

A rare primary leiomyosarcoma of the thyroid gland: a case report and literature review

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Case Report

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Abstract

Background Primary thyroid leiomyosarcoma(LMS) is very rare, with only 30 cases reported worldwide. Thyroid LMS should be diagnosed with caution and comprehensively evaluated considering clinical, imaging, and pathological data. It is a kind of fatal tumor with an extremely poor prognosis and lacks effective treatment regimens, and most patients die within 1 year of diagnosis. Here, we present a case report on a patient with Primary thyroid LMS.

Case presentation A 76-year-old woman presented with hoarseness, dysphagia, and dyspnea when lying down for the past 1 month visited our hospital. She had a history of right neck masses in the past 2 years. A hard, irregular tumor of approximately 8 cm × 5 cm × 5 cm was observed on the right lobe of the thyroid, the boundary between which and the surrounding tissues was unclear. The tumor anteriorly invaded the cervical muscles and interiorly invaded the right walls of the trachea and esophagus. Most tumor tissues were excised, a curative operation seemed impossible. Immunohistochemically, the tumor cells were positive for Calponin, vimentin and SMA, but negative for EMA, CK, P53, Desmin and S-100. Tumor recurrence and progression were considered two months after surgery, the patient refused follow-up treatment for personal reasons and died 4 months after surgery.

Conclusion Thyroid LMS accounting for merely 0.014% of primary thyroid tumors of unknown etiology. The diagnosis can only be confirmed upon a lack of evidence regarding epithelial differentiation or other types of sarcoma differentiation and when immunohistochemistry yields positive smooth muscle markers. Primary thyroid LMS is primarily surgically resected and no other effective treatment currently available. Disease progression is rapid, the prognosis is poor, and the 1-year survival rate is <10%. In the present study, a rare case of a 76-year-old female patient diagnosed with thyroid LMS was reported and a review of the literature is presented.

Background

Thyroid epithelial malignancies are most common, while sarcomas derived from mesenchymal tissues are rare. Thyroid sarcomas mostly including fibrosarcoma, angiosarcoma, and malignant hemangiopericytoma have been commonly reported among older individuals. Leiomyosarcoma (LMS) originates from mesenchymal cells differentiating from smooth muscle cells or mesenchymal smooth muscle cells and is common among men aged > 40 years. It often occurs in organs rich in smooth muscle cells including the uterus and gastrointestinal tract; however, it is rarely observed in soft tissues including blood vessels and the retroperitoneum. Thyroid LMS is rarer, accounting for merely 0.014% of primary thyroid tumors of unknown etiology but reportedly correlated with the Epstein-Barr virus infection [1].

Thyroid LMS often presents neck masses developing over a short term, usually confined to one lateral lobe of the thyroid gland. Imaging indicates masses with unclear boundaries, which are potentially associated with cystic degeneration, necrosis, or calcification, often with evidence regarding invasion to adjacent structures. Histologically, tumor cells originate from interwoven eosinophilic spindle cells, and

the nuclei are significantly atypical and polymorphic. The diagnosis of thyroid LMS requires comprehensive evaluation along with imaging and the assessment of clinical symptoms and immunohistochemical markers. The diagnosis can only be confirmed upon a lack of evidence regarding epithelial differentiation or other types of sarcoma differentiation and when immunohistochemistry yields positive smooth muscle markers [2].

Primary thyroid LMS is primarily surgically resected, including thyroidectomy and total resection with cervical lymph node dissection, and no other effective treatment currently available. Disease progression is rapid, the prognosis is poor, and the 1-year survival rate is < 10% [3]. Here, we report the case of a 76-year-old woman with thyroid LMS admitted to our hospital department and a review of the literature.

Case Presentation

A 76-year-old woman presented with hoarseness, dysphagia, and dyspnea when lying down for the past 1 month visited our hospital. She had a history of right neck masses in the past 2 years. The bilateral thyroid was asymmetric, and the trachea was offset to the left side. A mass of 8 cm × 6 cm was palpated on the right of the anterior neck area and the anterior edge of the sternocleidomastoid muscle, which was hard. The surface was rough, and the boundary was unclear, without undulation. No redness, swelling, or ulceration was observed around the mass, without upward and downward movement when swallowing, tongue movement, tremor, or vascular murmur. A mass of 2 cm × 2 cm was palpated in the left thyroid, which was hard. The surface was not smooth, and the boundary was unclear, without undulation.

The thyroid function test revealed no abnormalities. Whole-body examination revealed no abnormalities. Thyroid ultrasound examination revealed a mass of 6.7 cm × 5.4 cm in the right thyroid and 2–3 hypoechoic opacities in the left thyroid, of which the larger one was of 2.2 cm × 1.5 cm. Cervical contrast-enhanced computed tomography (CT) suggested (Fig. 1) a space-occupying mass in the right thyroid of approximately 8.4 cm × 5.1 cm × 5.2 cm, with multiple necrotic areas and plaque-like calcification. Contrast-enhanced imaging revealed heterogenous enhancement and involvement of the thyroid isthmus. Multiple nodular soft tissue density opacities were observed in the left thyroid, and the larger one was approximately 1.3 cm in diameter, displaying mild enhancement after contrast-enhanced imaging. Multiple enlarged lymph nodes were observed in the right neck and the submandibular region, and the larger one was approximately 2.0 cm in diameter.

A hard, irregular tumor of approximately 8 cm × 5 cm × 5 cm was observed on the right lobe of the thyroid, the boundary between which and the surrounding tissues was unclear. The tumor anteriorly invaded the cervical muscles and interiorly invaded the right walls of the trachea and esophagus. Multiple carcinous nodes were enlarged and fused into masses on the posterolateral side of sternocleidomastoid muscle, invading the anterior wall of the upper segment of the right common carotid artery and occluding the middle segment of the internal jugular vein owing to tumor compression. To protect the trachea, esophagus, right common carotid artery, vagus nerve, phrenic nerve, and recurrent laryngeal nerve, the left thyroid was completely resected and the right thyroid and isthmus containing most tumor tissues were

excised, the central lymph nodes were resected, and the thyroid tissues were resected from the occluded segment of the right internal jugular vein. Frozen intraoperative sections indicated that a malignant spindle cell tumor was present in the right thyroid and cervical lymph nodes and inclined to be undifferentiated carcinoma, and spindle cell proliferation with local papillary structures were observed in the left thyroid. Postoperative pathological examination suggested the presence of a malignant spindle cell tumor in the right thyroid (Fig. 2), and LMS was suspected in accordance with immunohistochemistry, and the tumor invaded the surrounding soft tissue; <left thyroid> nodular goiter was observed with local tumor involvement, and < central cervical lymph nodes > cancer tissues were examined (5/6). Figure 3 shows the results of immunohistochemistry, Vim (+), smooth muscle actin (SMA) (+), Calponin(+), Desmin (-), S-100 (-), epithelial membrane antigen (EMA) (-), and cytokeratin (CK) (-) (Fig. 3). The patient recovered smoothly and was discharged 5 d after surgery. Two months after surgery, she returned to our hospital for re-examination. Cervical ultrasound examination suggested that the right lobe of the thyroid was occupied by a giant tumor with an area of approximately 5.8 cm × 3.6 cm with an irregular morphology and unclear boundaries, and the internal echo was heterogeneous. Color doppler flow imaging (CDFI) indicated abundant blood flow signals in the periphery. Tumor recurrence and progression were thus considered. The patient refused follow-up treatment for personal reasons and died 4 months after surgery.

Discussion

Thyroid epithelial malignancies are the most common, such as papillary thyroid carcinoma and follicular thyroid carcinoma, whereas mesenchymal tumors are rare. Leiomyosarcoma originates from mesenchymal cells differentiated from smooth muscle cells or mesenchymal smooth muscle cells and is most common in the scalp, paranasal sinus, and the throat [4]. The etiology of thyroid LMS remains unknown but may be related to smooth muscles of the vascular wall of the thyroid capsule [5]. Thyroid LMS is very rare, with only 30 cases reported worldwide [3]. The incidence of thyroid LMS is more common among the elderly, among individuals aged 40–90 years, and the male:female ratio is 1:1.5. Most cases of thyroid LMS are unilateral, and only one case has been reported as bilateral [6]. Patients usually visit hospitals owing to the emergence of neck masses, which often enlarge rapidly over a short period without pain and are often accompanied by dyspnea, dysphagia, weight loss, and hoarseness. Thyroid function is usually normal. A radionuclide scan previously reported cold thyroid nodules. Ultrasound examination has generally reported unclear hypoechoic shadows with solid, partially cystic or calcified nodules. CT and magnetic resonance imaging (MRI) have previously reported that the tumor is a low-density mass with clear boundaries accompanied by dense calcification and necrotic sites. It is difficult to distinguish primary thyroid sarcoma from undifferentiated carcinoma through fine-needle aspiration cytology for thyroid tumors because undifferentiated carcinoma presents similar histological features to sarcoma [7]. The patient was an elderly woman with a 2-year history of masses in the right neck and received no special treatment during the course of the disease. Owing to rapid enlargement of masses in the past 1 month, symptoms including dyspnea and hoarseness manifested; hence, the patient visited our hospital. Preoperative thyroid function tests revealed normal findings.

Primary thyroid LMS should be diagnosed with caution and comprehensively evaluated considering clinical, imaging, and pathological data. Pathologically, LMS often displays infiltrative growth, is characterized by capsule invasion, and is often coupled with distant metastasis. Microscopically, tumor cells comprise spindle cells arranged in bundles, with red cytoplasmic staining, deeper nuclear staining, differently sized nuclei, and distinct atypia and are often coupled with hemorrhage and necrosis [8]. Immunohistochemistry critically facilitates the diagnosis and differential diagnosis of LMS. Moreover, the possibility of metastatic LMS needs to be ruled out, especially for LMS derived from organs including the uterus. Imaging examinations including CT help determine primary lesions and distant metastasis, and metastatic uterine LMS tissue usually expresses estrogen receptor (ER) and p16 [9]. Furthermore, it is necessary to distinguish thyroid LMS from the following types of cancers. Patients with medullary thyroid cancer usually have elevated blood calcium levels, with positive immunohistochemical markers including CK, thyroid transcription factor-1 (TTF-1), NSE, CgA, Syn, and Calcitonin. For undifferentiated thyroid tumors, on observing multiple sections, the presence of epithelial structures can be confirmed partly on the basis of positive immunohistochemical markers including CK and EMA; however, approximately 20% of patients present a loss of epithelial markers and negative smooth muscle markers [10]. Spindle cell tumors with thymus-like differentiation are histologically biphasic and comprise tightly interwoven spindle cell bundles and adenoid structures, with positive immunohistochemical markers including CK and CD117. Spindle cells occasionally present positive smooth muscle markers. Such tumors grow gradually and have metastatic potential and patients have a longer survival time [11]. Solitary fibrous tumors are [12] arranged in numerous ways and comprise a mixture of cell-sparse and cell-rich areas, with positive immunohistochemical markers including CD34, CD99, BCL-2, and vimentin.

Immunohistochemistry can help identify other spindle cell tumors including malignant peripheral neurilemmoma and synovial sarcoma, wherein focal CK is present in both. Spindle cells S-100 and SOX-10 of malignant peripheral neurilemmoma are positive, and the synovial sarcoma cell TLE1 was positive [13–14]. In a nutshell, primary leiomyosarcoma of the thyroid is very rare, and its diagnosis requires special cautiousness. Thyroid LMS can be diagnosed merely when there is a complete lack of epithelial cell differentiation and on obtaining clear evidence (histology, immunophenotype, or ultrastructure) indicating the presence of specific sarcoma differentiation, such as the expression of vimentin, SMA, and MSA, and the partial expression of Desmin, whereas CK, TG, calcitonin, S-100, and EMA are generally not expressed [15]. Herein, the tumor grew like a bundle of spindle cells, and the nucleus was obviously atypical and polymorphic. Furthermore, the tumor invaded the thyroid and surrounding tissues including fat and blood vessels. Vim (+), SMA (+), Desmin (-), S-100 (-), and CK (-) expression was consistent with that reported in the literature, upon immunohistochemistry.

Primary thyroid LMS is highly malignant. Most patients display distant metastasis upon tumor detection, and only a few patients have local lymphatic metastasis; most patients undergo hematogenous metastasis, which commonly spread to the lung and bone. Radiotherapy and chemotherapy cannot improve patient survival, and surgery is currently the most effective treatment method for primary thyroid LMS; however, local recurrence and metastasis still occur in 75% of patients. Thyroid LMS is a fatal tumor with an extremely poor prognosis and lacks effective treatment regimens, and most patients die

within 1 year of diagnosis [16]. For that reason, some studies explore the effectiveness of molecular-based treatment strategies. Day et al. reported that c-kit proto-oncogene was overexpressed in tumor cells in primary thyroid LMS [17], the product of which was a transmembrane tyrosine kinase receptor. Therefore, the feasibility of tyrosine kinase inhibitors as an adjuvant treatment for such patients is being investigated [18]. Another study attempted to treat a patient with lung metastatic primary thyroid LMS with imatinib mesylate capsules; however, it ultimately failed to prevent tumor recurrence and death [19]. Herein, although no distant metastasis occurred before surgery, it was intraoperatively observed that the cancer tissues invaded the surrounding tissues, and therefore radical surgery could not be performed. The tumor recurred in 2 months after surgery, and the patient died 4 months after surgery.

Conclusions

In summary, primary thyroid LMS is a rare malignant tumor, and all patients with rapidly enlarged masses in the anterior cervical region should be vigilant. Early diagnosis and treatment is of enormous significance. Immunohistochemistry serves as a definite diagnostic method to distinguish primary LMS from other thyroid malignancies. The prognosis of thyroid LMS is obviously poor, with no effective treatment method at present except for radical surgery.

Abbreviations

LMS: leiomyosarcoma ; CT: computed tomography ; CDFI: Color doppler flow imaging ; EMA: epithelial membrane antigen ; CK: cytokeratin ; SMA: smooth muscle actin ; MRI: magnetic resonance imaging ; ER: estrogen receptor ; TTF-1: thyroid transcription factor-1.

Declarations

Ethics approval and consent to participate

After ethical review, this study was approved by the Ethics Committee of Daping Hospital of Army Medical University. Written informed consent was obtained from the patient and her families for publication of this case report and any accompanying images.

Consent for publication

We obtained written informed consent from the patient for the publication of this case report and accompanying images.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SH collected the clinical data and wrote the manuscript as a major contributor. MH helped to write the manuscript. WGT and JJZ contributed to the management of the patient. BG reviewed the computed tomography findings and carried out the histopathologic evaluation. DLL carried out the operation on the patient and participated in writing the final manuscript as a corresponding author. All authors have read and approved the final manuscript.

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Figures

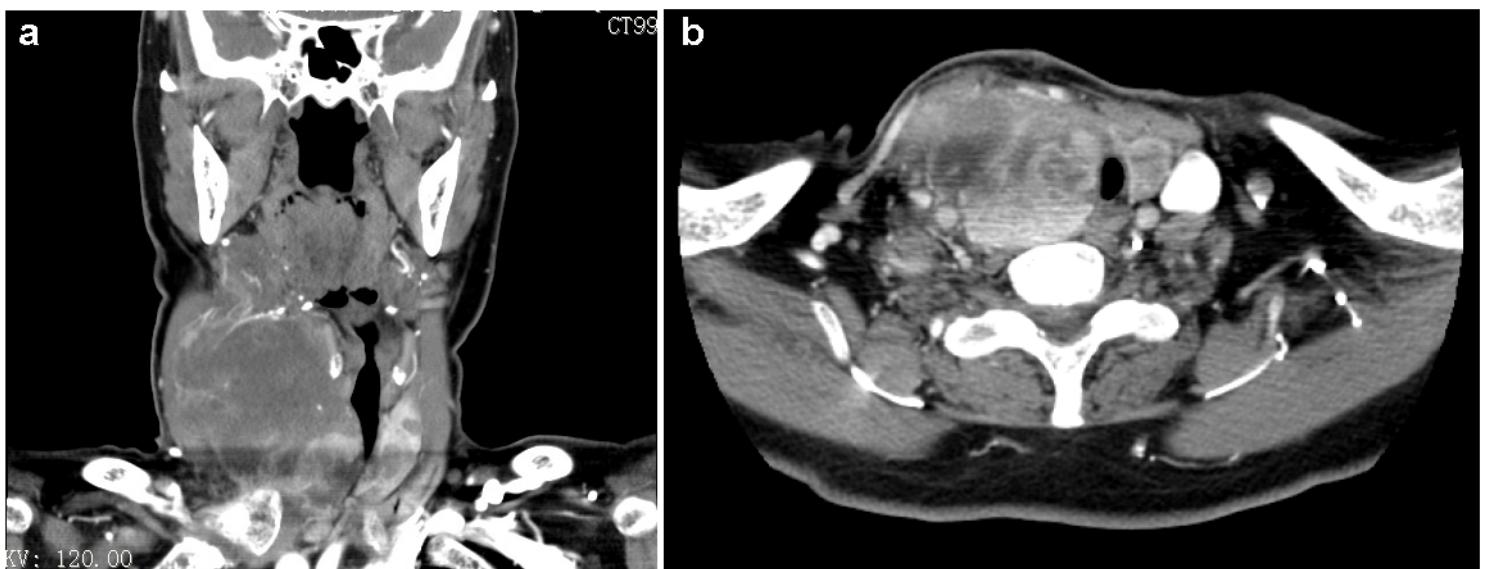


Figure 1

The findings of Computed topography. a) Computed topography demonstrated a space-occupying mass in the right thyroid of approximately $8.4 \text{ cm} \times 5.1 \text{ cm} \times 5.2 \text{ cm}$, with multiple necrotic areas and plaque-like calcification. b) Multiple nodular soft tissue density opacities were observed in the left thyroid, and the larger one was approximately 1.3 cm in diameter.

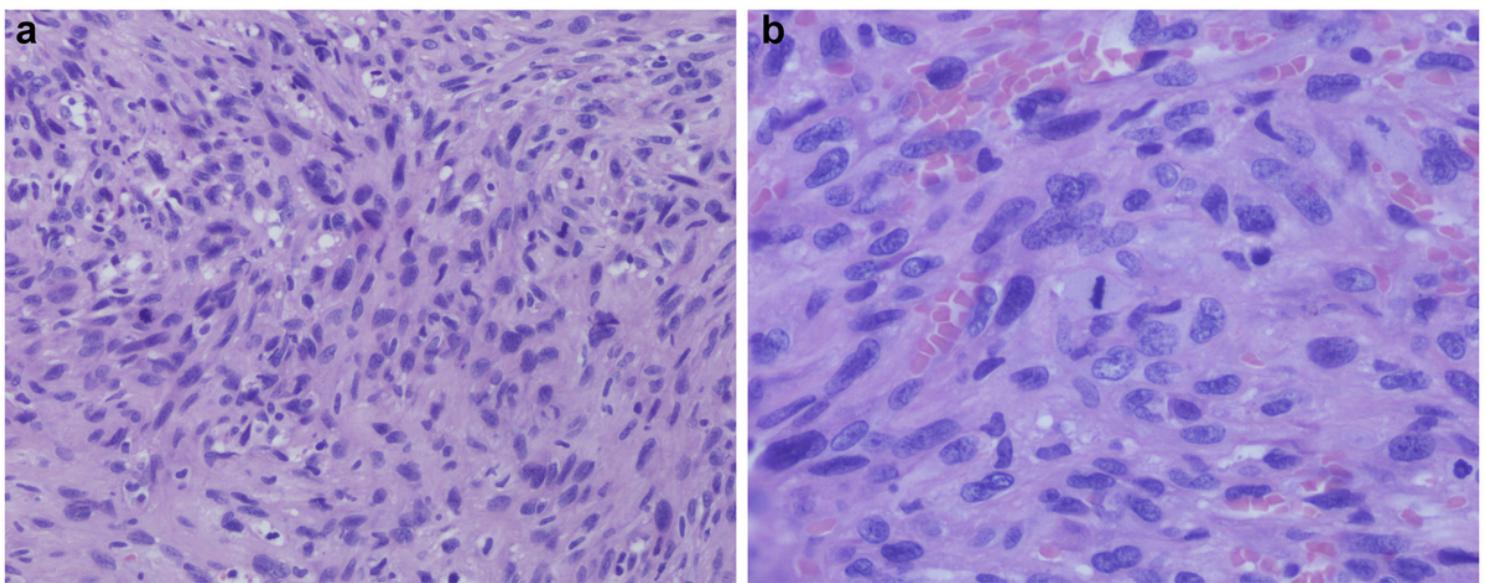


Figure 2

Histopathological character of the thyroid LMS. a) The tumor consisted of spindle cells arranged in interlacing fascicles $\times 200$.b) The tumor exhibited notable nuclear pleomorphism and atypical, giant cell formation $\times 400$.

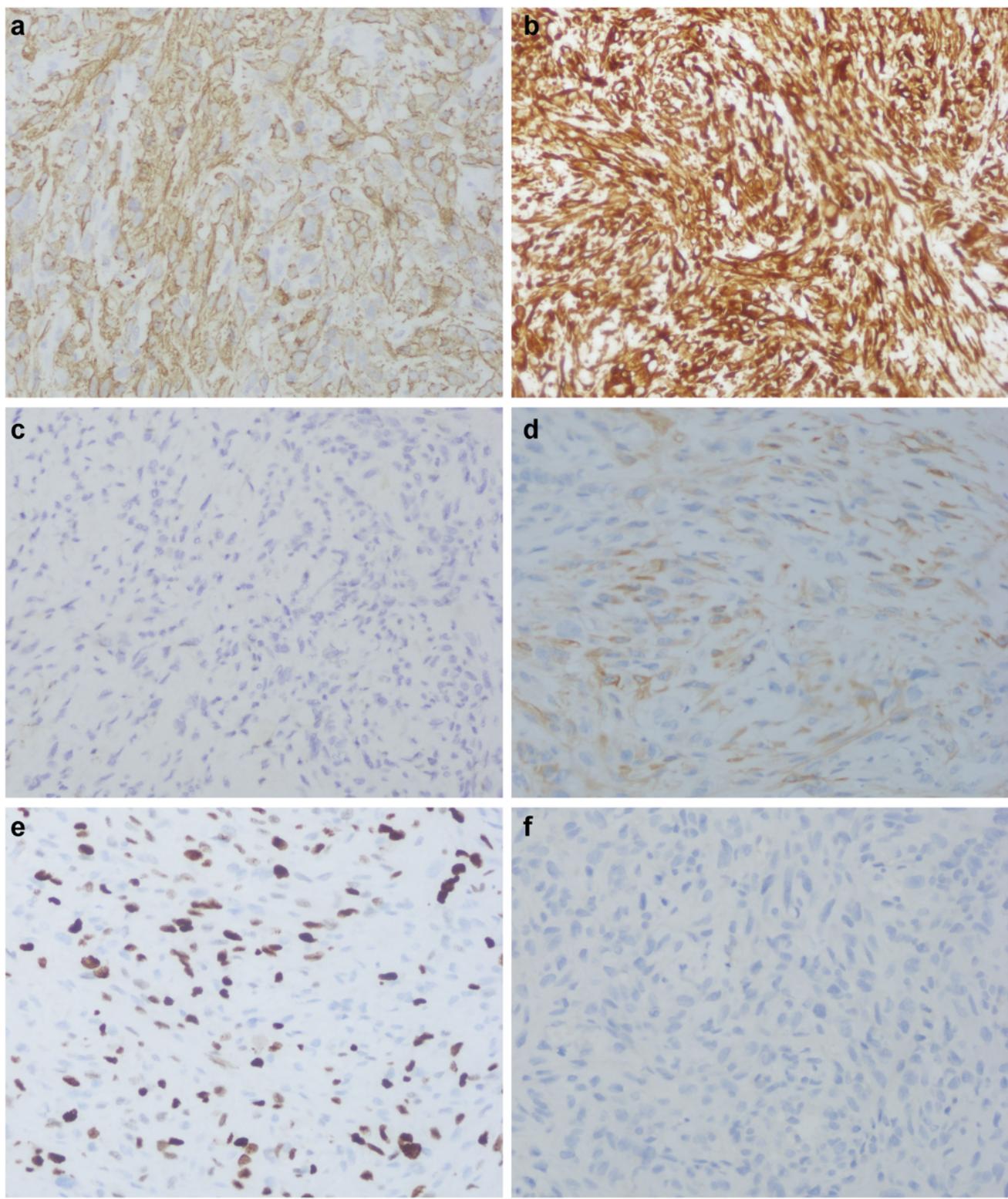


Figure 3

The immunohistochemical character of the thyroid LMS. a) SMA positive $\times 200$.b) Vimentin positive $\times 200$.c) S100 negative $\times 200$.d) Calponin positive $\times 200$.e) The Ki-67 index was about 40% $\times 200$.f) Desmin negative $\times 200$.

Supplementary Files

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