

Primary thyroid leiomyosarcoma: a case report and review of the literature

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SUMMARY: Primary thyroid leiomyosarcoma: a case report and review of the literature.

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Primary thyroid leiomyosarcoma (LMS) is an extremely rare tumor.

We report a case of a 47-year-old male with a rapidly growing neck mass and dysphagia. Preoperative investigations were diagnostic of

anaplastic carcinoma. Total thyroidectomy with partial esophagectomy and dissection of right infrahyoid muscles was performed. Through histological and immunohistochemical evaluations a primary thyroid high-grade LMS was diagnosed. At 2 months of follow-up a local recurrence was detected and consequently the patient was submitted to chemotherapy with partial response. He is still alive 9 months after surgery.

Diagnosis of primary thyroid LMS is difficult due to its similarity to other more common thyroid tumors. To date, there is no standard therapy and prognosis is poor.

KEY WORDS: Thyroid leiomyosarcoma - Thyroid carcinoma - Head and neck soft tissue sarcoma - Diagnosis - Treatment.

Introduction

Among all of the tumors of the thyroid gland, primary thyroid LMS accounts for 0.014% (1). To date, only 30 cases have been described in literature (2-6). This tumor is supposed to arise from smooth muscle cells of the capsular vessels of the gland (1, 7, 8).

Before a diagnosis of primary thyroid LMS, secondary leiomyosarcomas involving the thyroid gland must be ruled out through extensive investigations of the other organs. An accurate diagnosis requires the combined assessment of clinical, imaging and histologic data, and, above all, immunohistochemical evaluations.

Surgery is the main treatment while benefits of other therapies, as chemotherapy, radiotherapy, hormonal therapy and immunotherapy, are controversial (2, 7, 9-12).

The prognosis is poor with an estimated 1-year survival rate of 5-10% (9).

Case report

A 47-years-old man was referred to our Unit for a rapidly growing neck mass and dysphagia. Physical examination revealed a 5-6 cm firm mass in the right anterior cervical region fixed to superficial and deep tissue layers. The patient was clinically and biochemically euthyroid and thyroid autoantibodies were undetectable. Thyroid ultrasonography showed a heterogeneous hypodense mass (60x39x33 mm) of the right thyroid lobe, with peri- and intralesional vascular flow. Fine needle aspiration cytology was diagnostic of undifferentiated malignancy (Class 6 Bethesda). CT scan confirmed the presence of a bulky right cervical mass with no evidence of lym-

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phadenopathy and distant metastases (Figure 1).

At surgery, a hard and irregular mass of the right thyroid lobe, infiltrating the esophageal wall, was found. Consequently, a total thyroidectomy with partial esophagectomy and dissection of right infrahyoid muscles was performed. Postoperative course was uneventful and the patient was discharged 7 days after surgery in good conditions.

Histological examination showed a proliferation of elongated spindle-shaped cells arranged in

fascicular pattern with eosinophilic cytoplasm and hyperchromatic blunt nuclei with marked anisokaryosis (Figures 2, 3). Immunohistochemical evaluations documented a diffused reactivity with vimentin, desmin, smooth muscle actin (SMA) and muscle-specific actin. No reactivity was reported for thyroglobulin, TTF-1, Pax 8, calcitonin, cytokeratin AE1-AE3, EMA, S100, CD5, CD34, CD31 and MDM2. The conclusive diagnosis was primary thyroid high-grade LMS.

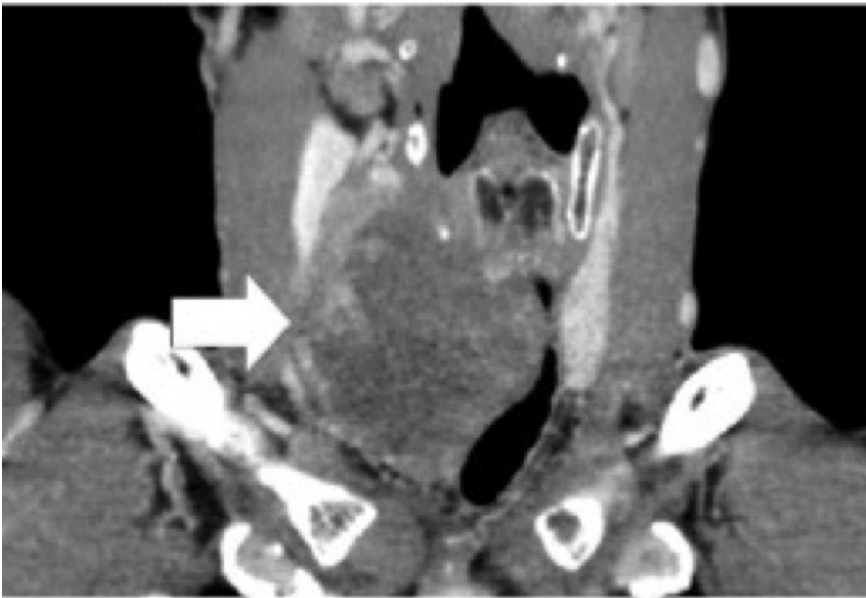


Figure 1 - CT scan shows the presence of a bulky right cervical mass (white arrow).

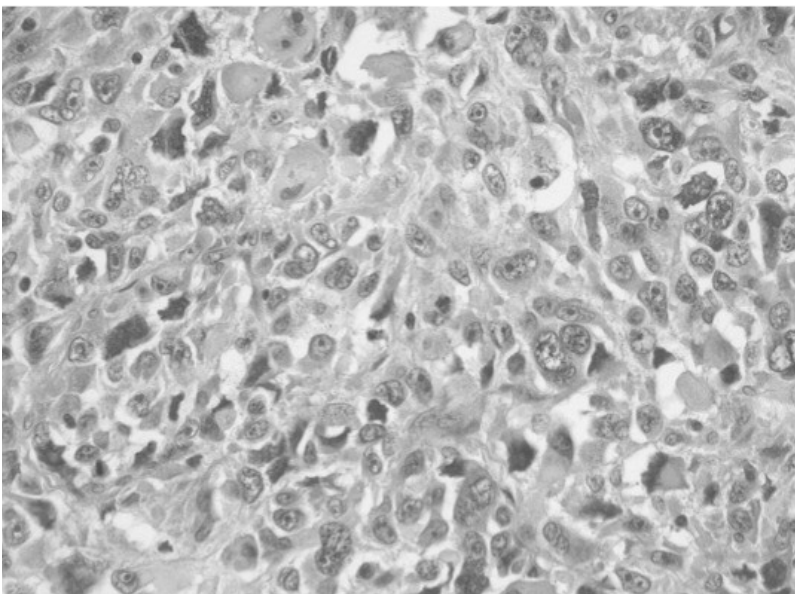


Figure 2 - Elongated spindle-shaped cells arranged in fascicular pattern (H&E, x200).

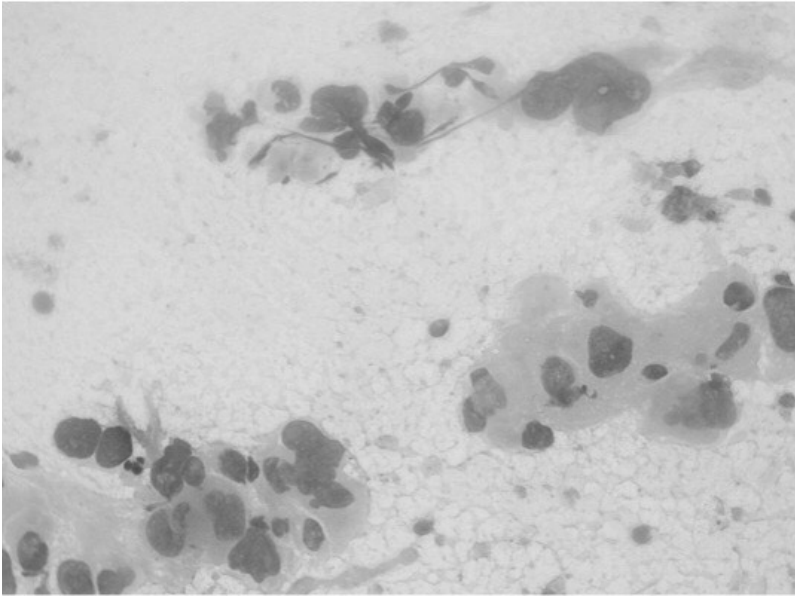


Figure 3 - Tumor cells with eosinophilic cytoplasm and hyperchromatic blunt nuclei with marked anisokaryosis (H&E, x400).

At 2 months of follow-up, a local recurrence was detected at ^{18}F -FDG PET/CT and it was confirmed at CT scan (Figures 4, 5). The patient was therefore submitted to chemotherapy, based on the association of Adriamycin and Ifosfamide, with partial response. He is still alive 9 months after surgery.

Discussion

Leiomyosarcoma is common in the gynecological and gastrointestinal systems and in the retroperitoneum. This tumor accounts for 4% of the head and neck sarcomas (13,14). Primary thyroid LMS is a very rare tumor, however, the number of reported cases is increasing due to the diagnostic immunohistochemical method. The present paper adds a new case to the literature.

This tumor seems to have a slight predilection for female patients and the mean age at diagnosis, including our case, is 63.4 years, with a range between 32 and 90 years. Additionally, a case of Epstein-Barr virus-associated primary thyroid LMS was reported in a 6-year-old child patient with congenital immunodeficiency.

Patients most commonly complain of a rapidly growing neck mass, as in our experience. Other symptoms can be dysphagia (as in our case), hoarseness, weight loss, dyspnea and arm pain (1-12, 15-20).

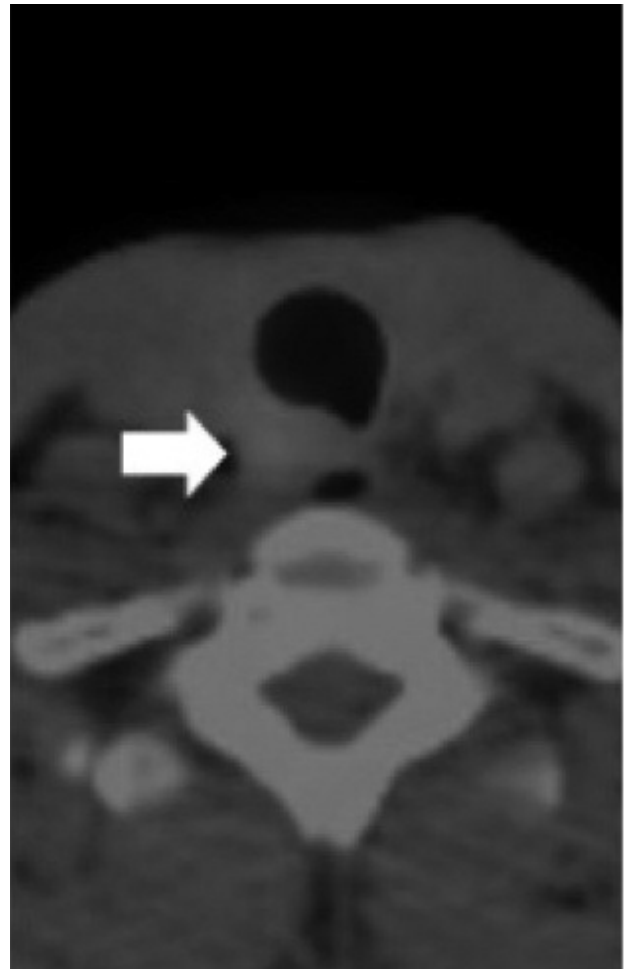


Figure 4 - Local recurrence at ^{18}F -FDG PET/CT (white arrow).



Figure 5 - Local recurrence at CT scan (white arrow).

Preoperative diagnosis can be extremely difficult, in fact, it has no characteristic imaging features that might be useful for diagnostic aims. The main differential pathologic diagnosis includes anaplastic thyroid carcinoma, spindle cell variant of medullary carcinoma, solitary fibrous tumor and spindle epithelial tumor with thymus-like differentiation (SETTLE). In our experience, as in other cases, the diagnosis of primary thyroid LMS was made after surgery on the immunohistochemical features of the tumor.

The majority of patients are euthyroid (4, 5, 8-12, 16-18, 20). Ultrasound can show an ill-defined or well-defined hypo-echogenic mass with calcified or cystic components (15). Thyroid isotope scanning can reveal a cold nodule or hyperplasia with increased and decreased uptake of radioactive iodine (1, 7). CT scan usually shows a low-density mass with calcification and necrosis (15) and, moreover, can reveal a direct tumoral invasion of the adjacent structures (15, 18). MR imaging can demonstrate a mass of intermediate signal on T2 and an isointense mass on T1 with a fair enhancement with gadolinium (15). Also fine needle aspiration cytology is used for the preoperative diagnosis but it might not be helpful to differentiate the rare primary thyroid LMS from the more frequent anaplastic carcinomas. In fact, anaplastic carcinomas sometimes show mor-

phological features similar to those of a sarcoma (11). At microscopic investigation, neoplastic cells are elongated, with abundant acidophilic fibrillary cytoplasm and with a nucleus generally centrally located and typically blunt-ended or 'cigar-shaped'. The degree of nuclear atypia is highly variable and also the mitotic activity varies considerably. Although high mitotic index is virtually diagnostic of malignancy, a primary thyroid LMS must be strongly suspected for a tumor that is widely necrotic, hemorrhagic and with significant atypia, even if the mitotic activity is low (5). The pattern of growth is usually fascicular.

Immunohistochemistry plays a key role in the diagnosis (21). Primary thyroid LMS shows reactivity for vimentin, smooth muscle actin (SMA), muscle-specific actin, smooth muscle myosin, desmin and H-caldesmon, while it typically stains negatively for cytokeratin, thyroglobulin, calcitonin and chromogranin (1).

Most patients have a poor prognosis despite an aggressive treatment from the beginning. To date, despite considerable improvements in oncology, an efficacious multidisciplinary treatment protocol is lacking (6). The surgical approaches reported in the literature vary between thyroid lobectomy to total thyroidectomy plus therapeutic modified radical neck dissection (4, 11, 20, 22-24). Because of the lo-

cally invasive characteristic of this tumor, some authors suggest radical surgery in order to obtain local control of the disease (10, 14, 18). In our experience, although radical surgery was performed, a local recurrence was detected after only 2 months of follow-up. To date, chemotherapy and radiotherapy has not shown any substantial therapeutic efficacy (9, 11, 12). Our patient was submitted to chemotherapy to treat the recurrence of disease with partial response only. In literature interesting data are reported in the management of uterus and thyroid leiomyosarcomas in case of overexpression of c-Kit proto-oncogene, a tyrosine kinase receptor. However, the effect of imatinib, a tyrosine kinase inhibitor, on the treatment of thyroid LMS needs to be observed in larger number of patients as no significant effect of this drug was currently noted on survival (10, 25). Additional antigens sporadically identified in primary thyroid LMS are estrogen and progesterone receptors, raising the possibility of hormonal responsiveness (17). Often, treatments can only produce palliative results, as in case of locoregional infiltrating disease. In this situation surgery can be performed to prevent esophageal or airway obstruction (4).

Conclusion

A new rare case of primary thyroid LMS has just been described. This tumor must be taken into account in patients with a rapidly growing neck mass. The final histological diagnosis requires immunohistochemical investigations to exclude other more frequent thyroid tumors. To date, radical surgery remains the mainstay of treatment while the effect of other therapies needs to be observed in larger number of patients to modify the current poor outcome.

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