# Primary Smooth Muscle Tumors of the Thyroid Gland

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**BACKGROUND.** Primary smooth muscle tumors of the thyroid gland are rare. To date, there are few cases reported of primary thyroid leiomyomas and leiomyosarcomas.

**METHODS.** One leiomyoma and four leiomyosarcomas arising within the thyroid gland were identified in the files of the Endocrine Tumor Registry of the Armed Forces Institute of Pathology. Histologic and immunohistochemical features were reviewed and follow-up obtained.

**RESULTS.** The patients included 2 females, ages 56 and 64 years, and 3 males, ages 45, 68, and 83 years. The patients presented with a mass in the thyroid gland that had increased in size over a number of months. All the tumors originated within a single lobe of the thyroid gland and measured from 1.1 to 9 cm in greatest dimension. Histologically, there was a fascicular pattern of growth comprised of spindle-shaped cells with blunt-ended nuclei. The leiomyoma was encapsulated, cytologically bland, and amitotic; the leiomyosarcomas were invasive with increased cellularity, pleomorphism, a high mitotic rate, necrosis, and hemorrhage. Immunohistochemical staining showed reactivity with vimentin, smooth muscle actin, muscle specific actin, and desmin. The patient with the leiomyoma was alive without evidence of disease 11 years after the initial presentation, with surgical resection as the only treatment. Three of the patients with leiomyosarcomas were dead within 2 years of diagnosis, in spite of aggressive therapeutic intervention. The remaining patient was still alive 10 months after initial presentation with multiple lung metastases.

**CONCLUSIONS.** Smooth muscle tumors of the thyroid gland are distinctive tumors. Leiomyosarcomas can be distinguished from anaplastic carcinoma, although patient outcome is uniformly unfavorable. ***Cancer* 1997; 79:579–87.**
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**KEYWORDS: thyroid, leiomyoma, leiomyosarcoma, spindle cell tumors, sarcomas, immunohistochemistry.**

The existence of primary thyroid sarcomas represents a contentious issue. Some authors believe that thyroid sarcomas are, in fact, anaplastic carcinomas with sarcomatous (spindle cell) features.[1–17] From the standpoint of treatment and prognosis, the histogenesis of thyroid ''sarcomas'' is academic, because these tumors, irrespective of the therapeutic intervention, are lethal.[1,2,8,9,12–14,17,18]

Primary thyroid smooth muscle tumors (leiomyomas and leiomyosarcomas) are rare. Isolated cases have been reported in the literature.[7,19–24] The authors report five additional cases of primary thyroid smooth muscle tumors, and discuss the clinical and pathologic features of these tumors, including their immunohistochemical findings, and contrast these findings with those reported in the literature. The current study findings document the existence of true smooth muscle tumors originating in the thyroid gland, and confirm that leiomyosarcomas arise de novo in the thyroid gland rather than representing a sarcomatous or spindle cell component of an anaplastic carcinoma.

## MATERIALS AND METHODS

One leiomyoma and four leiomyosarcomas of the thyroid gland were identified in the files of the Endocrine Tumor Registry at the Armed Forces Institute of Pathology. These 5 cases were identified in a review of 28,630 (0.017%) thyroid tumors seen in consultation between 1946 and 1996. Hematoxylin and eosin stained slides, available in all cases, were reviewed. The cases met the histologic criteria of smooth muscle tumors.[25]

Paraffin blocks and/or unstained slides were available in all cases. Four-micron sections were used for immunophenotypic analysis according to the avidin-biotin method of Hsu et al.[26] A basic commercially available antibody panel for each case included vimentin (mouse monoclonal, clone V9, 1:100 dilution [BioGenix Laboratories, San Ramon, CA]), smooth muscle actin (mouse monoclonal, clone 1A4, 1:8,000 dilution [Sigma Immuno Chemicals, St. Louis, MO]), muscle specific actin (mouse monoclonal, clone HHF35, 1:50 dilution [Enzo Diagnostics, Inc., Syosset, NY]), desmin (mouse monoclonal, clone DE-R-11, 1:200 dilution [Dako, Carpinteria, CA]), thyroglobulin (rabbit monoclonal, clone DAK-Tg6, 1:100 dilution [Dako]), a cytokeratin cocktail (AE1/AE3 and CK1), (AE1/AE3, mouse monoclonal, 1:50 dilution [Boehringer Mannheim, Indianapolis, IN] and CK-1, mouse monoclonal, 1:200 dilution [Dako]), S-100 protein (rabbit polyclonal, 1:800 dilution [Dakopatts, Glostrup, Denmark]), and chromogranin (mouse monoclonal, clone LK2H10, 1:1,600 dilution [Boehringer Mannheim Biochemicals]). Cytokeratin required predigestion for 3 minutes with 0.05% protease VIII (Sigma Chemical Co) in a 0.1 M phosphate buffer at a pH of 7.8 at 37 °C. Appropriate positive and negative controls were used throughout. In four cases there was insufficient or improperly fixed material with which to perform electron microscopy. In one case in which electron microscopy was performed, the cells were fragmented without subcellular detail, yielding no diagnostic information.

## RESULTS

### Clinical

The five patients with smooth muscle tumors had the following clinical findings (Table 1).

#### Case 1

A 56-year-old white woman presented with a nodule in the left lobe of the thyroid gland that had increased in size over the past few months. Radioactive iodine uptake scan showed a ''cold'' nodule. There were no other clinical abnormalities. The tumor was surgically shelled out with a rim of uninvolved thyroid parenchyma. At last follow-up, the patient remained without evidence of recurrence 11 years from the time of presentation.

#### Case 2

A 64-year-old white woman presented with a mass in the right lobe of the thyroid gland that had increased in size. There was no history of radiation exposure, nor was there another primary tumor. At surgery, the tumor extended into the surrounding soft tissue. Most of the tumor was resected, but residual tumor remained. Two months later, lung metastases were found, and 5 months later the patient died with evidence of widespread disease, including liver metastases and peritoneal and pleural implants (seen on computer axial tomography). Permission for an autopsy was not obtained.

#### Case 3

A 45-year-old white man presented with a mass in the left lobe of the thyroid, which extended down into the anterior mediastinum. The tumor had increased in size over the past 3 to 4 weeks. The patient also reported a 13.5-kg weight loss over a 3-month period. The tumor displaced the trachea to the right, causing a narrowing of the lumen by 50% (Fig. 1). The patient smoked 2 pack of cigarettes per day and drank 1 quart of alcohol per day. There was no history of radiation exposure nor of another primary tumor. A hemithyroidectomy was performed, followed by chemotherapy with doxorubicin. Within a few weeks, there was evidence of multiple lung metastases, which were confirmed histologically. The patient was still alive 11 months after the initial presentation.

#### Case 4

A 68-year-old white man presented with a few days' history of a mass in the anterior neck and thyroid gland. The patient reported hoarseness for a number of days. There was a single cold nodule in the left lobe of the thyroid gland as seen on thyroid scan. There was no history of radiation nor of another primary tumor. The tumor was described as rock hard and difficult to excise. Within a few months of diagnosis, lung metastases developed. The patient died 18 months after his initial presentation with widely disseminated disease (present on radiographic studies). Permission for an autopsy was not obtained.

#### Case 5

An 83-year-old white male presented with an enlarging thyroid mass with extension down into the substernal region. The patient reported dysphagia coincident with the development of the enlarging mass. The pa-

**TABLE 1**
**Clinical Features**

| | Age (yrs) | Gender | Size (cm) | Clinical presentation | Outcome |
|---|---|---|---|---|---|
| Leiomyoma | | | | | |
| Case 1 | 56 | F | 1.8 | Cold nodule | NED, 11 yrs |
| Leiomyosarcoma | | | | | |
| Case 2 | 64 | F | 7.5 | Multiple nodules | DWD, 5 mos |
| Case 3 | 45 | M | 9 | Enlarging mass and weight loss | Alive, 11 mos, DD (lungs) |
| Case 4 | 68 | M | 1.9 | Mass in thyroid | DWD, 18 mos |
| Case 5 | 83 | M | 5.5 | Substernal mass | DWD, 3 mos |

F: female; M: male; NED: no evidence of disease; DWD: dead with disease; DD: disseminated disease.

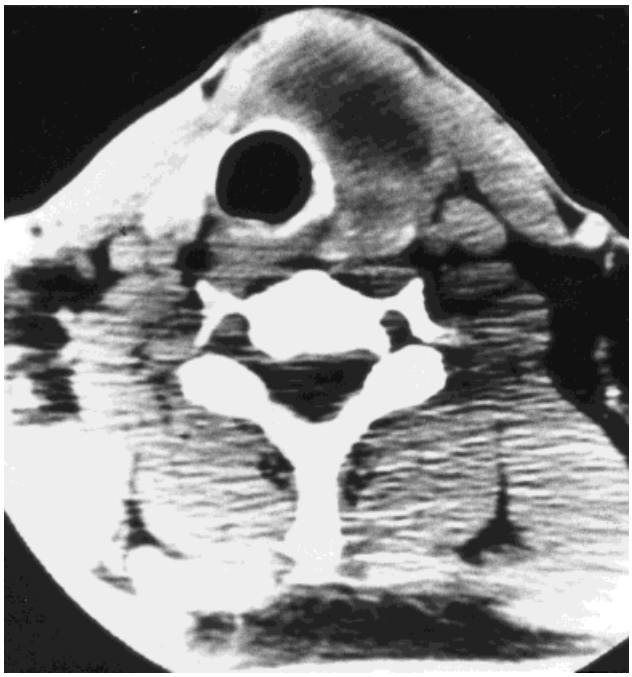

**FIGURE 1.** Case 3. Computed tomography image of thyroid mass, with tracheal compression and deviation.

tient denied radiation exposure, and there was no history of another tumor. Within a few weeks after excision, the patient developed multiple lung metastases, and died secondary to metastatic disease within 3 months of the initial presentation. Permission for an autopsy was not obtained.

### Pathologic Features

The leiomyoma (Case 1) was comprised of a well circumscribed and encapsulated tumor measuring a maximum of 1.8 cm in greatest dimension (Fig. 2A). The tumor was confined to the thyroid gland. The tumor cells were arranged in packets, bundles, or fascicles of smooth muscle fibers, intersecting in an orderly fashion. The cells were spindled, with blunt-ended, cigar-shaped, slightly hyperchromatic nuclei occupying a central location within the cytoplasm (Fig. 2B). The cells showed occasional cytoplasmic vacuoles. There was no evidence of capsular invasion, hemorrhage, necrosis, or mitotic activity. There was focal lymphocytic thyroiditis in the surrounding thyroid parenchyma.

The leiomyosarcomas were generally larger tumors, measuring from 1.9–9 cm in greatest dimension, and all shared similar histologic features. The tumors were unencapsulated, invading into and effacing the thyroid parenchyma. A few normal thyroid follicles were located at the periphery of the tumor, and were believed to represent trapped thyroid epithelium (Fig. 3A). The tumor cells infiltrated throughout the thyroid parenchyma, extending beyond the tumor capsule and thyroid capsule. Vascular invasion was present in all cases (Fig. 3B). In one case (Case 5) the tumor cells appeared to 'scroll off' a medium-sized blood vessel (Fig. 3C). The tumors were cellular, with a disordered fascicular growth pattern. The tumor cells were elongated or spindle-shaped with hyperchromatic, blunt-ended nuclei and abundant eosinophilic cytoplasm. The nuclei were generally centrally located within the cell, although there was variable placement. Perinuclear vacuoles were present. In many foci, the nuclei were markedly atypical and pleomorphic in appearance. There were on average 6 mitotic figures per 10 high-power fields (Fig. 3D). Areas of necrosis and hemorrhage were observed throughout the tumors. The remaining thyroid parenchyma was unremarkable, with the exception of focal lymphocytic thyroiditis.

### Immunohistochemistry

The leiomyoma showed immunoreactivity for smooth muscle actin and desmin. All of the leiomyosarcomas showed immunoreactivity with muscle specific actin, smooth muscle actin (Fig. 4A) and vimentin (Fig. 4B), with three of the four cases showing focal desmin reac-

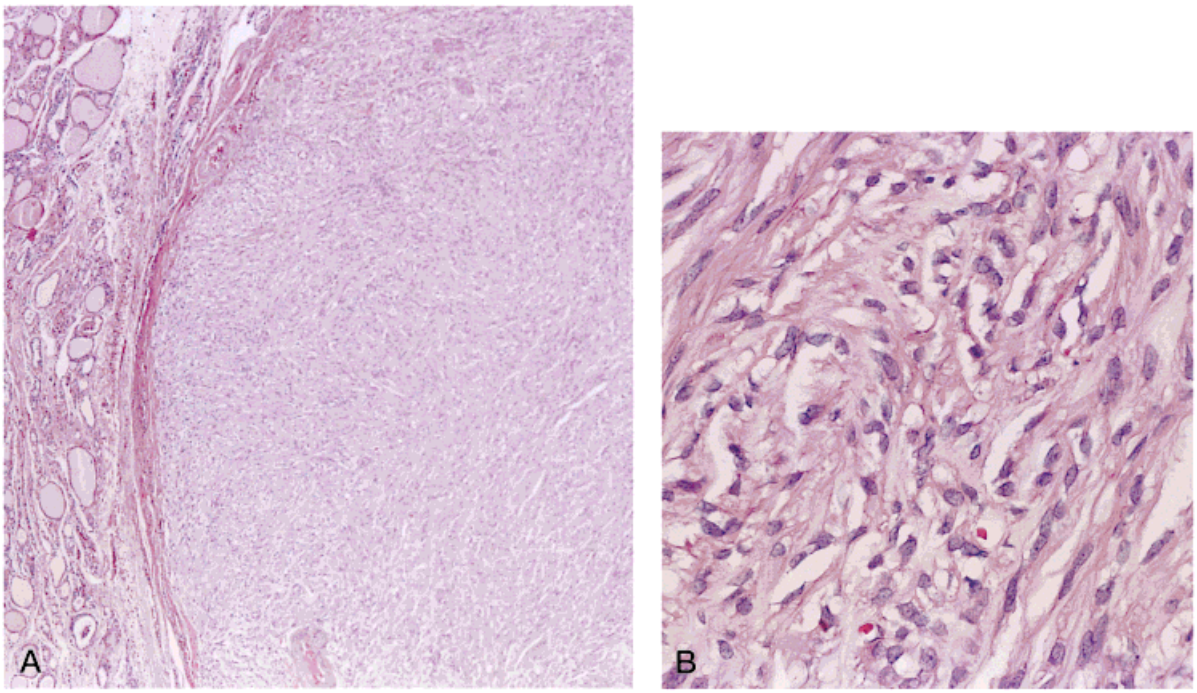


**FIGURE 2.** (A) Case 1. Well circumscribed and encapsulated thyroid leiomyoma. (B) Case 1. Thyroid leiomyoma showing spindled cells with blunt-ended, hyperchromatic nuclei that are centrally located.

tivity (Fig. 4C). Thyroglobulin, cytokeratin, chromogranin, and S-100 protein stains were negative for all cases (Fig. 4D) (Table 2).

## DISCUSSION

Primary sarcomas of the thyroid gland are infrequent[1,11,27–36] and primary smooth muscle tumors are rare.[7,19–24] The clinical data for the thyroid smooth muscle tumors that have been reported are summarized in Table 3. Similar to Case 1 in the current study, the two thyroid leiomyomas reported in the literature [19,21] occurred exclusively in women, presented as an isolated mass, were encapsulated and confined to the thyroid, and were cured with a lobectomy or partial thyroidectomy. The histology, immunohistochemistry, and electron microscopy of the reported leiomyomas confirmed that they were of smooth muscle origin.[19,21]

In contrast to their benign counterparts, the primary thyroid leiomyosarcomas (those reported in the literature and the cases in the current study) tended to occur in older patients, with roughly equal gender predilection (four women and three men). The leiomyosarcomas tended to be larger than their benign counterparts with malignant histologic features characterized by pleomorphism, prominent mitotic activity, necrosis, hemorrhage, and invasive and/or extrathyroidal growth. Thyroid leiomyosarcomas are invariably fatal, although follow-up was limited in the published reports (Table 3).[7,20,22–24] Immunohistochemical and ultrastructural evaluation were confirmatory of their smooth muscle derivation.[7,20,22–25,37–42] All the thyroid leiomyosarcomas occurred in patients who were without a primary smooth muscle tumor elsewhere. The exception was 1 case[20] in which the patient had undergone a hysterectomy for a uterine leiomyoma 29 years prior to the thyroid tumor. The possibility that the uterine tumor was misdiagnosed and actually represented a leiomyosarcoma must be considered. Even if the uterine tumor actually represented a low grade leiomyosarcoma rather than a leiomyoma (it is unlikely that a higher grade tumor would be confused with its benign counterpart), the probability that a low grade leiomyosarcoma would metastasize nearly 30 years after its removal appears remote and improbable. Furthermore, comprehensive studies have shown that of all the tumors that metastasize to the thyroid gland,[35,43–51] very few are sarcomas.[35,46,52–55]

Most reports in the literature of anaplastic thyroid carcinomas have demonstrated, through the use of immunohistochemical studies and electron microscopy, that the sarcoma-like tumors of the thyroid gland are in fact of epithelial histogenesis, i.e., anaplastic carcinomas.[2–6,31,22,8–11,14,16,17,22,31,56–58] These reports have shown that anaplastic carcinomas demonstrate dual expression

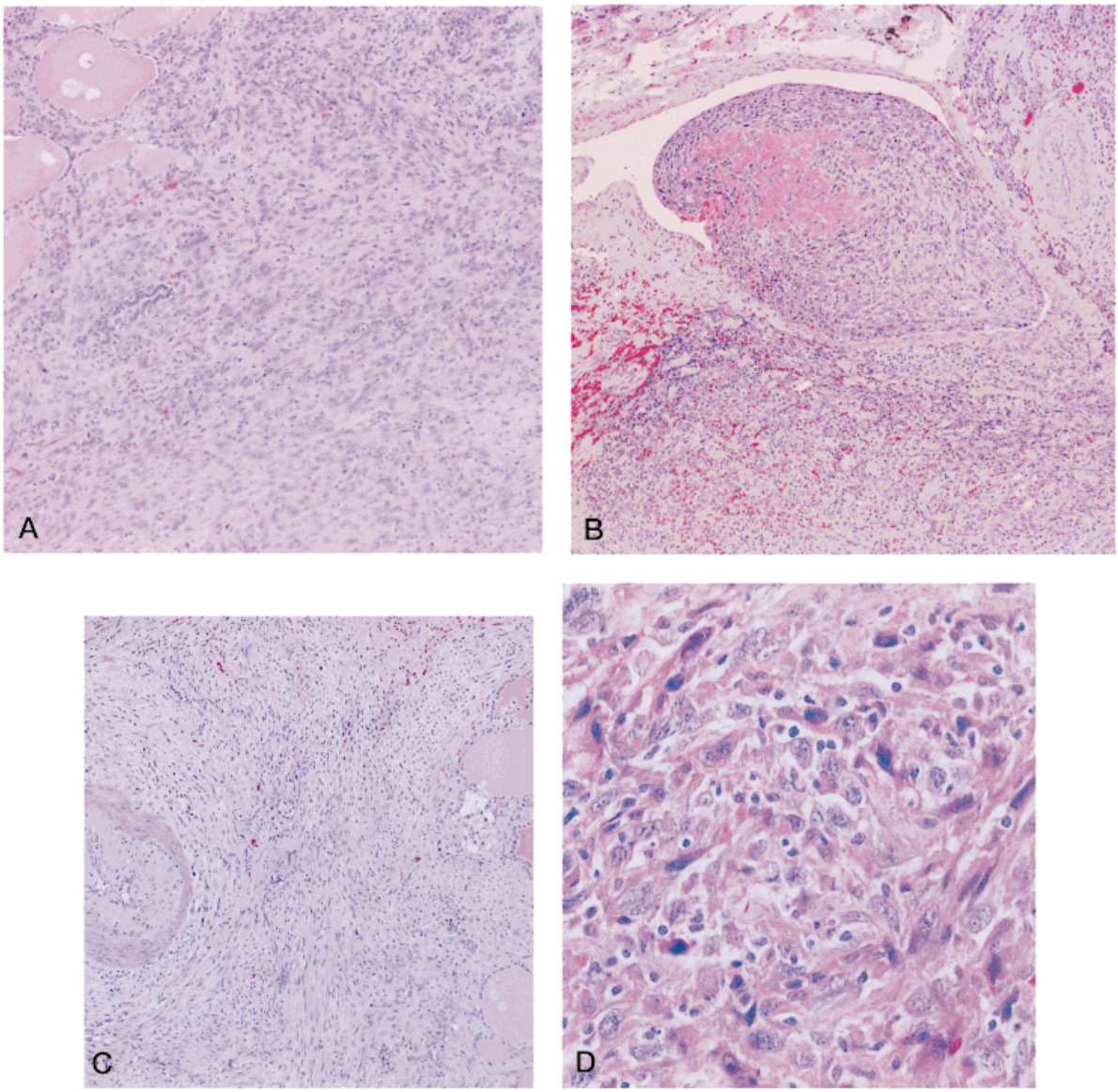


**FIGURE 3.** (A) Case 4. Normal thyroid follicles trapped at the periphery of this thyroid leiomyosarcoma. (B) Case 5. Thyroid leiomyosarcoma with infiltration beyond the thyroid capsule and with vascular invasion. (C) Case 5. Thyroid leiomyosarcoma demonstrating tumor cells coming off a medium-sized blood vessel. (D) Case 3. Mitotic figures seen in a pleomorphic spindle cell thyroid leiomyosarcoma.

of cytokeratin and vimentin,[3,4,8,9,11,14,16,17,56] occasional expression of thyroglobulin, but no reactivity with desmin, muscle specific actin, smooth muscle actin, chromogranin, or calcitonin.[2–4,8,9,11,14,17,58,59]

The World Health Organization classification of thyroid tumors indicates that it is very difficult or impossible to distinguish some thyroid sarcomas from undifferentiated carcinomas. A primary thyroid sarcoma should only be diagnosed when there is a complete lack of all epithelial differentiation and there is definite evidence of specific sarcomatous differentiation.[33] The authors believe that the preponderance of evidence in their cases supports a diagnosis of primary smooth muscle tumors of the thyroid gland. The existence of a thyroid leiomyoma is indisputable. Therefore, if a thyroid leiomyoma exists it is reasonable to presume that its malignant counterpart may also arise in this organ. The existence of thyroid leiomyosarcomas is reinforced by their clinical presentation and pathologic features. The leiomyosarcomas occurred as isolated masses that developed over a short interval, were not associated with a preexisting thyroid lesion

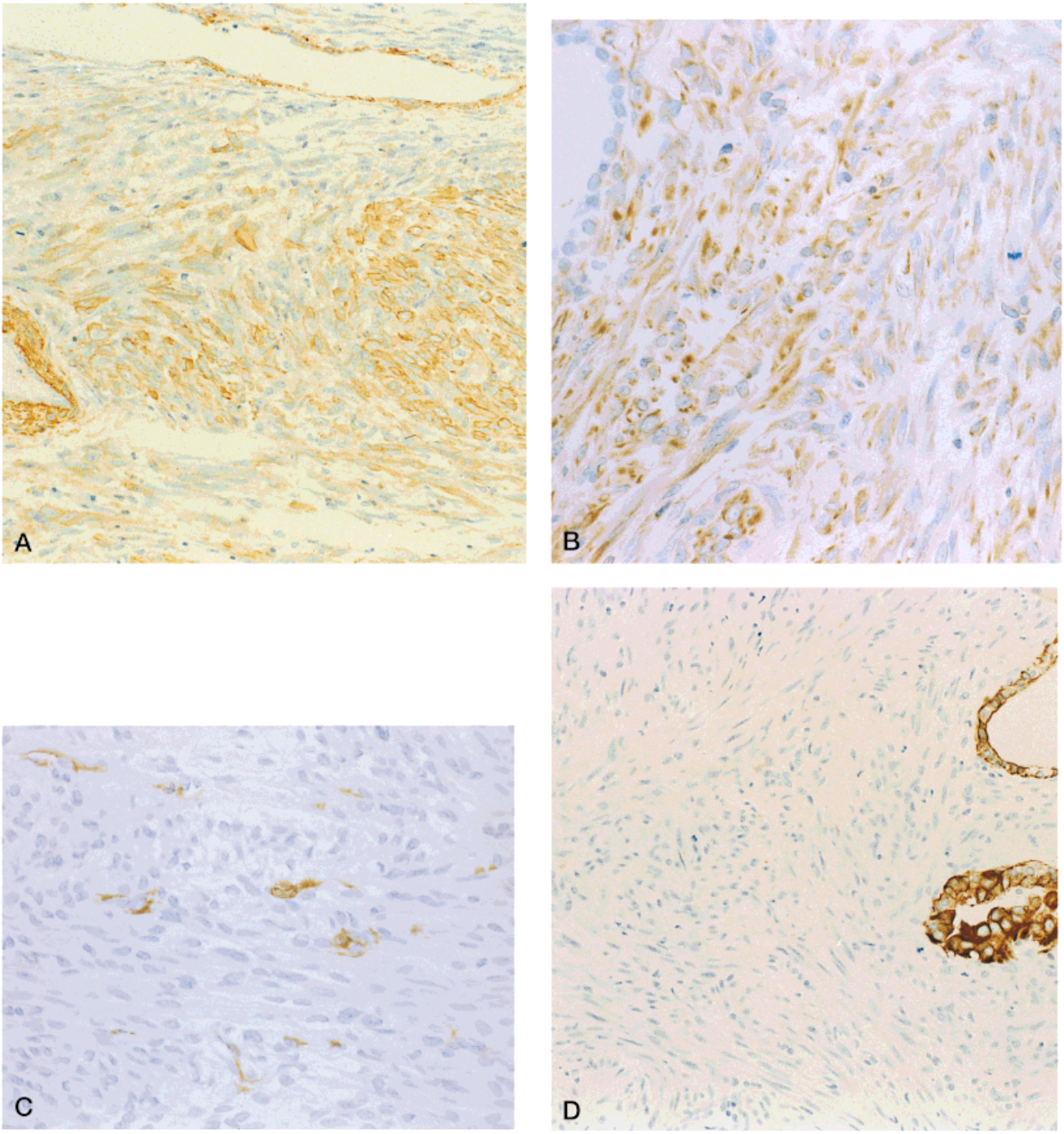


**FIGURE 4.** Immunohistochemical reactions demonstrated the following positive reactions in the leiomyosarcoma cells. (A) Case 3. Smooth muscle actin. (B) Case 4. Vimentin. (C) Case 2. Focal desmin. (D) Case 2. Keratin reaction in the epithelial cells of the thyroid but not in the leiomyosarcoma cells.

(goiter or neoplasm), and occurred in glands that had not been previously irradiated (external or radioiodine). Furthermore, none of the current study cases were patients with any history of a primary (smooth muscle) tumor elsewhere. These clinical features sharply contrast with those associated with either anaplastic carcinoma or metastatic leiomyosarcoma to the thyroid gland.

Pathologically, the leiomyosarcomas were confined to a single lobe with an infiltrative growth be-

**TABLE 2**
**Immunohistochemical Results**

| | SMA | MSA | Vimentin | S-100 | Desmin | Thyroglobulin |
|---|---|---|---|---|---|---|
| Leiomyoma | | | | | | |
| Case 1 | + | NA | NA | − | + | − |
| Leiomyosarcoma | | | | | | |
| Case 2 | + | + | + | − | − | − |
| Case 3 | + | + | + | − | + | − |
| Case 4 | + | + | + | − | + | − |
| Case 5 | + | + | + | − | + | − |

SMA: smooth muscle actin; MSA: muscle specific actin; S-100: S-100 protein; +: positive, −: negative; NA: not applicable.

**TABLE 3**
**Review of the Literature**

| | Age (yrs) | Gender | Size (cm) | Clinical presentation | Outcome |
|---|---|---|---|---|---|
| Leiomyoma | | | | | |
| Andrion et al.[21] | 45 | F | 1.5 cm | Firm, painless, palpable nodule | NED (6 yr FU) |
| Hendrick[19] | 3 | F | 3.5 cm | Mass, increasing in size | NED (4 yr FU) |
| Leiomyosarcoma | | | | | |
| Adachi et al.[20] | 74 | F | 12 cm | Mass, increasing in size | DWD, 1 mo |
| Chetty et al.[23] | 54 | F | 3.5 cm | Mass, cold on scan | Alive, LTF, 15 mos |
| Iida et al.[24] | 72 | F | 3 cm | 7 mos HO increasing size | DWD, 51 mos |
| Kaur and Jayaram[7] | NS | NS | NS | NS | DD, LTF, 1 yr |
| Kawahara et al.[22] | 82 | M | 5.5 cm | 1 mo HO mass and hoarseness | DWD, 4 mos |

F: female; M: male; NED: no evidence of disease; DD: disseminated disease; DWD: dead with disease; LTF: lost to follow-up; NS: not stated; FU: follow-up; HO: history of.

yond the capsule, showed morphologic characteristics of a malignant smooth muscle tumor,[25] and had an immunophenotype consistent with myogenic origin including vimentin, smooth muscle actin, muscle specific actin, and desmin. More important, these tumors were uniformly negative with thyroglobulin, keratin, chromogranin, and calcitonin, virtually negating the possibility of epithelial or neuroendocrine derivation from follicular epithelial cells or C cells, respectively.

The authors believe the histogenesis of thyroid smooth muscle tumors is, in all probability, from the thyroid vessels, i.e., smooth muscle in the vascular walls. In one of the current study cases (Case 5), a medium-sized vascular space appeared to be the point of origin of the tumor, with the neoplastic cells directly growing off the outer wall of the vessel. A similar histogenesis for smooth muscle tumors occurring in other unusual sites has also been proposed.[20,22,25,60] Furthermore, the classification of leiomyosarcomas includes three geographic groups: cutaneous and subcutaneous, deep soft tissue, and vascular origin.[25]

The authors believe that the constellation of clinical and pathologic findings in these cases supports the existence of primary thyroid leiomyosarcomas. Certainly, the possibility that the tumors have been inadequately sampled, potentially overlooking a small portion of epithelial differentiation or transitional zones between a differentiated thyroid tumor and the sarcomatoid foci (spindle cell), needs to be considered.[13,23,34] However, the cases in the current study have been extensively sampled.

Primary thyroid leiomyosarcomas share a similar biology with thyroid anaplastic carcinomas. These are high grade and aggressive tumors; three of four patients were dead within a short time after diagnosis.

## REFERENCES

1. Aldinger KA, Samaan NA, Ibañez M, Hill CS Jr. Anaplastic carcinoma of the thyroid. A review of 84 cases of spindle and giant cell carcinoma of the thyroid. *Cancer* 1978;41:2267–75.
2. Carcangiu ML, Steeper T, Zampi G, Rosai J. Anaplastic thyroid carcinoma:a study of 70 cases. *Am J Clin Pathol* 1985;83:135–58.
3. Dockhorn-Dworniczak B, Franke WW, Schröder S, Czernobilsky B, Gould VE, Böcker W. Patterns of expression of cytoskeletal proteins in human thyroid gland and thyroid carcinomas. *Differentiation* 1987;35:53–71.

4. Eckert F, Schmid U, Gloor F, Hedinger C. Evidence of vascular differentiation in anaplastic tumours of the thyroid:an immunohistological study. *Virchows Arch A Pathol Anat Histopathol* 1986;410:203–15.
5. Hedinger C. Sarcomas of the thyroid gland. In:Hedinger E. editor. Thyroid cancer. Berlin:Springer-Verlag, 1969:47–52.
6. Johannessen JV, Gould VE, Jao W. The fine structure of human thyroid cancer. *Hum Pathol* 1978;9:385–400.
7. Kaur A, Jayaram G. Thyroid tumors:cytomorphology of medullary, clinically anaplastic, and miscellaneous thyroid neoplasms. *Diagn Cytopathol* 1990;6:383–9.
8. LiVolsi VA. Surgical pathology of the thyroid. In:Major problems in pathology. Volume 2. Philadelphia: W.B. Saunders, 1991:253–70.
9. LiVolsi VA, Brooks JJ, Arendash-Durand B. Anaplastic thyroid tumors:immunohistology. *Am J Clin Pathol* 1987; 87:434–42.
10. Mills SE, Stallings RG, Austin MB. Angiomatoid carcinoma of the thyroid gland:anaplastic carcinoma with follicular and medullary features mimicking angiosarcoma. *Am J Clin Pathol* 1986;86:674–8.
11. Miettinen M, Franssila K, Lehto V-P, Paasivuo R, Virtanen I. Expression of intermediate filament proteins in thyroid gland and thyroid tumors. *Lab Invest* 1984;50:262–70.
12. Nel CJC, van Heerden JA, Goellner JR, Gharib H, McConahey WM, Taylor WF, et al. Anaplastic carcinoma of the thyroid:a clinicopathologic study of 82 cases. *Mayo Clin Proc* 1985;60:51–8.
13. Nishiyama RH, Dunn EL, Thompson NW. Anaplastic spindle-cell and giant-cell tumors of the thyroid gland. *Cancer* 1972;30:113–27.
14. Ordóñez NG, El-Naggar AK, Hickey RC, Samaan NA. Anaplastic thyroid carcinoma:immunohistochemical study of 32 cases. *Am J Clin Pathol* 1991;96:15–24.
15. Schneider V, Frable WJ. Spindle and giant cell carcinoma of the thyroid:cytologic diagnosis by fine needle aspiration. *Acta Cytol* 1980;24:184–9.
16. Schröder S, Dockhorn-Dworniczak B, Kastendieck H, Böcker W, Franke WW. Intermediate-filament expression in thyroid gland carcinomas. *Virchows Arch A Pathol Anat Histopathol* 1986;409:751–66.
17. Venkatesh YSS, Ordóñez NG, Schultz PN, Hickey RC, Goepfert H, Samaan NA. Anaplastic carcinoma of the thyroid:a clinicopathologic study of 121 cases. *Cancer* 1990;66:321–30.
18. Ibañez ML, Russell WO, Albores-Saavedra J, Lampertico P, White EC, Clark, RL. Thyroid carcinoma:biologic behavior and mortality. Postmortem findings in 42 cases, including 27 cases in which the disease was fatal. *Cancer* 1966; 19:1039–52.
19. Hendrick JW. Leiomyoma of thyroid gland. *Surgery* 1957;42:597–9.
20. Adachi M, Wellmann KF, Garcia R. Metastatic leiomyosarcoma in brain and heart. *J. Pathol* 1969;98:294–6.
21. Andrion A, Bellis D, Delsedime L, Bussolati G, Mazzucco G. Leiomyoma and neurilemoma:report of two unusual nonepithelial tumours of the thyroid gland. *Virchows Arch A Pathol Anat Histopathol* 1988;413:367–72.
22. Kawahara E, Nakanishi I, Terahata S, Ikegaki S. Leiomyosarcoma of the thyroid gland:a case report with a comparative study of five cases of anaplastic carcinoma. *Cancer* 1988; 62:2558–63.
23. Chetty R, Clark SP, Dowling JP. Case report:leiomyosarcoma of the thyroid:immunohistochemical and ultrastructural study. *Pathology* 1993;25:203–5.
24. Iida Y, Katoh R, Yoshioka M, Oyama T, Kawaoi A. Primary leiomyosarcoma of the thyroid gland. *Acta Pathol Jpn* 1993;43:71–5.
25. Enzinger FM, Weiss SW. Leiomyosarcoma. In: Soft tissue tumors. 3rd edition St. Louis: C.V. Mosby, Co., 1988:491–510.
26. Hsu SM, Raine L, Fanger H. Use of avidin-biotin peroxidase complex (ABC) in immunoperoxidase techniques. A comparison between ABC and unlabeled antibody (PAP) procedures. *J Histochem Cytochem* 1981;29:557–80.
27. Bosse MD. Hemangioendothelial sarcoma of thyroid. *Arch Pathol Lab Med* 1943;36:316.
28. Chan YF, Ma L, Boey JH, Yeung HY. Angiosarcoma of the thyroid. An immunohistochemical and ultrastructural study of a case in a Chinese patient. *Cancer* 1986;57:2381–8.
29. Chesky VE, Dreese WC, Hellwig CA. Hemangioendothelioma of the thyroid. Review of the literature and report of a case. *J Clin Endocrinol Metab* 1953;13:801–8.
30. Chesky VE, Hellwig CA, Welch JW. Fibrosarcoma of the thyroid gland. *Surg Gynecol Obstet* 1960;111:767–70.
31. Fisher ER, Gregorio R, Shoemaker R, Horvat B, Hubay C. The derivation of so-called giant-cell and spindle cell undifferentiated thyroidal neoplasms. *Am J Clin Pathol* 1974; 61:680–9.
32. Glass HG, Waldron GW, Brown WG. Coexistant sarcoma, adenocarcinoma and Hashimoto's disease in a thyroid gland. *Cancer* 1956;9:310–6.
33. Hedinger C, Williams ED, Sobin LH. Histologic typing of thyroid tumors. In:World Health Organization International histologic classification of tumors. 2nd edition. Berlin: Springer-Verlag, 1988:13–5.
34. Meissner WA, Warren S. Other benign tumors and other sarcomas. In:Atlas of tumor pathology. Series 2. Fascicle 4. Washington, DC: Armed Forces Institute of Pathology, 1969:53, 123–6.
35. Shimaoka K, Sokal JE, Pickren JW. Metastatic neoplasms in the thyroid gland. Pathological and clinical findings. *Cancer* 1962;15:557–65.
36. Shin W-Y, Aftalion B, Hotchkiss E, Schenkman R, Berkman J. Ultrastructure of a primary fibrosarcoma of the human thyroid gland. *Cancer* 1979;44:584–91.
37. Ghadially FN. Myofilaments in leiomyoma and leiomyosarcoma. In:Ultrastructural pathology of the cell and matrix. 3rd edition. Volume 2. London: Butterworths, 1988:862–71.
38. Osborn M, Weber K. Tumor diagnosis by intermediate filament typing:novel tool for surgical pathology. *Lab Invest* 1983;48:372–94.
39. Rangdaeng S, Truong LD. Comparative immunohistochemical staining for desmin and muscle-specific actin:a study of 576 cases. *Am J Clin Pathol* 1991;96:32–45.
40. Roholl PJM, Elbers HRJ, Prinsen I, Claessens JAJ, van Unnik JAM. Distribution of actin isoforms in sarcomas:an immunohistochemical study. *Hum Pathol* 1990;21:1269–74.
41. Schürch W, Skalli O, Seemayer TA, Gabbiani G. Intermediate filament proteins and actin isoforms as markers for soft tissue tumor differentiation and origin:I. Smooth muscle tumors. *Am J Pathol* 1987;128:91–103.
42. Truong LD, Rangdaeng S, Cagle P, Ro JY, Hawkins H, Font RL. The diagnostic utility of desmin. A study of 584 cases and review of the literature. *Am J Clin Pathol* 1990;93:305–14.

43. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma. Analysis of 1000 autopsied cases. *Cancer* 1950;3:74–85.
44. Czech JM, Lichtor TR, Carney JA, van Heerden JA. Neoplasms metastatic to the thyroid gland. *Surg Gynecol Obstet* 1982;155:503–5.
45. Elliott RHE Jr. Frantz VK. Metastatic carcinoma masquerading as primary thyroid cancer:a report of authors 14 cases. *Ann Surg* 1960;151:551–61.
46. Ivy HK. Cancer metastatic to the thyroid:a diagnostic problem. *Mayo Clin Proc* 1984;59:856–9.
47. McCabe DP, Farrar WB, Petkov TM, Finkelmeier W, O'Dwyer P, James A. Clinical and pathologic correlations in disease metastatic to the thyroid gland. *Am J Surg* 1985;150:519–23.
48. Mortensen JD, Woolner LB, Bennett WA. Secondary malignant tumors of the thyroid gland. *Cancer* 1956;9:306–9.
49. Silverberg SG, Vidone RA. Metastatic tumors in the thyroid. *Pacif Med Surg* 1966;74:175–80.
50. Watanabe I, Tsuchiya A. Secondary carcinoma of the thyroid gland. *Jpn J Surg* 1980;10:130–6.
51. Wychulis AR, Beahrs OH, Woolner LB. Metastasis of carcinoma to the thyroid gland. *Ann Surg* 1964;160:169–77.
52. Bode-Lesniewska B, Schröder S, Gemsenjäger E, Stäubli M, Pfaltz M. Leiomyosarcoma in the thyroid gland—primary or metastatic tumor? *Pathologe* 1994;15:303–7.
53. Cruickshank JC. Case report:leiomyosarcoma metastatic to the thyroid gland. *Ear Nose Throat J* 1988;67:899–910.
54. Gattuso P, Castelli MJ, Reyes CV. Fine needle aspiration cytology of metastatic sarcoma involving the thyroid. *South Med J* 1989;82:1158–60.
55. Shimota H, Satoh T, Ishi K, Iwase A. An autopsy case of primary lung leiomyosarcoma. *Jpn J Clin Pathol* 1991;39:666–70.
56. Beltrami CA, Criante P, Di Loreto C. Immunocytochemistry of anaplastic carcinoma of thyroid gland. *Appl Pathol* 1989;7:122–33.
57. Graham H, Daniel C. Ultrastructure of an anaplastic carcinoma of the thyroid. *Am J Clin Pathol* 1974;61:690–6.
58. Ryff-de Léche A, Staub J-J, Kohler-Faden R, Müller-Brand J, Heitz PU. Thyroglobulin production by malignant thyroid tumors. An immunocytochemical and radioimmunoassay study. *Cancer* 1986;57:1145–53.
59. Hales M, Rosenau W, Okerlund MD, Galante M. Carcinoma of the thyroid with a mixed medullary and follicular pattern. Morphologic, immunohistochemical, and clinical laboratory studies. *Cancer* 1982;50:1352–9.
60. Kuruvilla A, Wenig BM, Humphrey DM, Heffner DK. Leiomyosarcoma of the sinonasal tract. A clinicopathologic study of nine cases. *Arch Otolaryngol Head Neck Surg* 1990;116:1278–86.