



Case report

Primary synovial sarcoma of thyroid gland: A case report and review of literature

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ARTICLE INFO

Keywords:

Synovial cell sarcoma
Thyroid gland
Case report

ABSTRACT

Introduction and importance: Synovial cell sarcoma (SS) is an extremely rare mesenchymal malignancy, representing nearly 10% of all soft-tissue sarcomas. These high-grade soft tissue sarcomas commonly arise in the para-articular regions of lower extremities. However, 15% of Synovial sarcomas has been described at Unusual locations, including head, neck, and trunk. Herein, we describe the twelfth case of primary synovial cell sarcoma of thyroid with a literature review.

Case presentation: A 43-year-old woman presented with complaint of a progressive neck mass for the last five-months. She developed with dysphagia and dyspnea nearly 2 months prior, without signs of hoarseness, and weight loss. Ultrasonography in which revealed a heterogeneous, hypervascularized thyroid mass. After total thyroidectomy immunohistochemistry was in favor of primary synovial cell sarcoma of thyroid. The diagnosis was confirmed via Molecular genetic analysis of the SYT-SSX fusion gene transcript using the RT- polymerase chain reaction method. Clinical Discussion: Primary thyroid SVS is an extremely rare malignancy with poor biological behavior. SVS has been known for its tendency to local and distal re-occurrence after a few years of treatment. SS can be classified into two subtypes of monophasic or biphasic based on the presence of mesenchymal and/or epithelial components. Accordingly, the most accurate diagnostic tool for SS is considered to be molecular genetic analysis for SYT/SSX fusion transcript.

Conclusion: Herein, we reported an extremely rare case of SVS of thyroid gland. These high-grade soft tissue sarcomas mainly present with an asymptomatic rapid growing neck mass. Unspecific clinical presentations and extreme rarity of this disorder, make the diagnosis of thyroid SVS very challenging. Due to paucity of data, there is not enough evidence to establish a reliable mortality rate. However, the prognosis of thyroid SVS seems unfavorable.

1. Introduction

Synovial cell sarcoma (SS) is an extremely rare mesenchymal malignancy, representing nearly 10% of all soft-tissue sarcomas [1]. These high-grade soft tissue sarcomas commonly arise in the para-articular regions of lower extremities. However, 15% of Synovial sarcomas has been

described at Unusual locations, including head, neck, and trunk [2]. Accordingly, almost all Synovial sarcomas have been associated with specific chromosomal changes [$t(X; 18)$ (p11.2; q11.2)] leading to expression of a chimeric (SYT-SSX) gene transcript [3]. Primary synovial

cell sarcoma of thyroid is exceedingly rare. To our knowledge, only 11 cases have been reported in the English literature [1,4–13]. Herein, we describe the twelfth case of primary synovial cell sarcoma of thyroid with a literature review. This study was reported in line with the SCARE criteria [14].

2. Case presentation

A 43-year-old woman presented with complaint of dysphagia and dyspnea 7 months prior to her admission. In the last five months, she started to have a progressive neck mass, without signs of hoarseness, and

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<https://doi.org/10.1016/j.ijscr.2021.106245>

Received 13 May 2021; Received in revised form 16 July 2021; Accepted 24 July 2021

Available online 26 July 2021

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weight loss. She was previous case of hypothyroidism, on levothyroxine. Family history revealed diffused goiter in her aunt and first cousin. On examination, there was a firm, non-tender, macronodular, fixed midline mass measuring 10x7cm in diameter without signs of lymph node enlargement (Fig. 1). Routine laboratory studies, including thyroid function tests were unremarkable.

She underwent cricothyroid ultrasonography in which revealed heterogeneous, hypervascularized and mixed (solid and liquid) thyroid mass. There was a 93x46x15mm hypoechoic nodule in lower part of left thyroid gland, suggestive for primary thyroid mass. There were multiple hypoechoic nodules in the right lobe, largest being 34x28 mm in diameter. There was no sign of cervical lymphadenopathy. Furthermore, cervical CT scan with IV contrast revealed a heterogeneous thyroid mass with a 90 * 45 * 65 mm thyroid nodule with internal necrotic view. Accordingly, there were no signs of tumor invasion to larynx, trachea, esophagus, carotid arteries, jugular veins, and cervical spines. The fine needle aspiration (FNA) cytology was in favor of undifferentiated cell carcinoma of thyroid gland. Due to high suspicions for thyroid malignancy, the patient was scheduled for total thyroidectomy. Prior to her surgery, the patient underwent Thoracoabdominal CT scan which showed no signs of distant metastasis (Fig. 2).

3. Treatment

Pre-operative management was considered. Total thyroidectomy was conducted under general anesthesia with the purpose of complete resection of the tumor and involved lymph nodes. There was an encapsulated mass about 100 * 80 * 40 mm diameter. When trying for total excision, the capsule was ruptured and multiple segments of necrotic mass were taken out. No lymphadenopathy or distant metastasis was present. The cut surface showed a creamy, and elastic solid mass with storiform pattern. On microscopy, the tumor was consisted of fascicles and sheets of monophasic spindle cell growth pattern with oval nuclei (Fig. 3). Subsequent immunohistochemistry showed immunoreactivity for EMA, cytokeratin (CK 7, CK 19), BCL-2, and TLE1. However,

tumor cells were negative for S-100, CD99, CD-31 and CD-34 with KI-67 index of 5% (Fig. 4). The diagnosis was confirmed via Molecular genetic analysis of the SYT-SSX fusion gene transcript using the RT- polymerase chain reaction method.

4. Outcome and follow-up

The post-operative course was uneventful without any signs of short-time complications. Patient was started on 6 cycles of doxorubicin and ifosfamide and radiotherapy. She was discharged 6 days following her procedure without any discomfort. The patient was scheduled for monthly cricothyroid ultrasonography, and Contrast-enhanced computed tomography (CT) of thoracic and abdominal every 3 months for evaluation of distant metastasis. Fortunately, the patient showed no signs of local or distant metastasis during her monthly follow-up visits.

5. Discussion

Thyroid sarcoma, a pluripotential mesenchymal neoplasia, is generally a high-grade aggressive tumor [1]. Primary thyroid SVS is an extremely rare malignancy with poor biological behavior. That said, SVS has been known for its tendency to local and distal re-occurrence after a few years of treatment [12]. Prior to 1940, most cases of thyroid anaplastic carcinomas were in fact mistakenly labeled as synovial sarcoma [11]. To best of our knowledge, only 12 cases of primary thyroid synovial sarcomas (including the present case) have been reported in English literature (Table 1). SS typically affect patients during adolescence and adulthood. However, in SVS of thyroid gland the mean age at the time of diagnosis was 39.7 (range 15–72). Accordingly, men are more affected than females with a 2:1 sex ratio.

The most common clinical finding of SVS is an asymptomatic rapid growing neck mass, mimicking anaplastic thyroid carcinoma. Other manifestations include Excessive salivation, hoarseness, dysphagia, and dysphonia which is mostly associated with compression effects by the rapidly growing tumor. Unspecific clinical presentations and extreme



Fig. 1. Diffuse thyroid enlargement seen in the patient.

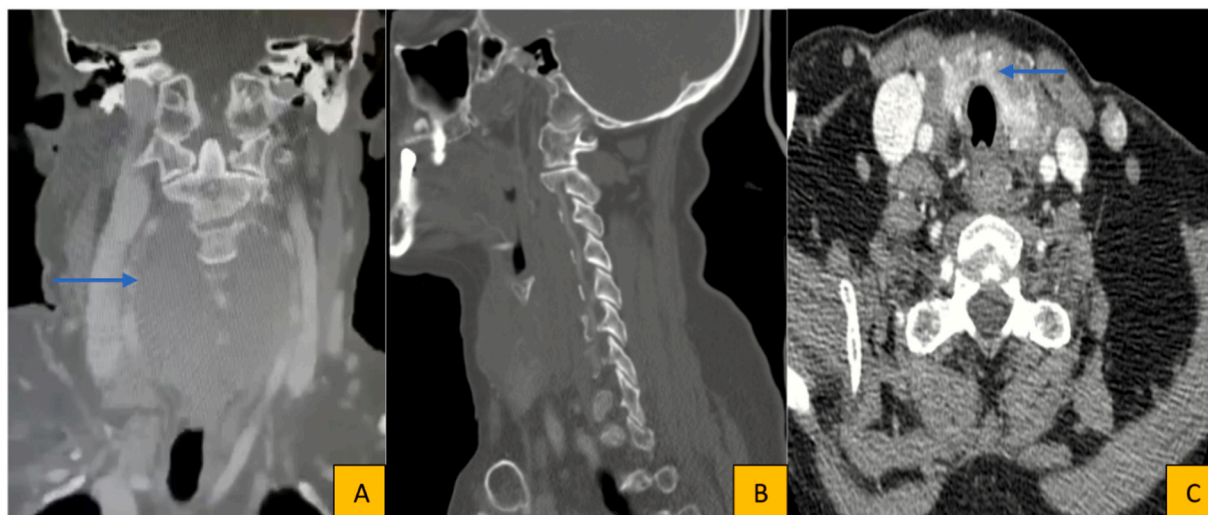


Fig. 2. Cervical CT scan with IV contrast. Blue arrows outline thyroid mass without signs of invasion to surrounding structures.

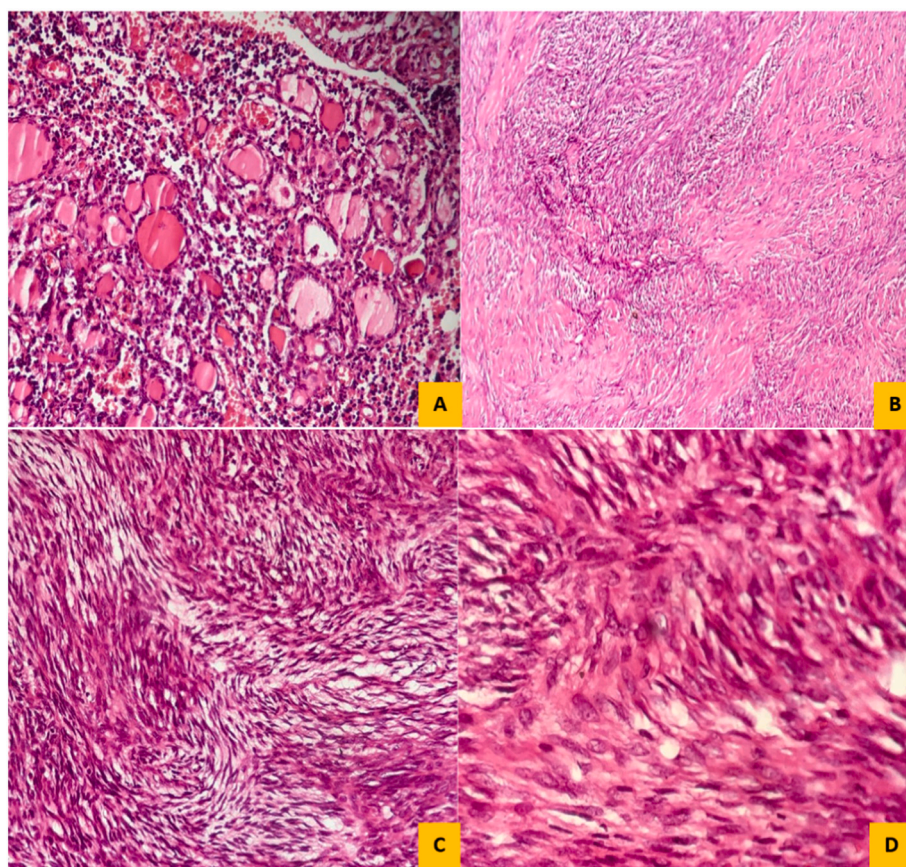


Fig. 3. Histologic evaluation with H&E staining of the thyroid specimen revealed spindle cells with fibrotic-like appearance and focally whorled pattern.

rarity of this disorder, make the diagnosis of thyroid SVS very challenging. Imaging studies including ultrasound, magnetic resonance imaging (MRI), and CT scan of the neck could be used to assess the location, size, vascularization, and local invasion of primary tumor to surrounding structures. However, radiologic evaluations fall short in differentiation of SVS from other thyroid malignancies. Pre-operative Fine needle aspiration (FNA) is not a reliable diagnostic tool, and it could be misleading. In fact, three cases of SVS were misdiagnosed as medullary, follicular, and papillary thyroid carcinoma by FNA (Table 1).

Histologic, Immunohistochemistry (IHC), and molecular analyses are considered as the cornerstone of SVS recognition. Histomorphologically, SS can be classified into two subtypes of monophasic or biphasic based on the presence of mesenchymal and/or epithelial components. Biphasic SS, consisted of both spindle and epithelioid cells, is considered to be more common ($n = 8$, 66.6%) and is diagnostically less challenging especially in common locations [11]. The monophasic subtype on the other hand, is mainly composed of spindle cells, in which accurate diagnosis is extremely challenging. Common differentials of monophasic

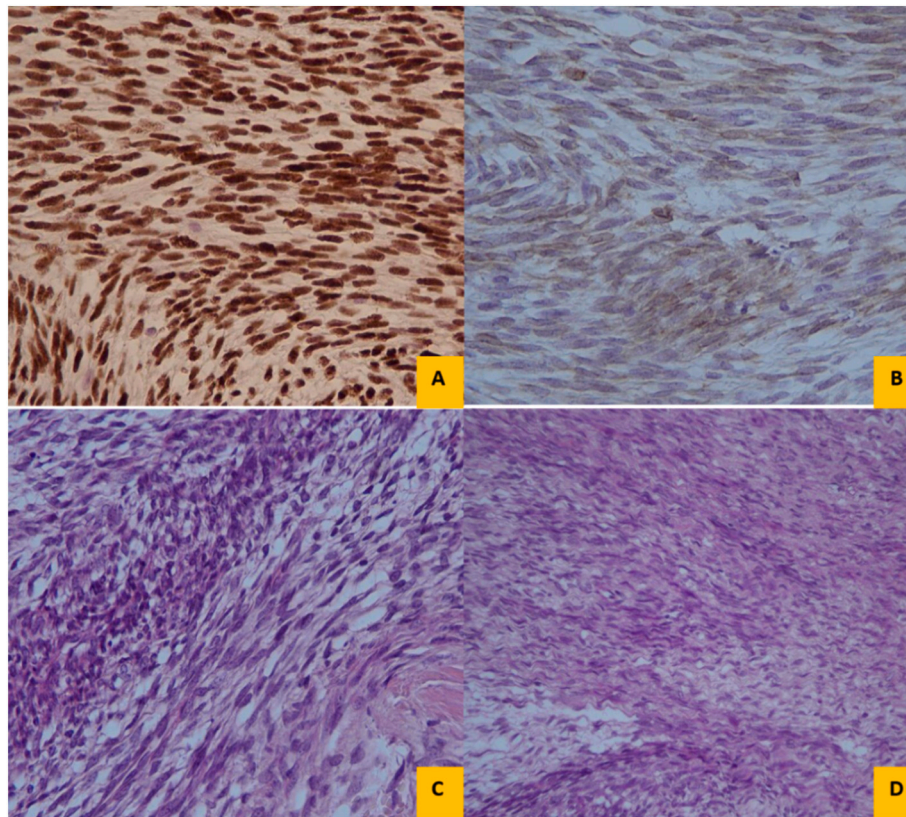


Fig. 4. Immunohistochemistry showed immunoreactivity for TLE1 (A), BCL-2 (B), and EMA (C, D).

Table 1

Review of literature (12 Cases of thyroid synovial sarcoma).

Study	Sex/age	Initial clinical symptoms	Preoperative diagnosis by FNAB	Initial treatment	Mono- or biphasic	Relapse (month after surgery)	Last follow-up (month after surgery)
Roth [1]	M/15	Excessive salivation/otalgia	No	Total thyroidectomy and cobalt therapy	Biphasic	Not mentioned	Not mentioned
Kikuchi [2]	M/60	Hoarseness/palpable mass	Yes/MTC (medullary thyroid carcinoma)	Total thyroidectomy neck dissection partial resection of thyroid and cricoid cartilages	Biphasic	Local, lung (18 Months)	Dead of disease (36 months)
Jang [3]	M/15	Palpable mass	Yes/FL (follicular lesion)	Total thyroidectomy, left Neck dissection	Biphasic	not mentioned	Not mentioned
Ryu [4]	F/72	Dysphagia/hoarseness/palpable mass	Yes/CC (cystic change)	Thyroidectomy, tracheal fenestration	Monophasic	Local, lung (0.5 months)	Dead of unknown cause (3 months)
Ghafouri [5]	F/44	Rapidly growing mass	No	Total Thyroidectomy with Incomplete excision	Monophasic	Not mentioned	Not mentioned
Boudin [6]	M/55	Rapidly growing mass	No	Thyroidectomy with, Incomplete excision, CRT	Monophasic	Local/0.5 months Surgery and RT	Alive without disease (10 months)
Bansal [7]	F/28	Rapidly growing mass/dysphagia/weight loss	No	Total thyroidectomy	Biphasic	Not mentioned	Not mentioned
Murro [8]	M/41	Dysphonia/left neck mass	No	Total thyroidectomy, laryngopharyngo-esophagectomy	Biphasic	Not mentioned	Not mentioned
Shi [9]	M/31	Asymptomatic mass	No	Total Thyroidectomy with Incomplete excision	Biphasic	Upper neck cervical lymph nodes (chemoradiation and re-excision)	Alive without disease (36 months)
Zahran [10]	M/47	Rapidly growing mass	No	Total thyroidectomy	Biphasic	Not mentioned	Alive without disease (12 months)
Dilamer [11]	M/26	Neck mass	Yes (papillary carcinoma)	Total thyroidectomy	Biphasic	Local recurrence (chemo immunotherapy)	Dead of disease (41 months)
Our case	F/43	Dysphagia/neck mass	Yes	Total thyroidectomy	Monophasic	Not mentioned	Alive without disease (6 months)

SS being other spindle cell sarcomas, including leiomyosarcoma, rhabdomyosarcoma, fibrosarcoma, malignant peripheral nerve sheath tumor (MPNST), and spindle epithelial tumor with thymus-like differentiation (SETTLE) [15,16]. Immunohistochemically, SS typically is positive for epithelial markers including EMA, cytokeratin (CK 7, CK 19), and also the tumors react positively to vimentin, CD 99, and bcl-2 which help distinguish them from other types of sarcomas. However, IHC may yield conflicting results since there have been reports of epithelial cell markers expression in anaplastic cell carcinoma, MPNST, and carcinosarcoma [11,15].

Accordingly, the most accurate diagnostic tool for SS is considered to be molecular genetic analysis for SYT/SSX fusion transcript. In almost all cases of SS, this chromosomal translocation [t(X; 18) (p11.2; q11.2)] could be detected using frozen or paraffin embedded tissues via real-time reverse transcriptase polymerase chain reaction (RT-PCR) or FISH [1].

Due to rarity of the disease, there is very limited data on the optimal treatment. Since synovial cell sarcomas are considered as highly aggressive and infiltrative tumors, wide excision surgical removal with tumor-free margins is suggested. However, wide margin-free surgical resection cannot always accomplish because of the large tumor size and the proximity to vital structures in the head and neck region. In all 12 cases of SS, total thyroidectomy was the initial treatment option, in which in four patients was the only therapeutic approach (including ours) [7,10,11] with two patients underwent cervical lymph node dissection. That said, lymph node dissection is not generally recommended for management of sarcomas, except when nodal involvement is suspected. As usual for sarcomas, chemoradiotherapy is generally recommended given their invasive nature, and high risk of local and distant metastasis. Adjuvant chemotherapy with ifosfomide may be considered which can lead to cancer stabilization and lower chance of recurrence [1,17].

Due to paucity of data, there is not enough evidence to establish a reliable mortality rate. To best of our knowledge, 3/12 patients passed away and all three had local or distant metastasis. The most common location for distant metastasis was the lungs and local recurrence was reported in two patients. Overall, the prognosis of thyroid SVS seems unfavorable with tumor size, location and radicalness of surgical resection being the most probable prognostic values.

6. Conclusion

Herein, we reported an extremely rare case of SVS of thyroid gland. These high-grade soft tissue sarcomas mainly present with an asymptomatic rapid growing neck mass. Unspecific clinical presentations and extreme rarity of this disorder, make the diagnosis of thyroid SVS very challenging. Due to paucity of data, there is not enough evidence to establish a reliable mortality rate. However, the prognosis of thyroid SVS seems unfavorable.

Ethics approval and consent to participate

The purpose of this research was completely explained to the patient, and was assured that their information will be kept confidential by the researchers. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal. The present study was approved by the medical ethics committee of the academy.

Source of funding

No funding was obtained for this study.

CRedit authorship contribution statement

SS and M.SH – drafted the manuscript and provided images and histologic evaluations. MS and OO- helped with the draft and reviewed the literature. RS – Supervisor (corresponding author), provided initial feedback and reviewed the final manuscript. The authors read and approved the final manuscript.

Guarantor

Ramin Shekouhi

Research registration

Not applicable.

Patient's perspective

The patient satisfied and was comfortable one month after the operation.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

Not applicable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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