A Rare Primary Tumor of the Thyroid Gland: A New Case of Leiomyoma and Literature Review

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Yanling Zhang[1,2], Heng Tang[2], Huaiyuan Hu[2] and Xiang Yong[2]

[1]Department of Oncology, Wanbei Coal-Electricity Group General Hospital, Suzhou, China.
[2]Department of Pathology, Wanbei Coal-Electricity Group General Hospital, Suzhou, China.

ABSTRACT: Primary leiomyomas of the thyroid are very rare. We here report a case of a 53-year-old woman with a painless mass at the right thyroid, revealed by physical examination. The patient underwent a lobectomy. Frozen sections showed a spindle cell tumor of the thyroid gland. The nuclei of some of the tumor cells were obviously enlarged and deeply stained. Pseudocapsule invasion was observed in small foci. Samples showed neither mitosis nor necrosis and the nature of the tumor was difficult to determine. Paraffin sections showed a well-circumscribed nodular composed of intersecting fascicles of spindled to slightly epithelioid cells with eosinophilic cytoplasm and blunt-ended, cigar-shaped nuclei. We observed no significant nuclear atypia, mitotsis, or necrosis. Immunohistochemical staining showed the tumor cells to be positive for α-smooth muscle actin and h-caldesmon but negative for TG, TTF1, PAX8, S-100, CT, CK, and CD34. The ki-67 index was very low (<1%). Primary thyroid leiomyoma is rare and difficult to diagnose using frozen sections. Diagnosis requires immunohistochemical staining. Leiomyoma may be mistaken for other thyroid tumors also characterized by spindle cells.

KEYWORDS: leiomyoma, smooth muscle tumors, thyroid neoplasma

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CORRESPONDING AUTHOR: Xiang Yong, Department of pathology, Wanbei Coal-Electricity Group General Hospital, Suzhou, Anhui Province, China.
Email: 15385741966@163.com.

Introduction

Primary mesenchymal tumors of thyroid include smooth muscle tumors, solitary fibrous tumors, vascular tumors, and nerve sheath tumors.[1] Primary smooth muscle tumors of the thyroid gland are rare, most of them being leiomyosarcomas rather than leiomyomas.[2] To date, only 6 cases of leiomyoma have been reported.[3–8] The present report describes a new case of primary leiomyoma of the thyroid gland in a 53-year-old Asian woman, and frozen sections showed a spindle cell tumor of the thyroid gland, but HE (hematoxylin-eosin) and immunohistochemical staining indicated that the tumor was leiomyoma.

Case Report

A 53-year-old Asian woman was admitted to the hospital because of a firm, painless, palpable nodule localized in her right thyroid. Physical examination revealed a nodule 24 mm in diameter with a smooth surface in the right lobe of the thyroid gland. Radioactive iodine uptake scan showed a "cold" nodule. No cervical lymph nodes were palpable. Thyroid function tests, including T3, T4, and TSH, showed no remarkable findings, but TG < 0.20, ATG-Ab, and TPO-Ab were significantly elevated, suggesting that chronic lymphocytic thyroiditis should be considered. Ultrasound evaluation revealed that the patient had a 24 mm × 18 mm low echo-level nodule in the right thyroid lobe (Figure 1). The patient underwent surgery and a total thyroidectomy was performed in the right lobe. The diagnosis made using frozen sections was spindle cell tumor of the thyroid, possibly benign. The patient showed no evidence of recurrence or metastatic disease 6 months after surgery.

Pathology

The hemithyroidectomized specimen measured 5.0 cm × 3.0 cm; the tumor nodule consisted of a well-circumscribed mass measuring 2.4 cm × 1.8 cm × 1.5 cm. On section, the cut surface was bulging and showed glistening gray tissue (Figure 2).

Frozen sections showed a well-circumscribed single nodule with an incomplete fibrous pseudocapsule. The nuclei of some of the tumor cells were obviously enlarged and deeply stained. Suspicious pseudocapsular invasions were observed in small foci, but mitosis and necrosis were absent (Figure 3). The diagnosis made using frozen sections was spindle cell tumors of the thyroid gland. Immunohistochemical staining was performed to rule out other malignant spindle cell tumors.

Microscopic examination of histologic sections showed a uniform tumor pattern consisting of intersecting fascicles of cells. The cells were spindled, with blunt-ended, cigar-shaped, slightly hyperchromatic nuclei occupying a central location within the pale eosinophilic cytoplasm. The cells showed occasional cytoplasmic vacuoles. The tumor cells showed mild pleomorphism, but there were no visible areas of hemorrhage or necrosis. No mitotic figures were identified (0/10HPF). The tumor displayed focal myxoid changes. At times, the surrounding thyroid tissue showed hyperplastic follicles with sparse foci of lymphocytic infiltration of the intervening stroma. A slightly diffuse lymphocytic infiltration was also observed in many fields of the tumor (Figure 4).

Immunohistochemistry (Dako, Carpinteria, CA, USA) showed tumor cells to be positive for vimentin, α-smooth muscle actin (SMA; Figure 4), and h-caldesmon and negative for

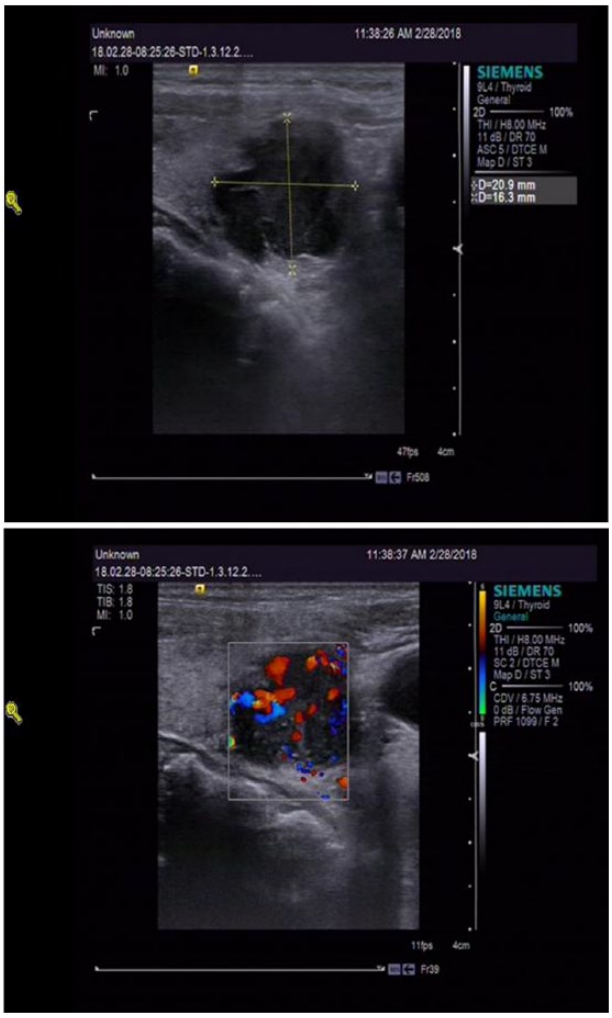

Figure 1. Ultrasound evaluation revealed that the patient had a 24-mm × 18-mm, well-circumscribed nodule in the right thyroid lobe.

TG, TTF1, PAX8, S-100 protein, CT, CD34, and AE1/AE3. The diagnosis of thyroid gland leiomyoma was made in this way.

Discussion

Primary thyroid leiomyomas are rare, with only 8 cases been reported to date[3–8] (Table 1). The median age is 45 years (range 3-61 years); 4 cases were women and other 2 cases were man. Leiomyoma usually presents as a painless, slowly growing nodule.[3,5–8] Most reports in the literature showed that the thyroid function test is often normal and thyroid scans can show a cold nodule.[4–8] Usually, the nodule measures <3.5 cm,[3–7] whereas larger neoplasms (9 cm) were observed in 1 case.[8] In the current case, the clinical features and ultrasound findings were also consistent with the literature report, but blood examination showed TG < 0.20 and that ATG-Ab and TPO-Ab were significantly higher, indicating that the patient had chronic lymphocytic thyroiditis. Paraffin sections also confirmed this finding, which was consistent with those reported by Thompson et al.[5]

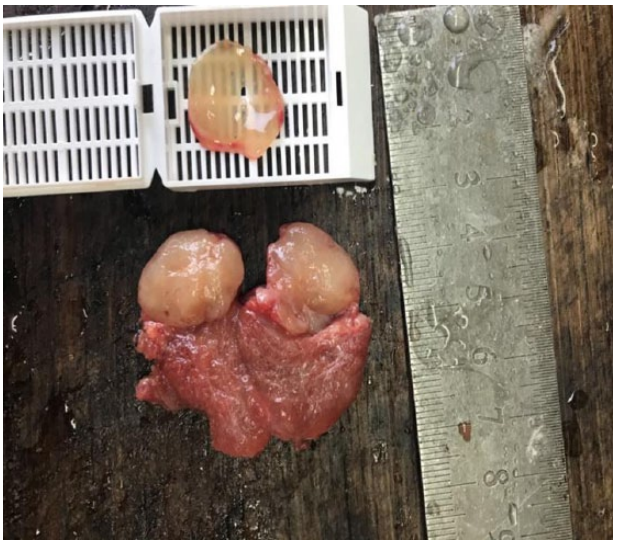

Figure 2. The tumor nodule consisted of an apparently encapsulated mass measuring 2.4 cm × 1.8 cm × 1.5 cm. The cut surface was bulging and showed glistening gray tissue.

In a review of published case reports, we observed that frozen section analysis was performed in 2 cases. In one of these cases, the diagnostic team also evaluated fine needle aspiration results and considered a diagnosis of medullary carcinoma,[4] and in the other case, they considered a diagnosis of benign spindle cell tumors.[6] This suggested that it is difficult to diagnose leiomyoma using frozen sections alone. Our case was consistent with literature showing that spindle tumor cells with enlarged and deeply stained nuclei and suspicious pseudocapsular invasion render frozen section diagnosis more difficult. We initially suspected anaplastic carcinoma or sarcoma of the thyroid gland, but we observed no mitosis, necrosis, or true invasion. These situations suggest that definitive diagnosis of intrathyroidal spindle cell neoplasm should be deferred until a thorough morphological and immunohistochemical examination of paraffin embedded tissue can be performed.

Leiomyomas are characterized by spindle cells with centrally located cylindrical, blunt-ended nuclei, which are arranged with short intersecting bundles. They are well circumscribed, cytologically bland, and amitotic. Immunohistochemical staining showed reactivity with SMA, h-caldesmon, and desmin.[3-8] Our histopathologic and immunohistochemical findings were also consistent with these statements.

Many epithelial and stromal tumors of the thyroid,[9] including papillary carcinoma with exuberant nodular fasciitis-like stroma,[10] spindle cell variants of medullary thyroid carcinoma (MTC),[11] anaplastic carcinoma,[12] follicular thyroid adenoma,[13] spindle epithelial tumor with thymus-like differentiation (SETTLE),[14] and carcinoma showing thymus-like differentiation (CASTLE),[15] leiomyosarcoma,[2] Schwann cell tumors,[16] and solitary fibrous tumors[17] may exhibit spindle cell morphology and need to differentiated from leiomyoma.

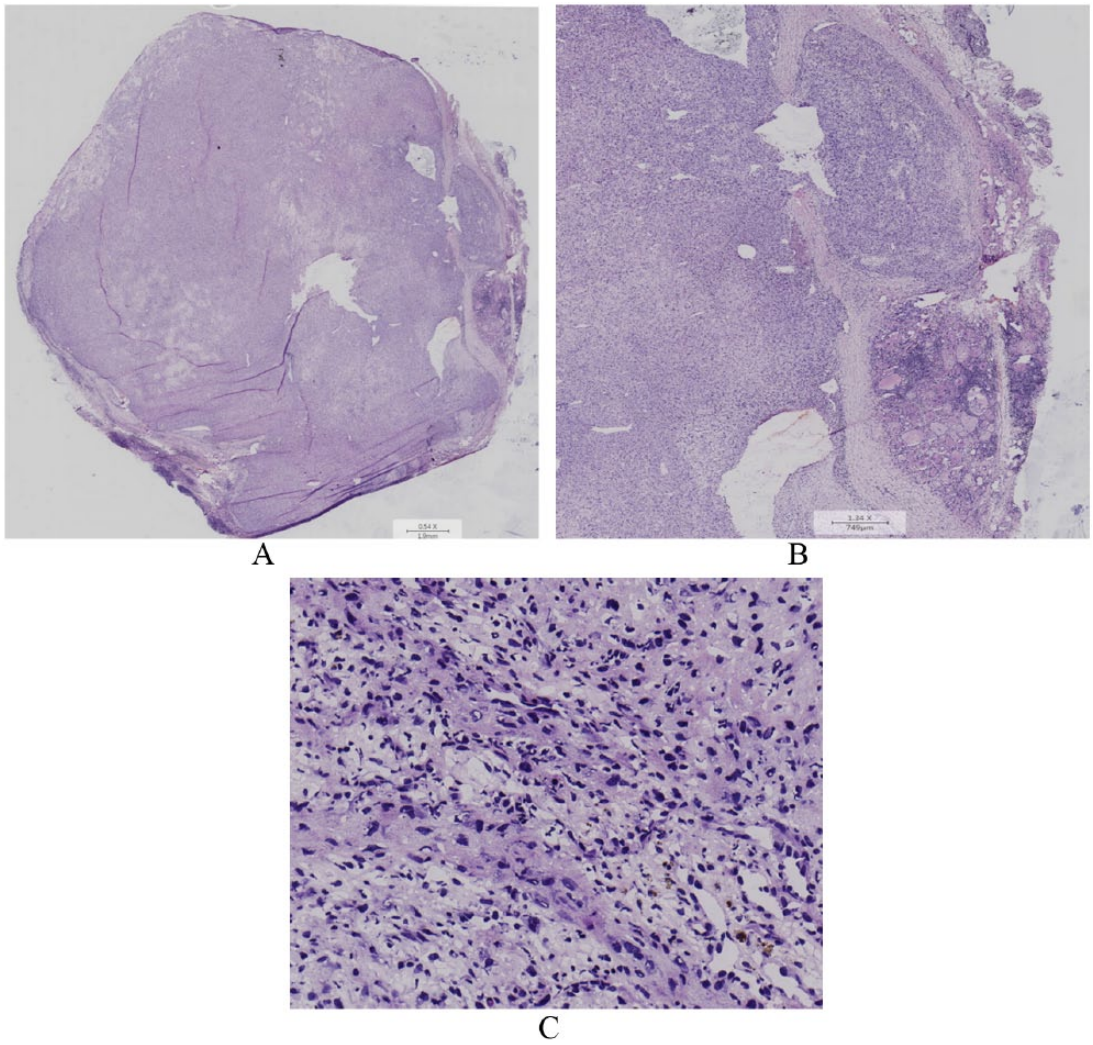

Figure 3. (A) Frozen sections showed a well-circumscribed single nodule with an incomplete fibrous pseudocapsule, (B) suspicious pseudocapsule invasion was observed in small foci, and (C) some of the tumor cells were visibly enlarged and deeply stained.

Papillary thyroid carcinoma (PTC) with exuberant nodular fasciitis-like stroma was first reported by Chan et al.[18] This rare variant of PTC is characterized by a prominent spindle cell proliferation with small foci of papillary carcinoma. The stromal components in these tumors resemble the appearance of nodular fasciitis or fibromatosis of the soft tissues, and this may occupy 60% to 70% of the tumor. Immunohistochemical and ultrastructural analyses have shown that the spindle cells exhibit some characteristics of myofibroblasts and could be positive for SMA. Thorough sampling to detect epithelial components could help differentiate leiomyoma from this rare variant of PTC.

Medullary thyroid carcinoma with predominant spindle cell morphology is rarer than other forms of MTC. Microscopic examination revealed spindle-shaped tumor cells in a diffuse pattern may resemble leiomyoma. But medullary carcinoma cells with granular amphophilic cytoplasm and a nucleus with fine chromatin. Immunohistochemical analysis showed tumor cells to be positive for CT, CEA, CD56, Syn, and CgA and negative for SMA; h-caldesmon could differentiate it from leiomyoma.

Anaplastic carcinoma[12] contains 3 main patterns: giant cell, squamoid, and spindle cell. Spindle cell anaplastic carcinomas resemble sarcomas, with a fascicular pattern of spindle cells, marked atypia, and mitotic activity. Even without an epithelial-biphasic or well-differentiated component, focal keratin positivity is common in anaplastic carcinomas. Histologically, leiomyoma lacks nuclear atypia, mitotics, and necrosis. No epithelial differentiation was observed in any part of the tumor, and immunostains for keratins were negative. Smooth muscle markers were uniformly positive, confirming the diagnosis.

The most important differential diagnosis was leiomyosarcoma.[2] Primary thyroid leiomyosarcomas were very rare and histologic examination showed marked atypia, mitotic activity, areas of coagulative necrosis, and invasion of surrounding tissue.

In our patient, the diagnosis of leiomyoma was favored because only a slight nuclear atypia was founded and lack of mitotic activity, coagulative necrosis, and invasion of surrounding tissue. Immunohistochemical analysis showed the ki-67 index $<1\%$, which ruled out leiomyosarcoma.

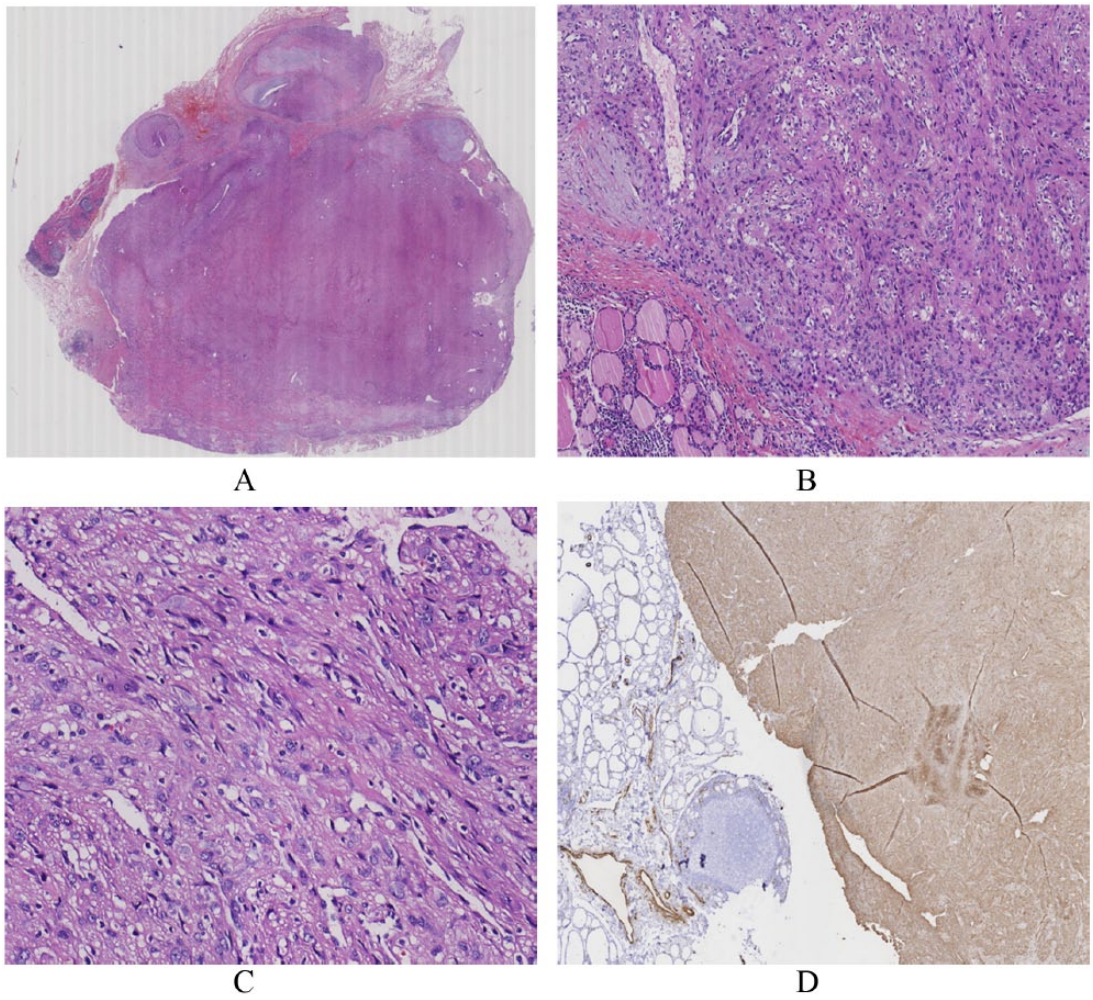

Figure 4. (A and B) Well-circumscribed and encapsulated thyroid leiomyoma in which the surrounding thyroid tissue showed hyperplastic follicles with sparse foci of lymphocytic infiltration of the intervening stroma. (C) A uniform tumor pattern consisting of intersecting fascicles of cells. (D) The tumor cells were positive for α-smooth muscle actin.

Table 1. Summary of all previously reported cases.

	AGE, Y	GENDER	SIZE, CM	CLINICAL PRESENTATION	OUTCOME
Hendrick[3]	3	F	3.5	Mass, increasing in size, cold nodule	NED, 4 y
Andrion et al[4]	45	F	1.5	Firm, painless, palpable nodule	NED, 5 y
Thompson et al[5]	56	F	1.8	Mass, increasing in size, cold nodule	NED,11 y
Biankin and Cachia[6]	61	F	3	Mass, increasing in size, cold nodule	NED, 6 mo
Erkilic et al[7]	40	M	3	Mass, increasing in size, cold nodule	NED, 5 y
Mohammed et al[8]	9	M	9	Mass, increasing in size, cold nodule	NED, 2 y

The absence of an epithelial component and negative findings for CK, TG, TTF1, and PAX8 ruled out other types of spindle cell tumors of the thyroid derived from epithelial components, such as follicular thyroid adenoma,[13] SETTLE,[14] and CASTLE.[15] The absence of S-100 and CD34 markers ruled out Schwann cell tumors[16] and solitary fibrous tumors.[17]

Leiomyoma of the thyroid is a benign tumor, so the treatment of choice is surgery. Further treatment is unnecessary. In our case, the patient was still disease free 6 months after surgery, and long-term disease-free survival has been reported for other patients.[3-8]

Conclusions

Primary thyroid leiomyoma is a rare tumor, which is difficult to diagnose using the frozen section technique alone. It must be distinguished from various other thyroid spindle cell tumors, especially malignant spindle cell tumors.

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Author Contributions

YZ wrote the manuscript and performed the literature review. HH revised the manuscript for important intellectual content. YZ and XY were major contributors to writing the manuscript. All authors read and approved the final manuscript.

Ethical Approval

Ethical approval is not applicable because this article does not contain any studies with human or animal subjects.

Informed Consent

Written informed consent for publication of this case report and any accompanying images was obtained from the patient's parents.

ORCID iD

Xiang Yong https://orcid.org/0000-0002-0787-9797

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