

CASE REPORT

Metastatic leiomyosarcoma of the thyroid: A rare entity

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Abstract

Cancer metastasis to the thyroid gland from non-thyroid sites is a rare presentation in clinical practice. The most frequent primary cancers that metastasise to the thyroid are renal cell carcinoma, followed by colorectal, lung and breast. We report a case of a 64-year-old Malay lady who presented with anterior neck swelling 4 years after an initial diagnosis of uterine leiomyosarcoma. She had undergone a hysterectomy procedure four years ago. Fine needle aspiration cytology of the thyroid mass suggested undifferentiated thyroid carcinoma. After multi-disciplinary discussion, the patient underwent thyroidectomy and the final histopathological diagnosis was metastatic leiomyosarcoma of the thyroid. The diagnosis was aided by an immunohistochemistry panel of positive myogenic markers, negative epithelial markers as well as the previous medical history of uterine leiomyosarcoma. Metastatic leiomyosarcoma of the thyroid may mimic primary undifferentiated (anaplastic) thyroid carcinoma (UTC) with a sarcomatoid pattern, medullary thyroid carcinoma (MTC) with spindle cells morphology and spindle cell tumour with thymus-like differentiation (SETTLE). Hence, a multidisciplinary approach must be practised by pathologists, surgeons and radiologists to consider metastatic lesions of the thyroid gland, especially when a previous history of cancer exists or is suspected.

Keywords: Metastatic thyroid cancer, leiomyosarcoma

INTRODUCTION

The classification of the smooth muscle tumours of the thyroid as described by WHO includes leiomyomas and leiomyosarcomas.^{1, 2} Uterine leiomyosarcoma metastatic to the thyroid is an extremely rare disease. Only 6 cases have been reported worldwide.^{2,9,10,11,12,13} It may present as a single or multiple lesions. Positive expression of myogenic markers and negative expression of epithelial markers are very useful in establishing the diagnosis of leiomyosarcoma. Metastatic leiomyosarcoma has to be differentiated from other primary spindle cell tumours of the thyroid. The differential diagnoses of spindle cell tumours of the thyroid include undifferentiated (anaplastic) thyroid carcinoma (UTC) with a sarcomatoid pattern, medullary thyroid carcinoma (MTC) with spindle cells morphology and spindle cell tumour with thymus-like differentiation (SETTLE).¹ Correlation with

clinical history and radiological findings are crucial in establishing the diagnosis of metastatic leiomyosarcoma. The treatment depends on whether the metastasising tumour is widespread or isolated. In the former, the prognosis is poor and the survival rate is dismal.^{2,3}

CASE REPORT

A 63-year-old lady presented with left anterior thyroid swelling for 6 months duration. The swelling was rapidly increasing in size. However, no obstructive symptoms were experienced by the patient. No cervical lymphadenopathy was noted. The patient had a previous history of uterine leiomyosarcoma and had undergone a total abdominal hysterectomy and bilateral salphingoophorectomy (TAHBSO) for the past 4 years. The patient was planned for a course of chemotherapy but then was abandoned due to poor response. Lung metastases was noted

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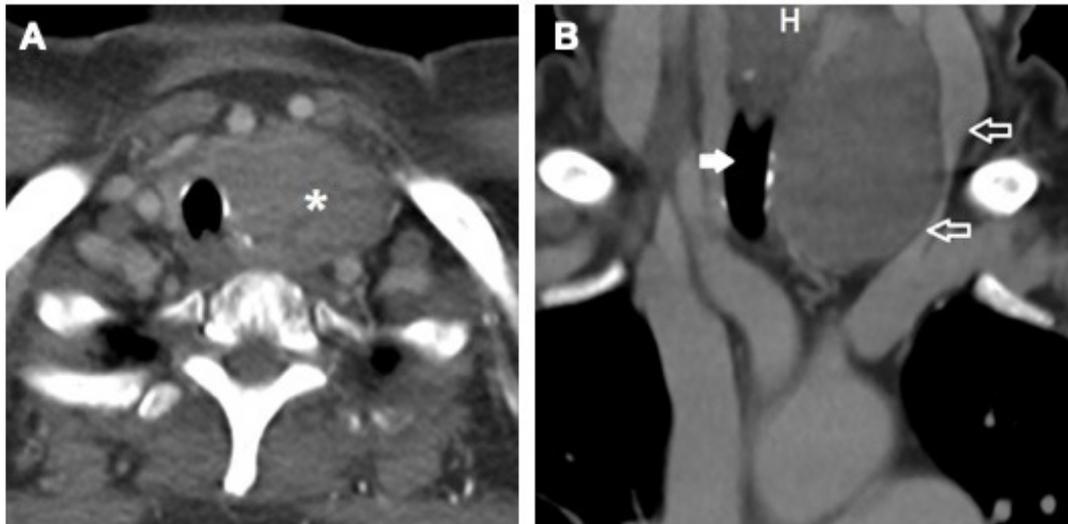


FIG. 1: CT scan. A) axial view shows heterogeneous lesion (*) arising from left thyroid gland with the presence of specks of peripheral calcification. B) coronal view displays the lesion causing displacement of the trachea (arrow) and adjacent left common carotid artery (open arrows).

about a year after the initial diagnosis of uterine leiomyosarcoma followed by thyroid swelling 4 years after that.

The physical examination revealed an enlarged thyroid mass that moves with deglutition but not by tongue protrusion. The mass was soft to firm in consistency. The patient was clinically and biochemically euthyroid. Ultrasound of the neck showed a solitary nodule arising from the left thyroid lobe measuring 6.6cm x 5.7cm x 4.8cm. On CT scan, the lesion showed heterogeneous enhancement post-contrast. The adjacent trachea, left common carotid artery and internal jugular vein were displaced by the tumour (Figure 1). Multiple lungs, bone, left

adrenal gland and liver metastases were also noted. Fine needle aspiration cytology (FNAC) revealed hypercellular pleomorphic spindle cells that suggestive of undifferentiated carcinoma (Figure 2). Subsequently, a total thyroidectomy was done. Postoperatively she was discharged on day 3 with a suppression dose of thyroxine.

The histopathological examination shows a hypercellular spindle cell tumour which composed of moderate to markedly pleomorphic cells arranged in interlacing fascicles with eosinophilic cytoplasm and hyperchromatic nuclei. Mitosis is noted around 10 in 10hpf including the aberrant form. Necrosis is present. The neoplastic cells are positive for

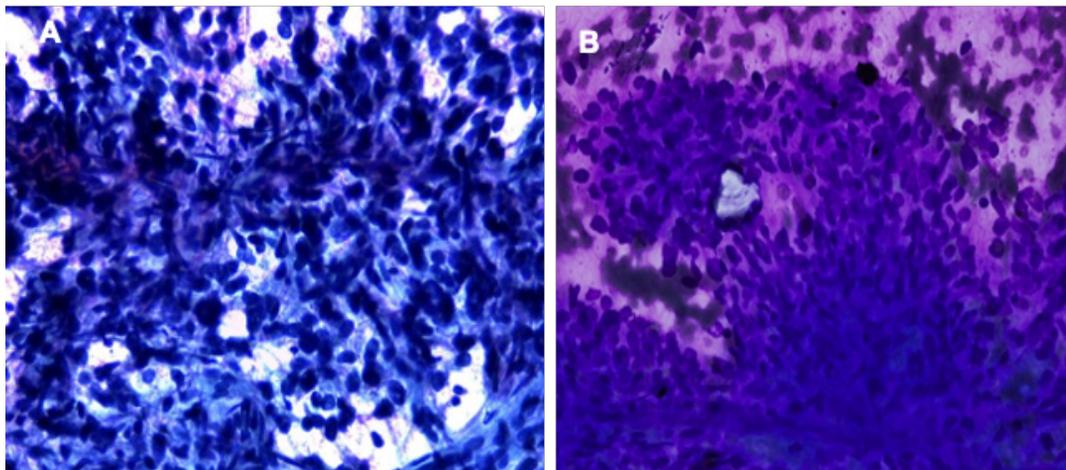


FIG. 2: Fine needle aspiration cytology of the thyroid shows hypercellular smear with clusters of spindle and pleomorphic cells by PAP (A) and MGG (B) stains, respectively. (400x magnification)

smooth muscle actin (SMA), caldesmon and desmin (Figure 3). Occasional positivity of thyroglobulin in native thyroid follicles is seen. The tumour cells are negative for myogenin, S100, calcitonin, synaptophysin, chromogranin CKAE1/AE3, EMA and TTF1. The diagnosis of leiomyosarcoma is made based on morphological

and immunohistochemical findings. However, in view of the previous history of uterine leiomyosarcoma, metastatic leiomyosarcoma of the thyroid was the most possible diagnosis. Postoperatively, the patient was well and currently on replacement thyroxine therapy, calcium supplement and palliative therapy.

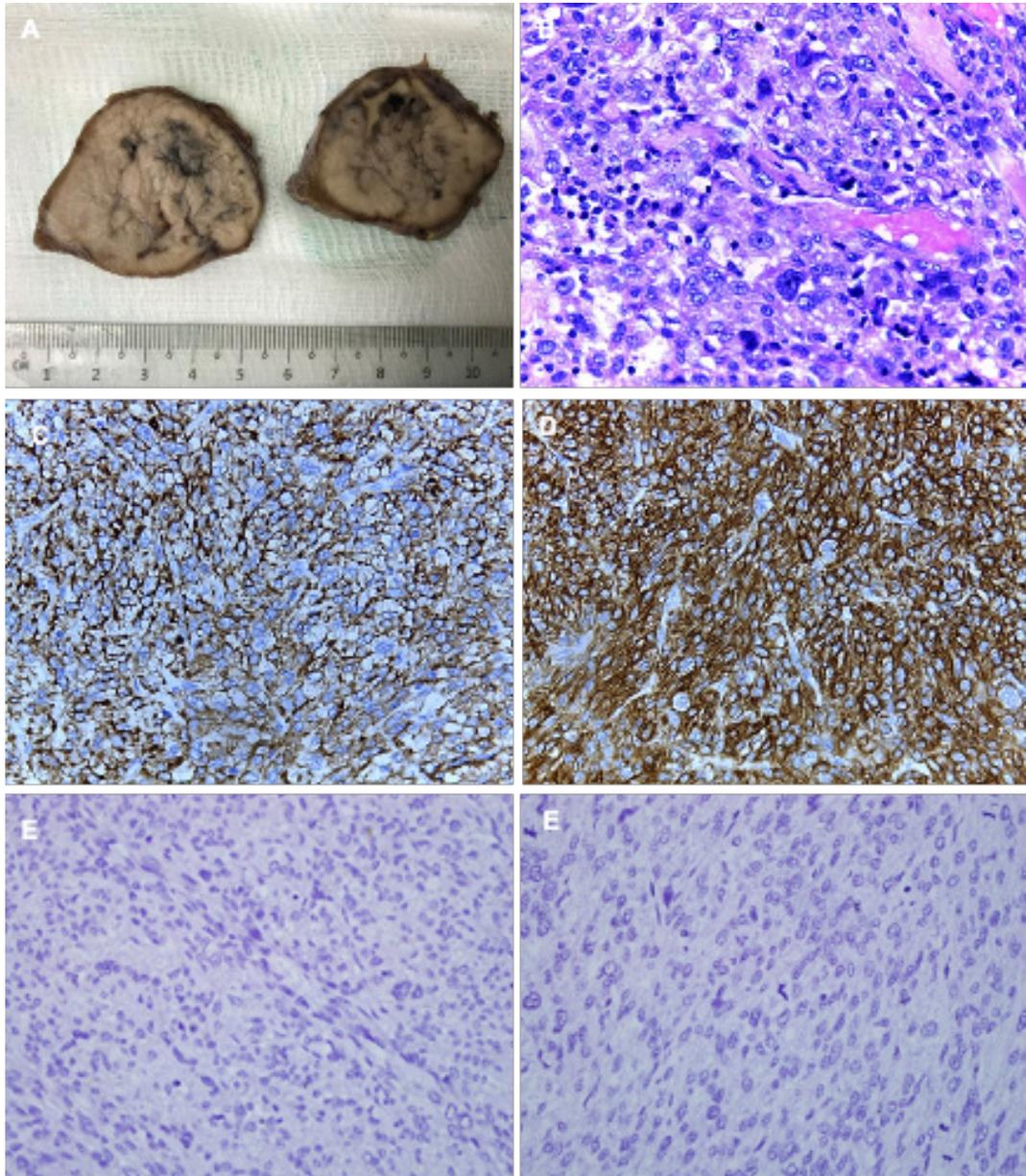


FIG. 3: Histopathological examination of the left thyroid. A) The cut section of the left thyroid lobe revealed a fairly circumscribed whitish tan lesion surrounded by a thin rim of native thyroid parenchyma. The cut surface of the lesion appears whorled with areas of necrosis and haemorrhage. B) Moderate to markedly pleomorphic tumour cells with large, irregular nuclei and coarse chromatin (H&E stain, 400x magnification). C) Diffuse caldesmon positivity of the tumour cells (400x magnification). D) Diffuse SMA positivity of the tumour cells (400x magnification). E) The tumour cells are diffusely negative towards TTF1. F) Tumour cells also negative for calcitonin (400x magnification).

DISCUSSION

The occurrence of tumours metastasising to the thyroid has been reported in less than 0.1% of thyroid malignancies.⁴ Tumours spread to the thyroid gland via direct local extension or haematogenous route. Sarcomas of the uterus are aggressive tumours that have a greater tendency to disseminate through vascular channels. Leiomyosarcoma of the uterus usually spread to the lungs, liver and bones. Though rich in blood supply, the thyroid gland is a rare site for metastasis. This could be explained by the rapid blood flow in the highly vascularised thyroid tissue which prevents the adhesion of tumour cells to the thyroid.⁵ Primary tumours that frequently metastasise to the thyroid include kidney, lung, breast and head & neck tumours.⁶ Metastatic uterine leiomyosarcoma of the thyroid is a very rare entity. Thorough English literature searches using Google scholar showed only 6 cases of metastatic leiomyosarcoma of the thyroid originating from the uterus have been reported.^{2,9-13}

The clinical presentation of metastatic lesions is more or less similar to primary thyroid tumours.⁵ The patient usually comes with a thyroid mass and may be accompanied by compressive symptoms. Other features include hoarseness of voice, dysphagia, dyspnoea and loss of weight loss. A rapidly growing thyroid mass with obstructive symptoms is more suggestive of anaplastic thyroid carcinoma rather than metastatic leiomyosarcoma of the thyroid.² However, the sudden appearance of a thyroid mass after the diagnosis of a primary tumour most likely indicates the secondary involvement of the thyroid.⁶

Radiologically, there are no specific sonographic findings for a metastatic thyroid nodule. However, multiple thyroid nodules without evidence of microcalcification may be suggestive of a metastatic nodule.⁷ There are reported cases of metastatic thyroid nodule from uterine leiomyosarcoma showing hypoechoic solid nodules on ultrasound and infiltrative features in CT scan.^{2,8} These metastatic thyroid nodules also showed increased 18F-FDG uptakes in PET/CT scanning which can be useful in assessing a patient who is being considered for surgical intervention.⁸

Undifferentiated (anaplastic) thyroid carcinoma (UTC) with a sarcomatoid pattern, medullary thyroid carcinoma (MTC) with spindle cells morphology and spindle cell tumour with thymus-like differentiation (SETTLE) need to be

excluded in order to diagnose leiomyosarcoma of the thyroid as in our present case.¹ Therefore, a panel of immunohistochemistry plays a major role in establishing the diagnosis. Anaplastic thyroid carcinoma is not immunoreactive for TTF1 and thyroglobulin. Immunopositivity of CKAE1/AE3 and EMA with immunonegativity of myogenic markers such as SMA and caldesmon are suggestive of undifferentiated (anaplastic) thyroid carcinoma.³ Spindle cells medullary carcinoma of the thyroid usually show strong positivity towards calcitonin, chromogranin, synaptophysin and CEA but negative for myogenic markers. SETTLE differs from leiomyosarcoma in the term of its lobulated appearance and biphasic pattern of the tumour.³ CKAE1/AE3 & CK7 are strongly positive for both components glandular and mesenchymal elements. On rare occasions, myoepithelial marker positivity is expressed by the spindle cell component of the tumour. Thus, high mitotic activity with more marked nuclear hyperchromasia and cellular pleomorphism are in favour of leiomyosarcoma rather than SETTLE.⁴

Preoperative diagnosis of leiomyosarcoma of the thyroid is challenging.³ The origin of the tumour should be determined whether it is a primary lesion arising from the thyroid, non-thyroid cervical region leiomyosarcoma or metastasis from the soft tissue, pelvic organs or any other distant sites. A multidisciplinary approach consisting of surgeons, radiologists and pathologists working as a team is very effective for establishing the diagnosis.^{1,3} Relevant clinical and past medical history of the patient provided by primary care physician in collaborating with radiological findings are very valuable information for helping pathologist to come to the final diagnosis. This information can be obtained via multidisciplinary discussion among the experts.

Selection of the treatment for metastatic thyroid lesions can be surgical or non-surgical depending on the individual case. In the majority of cases, palliative care is the choice of treatment.⁵ Total thyroidectomy or lobectomy is aimed for local disease control and long term cure in selected patients.^{5,6} The choices between surgical treatment and palliative care in thyroid metastasize depends on patient fitness¹ and comorbidity² and the likelihood of the success of surgical treatment.⁵ In indolent primary malignancy and isolated thyroid metastasise in otherwise fit patient, surgical treatment is the treatment of choice to improve symptoms and

aim for long term cure.⁵ The mean survival in a patient treated non-surgically is lower than the patient treated with thyroidectomy with and without adjuvant therapy.^{5,6} As reported by Nakhjavani *et al.*, 1997, a patient who underwent thyroidectomy or thyroidectomy with adjuvant therapy has 34 months of mean survival as compared to 25 months of mean survival in patient who not underwent a surgical treatment. The surgical treatment in selected cases will prolong the survival rate of the patient. As lymph node involvement is rare in secondary thyroid carcinoma, neck dissection is not recommended.⁵

The diagnosis of metastatic leiomyosarcoma of the thyroid is a challenge due to its rarity. Correlation with clinico-radiological findings and a multidisciplinary approach are needed in complimentary to histopathological diagnosis. Though the treatment is mainly palliative, early detection with surgical thyroidectomy promises an increased survival time in this group of patients.

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Conflict of interest: The authors declare no conflict of interest.

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