Neurogenous Tumors of the Mediastinum: 
A Clinicopathologic Study Based on 50 Cases*

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During the past 20 years, a number of excellent articles concerned 
with neurogenous neoplasms of the mediastinum have appeared.1,4,12 All the observers, except the Japanese,1 are in agreement 
that these probably represent the most common mediastinal neoplasms, particularly in the posterior mediastinum. Furthermore, there is general assent to the 
idea that it is not possible to classify these neoplasms either on the basis of clinical signs or symptoms or by means of radiologic findings. Only thoracotomy and biopsy allow for the establishment of a definite diagnosis of a particular mediastinal tumor as being neurogenous in nature, as well as whether it is benign or malignant.

On a number of points, however, various compilators have had divergent experiences: (1) the incidence of anterior mediastinal neurogenous neoplasms; (2) the incidence of cancer in neurogenous tumors; (3) the frequency of association of malignant schwannoma with von Recklinghausen's disease; (4) the sex distribution in nerve sheath neoplasms; (5) the relative frequency of intraspinal extension of nerve sheath tumors as compared with sympathetic neurogenous tumors; (6) the prognosis of partially differentiated ganglioneuromas and neuroblastomas. It is hoped that the present compilation, one of the largest available, will shed some light on these disputed areas.

Materials and Methods

The records of all cases on file in the Laboratory of Surgical Pathology of the Columbia University College of Physicians and Surgeons, in which a diagnosis of a neurogenous tumor was rendered, were studied. All cases in which the tumor was only partly within the mediastinum were excluded from the present study. The pathologic findings and treatment were noted. The clinical aspects of each case were studied with regard to age, sex, symptoms and clinical findings. In this study, we have used the following classification of neurogenous tumors:

1. Tumors of nerve-sheath origin: (1) neurilemmoma; (2) neurofibroma; and (3) malignant schwannoma.

2. Tumors of the sympathetic nervous system: (1) mature ganglioneuroma (well-differentiated); (2) partially differentiated ganglioneuroma (ganglioneuroblastoma); and (3) neuroblastoma (sympathico-blustainoma).

The roentgenologic findings were noted. A total of 50 cases of neurogenous neoplasms, presenting primarily in the mediastinum, were found acceptable for evaluation. The tumors consisted of 14 neurilemmomas, ten neurofibromas, two malignant schwannomas, seven mature ganglioneuromas, seven partially differentiated ganglioneuromas (ganglioneuroblastomas) and ten neuroblastomas (sympathicoblastomas).

Observations

Of the 50 neurogenous neoplasms reviewed, 26 were nerve sheath in origin and 24 were considered to be derived from the sympathetic nervous system. Of the entire group, 12 were considered histologically to be malignant (24.0 per cent). All but three neoplasms were located partially or wholly in the posterior mediastinum, principally in the costovertebral gutter. One neurilemmoma arose in the anterior mediastinum between the parietal pleura and ribs, one ganglioneuroma (mature variety) arose in the anterior mediastinum on either side of the subclavian vein and lay against the
first and second ribs, and one neurofibroma was found in the anterior mediastinum lying on the visceral pleura of the apex of the lung.

_Nerve Sheath Neoplasms_

Fourteen of the 26 nerve sheath neoplasms were neurilemmomas, ten were neurofibromas, and two were malignant schwannomas. Although there was a greater range in age among the neurofibromas, their average age and that of the neurilemmomas were similar (Table 1). The neurofibromas, as expected, tended to be multiple, while the other neurogenous neoplasms were solitary. There was a definite predominance of women, especially in the case of the neurilemmomas. These neoplasms showed a predilection for the superior portion of the mediastinum.

_Neurilemmomas_

The commonest neoplasm in this study was the neurilemmoma. The majority were detected incidentally during routine roentgenologic surveys of the chest. Compression of nerve roots may explain the pain in one case and intraspinal extension of the sensory changes in the other case. In no case did the neoplasm, by virtue of its size, give rise to tracheobronchial displacement with subsequent coughing and dysphagia. Grossly, the tumors appeared encapsulated and ranged in greatest diameter from 4.5 to 10 cm. Approximately 30 per cent were firm, with a gray-tan surface, while the remainder showed degenerative phenomena especially cystic alterations and hemorrhage. No definite pattern of type or extent of degeneration, as related to the size of the tumor, could be determined. Five of the neurilemmomas extended intraspinally through intervertebral foramina, but only one produced symptoms directly traceable to this extension.

Microscopically, a connective tissue capsule was always found. Where adequate tissue was available, a spindle cell pattern with palisading was seen in all but one case (Fig. 1). The degree of palisading, however, varied markedly from two rows of nuclei to eight or ten rows. The cystic changes of the Antoni type B growth were accentuated in ten cases. In only one case was there complete absence of degeneration. Vascular thickening as a result of perivascular hyalinization was present in 55 per cent of all the neurilemmomas. Similarly, in 55 per cent of the cases clusters as well as single intact and necrotic foam cells were observed. Pleomorphic nuclei were prominent in three cases, but mitoses were not apparent (Fig. 2). Calcific deposits were noted in five cases, hemosiderin in nine, and recent or old thrombi in eight cases (Fig. 3). Perivascular lymphocytic infiltrates were prominent in seven cases and hyaline degeneration in seven cases. Eleven of the patients are alive and well without evidence of recurrence after radical removal of the tumor, while three have died of unrelated diseases (Table 2).

_Neurofibromas_

Only three of our ten patients with neurofibroma had any stigmata of von Recklinghausen's disease. In all but one

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**Table 1—Clinical Findings in 50 Neurogenous Mediastinal Tumors**

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Sex</th>
<th>Age Range (Yrs)</th>
<th>Symptoms</th>
<th>Cough</th>
<th>Pain</th>
<th>Sensory</th>
<th>Avg. Tumor Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurilemmoma</td>
<td>4 M</td>
<td>29-77</td>
<td>53</td>
<td>11</td>
<td>0</td>
<td>2</td>
<td>6.5 cm</td>
</tr>
<tr>
<td>Neurilemmoma</td>
<td>10 F</td>
<td>29-77</td>
<td>53</td>
<td>11</td>
<td>0</td>
<td>2</td>
<td>6.6 cm</td>
</tr>
<tr>
<td>Malignant Schwannoma</td>
<td>2 M</td>
<td>34</td>
<td>34</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>6.0 cm</td>
</tr>
<tr>
<td>Mature Ganglioneuroma</td>
<td>6 M</td>
<td>9-52</td>
<td>21</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>6.0 cm</td>
</tr>
<tr>
<td>Partially Differentiated Ganglioneuroma</td>
<td>5 M</td>
<td>47 yrs.</td>
<td>12</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6.5 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2½ yrs.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>5 M</td>
<td>-8 yrs.</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>6.5 cm</td>
</tr>
</tbody>
</table>
case, the lesions were detected as a result of routine chest x-ray films. One patient presented with cough apparently a result of mechanical compression of the trachea by the tumor (Table 1). There was a greater age range with these tumors than with the neurilemmomas, but the average was the same. In no case was there demonstrable sarcomatous transformation. All but one of the neurofibromas were located in the posterior mediastinum. One tumor apparently involved the vagus nerve and was located in the middle mediastinum and projected into the anterior mediastinum. All the tumors were well-circumscribed and grossly appeared to be encapsulated. Approximately 90 per cent presented a bosselated external surface. In only one case was there cystic alteration; the others presented a firm to rubbery cut surface.
with no grossly visible degeneration. The tumors were associated with intercostal nerves or a sympathetic trunk. Microscopically, true connective tissue capsules were absent. Palisading and Verocay bodies were absent. Blood vessel thickening was present in four cases, but thrombus formation was noted in only one. Isolated and grouped foam cells were seen in three cases, hemosiderin in two, hyaline degeneration in four and calcification in one case. Perivascular lymphocyte accumulations were prominent in two cases. Seven of the ten patients are alive and well without evidence of disease. Three patients have been lost to follow-up (Table 2).

Malignant Schwannoma

Both cases occurred in men in the mid-30's. Grossly they were approximately the same size as the other nerve sheath neoplasms. One case showed cystic alterations on the cut surface while the other was gray-white and whorled. Both cases showed extensive infiltration of adjacent tissues. In the one case, the infiltration was confined to the adjacent pleura, lung and lymph nodes, while in the other there were distant metastases to the liver, adrenals, kidneys, pancreas, lungs and lymph nodes at necropsy. Microscopically, hypercellularity, cellular and nuclear pleomorphism, and moderate numbers of mitotic figures were characteristic (Fig. 4). The majority of the cells were spindled, and whorling was noted in some areas. Both cases revealed thickened blood vessels and varying degrees of necrosis. The patient with metastases died seven years after partial removal of the lesion. The other patient, after partial removal of the tumor, has been lost to follow-up.

Sympathetic Neurogenous Neoplasms

Seven of the ganglioneuromas were of

Table 2—Follow-up Data on 44 Neurogenous Mediastinal Tumors

<table>
<thead>
<tr>
<th>Neurilemmoma</th>
<th>11</th>
<th>3</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurofibroma</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Malignant Schwannoma</td>
<td>-</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mature Ganglioneuroma</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Partially Differentiated Ganglioneuroma</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

*No evidence of disease.

Table 2—Follow-up Data on 44 Neurogenous Mediastinal Tumors

Death from Unrelated Cause

Alive NED* Of Tumor

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Neurilemmoma      11    3    0
Neurofibroma       7     0    0
Malignant Schwannoma -     0    1
Mature Ganglioneuroma 6     1    0
Partially Differentiated Ganglioneuroma 4     0    1
Neuroblastoma      5     0    5

*No evidence of disease.
the mature and seven were of the partially differentiated variety. In addition, there were also ten neuroblastomas. All of these neoplasms occurred in much younger individuals than did those of nerve sheath origin. These neuroblastomas were equally distributed between the sexes while both varieties of ganglioneuroma occurred more frequently in women (Table 1). The neoplasms were all of the same general order of size as those of nerve sheath origin. One of the mature and two of the partially differentiated ganglioneuromas had intraspinal extensions.

**Mature Ganglioneuromas**

These tumors occurred in an older age group than did the undifferentiated variety. Five of these tumors were asymptomatic while two others caused cough and pain. The tumors grossly appeared encapsulated and usually had bosselated external surfaces. The cut surfaces showed no gross degenerative alterations in four cases, while the others demonstrated cyst formation, gelatinous areas and focal areas of yellow softening. In two cases calcification was grossly demonstrable. Attachment to the sympathetic trunk was demonstrated in two cases and to intercostal nerves in three instances. Microscopically, the tumors were composed of nests of and isolated mature ganglion cells in an edematous, neuromatous, Schwann cell and fibrous stroma (Fig. 5). The whole was enclosed by a connective tissue capsule. Many of the ganglion cells showed degenerative phenomena in the form of calcification, cytoplasmic vacuolization and nuclear pyknosis. In two of the cases varying amounts of adipose tissue were present in the stroma. Blood-vessel wall thickening and thrombus formation was absent. Six patients are alive and without evidence of recurrence after complete removal of the neoplasm. One patient died of an unrelated disease, necropsy revealing no extension of the neurogenous tumor to adjacent or distant structures (Table 2).

**Partially Differentiated Ganglioneuromas**

These neoplasms occurred in a younger age group than did the mature ganglioneuromas. All but one of the patients were less than 20 years of age. Women predominated by a 2:1 ratio. All of these tumors were located in the posterior mediastinum except for one case, in which

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**Figure 4:** Malignant schwannoma. Note the hypercellularity due to spindle-shaped cells with atypical and pleomorphic nuclei.
the tumor lay on either side of the subclavian vein with its medial surface resting on the neck of ribs 3, 4, and 5. Four of the tumors produced symptoms: dyspnea, cough, pain and sensory changes. In two of the cases it was possible to demonstrate extension into an intervertebral foramen. In four cases a capsule could be recognized grossly. Cystic alteration was present in one case, while the others were grossly firm and gray-tan. Attachment to intercostal nerves or the sympathetic trunk was shown in all but two cases. The imposing histologic feature was the admixture of cells varying in maturity from sympathogonia to mature ganglion cells. In most cases the immature cells predominated. The stroma was essentially composed of neuromatous, Schwann cell, and fibrous tissue complex (Fig. 6). In three cases microscopic calcification was noted. Occasional perivascular clusters of lymphocytes were noted in almost all cases. Adipose tissue was present in one case, hemosiderin in one case and hyaline degeneration in one. Four patients are alive and well two to ten years after either partial or complete removal of the tumor. In one case, a large amount of tumor was left behind at operation and the patient remains well, with radiologic evidence of residual tumor six years after surgery. One patient died three years after partial removal of the tumor with metastases in the left adrenal, liver, ribs, skull and lymph nodes. Two patients have been lost to follow-up (Table 2).

Neuroblastoma

This tumor occurred in a much younger age group than did any of the other neurogenous tumors. There was an equal sex distribution. All but one of the patients had symptoms referable to the tumor, such as dyspnea, pain, cough and sensory alterations (Table 1). None of the lesions showed extensions intraspinally. Grossly, the neoplasms were of approximately the same order of size as the tumors previously discussed. Capsular invasion and penetration were found in two cases. Gross calcification was present in two cases and cyst formation in three cases. Capsules were grossly demonstrable in four cases. Histologically, the predominating cell was round to oval, had a small amount of cytoplasm and a prominent hyperchromatic nucleus. Occasionally,

**Figure 5:** Mature ganglioneuroma. Note mature sympathetic ganglion cells with satellites set in a neurofibromatous stroma (H. and E. x 112).
cells with more abundant eosinophilic cytoplasm were observed. In approximately 60 per cent of the cases, pseudorosettes were seen. No mature ganglion cells were noted in any of the tumors. Five of the patients are alive three to 15 years after total or partial removal of the tumor. Four of these patients had postoperative radiation. One patient died three hours after operation and the remaining four died six months to three years after partial removal of the tumor (Table 2). Of these last patients, two received radiation therapy and two did not; the longest survivor in this group received radiation therapy.

**DISCUSSION**

If the partially differentiated ganglioneuromas (ganglioneuroblastomas) are excluded from primary consideration as malignant tumors then the incidence of cancer in our group of neurogenous tumors is 27 per cent. This figure is slightly higher than the figures of 10 per cent to 20 per cent that are usually quoted, but considerably less than others. In keeping with most published series, the tumors of nerve sheath origin comprise the greatest group among the neurogenous tumors; the neurilemmomas constituting the largest single type of tumor. One interesting feature was that although the great majority of the tumors were located in the posterior mediastinum, a sufficient number were present in the anterior and middle mediastinum to prevent using radiologic location of the neoplasm as a dogmatic diagnostic criterion of neurogenous tumors.

Regarding the nerve sheath neoplasms, the most outstanding clinical finding was the very lack of symptoms, almost all of the tumors being detected on routine chest x-ray examination in the form of a sharply circumscribed, round or oval, homogenous mass. From a histologic point of view, almost all of the neurilemmomas showed degenerative changes while this was distinctly uncommon with the neurofibromas. In addition, encapsulation was present in all the neurilemmomas and in none of the neurofibromas. Blood vessel thickening was much more frequent in the neurilemmomas than the neurofibromas. We have not classified any of our neurilemmomas as so-called "ancient neurilemmomas" because of our inability to establish this histologic

*Figure 6: Partially differentiated ganglioneuroma. Note immature ganglion cells and sympatheticoblasts in a feathery Schwann cell background (H. and E. x 230).*
distinction in these tumors. Three of the neurilemmomas contained numerous cells with pleomorphic nuclei. It is worth reiterating that this cytologic finding has no bearing on the natural history of the tumor and is not, in and of itself, to be considered a sign of malignant disease.

One of the striking features is the fact that none of our neurofibromas showed malignant degeneration, and in our two cases of malignant schwannoma there was neither clinical nor pathologic evidence of von Recklinghausen’s disease. This is in contrast to the findings of Hollingsworth and Saxen who noted that malignant degeneration of neurofibromas was common. In Ackerman’s series, three of his four cases of malignant schwannoma occurred in patients with von Recklinghausen’s disease. It is of interest to note that the rare malignant schwannoma may be the cause of hypoglycemia. In contrast to a recent report, the two patients with malignant nerve sheath tumors were in a younger age group than the majority of the patients with benign tumors. Another contrast to previous compilations lies in the 2:1 predominance of women over men in the case of nerve sheath tumors; the malignant types, however, occurred in men exclusively. No significance is attached to this sex distribution.

The various sympathetic neurogenous tumors occurred in a decidedly younger age group than did the tumors of nerve sheath origin. It is of interest to note that the mature ganglioneuromas occurred in a slightly older age group than did the partially differentiated ones. This clinical finding would tend to substantiate the contention that with increasing age there is a decrease in the immaturity of the cells. However, from a morphologic standpoint none of our partially differentiated tumors showed a tendency to alter its pattern toward the more mature as the patient grew older.

In our cases, as contrasted with another series, intraspinal extension was more common in the nerve sheath neoplasms than in those of sympathetic origin. Furthermore, more of the sympathetic neurogenous tumors gave rise to symptoms. It is difficult to explain this on the basis of size alone, since all of the neurogenous neoplasms were in approximately the same size-range. However, if one discounts the neuroblastomas (sympathicoblastomas), then the frequency of symptoms in both classes of tumors is similar. In this tumor, the frequent involvement of adjacent soft tissues and organs might well account for the greater frequency of complaints referable to the tumor. The prognosis of the partially differentiated ganglioneuroma, whether partially or completely removed, was relatively good. This fact is attested to by the fact that only one of the patients is known to have died of this tumor. Furthermore, this one case tends to point-up the fact that although there is not a great prognostic difference between the mature and partially differentiated varieties of ganglioneuromas, the latter is to be considered less favorable. One of the most striking facets in the group of sympathetic neurogenous tumors, in the present series, is the relatively slow growth, lateness of metastasis, and relatively good prognosis of the sympathicoblastomas. This may well be related to the present mode of therapy, which combines surgery with subsequent radiotherapy.

**SUMMARY**

Fifty cases of neurogenous tumors of the mediastinum have been reviewed. All but three of the tumors were located in the posterior mediastinum. The most common neoplasm was the neurilemmoma and the most infrequent the malignant schwannoma. There was no example of malignant degeneration of neurofibromas. In neither of our two cases of malignant schwannoma did the patients have von Recklinghausen’s disease. In the tumors of nerve sheath origin, the neuroblastomas have the worst prognosis and the immature ganglioneuroma had only a slightly worse prognosis than the mature variety. The treatment
of this entire group, with the additional use of radiation in the case of neuroblastoma, is surgical extirpation.

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Resumen

Se han revisado 50 casos de tumores neurogénicos del mediastino. Con excepción de tres, todos los demás estaban en el mediastino posterior. El más común fue el neurilemoma y el menos frecuente fue el schwannoma maligno. No hubo caso de degeneración maligna de los neurofibromas. En ninguno de los dos casos de schwannoma maligno tuvieron los enfermos la enfermedad de Recklinghausen. En los tumores originados en la vaina, los neuroblastomas son los de peor pronóstico y los ganglioneuromas inmaduros tienen un pronóstico ligeramente más malo que los maduros. El tratamiento es la extirpación quirúrgica agregando la radiación en el caso del neuroblastoma.

Résumé

Cinquante cas de tumeurs neurogènes du médiastin ont été passés en revue. Toutes les tumeurs sauf trois étaient localisées au médiastin postérieur. Le néoplasme le plus commun fut le neurilémome et le moins fréquent le schwannome malin. Il n'y eut aucun cas de dégénérescence maligne de neurofibromes. Dans aucun des deux cas de schwannome malin les malades ne furent atteints de maladie de Recklinghausen. Dans les tumeurs dont l'origine est la gaine du nerf, les neuroblastomes ont le plus mauvais pronostic, et le ganglioneurome immature a seulement un pronostic légèrement moins mauvais que la variété mature. Le traitement de ce groupes entier est l'extirpation chirurgicale associée à l'emploi de radiothérapie dans le cas de neuroblastome.

Zusammenfassung

50 Fälle von neurogenen Mediastinal tumoren wurden beschrieben. Alle mit Ausnahme von 3 Tumoren waren im posterioren Mediastinum lokalisiert. Das häufigste Neoplasma war das Neurilemom und das seltenste, das bösartige Schwannom. Es fanden sich keine Beispiele einer malignen Degeneration der Neurofibrome. In keinem unserer beiden Fälle bösartiger Schwannome hatten die Patienten eine Recklinghaus-