CASE REPORT

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PRIMARY SCHWANNOMA IN A CERVICAL LYMPH NODE

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Abstract: Background. Spindle cell neoplasms within lymph nodes are rare and include benign and malignant tumors and primary and metastatic tumors such as palisaded myofibroblastoma, leiomyoma, leiomyosarcoma, reticular cell neoplasms, and vascular sarcomas. Ancillary studies may help distinguish these neoplasms.

Methods. A 77-year-old white woman was seen with a painless, slowly growing mass of the left neck. Her clinical history was noncontributory. An excisional biopsy was performed without complication. There has been no recurrence, to date, of the lesion.

Results. Gross examination, microscopic examination, immunohistochemistry, and ultrastructural studies were consistent with the diagnosis of schwannoma arising within a lymph node.

Conclusions. We report the first case of intranodal schwannoma arising in a cervical lymph node. The recognition of intranodal schwannoma is important because it is cured with excision, whereas some of the other diagnostic considerations for a spindle cell lesion within a lymph node may require radiation or chemotherapy. © 2009 Wiley Periodicals, Inc. Head Neck 32: 964–969, 2010

Keywords: schwannoma; cervical lymph node; spindle cell lesion; primary

Spindle cell lesions within lymph nodes are usually attributed to metastatic disease. The most likely diagnostic possibilities include metastatic spindle cell carcinoma, metastatic spindle cell melanoma, and metastatic sarcoma. Primary spindle cell neoplasms within lymph nodes are rare and include entities such as palisaded myofibroblastoma, leiomyoma, dendritic cell neoplasms, angiosarcoma, and Kaposi’s sarcoma.

We present a case of a lesion within a lymph node, which exhibits the classic histology, immunohistochemical profile, and ultrastructural characteristics of a schwannoma. Schwannomas occur in many locations but, to date, there is no report of a schwannoma arising as a primary neoplasm within a lymph node. Schwannomas are benign lesions that do not show malignant
behavior, and metastasis of a schwannoma to a lymph node has not been described. Although schwannoma with malignant transformation may lead to nodal metastasis, the lesion described here lacks the features of malignant peripheral nerve sheath tumor. Therefore, we believed that this lesion was a primary schwannoma arising within a lymph node. The following discussion addresses the differential diagnosis of spindle cell lesions within lymph nodes, and how these criteria apply to the lesion presented in this case.

**CASE REPORT**

A 77-year-old white woman was seen with a painless, slowly growing mass of the left neck. Her clinical history was unremarkable. An excisional biopsy was performed without complication. There has been no recurrence, to date, of the lesion.

The specimen was received fresh, and then gross examination was performed and the mass was serially sectioned. A portion of the tissue was frozen for ultrastructural study. The tissue was fixed in 1% formalin, embedded in paraffin, and processed routinely, and thin sections were stained with hematoxylin-eosin stain.

Additional sections were deparaffinized and rehydrated. The slides were incubated with primary antibodies against S-100 protein, fascin-1, smooth muscle actin, desmin, CD146, CD35, CD45, CD21, CD23, pan-cytokeratin, epithelial membrane antigen, and a pan-melanoma cocktail. A second incubation was performed with secondary antibody to biotinylated mouse anti-human immunoglobulin G (Dako). The detection was executed using 3,3′-diaminobenzidine as a chromogen, counterstained with hematoxylin.

On gross examination, the lesion was observed as a circumscribed, light-tan, firm mass (1.5 cm × 1.0 cm × 1.0 cm) with a discrete capsule and focal cystic changes. Microscopically, the lesion consisted of a well-circumscribed, encapsulated, round, nodular lesion composed of spindle cells. A dense, collagenous capsule surrounded the nodule, underlying a thin, compressed rim of benign lymphoid tissue. Small follicular centers and subcapsular sinuses were present at the periphery, indicating true lymph node architecture (Figure 1A). Cytologically, the tumor cells displayed spindled nuclei with tapered ends, even chromatin distribution, and pale pink, abundant cytoplasm.

Occasionally, nuclei were compact, round to ovoid. Some areas showed increased cellularity (Figure 1B). Verocay bodies were identified within these cellular areas (Figure 1C). Other areas were less cellular, with spindle cells arising in a loose stroma (Figure 1D). Cystic areas, without an epithelial lining, were present within the lesion. Necrosis and mitotic figures were absent.

Immunoperoxidase staining showed diffuse, strong cytoplasmic positivity for S-100 protein (Figure 1E) and fascin-1. Additionally, CD146 staining showed focal positive membranous staining. Smooth muscle actin staining highlighted the blood vessels, whereas all other stains were negative (see Table 1).

The frozen tissue submitted for electron microscopy showed cells with prominent, convoluted, moderately thin cytoplasmic processes lacking pinocytotic vesicles. The cells were lined by continuous basal lamina material (Figure 1F).

**DISCUSSION**

A schwannoma is a benign tumor consisting of differentiated neoplastic Schwann cells. The tumors are typically encapsulated, well-circumscribed lesions that appear light tan and glistening on gross examination. They may include areas of hemorrhage or cyst formation, but characteristically are devoid of necrosis. Microscopically, they are composed of spindle-shaped Schwann cells that are arranged in alternating patterns of cellular areas, with palisading growth (Antoni A, Figure 1B), and less cellular, loosely arrayed areas with a lipidized background (Antoni B, Figure 1D). The Antoni A areas may contain Verocay bodies (Figure 1C). Prominent blood vessels with hyalinization, in a background of hemorrhage, are a common feature. Several variants of schwannomas are described, including cellular, melanotic, and plexiform types.1

The immunohistochemical profile of the schwannoma includes diffuse, strong positivity for S-100 (Figure 1E), frequent expression of Leu-7 (CD57), and occasional, focal positivity for glial fibrillary acidic protein (see Table 1). In addition, fascin-1 is an actin-bundling protein that is expressed in specialized cells with extensive surfaces or migratory potential such as neurons, glia, dendritic cells, macrophages, skeletal and smooth muscle, and endothelial cells, but...
not in normal epithelial cells. Fascin-1 is positive in our case of schwannoma, which supports its neural origin and morphology, particularly with regard to cytoplasmic processes. Desmin, smooth muscle actin, and keratin stains are negative. Electron microscopy shows prominent basal lamina surrounding cell processes (Figure 1F) and Luse bodies.

Schwannomas can be found wherever peripheral nerves are located. Most commonly, schwannomas arise from small to medium-sized peripheral nerves of the head and neck, as well as extensor surfaces of the extremities. Spinal and cranial nerves, including the vestibular division of the eighth cranial nerve (the well-known bilateral acoustic schwannomas associated with type 2 neurofibromatosis) may also be involved, and approximately 40 cases of central nervous system schwannomas have been reported.

In general, schwannomas are benign and do not show malignant behavior (including metastasis), with the exception of a rare subset of schwannomas that undergo malignant...
transformation. Such transformation should be suspected when there is accelerated growth or development of pain.¹ Malignant peripheral nerve sheath tumor and angiosarcoma are the described malignant neoplasms that may arise within a schwannoma.¹

Malignant peripheral nerve sheath tumor features fasciculated growth, similar to fibrosarcoma, with tightly packed, hyperchromatic spindle cells with abundant, pale pink cytoplasm. Necrosis and brisk mitotic activity, with at least 4 mitoses per high power field, is seen in 75% of cases. Some investigators have found that malignant peripheral nerve sheath tumor arising in a schwannoma typically is of the epithelioid variant.² Malignant peripheral nerve sheath tumor may focally express S-100, but not in a diffuse pattern as in schwannoma. This difference in staining pattern may be useful in differentiating these entities. Electron microscopy is usually noncontributory.

Epithelioid malignant change is a newly described lesion which is believed to be a precursor lesion to epithelioid malignant peripheral nerve sheath tumor.² “Atypical schwannoma with epithelioid cells” is the suggested nomenclature.² The term was coined after examination of a series of schwannomas with the evidence of malignant change, wherein a subset showed small clusters or scattered single cells with enlarged vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm. These cells resembled tumor cells seen in cases of epithelioid malignant peripheral nerve sheath tumor, but were scattered amid benign Schwann cells. In 1 of these cases, areas of epithelioid malignant change were present within the same benign schwannoma along with a focus of epithelioid malignant peripheral nerve sheath tumor. In 1 of these cases, areas of epithelioid malignant change were present within the same benign schwannoma along with a focus of epithelioid malignant peripheral nerve sheath tumor. In 1 of these cases, areas of epithelioid malignant change were present within the same benign schwannoma along with a focus of epithelioid malignant peripheral nerve sheath tumor.² Despite their resemblance to epithelioid malignant peripheral nerve sheath tumor, the behavior of these tumors is uncertain, as follow-up data have been limited. These changes were not identified in our case.

Table 1. Immunohistochemical staining results.

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Positive staining</th>
<th>Negative staining</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-100 protein</td>
<td>Schwannoma, melanoma</td>
<td>Carcinoma, smooth muscle tumors, vascular tumors</td>
<td>Positive, diffuse cytoplasmic</td>
</tr>
<tr>
<td>Pan-melanoma cocktail</td>
<td>Melanoma</td>
<td>Schwannoma, carcinoma, smooth muscle tumors, vascular tumors</td>
<td>Negative</td>
</tr>
<tr>
<td>Cytokeratin cocktail</td>
<td>Carcinoma</td>
<td>Schwannoma, carcinoma, smooth muscle tumors, vascular tumors</td>
<td>Negative</td>
</tr>
<tr>
<td>Desmin</td>
<td>Smooth muscle tumors, skeletal muscle tumors</td>
<td>Carcinoma, melanoma, schwannoma</td>
<td>Negative</td>
</tr>
<tr>
<td>Smooth muscle actin</td>
<td>Smooth muscle tumors</td>
<td>Schwannoma, melanoma, carcinoma</td>
<td>Positive in blood vessels, negative in tumor cells.</td>
</tr>
<tr>
<td>Fascin-1</td>
<td>Histiocytic lesions, vascular tumors, lipogenic tumors, neurogenic tumors, skeletal and smooth muscle tumors</td>
<td>Carcinoma</td>
<td>Positive, strong cytoplasmic staining.</td>
</tr>
<tr>
<td>Epithelial membrane antigen</td>
<td>Adenocarcinoma, meningioma</td>
<td>Schwannoma, some carcinomas</td>
<td>Negative</td>
</tr>
<tr>
<td>CD21</td>
<td>Follicular dendritic cell sarcoma, some leukemia/lymphoma</td>
<td>Schwannoma, carcinoma, melanoma</td>
<td>Positive in follicular dendritic cells, negative in tumor cells.</td>
</tr>
<tr>
<td>CD23</td>
<td>Follicular dendritic cell sarcoma, some leukemia/lymphoma</td>
<td>Schwannoma, carcinoma, melanoma</td>
<td>Positive in follicular center cells, negative in tumor cells.</td>
</tr>
<tr>
<td>CD35</td>
<td>Follicular dendritic cell sarcoma, some lymphomas</td>
<td>Schwannoma, carcinoma, melanoma, other histiocytic lesions</td>
<td>Positive in follicles, negative in tumor cells.</td>
</tr>
<tr>
<td>CD45</td>
<td>Most white blood-cell derived lesions</td>
<td>Carcinoma, sarcoma, melanoma</td>
<td>Positive in lymphoid cells, negative in tumor cells.</td>
</tr>
<tr>
<td>CD146</td>
<td>Melanotic schwannoma and other neurogenic tumors, vascular sarcomas, some carcinomas, some melanomas, smooth muscle tumors</td>
<td>Most carcinoma, normal melanocytes</td>
<td>Focally positive in tumor cells.</td>
</tr>
</tbody>
</table>

Primary Schwannoma in a Cervical Lymph Node
Angiosarcoma may have a spindled or epithelioid morphology, but the diagnosis is made by the presence of rudimentary vessels with irregular, sinusoidal patterns, arranged around islands of tissue in a destructive manner, which was not seen in our case. Sampling is important to correctly identify the lesion, as some areas will display flattened endothelium, whereas in other areas, the endothelium appears neoplastic. Characteristically, angiosarcoma stains for vascular markers, including CD34, CD31, and von Willebrand factor. Kaposi sarcoma may also arise as a primary lesion in a lymph node and will present the morphology of irregular blood vessels with suspicious cytology. Other malignant spindle cell neoplasms that may feature metastasis to lymph nodes and are easily differentiated with immunohistochemical stains include metastatic spindle cell carcinoma (cytokeratin positive) and metastatic spindle cell melanoma (HMB-45 positive). These stains were negative in our case, excluding the diagnosis of melanoma or carcinoma.

Reticulum cell sarcomas (follicular dendritic cell, interdigitating reticular cell, and fibroblast reticular cell types) are another group of tumors that arise as intranodal or extranodal lesions, from precursors that occur naturally within the lymph node. The interdigitating type shows diffuse positivity for S-100 protein, which could pose a diagnostic difficulty, especially as the gross morphology resembles our case (a spindle cell lesion obliterating most of the lymphoid component and compressing a thin rim of normal tissue at the periphery), but the cell morphology is distinctive. Also, reticulum cell sarcomas show positive immunoperoxidase staining for CD 21, CD23, and CD35, which were negative in our case. Reticulum cell sarcomas have vesicular nuclei with prominent nucleoli and prominent cytoplasmic processes not seen in Schwann cells. Additionally, a prominent lymphoid population is also seen intermixed with the tumor cells. Also, distinct ultrastructural features are seen for each subtype of reticulum cell sarcomas, which are clearly unlike those seen in schwannoma.

Benign spindle cell lesions identified within the lymph nodes include leiomyoma, palisaded myofibroblastoma, inflammatory myofibroblastic tumor (pseudotumor), and Mycobacterium-infected lymph nodes. Leiomyomas can have very similar morphology and will express desmin and smooth muscle actin, but do not express S-100 as the schwannoma. The palisaded myofibroblastoma, believed to arise from the smooth muscle or myofibroblasts, expresses actin but lacks S-100 protein, as well as synaptophysin, desmin, keratin, and epithelial membrane antigen. These lesions show very similar morphology to schwannoma, and the occurrence of the case presented here within a lymph node is strongly reminiscent of the palisaded myofibroblastoma, but without the immunohistochemical profile to support the diagnosis. Inflammatory myofibroblastic tumor (inflammatory pseudotumor of lymph nodes) is another lesion in the differential diagnosis and is characterized by a histiocytic and fibroblastic, non-neoplastic proliferation involving the lymph node connective tissue framework and associated vascular lesions. The lesions are usually associated with the hilum, trabeculae, or capsule, with abundant intermixed inflammatory cells, including lymphocytes, plasma cells, and neutrophils. S-100 protein is negative in these tumors. Mycobacterium infection, when occurring as the “mycobacterial spindle cell pseudotumor” is usually suspected because of a clinical history of immunosuppression, documented prior infection, or Bacillus Calmette Guerin vaccination and will not have the same morphologic, immunohistochemical, or ultrastructural characteristics as schwannoma.

Other rare spindle cell lesions reported as arising in lymph nodes include anthracotic and anthracosilicotic spindle cell pseudotumors of mediastinal lymph nodes, which show abundant anthracotic pigment and birefringent, needle-shaped silicate crystals. Spindle and histiocytoid hemangioendothelioma has also been reported in the lymph node as a primary lesion. These lesions will also be S-100 protein negative.

In summary, among the spindle cell lesions that arise within the lymph nodes, only a schwannoma would present with the pattern of immunohistochemical staining and ultrastructural characteristics seen in this case, and in the absence of atypia, malignant tumors are excluded from the differential diagnosis. Therefore, we present the only known report, to date, of a schwannoma arising within a lymph node.

REFERENCES


