilic fibroblasts and myofibroblasts with variable tapering or plump vesicular nuclei arranged in fascicles. These fascicles infiltrate the surrounding residual muscle fibers. Individual cells are well separated by collagen and no atypical mitoses are present. H & E, original magnification × 200.

In the recent literature the peroneal nerve was also the most frequently involved nerve, with 40 cases reported in a review in 2001 by Coleman, et al.48 In the LSUHSC review the lower extremity was the most common location of ganglion cysts, with 61% of tumors, followed by the upper extremity with 27%.

Epidermoid cysts usually do not arise within the nerve itself, but may compress an adjacent nerve. The epidermoid cyst in this series involved the sciatic nerve close to the sciatic notch. In two case reports epidermoid cysts that compressed the lateral branch of the superficial peroneal nerve50 and the digitalis plantaris communis nerve have also been presented.58

Comparison of LHN and Perineuriomas. Localized hyper trophyic neuropathy of a peripheral nerve results from hyperplasia of schwann and/or perineural cells in an onion bulb–like manner, which leads to fascicular enlargement. There is a moderate length of localized cylindrical or fusiform swelling in the course of a major peripheral nerve, usually in a limb. Histologically, there is a striking proliferation of perineurial cells in a whorl formation surrounding each individual myelinated axon with marked endoneural fibrosis and also fibrotic replacement of the perineurium. Myelin is either lost or greatly diminished in thickness.32,67

Unfortunately, the term LHN has been used in the literature to denote two distinct unrelated lesions: 1) a rare, nonhereditary localized proliferation of schwann cells characterized by an onion-bulb formation, which is now solely referred to as LHN; and 2) a more common intraneural tumor composed of perineurial cells with a pseudo–onion bulb formation, which is now called perineurioma.

Johnson and Kline30 observed the perifascicular perineurium of LHN lesions, as now defined, to be defective, attenuated, fibrotic, or hyalinized due to a postulated damage to the perineurium with a breakdown of the perfusion barrier as the primary event in the pathogenesis of the lesion.17,19 Gruen, et al.,31 however, found no history of significant trauma in most LHN cases or for that matter in those previously

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reported in the literature. They proposed that the pathophysiological proliferative response in LHN may be a reaction to an unknown chemical, toxic, or compressive mechanical injury, or a neoplastic process.

Localized hypertrophic neuropathy affects children or young adults, with a predilection in the LSUHSC series for the sciatic nerve in the leg, followed by the median nerve and the brachial plexus. In the English-language literature spanning the last 10 years, Simmons, et al., reported two cases each for the brachial plexus, and one each for the radial, femoral, and sciatic nerves. Stumpo, et al., reported bilateral LHN involvement of the brachial plexi in a patient, whereas Isaac and colleagues reported LHN involvement of the radial nerve and Takao, et al., LHN enlargement and femoral nerve involvement. The tumor was also found in the tibial division of the sciatic nerve by Suarez, et al., and femoral nerve involvement. The tumor was also found in the tibial division of the sciatic nerve by Suarez, et al., and in the common peroneal nerve, as reported by Heilbrun and associates.

Lipomas. There are four lipomatous conditions that can affect a nerve: a solitary lipoma may cause neural compression; “macrodystrophia lipomatosa” may produce overgrowth of the hand or fingers; an encapsulated lipoma can be located in the nerve; and lipofibromatous hamartoma of the nerve can occur. The usually fatty tumors are benign, globose or ovoid, and subcutaneous. They have a fine capsule, are composed entirely of adipose tissue (Fig. 5), and usually do not involve nerves. Exceptions occur when a large lipoma envelops or compresses a nerve, or originates at a deeper level in the limb and compresses or entraps a nerve, producing symptoms. In these exceptions, removal is not easy and neural damage can result. Lipomas usually surround a nerve and removal is difficult if this occurs at a plexal level, especially if there has been a previous unsuccessful surgical attempt.

In the LSUHSC series, the upper extremity was the site of seven (58%) of the 12 lipomas, followed by the brachial plexus (four lesions [33%]); and one lipoma involved the sciatic nerve. This finding agrees with the literature in which lipomas involving nerves were prevalent. Focusing on English-language publications from the preceding 10 years, we found a preponderance of lipomas involving the upper extremity, with Babins and Lubahn presenting five palmar lipomas that compressed the median nerve. Goldstein, et al., presented a perineural lipoma that caused nerve compression when postoperative edema developed after vascular graft placement. Three lipomas were presented that involved the PIN branch of the radial nerve, two by Nishida and colleagues and one by Hashizume and associates. One lipoma, reported by Zvijac, et al., compressed the suprascapular nerve and, according to Resende, et al., one each compressed the peroneal and posterior tibial nerves.

Less frequently, lipomas have their origin in the nerve and have an intraneural component, but largely form an extraneural mass. Experience with a sciatic lipoma at the buttck level required a partial interfascicular dissection for complete removal.

Unfortunately, there is also a small but significant group of patients who have a lipohamartomatous condition, in which there is a significant fatty–fibrous mass within the nerve. There were four such cases in the LSUHSC series involving the median nerve. A literature search of the preceding 10 years revealed four radial, three median, and one ulnar nerves involved by lipofibromatous hamartomas in five publications. The usual surgical management of lesions at LSUHSC was section of the transverse carpal ligament and decompression rather than an attempt to remove the lipomatous tissue. When serious loss of median nerve function occurs, more extensive surgery is required. An internal neurolysis can be performed, with reduction of the bulk of the tumor from around individual fascicles, or for a more focal lipohamartoma resection and repair can be done.

Vascular Tumors. Tumors of vascular origin and other arterial or venous anomalies can either envelop or compress a nerve or, less frequently, arise within it. Examples in the present series include venous angiomas, hemangiomas, hemangiopericytomias, glomus tumors, and hemangioblastomas. A literature search revealed no venous angiomas involving peripheral nerves. One hemangioma of the median nerve was presented in the English-language literature.
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spanning the past 10 years by Ergin, et al.,14 and one each of the PIN and posterior tibial nerves by Busa, et al.,14 and Vigna, et al.,23 respectively. There were hemangiomas in the LSUHSC series, two involving the ulnar nerve and one the peroneal nerve (Fig. 6). A hemangiopericytoma of the sciatic notch presenting as sciatica was documented by Harrison, et al.34 In a review of English-only literature covering a 10-year period, there were four glomus tumors involving the peripheral portions of digital nerves, as occurred in one LSUHSC case, one lateral cutaneous nerve, and two peripheral nerve hemangioblastomas, one affecting the sciatic nerve at the mid-thigh level28 and the other affecting the radial nerve. Another tumor in this group, although not experienced by the authors, is a hemangiosarcoma.

Hemangiopericytomas can arise in the mediastinum and grow superiorly to envelop or become adherent to the brachial plexus. These tumors can behave in a malignant fashion and metastasize to other sites, even to the brain. They usually cannot be removed entirely from the plexus and complete removal is difficult even if the plexus is not involved.

Hemangioblastomas are much more common in the central rather than the peripheral nervous system, and such tumors located in or involving a peripheral nerve are extremely rare in the literature. The histological characteristics of these lesions are similar to those seen in central nervous system lesions. The tumor is cellular and multinodular with areas of microcystic degeneration. A hemangioblastoma of the nerve involves primarily the epineurium, but invasion of the fascicles by tumor cells (called “stromal cells”) is often seen. Stromal cells have round nuclei and vacuolated lipid-rich cytoplasm, and they fill the interstices between innumerable capillaries. The single hemangioblastoma in this series involved the median nerve at the elbow level and required an interfascicular dissection to clear the fascicles of tumor. Some years later this lesion recurred and total resection of the involved segment of the nerve followed by graft repair was necessary.

Desmoid Tumor. The desmoid tumor is very fibrous and adherent to neighboring nerves and other structures. Although desmoids are benign, they tend to be invasive of soft tissues and, if close to a nerve, such a tumor can envelop and be quite adherent to it. These tumors are composed of well-collagenized uniform fibroblasts with rare mitoses (Fig. 4).

The most frequent site of origin is the abdominal musculature, but desmoids can originate in the neck, shoulder, upper arm, and lower extremity, where they can involve soft tissue and can compress, incorporate, or adhere to major nerves. In the current series the brachial plexus was the involved site of six (55%) of the 11 desmoid tumors that were presented. A literature search revealed five single case reports25,26,59,77 and one report of seven patients78 with brachial plexus involvement by desmoid tumors. In our series, the sciatic nerve was involved in two cases. In the LSUHSC series there was a desmoid of the median nerve, and Ferarese, et al.,20 published one case of radial nerve involvement by a desmoid tumor. Brgeon, et al.,4 reported two cases of sciatic nerve involvement by desmoid tumors and one case by Fuchs and colleagues,22 also involved the sciatic nerve.

Desmoid tumors have poorly delineated surgical margins.24 Despite what would appear to be gross-total excision, recurrence is common, especially if wide resection is difficult because of contiguous important neural or vascular structures. Excision is the treatment of choice for these tumors. Gross-total excision with microscopically negative margins has been reported to produce recurrence rates of 5 to 50%, whereas excision with microscopically positive margins produce recurrence rates as high as 90%.1,4,15,30,44,52

Radiation therapy may control low-grade growth and external-beam radiation (55 Gy) improves local control in patients in whom the tumor margins prove positive for tumor cells.24,47,53 Some series have shown a significant injury to the brachial plexus in patients receiving as little as 40 Gy, however.24

Tamoxifen has been used as a chemotherapeutic adjunct to surgery mainly in locations other than the peripheral nerve for desmoids; however, the reduced recurrence rates that have been shown24,36,66,71 are variable and there have also been late recurrences in some cases.24,54,55 Cytotoxic therapy with vincristine, actinomycin D, and cyclophosphamide has been shown to have an effect and corticosteroid medications rarely have been shown to cause tumor regression.24

Myositis Ossificans and Osteochondroma. Myositis ossificans is a disorder related to previous trauma or surgery. In this series four cases were encountered, two affecting the brachial plexus and two in the upper extremity involving the median or radial nerve. Such a lesion usually produces a hard mass of tissue that surrounds adjacent nerves, vessels, muscles, tendons, and occasionally bone. Given that neurolysis of the nerve often dramatically improved symptoms, as in the case involving the brachial plexus, complete resection of these masses was not performed. The tumor may be symptomatic owing to neural involvement, vascular involvement, or both. Removal of these masses can be technically difficult. Although the origin is different, an occasional lipoma can also become calcified after trauma or previous surgery. An English-only literature search covering the preceding 10 years revealed no cases of myositis ossificans, but instead “neuritis ossificans” in which the ossifying process was intraneural.37,72,78

Four osteochondromas involved a nerve in this series, and 50% involved the peroneal nerve. A review of English-language literature spanning 10 years demonstrated eight cases of osteochondromas of the nerve, with the peroneal nerve involved in seven of them12,22 and the musculocutaneous nerve involved in one.40

Ganglioneuromas, Cystic Hygromas, Triton Tumors, and Meningiomas. A literature review spanning the past 10 years revealed no peripheral nerve ganglioneuromas, cystic hygromas, or triton tumors. Among reports written in English there was one of a radial nerve meningioma1 and another of a benign triton tumor or neuromuscular choristoma of the left brachial plexus reported by Van Dorpe, et al.49 There were only a few of these tumors in the LSUHSC series,4 as well as outlined in Results.

Myoblastoma or Granular Cell Tumor. These tumors are formed of a mixture of plump and somewhat angular cells with an eosinophilic granular cytoplasm, in which the granules represent a large number of lysosomes. The cells have small, regular, hyperchromatic nuclei. Occasional cells have one or several eosinophilic cytoplasmic globules, which at times exhibit a periglobular halo. Also seen are “angulate
surgical exposure to determine the normal anatomy both adjacent and proximal to the lesion before skeletonizing the involved nerve away from the lesion.

Lymphangiomas. When these tumors involve a nerve, they have many of the same characteristics as myoblastomas. Lymphangiomas have cells of a lymphoid nature, which tend to spread as a sheet of tumor tissue enveloping structures rather than forming a true mass lesion. Two lymphangiomas were reported in this LSUHSC series and they involved the brachial plexus and the median and ulnar nerves. A literature review revealed only one ulnar and one posterior tibial nerve lymphangioma. Surgical excision is performed in the same manner as that used to treat a myoblastoma.

Malignant Tumors of Non–Neural Sheath Origin

Malignant tumors with a non–neural sheath origin usually involve nerves by direct extension from the primary site, but these tumors may occasionally metastasize to nerve or tissues adjacent to the nerve. Management of these tumors must be individualized because there is wide variability in presentation and the extent of involvement related to the individual behavior of each type of cancer.

A literature search for malignant PNNSTs over the last 10 years demonstrated the primary lymphoma involving the radial nerve at our institution, which we already mentioned, and six cases of primary non-Hodgkin lymphoma, four of which involved the sciatic nerve. There were 15 patients with malignant fibrosarcoma or desmoid tumors in the brachial plexus. An intraneural synovial sarcoma of the median nerve at the wrist was reported by Chesser and coworkers. Breast carcinoma can result in neural injury due to radiation-induced fibrosis, recurrent carcinoma with invasion of the plexus, or both. The specific diagnosis often cannot be resolved without an operation and biopsies at multiple sites. Several criteria are used to identify carcinomatous compression or invasion, including a palpable or definite mass seen on CT or MR images and the involvement of specific plexal elements, especially the lower trunk, medial cord, or its outflows. Less definite but also suggestive of carcinoma are severe pain, especially in the distribution of specific plexal elements, and the absence of lymph edema.

Metastasis to nerves can also occur with melanoma, thymoma, and lung, pancreatic, and prostate cancers; most of these metastases involve spread of the disease to the brachial plexus. Those lesions at an infraclavicular axillary level appear to present by direct extension, whereas spread of disease from nearby lymph nodes is more common with breast cancer involving the supraclavicular plexus.

Proposed criteria thought to favor breast carcinoma includes the presence of a Horner syndrome, a history of a radiation dose less than 60 Gy, and presentation in the first few years after mastectomy. The presence of a Horner syndrome in a study by Lederman and Wilbourn was indicative of neoplastic brachial plexopathy, rather than radiation-induced plexopathy. We have seen exceptions to these criteria. For example, several women have presented with breast carcinoma within one or more plexal elements 15 or more years after initial treatment of the breast lesions.

Surgical indications for metastatic lesions included pain and paresthesias, progressive deficit, and usually a palpable and very tender mass.

Another type of cancer involving the nerve and particularly the plexus is pulmonary metastatic disease. Lung cancer may involve the brachial plexus by direct extension and most often produces a Pancoast syndrome. This syndrome, which occurred in seven of nine patients with metastases to the brachial plexus, sometimes occurs as a result of local extension of a pulmonary apical tumor with involvement of the C-8, T-1, and T-2 nerves. There usually is shoulder pain radiating in the ulnar distribution of the arm, often with radiological evidence of the destruction of the first and second ribs. If pain is a severe problem, a palliative approach can consist of posterior subscapular resection of the first rib and subtotal resection of the apical tumor to decompress the lower elements of the plexus. This procedure, combined with cervical laminectomy for associated epidural metastatic disease is also palliative. Occasionally, a high contralateral open cervical cordotomy also helps control the pain associated with a Pancoast syndrome. The main focus of this palliative operation is to alleviate pain and decompress the compressed or entrapped plexal elements.

True metastatic disease involving a nerve is seen with lymphoma, bladder cancer, and melanoma, although these lesions are less common than breast or pulmonary cancer. With melanomas involving the plexus, removal of the tumor from any epineural attachment has sufficed. The surgical approach is followed by local irradiation. A similar approach is also appropriate for lymphomas, at least for palliative treatment of these tumors.

Conclusions

Although not as numerous as the neural sheath tumors presented in our companion article, non–neural sheath tumors have a greater variety of types of tumors. Benign tumors involved the brachial and pelvic plexi and peripheral nerves, whereas malignant tumors more frequently tended to involve the brachial plexus. The location of benign tumors was relatively similar, with 39 tumors located in the upper extremities, 38 tumors in the lower extremities, and 33 in the brachial plexus region. There was only one tumor located in the pelvic plexus. The reasons for these predictions for certain locations are unknown at this time. The most common lesion was the ganglion cyst, which occurred mainly in the lower extremities and, particularly, in the peroneal nerve. The next most prevalent tumor was the LHN lesion, which involved the upper and lower extremities.
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ties equally. Of the malignant lesions, breast carcinoma and lung carcinoma were the most common lesions to metastasize to a nerve.

The literature review documented the paucity of publications of cases of benign PNNSTs and underscores the fact that the present LSUHSC series is one of the largest in the literature to date.

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