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Well-Differentiated Liposarcoma Localized to the Thyroid Gland

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What Is Known about This Topic?

- Most cases of liposarcoma are treated with surgery. Adjuvant radiation therapy is used in a few cases. The role of chemotherapy, either adjuvant or neoadjuvant, remains to be determined. Given the paucity of cases, a definite treatment protocol has not been established for the management of this pathology.

What Does This Case Report Add?

- This case report presents the 13 cases of liposarcoma of the thyroid gland described in the literature, with summary of treatment and patient outcome 9 months postoperatively. It also highlights the discussion involved in making decisions regarding adjuvant management of the patient in case. It reinforces that surgery is a good option as initial management and highlights that patients with early stage cancer, such as the patient in case, may do well without any adjuvant treatment – either with radiation therapy or chemotherapy. Given the rarity of this pathology and thus scarce existing data regarding its management, our case report adds more strength to evidence regarding the treatment of this pathology.

Keywords
Liposarcoma · Thyroid gland · Well-differentiated type

Abstract
Liposarcoma of the thyroid gland is a pathology that is rarely encountered in clinical practice, given the paucity of these cases. For the same reason, a definite treatment protocol has not been established for these cases. We present a case of a 49-year-old man who presented with a thyroid mass that was found to be a well-differentiated liposarcoma and was treated surgically with no adjuvant therapy other than close surveillance with clinical examination and MRI scans. On his most recent clinical visit, 9 months after surgery, there was no clinical or radiologic evidence of recurrence and the patient is doing well with good speech and swallow functions and no new symptoms. We also summarize all the cases of this rare pathology presented thus far to the best of our knowledge.

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Introduction

Liposarcoma of the thyroid is an extremely rare lesion. To our knowledge only 12 cases [1–9] of this tumor have been reported thus far and here we report the 13th case. Due to the paucity of literature regarding this lesion, the optimal treatment protocol for this cancer has not been definitively established. Currently, surgery remains the primary modality of treatment with adjuvant radiation therapy being employed in some cases. It is not clear whether chemotherapy has any role in the initial treatment of this rare lesion, which tends to show a more localized behavior.

Case Presentation

We present the case of a 49-year-old gentleman who initially began experiencing pain between his shoulder blades for a week and subsequently noticed a left neck mass while he was shaving. He denied neck pain, dysphagia, difficulty breathing, voice changes, or fatigue. He had no history of thyroid problems, weight loss, night sweats, easy bruising, or bleeding, and no history of radiation exposure or trauma to the area. CT scan of the neck with contrast was obtained and revealed a 15.4-cm vertical × 7.7-cm lateral × 6.7-cm anteroposterior nonenhancing isodense mass of the left neck extending from the hyoid down to the arch of the aorta, displacing the carotid laterally (Fig. 1). The right thyroid enhanced normally with contrast and the left neck mass was contiguous with the thyroid but did not enhance as significantly. The trachea and esophagus were deviated rightward. A flexible fiberoptic laryngoscopy was performed which showed extensive cobblestoning in the posterior oropharynx with deviation of the airway at the level of the mass. Symmetric true vocal cord motion was noted but the left pyriform sinus appeared slightly compressed. No mucosal lesions or masses were noted within the upper aerodigestive tract to the level of the larynx. The subglottis was visualized and appeared patent. A fine needle aspiration biopsy of the left neck mass was performed and the cytology was negative for malignant cells. Despite benign cytopathology and a relative lack of symptoms, a left thyroid lobectomy was offered to the patient due to the concerning size and appearance of this lesion. The patient then had an elective left thyroid lobectomy, isthmusectomy, and limited central neck dissection (Fig. 2, 3). The left recurrent laryngeal nerve was adherent to the capsule of the mass but was dissected free with care. Nerve monitoring (NIM-Response 3.0 Nerve Monitoring System; Medtronic) was performed through the entirety of the procedure and good electrophysiological function was maintained throughout the dissection. Immunohistochemistry of the surgical specimen was positive for S100 (Fig. 4) but negative for TTF1, thyroglobulin, and cytokeratin. Histopathology demonstrated clearly defined lipoblasts. The final diagnosis was a well-differentiated, grade 1 liposarcoma, with the tumor measuring 15.8 cm at the greatest dimension and margins negative for tumor. The isthmus margin on the remaining right thyroid lobe was benign. All the cervical lymph nodes excised were negative for malignancy. Based on these pathology findings, the patient was deemed as having a stage IB (T2b, N0, Mx, G1) liposarcoma of the thyroid gland. His case was discussed in our multidisciplinary tumor board and consensus was to observe the patient without any adjuvant treatment. The possibility of adjuvant radiation therapy was considered and discussed as well, but it was felt that there was not adequate evidence to support this approach currently. Postoperatively, the patient was swallowing well and breathing well with a strong voice. Repeat flexible fiberoptic laryngoscopy demonstrated normal and symmetric true vocal cord motion.

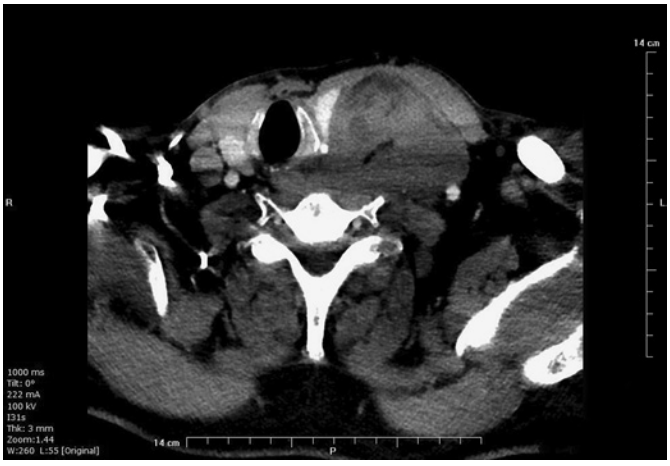

Fig. 1. Transverse view of the CT scan of the neck demonstrating an enlarged left cervical mass with compression of the surrounding structures.

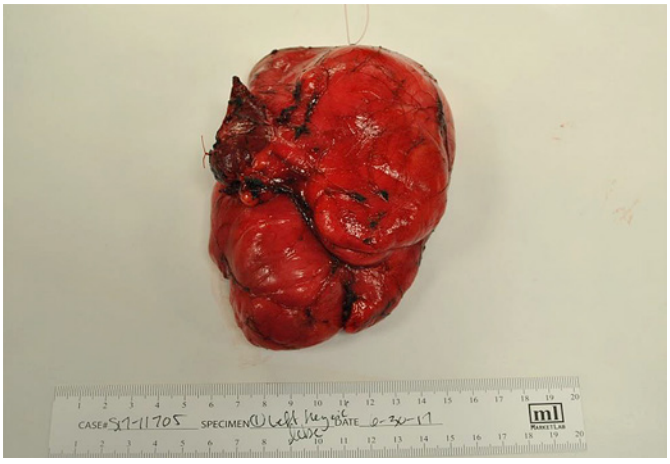

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Fig. 2. Gross image of the thyroid gland prior to sectioning.

Discussion

Epithelial cancers of the thyroid gland constitute the majority of thyroid malignancies (about 95%) and include papillary, follicular, hurtle cell, anaplastic, and

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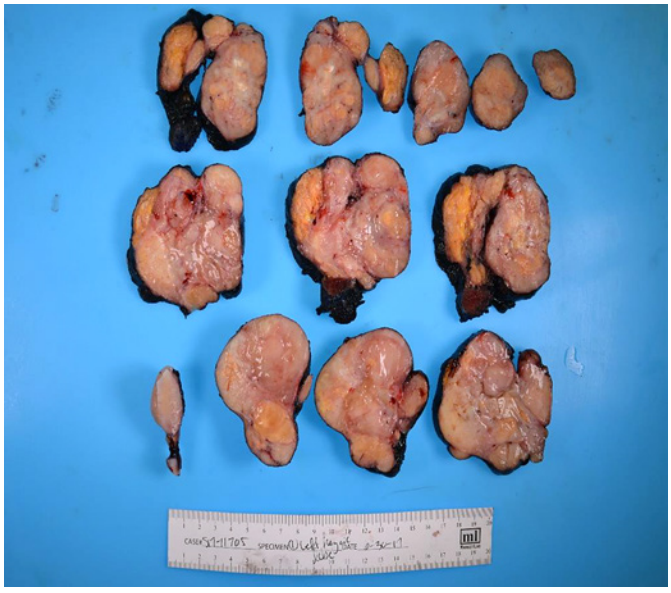

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Fig. 3. Gross images of the thyroid gland after sectioning.

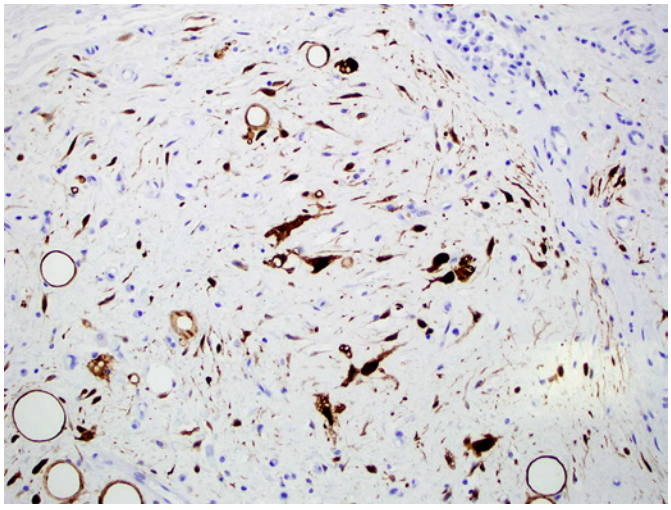

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Fig. 4. Immunohistochemistry demonstrating S100 positivity of the liposarcoma.

medullary thyroid cancers. The nonepithelial cancers constitute less than 5% of all thyroid malignancies and include primary thyroid lymphoma, malignant teratoma, primary squamous cell cancers, and thyroid sarcomas [5, 10]. Thyroid sarcomas constitute less than 1% of all thyroid malignancies [8]. Fibrosarcoma [5], leiomyosarcoma [5], malignant hemangioendothelioma [3], malignant diffuse hemangiopericytoma [5], osteogenic sarcoma [5], chondrosarcoma [5], and liposarcoma [1–8] are the various sarcomas reported to have occurred as primary thyroid sarcomas [10].

Liposarcoma is one of the most common soft tissue sarcomas overall, accounting for 18–20% of these tumors. They show a male predominance and tend to occur in the fifth decade. Childhood liposarcomas are rare. It commonly arises in the extremities or in the retroperitoneal space. Histologically, the most recent World Health Organization classification of soft tissue tumors recognizes 5 categories of liposarcomas: (1) well-differentiated (also known as atypical lipomatous tumor) which includes the adipocytic, sclerosing, and inflammatory subtypes, (2) dedifferentiated, (3) myxoid, (4) round-cell, and (5) pleomorphic types [11]. A spindle cell variant of the well-differentiated type is also recognized. Immunohistochemistry staining for S100 may aid the diagnosis [3, 5] in the setting of lipoblasts and suggestive clinical picture, though the presence of lipoblasts by themselves does not indicate a diagnosis of liposarcoma. Specific histologic types tend to show a preference for specific anatomic locations in their occurrence. Well-differentiated liposarcomas commonly tend to occur in the deeper soft tissues of the limbs and the retroperitoneum. The majority of the myxoid, round-cell, and pleomorphic liposarcomas occur in the limbs, and dedifferentiated liposarcomas occur predominantly in the retroperitoneum. Well-differentiated liposarcomas are the most indolent type and rarely metastasize. However, they can progress to dedifferentiated forms, which tend to have a high metastatic potential depending on the extent of dedifferentiation [5].

Primary liposarcoma of the thyroid is an extremely rare tumor with less than 15 reported cases in the English literature thus far. A review of PubMed from 1986 to 2017 yielded only 12 case reports of this pathology (Table 1). Most of the reported cases had myxoid [3, 5, 7] or pleomorphic [4, 5] histology (3 cases each), 2 had well-differentiated [6, 9] histology, and the histologic types in the other 4 cases [1, 2, 8] were not specified.

Similar to other sarcomas, complete surgical excision remains the treatment of choice for these tumors. In the head and neck, the extent of resection is often limited by the close proximity to vital structures, which can result in significant morbidity. Adjuvant radiation therapy is often recommended for high-risk features such as positive surgical margins or high-grade histopathology. Studies have demonstrated the radiosensitivity of liposarcomas with decreased local recurrence rates in patients receiving adjuvant radiation, although they did not find an improvement in overall survival or the rate of distant metastasis

Table 1. Patient and tumor characteristics, initial treatment, clinical course, and outcomes for the cases of primary thyroid liposarcomas reported thus far in the English literature

	Study, year	Sex	Age, years	Histology	Initial treatment	Clinical course and outcome
1	Nielsen et al. [1], 1986	M	NS	NS	Unknown	Unknown
2	Griem et al. [2], 1989	M	23	NS	Surgery alone	Alive and free of disease at 22 months
3	Andrion et al. [3], 1991	F	56	Myxoid liposarcoma	Surgery alone	Died 2 months after surgery
4	Awad et al. [4], 2003	F	50	Pleomorphic liposarcoma	Surgery + adjuvant RT	Stable for 8 months and then relapse with skin, bone, lung, and liver metastases – no response to chemotherapy course – expired 9 months later
5	Awad et al. [4], 2003	M	71	Pleomorphic liposarcoma	Surgery + adjuvant RT	Alive at 6 months with no evidence of cancer
6	Mitra et al. [5], 2004	F	49	Myxoid liposarcoma	Surgery + adjuvant RT	Stable for 7 months and then relapse with subcutaneous scalp, lung, and liver metastases – received 1 cycle of doxorubicin + ifosfamide which was discontinued due to intolerance – expired 10 months later
7	Mitra et al. [5], 2004	M	71	Pleomorphic liposarcoma	Surgery + adjuvant RT	Stable for 11 months and then relapse with pulmonary metastases – treated with 3 cycles of single agent doxorubicin with no response – also developed bone metastases at 14 months – still alive at the time of case report
8	Kilic et al. [6], 2007	M	40	Well-differentiated liposarcoma	Surgery + adjuvant RT	Alive at 2 years
9	Huang et al. [7], 2009	F	59	Myxoid liposarcoma	Surgery alone	Stable for 1 year and then relapse with bone metastases – expired later
10	Kumar et al. [8], 2014	F	72	NS	Surgery + adjuvant RT	Alive at 2 years
11	Kumar et al. [8], 2014	F	65	NS	Surgery + adjuvant RT	Alive at 2 years
12	Guarda et al. [9], 2018	F	82	Well-differentiated liposarcoma	Surgery alone	Alive and free of disease on follow-up

NS, not specified.

[5]. However, it is difficult to draw definitive conclusions on the benefits of adjuvant radiation therapy on local control and survival when these retrospective series had small patient cohorts and an inherent selection bias. This point is well demonstrated in a study by Gritli et al. [12]. This is a retrospective review of 15 cases of head and neck liposarcoma over 32 years, of which there was only 1 case of well-differentiated liposarcoma of the thyroid. Overall, their 5-year survival rate was 87% for patients treated with surgery alone, 75% for patients treated with surgery followed by adjuvant radiotherapy, and 0% for patients treated with radiotherapy alone.

Surgery was the initial treatment modality advocated in all the reported cases [2–9]. Adjuvant radiation therapy was also performed in most cases [4–6, 8] but no clear criteria were applied. Chemotherapy was administered in 3 cases [4, 5] after recurrence, which in all 3 cases was in the form of distant metastatic disease. In 2 of these cases [4, 5], a response to chemotherapy was not seen and in the other case [5] chemotherapy was discontinued due to

intolerance. We have summarized the initial and subsequent treatments used, the clinical courses, and the outcomes for the reported cases in Table 1.

With the current available data, a correlation between the outcomes of the cases to the initial treatments they received cannot be made, since the stage of the initial cancer is not accurately specified for the cases (stage includes the grade for sarcomas). In general, it seems that the tumors did not respond well to conventional chemotherapy used for the treatment of soft tissue sarcomas (doxorubicin with ifosfamide). Recently, eribulin has been approved for the treatment of unresectable or advanced (metastatic) liposarcoma of the extremities or retroperitoneum after progression on an anthracycline-based regimen [13]. This data may be extrapolated for the treatment of liposarcoma of the thyroid, especially since there are no established protocols for the treatment of relapsed/metastatic thyroid liposarcoma at the present time. Admittedly, further substantive investigation will be limited given the rarity of this lesion.

Statement of Ethics

The subject in the case report gave his informed consent. There was no need for institutional review board approval as it is only a case report with a review and did not have a study protocol. No animals were used.

Disclosure Statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

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