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Case report

Head and neck synovial sarcoma in a woman with previous lymphoma and papillary thyroid carcinoma

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Summary
Synovial sarcoma is a rare malignant mesenchymal neoplasm that rarely arises in the head and neck and thyroid lodge. Researchers have documented only few cases in the literature. We present the case of a young woman diagnosed with synovial sarcoma that originated in the thyroid region one year after a total thyroidectomy for a primary papillary carcinoma and eight years after chemo-radiotherapy for a lymphoma.

Key words: head and neck tumor, synovial sarcoma, thyroid tumor, Hodgkin lymphoma, breast cancer

Background

Synovial sarcoma (SS), described for the first time by Jernstrom in 1954, is a malignant mesenchymal neoplasm. It is rarely observed in the head and neck region[1,2], and exhibits varying degrees of epithelial and mesenchymal differentiation, with biphasic and monophasic types as common variants. Most (70%) originate in the deep soft tissues of the lower and upper limbs, often near the joints. About 15% originate in the trunk, while only 5-7% originate in the head and neck area. The characteristic t(X;18)(p11.2;q11.2) translocation results in the transcription of the SYT-SSX fusion gene, which defines synovial sarcoma[1,3].
The average age for a synovial sarcoma diagnosis is typically in the late thirties[3].
Herein, we present the case of a synovial sarcoma located in the thyroid region in a young woman with previous chemo-radiotherapy treatment for Hodgkin lymphoma and multifocal papillary microcarcinoma of the thyroid. During follow-up, she also developed breast cancer.

Case presentation

A 36-year-old woman who underwent chemo-radiotherapy in 2008 for Hodgkin Lymphoma of the mediastinum and neck, and total thyroidectomy in early 2015 for three papillary carcinoma, follicular variant was referred to our center in 2016 for sudden and worsening dysphonia and dysphagia over several weeks. Magnetic resonance imaging (MRI) re-

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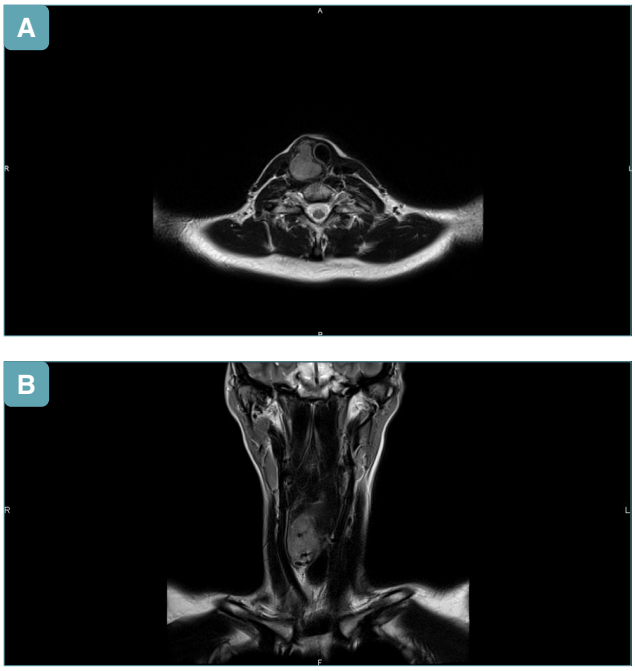

Figure 1. (A-B) The preoperative RMN shows a nodule on the right side of the thyroid "bed", close to the esophagus and cricoid cartilage, without any obvious involvement.

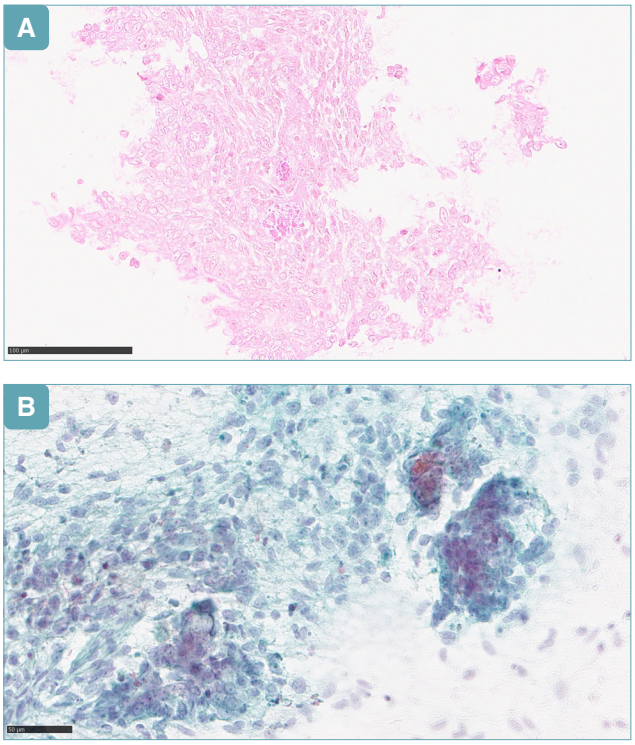

Figure 2. The cytological morphology assessed by a H&E staining (A) and PAP staining (B), shows the unusual architectural and cytological features due to spindle and epithelioid cells. The cells are characterized by fine nuclear chromatin and barely evaluable nulceoli, with fusate and epithelioid morphology and scarce clear cytoplasm.

vealed a 2.8x4.4 cm lesion in the right thyroid side, described as suspected pathological tissue. The lesion displaced the trachea and the esophagus to the left, being near the esophageal wall and the post-cricoid hypopharynx. No clear signs of cricoid cartilage infiltration were observed, and no nodal metastases were present after RMI and US exam (Fig. 1A-B). Total body imaging studies, including total body computed tomography (CT) and positron emission tomography (PET), did not detect any distant metastases.

A preoperative fine-needle aspiration identified malignant epithelioid cancer cells with a solid and papillary architecture interspersed with spindle cells. Necrosis was observed in some areas. The cells showed papillary fronds, overlapping nuclei, more regular nuclear border, sometimes with clear appearance, and clearly distinguishable nucleoli (Fig. 2 A-B). No other classic cytological changes typical of true papillary carcinoma were observed. The spindle cells were atypical, more regular in morphology than epithelioid cells, and did not stain with keratin. Immunostaining for keratin AE1-AE3 showed strong immunoreactivity in the papillary component.

In October 2016, at our hospital, the patient underwent total laryngectomy due to cricoid cartilage involvement which needed a complete laryngeal resection, while the esophageal adventitia could be easily detached from the tumor.

Grossly, the tumor infiltrated the cricoid perichondrium and skeletal musculature "ab extrinsic".

The histology revealed a neoplasm with two distinct cellular components, a predominant epitheiolid component, characterized by cuboidal-columnar cells and pluristratified epithelium admixed with a spindle cell component (Fig. 3 A,B). The epithelioid cells displayed architectural features resembling papillary carcinoma of the thyroid, featuring clear nuclei, irregular nuclear borders, nuclear overlapping without pseudo inclusions, and occasional clear cell changes devoid of mucin. In contrast, the spindle cells were overtly atypical, displaying mitosis with a fascicular pattern of growth (Fig. 3 B). The neoplasm showed extensive areas of necrosis (in approximately 65% of the tumor) and increased mitotic activity in both components (> 10 mitoses in 10 high-power fields at 40x magnification) (Fig. 3 C). These findings suggested a malignant high-grade tumor. The biphasic pattern ruled out

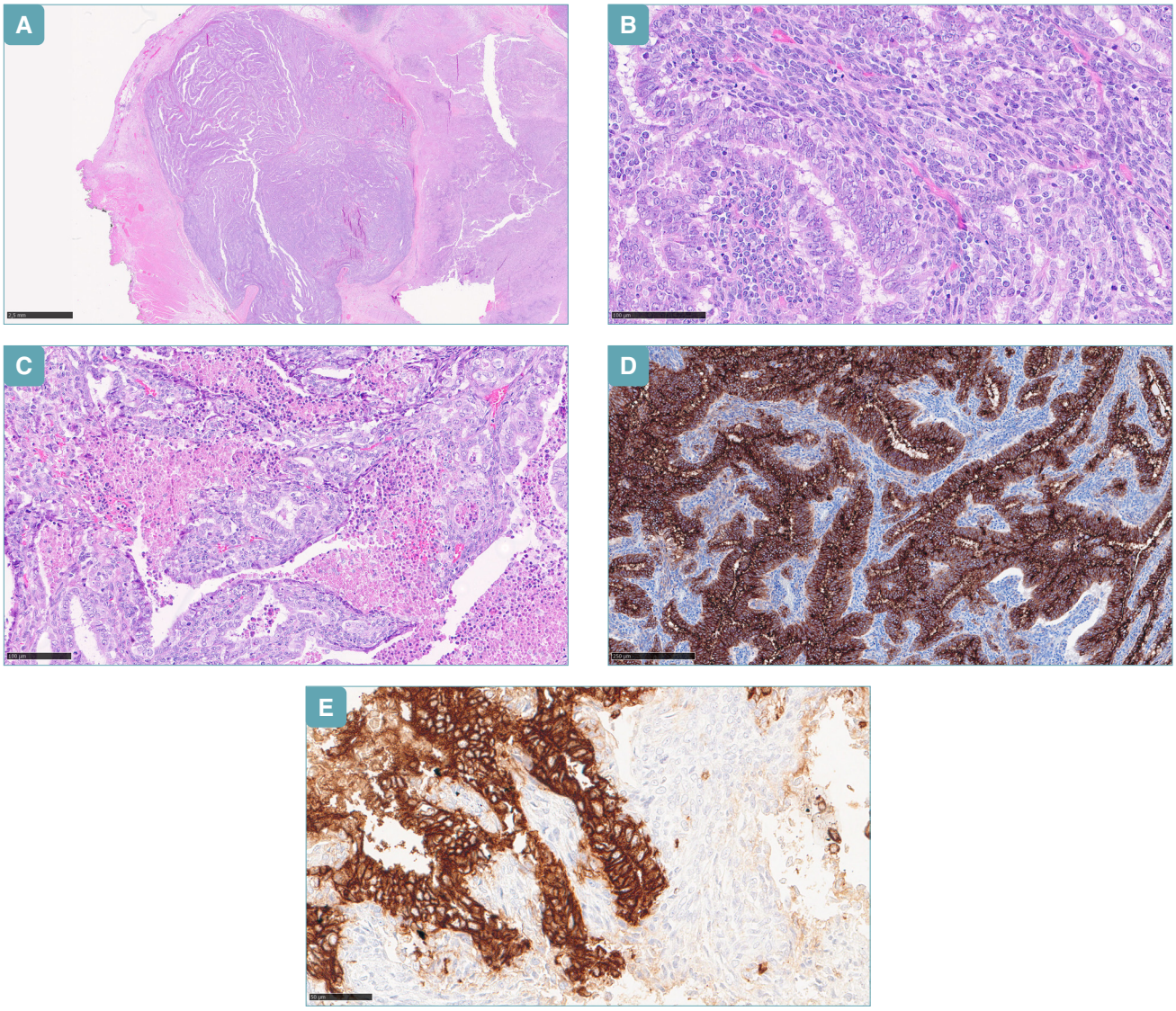

Figure 3. The H&E stain of the neoplasm of a low magnification that showed a nodular growth and a papillary pattern (A); the tumor-shows the typical morphology of biphasic synovial sarcoma, with papillary fronds, necrosis and atypical mitosis easily assessed in both components. (B,C); EMA staining the epithelial component in histology (D) and keratin staining the epithelial component in cytology (E); the epithelial component heavily stained, whereas the spindle component was negative.

a high-grade primary thyroid tumor, such as papillary carcinoma, and was indicative of synovial sarcoma (SS). Immunohistochemical staining (IHC) showed reactivity for EMA and keratin AE1-AE3, while both neoplastic components were negative for TTF1 and thyroglobulin (Fig. 3 D,E). FISH revealed a rearrangement of 18q11 (SS18) involving both the epithelial and spindle components in more than 15% of neoplastic cells (Fig. 4). Following a thorough evaluation of the morphology, along with the SS rearrangement, a diagnosis of biphasic synovial sarcoma was confirmed, with involvement of the perichondrium of the cricoid cartilage and the skeletal musculature.

Following the surgery, adjuvant therapy with chemotherapy (ifosfamide 9 g/m^2 plus EpiAdriamicin 120 mg/m^2) began from May 12, 2016, to January 20, 2017, for three cycles, last cycle with low dose due to medullary toxicity, associated with IMRT radiotherapy 54 Gy for 30 fraction (1.8 Gy/Day) for a total of 43 days.

In February 2017, during a routine post-surgery exam-

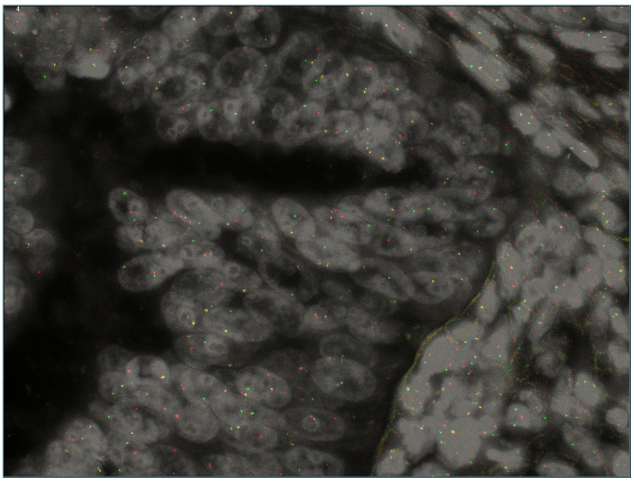

Figure 4. FISH analysis for a SYT-SSX shows a single yellow signal and a red and green split signal due to a rearrangement. The translocation was observed in the epithelial (left) and mesenchymal (right) components of the image.

ination, tumoral relapse was detected in the subcutaneous tissue near the radiotherapy field. The relapse was promptly treated with surgery.

Subsequent follow-ups remained uneventful until February 2022 when the woman underwent a right mastectomy with axillary sentinel lymph node resection. The diagnosis revealed an invasive ductal carcinoma of the breast no special type (NST).

The tumor showed the following biological parameters: ER > 95%; PgR > 95%; Ki-67 15% and Her-2/Neu 1+ (20% of neoplastic cell).

The patients had undergone genetic counseling at our institute due to numerous tumors, with the suspicion of Li-Fraumeni syndrome. TP53 analysis did not show any genetic alterations that could explain these tumors.

To date, after the last oncological treatment for breast cancer, the patient has not experienced any other tumoral relapses up to end of January 2025.

Discussion

This case presents several noteworthy discussion points.

Cytology revealed the biphasic composition of the neoplasm, with two distinct cell populations: an epithelioid population positive for keratins, and a spindled population negative for keratins. The cytological aspects, the presence of necrosis and a papillary arrangement without clear aspects referable to primary papillary carcinoma of the thyroid oriented lead to a diagnosis of malignant neoplasm, to be defined after surgical resection.

The differential diagnosis was challenging. This tumor showed two distinct patterns, epithelioid and spindled, which are highly unusual for a relapse or metastasis of a thyroid tumor. Typically, papillary thyroid carcinoma may exhibit various patterns, such as Warthin-like and sclerosing patterns, but none with overtly stromal malignant features. Necrosis is generally observed only in high-grade primary thyroid carcinomas, such as the insular type. Other head and neck primary tumors sharing similar architectural and cytological features, particularly CASTLE, SETTLE and CEFTE tumors, were considered [4,5,6].

Thyroid carcinoma with thymus-like features (CASTLE) is exceedingly rare, accounting for only 0.1-0.15% of cases, displays histological features overlapping with those of thymic tissue and exhibits positive staining for CD5, p63, and keratin in immunohistochemical analyses[5]. However, in this case in the CASTLE tumor, TTF1 and the rearrangement of SS18 were negative, which proved helpful in distinguishing it from the synovial sarcoma. CASTLE tumors generally have an indolent behavior, and their management requires careful coordination within a multidisciplinary team[5].

SETTLE is a rare tumor that exhibits a lobulated architecture with epithelioid cells producing mucin intermingled with spindle cells. While SS shares some morphology overlap with SETTLE, it lacks mucinous cells from a morphological standpoint. Spindle epithelial tumor with thymus-like differentiation (SETTLE) is reported in young individuals and demonstrates notable immunohistochemical staining similarities with our case. The key in differential diagnosis lie in synovial sarcoma, which exhibit rearrangement for t(X,18)[1,3,7].

Another rare entity is carcinoma of the thyroid with Ewing family tumor elements (CEFTE). This tumor, also found in young individuals, displays a biphasic pattern and an adamantinoma-like feature with a favorable prognosis. This tumor shows a rearrangement of EWING sarcoma gene and lack of SS18 rearrangement[7].

Another consideration is the likelihood that this woman had previously developed lymphoma, thyroid cancer and breast carcinoma. This is an extremely rare occurrence in a normal person, even a young person with no particular genetic alterations. The connection between these occurrences is challenging.

It is well known that patients treated at a young age for Hodgkin lymphoma have an increased risk of developing malignant tumors, including thyroid tumors, sarcomas, and breast tumors [7].

Andrea K Ng et al. have shown a high relative risk

(RR) for the development of other neoplasms following therapy for Hodgkin lymphomas, with RR reported to be 5.6 for thyroid tumors, 26.6 for sarcomas, and 6.7 for breast carcinomas[8]. The carcinogenic role of radiotherapy is well recognized, particularly for papillary thyroid carcinomas and SS[8,9].

The prognosis of this tumor is poor. From a paper by William J. Harb, the head and neck SS was reported in < 5% of all sarcomas of the head and neck area. Prognosis is better when surgery is combined with RT or CT, with multimodality treatment, as done in our case [10].

Other morphological parameters are used to know the "aggressiveness" of the tumor like maximum diameter, location, age, organs involved and other histological parameters like extensive necrosis, vascular invasion and number of mitosis. Therefore, the recurrence is ~45%, while the range of survival is 23% to 45% at 5 years and at 10 years ranges from 23.2% to 30% [11]. However, these data are related to the therapy used to treat the tumor, surgical only or a multimodality treatment using RT and CT. This last approach gives a better chance of survival. However, after relapse, the prognosis of our patient is not only related to the SS, but also to breast cancer with a complex medical situation.

Conclusions

SS, which is rare in the head and neck, is a clinically significant tumor that can pose challenges in terms of differential diagnosis, particularly in preoperative or needle aspiration settings. It becomes particularly relevant in patients with a history of prior treatment for Hodgkin lymphoma at a young age, as they exhibit an elevated risk of developing subsequent malignant neoplasms, including sarcomas.

The presented case aligns with the observed trend in such patients, emphasizing the specific risk of developing thyroid tumors and other malignancies alongside sarcomas. This underscores the importance of considering SS in the differential diagnosis, especially when dealing with individuals who have a history of treatment for Hodgkin lymphoma. A heightened awareness of the potential for various malignancies in these patients can contribute to early detection and more effective management strategies.

Conflict of interest statement

The authors declare no conflicts of interest.

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Author's contribution

All the authors contributed equally to produce this manuscript.

Ethical consideration

Our study was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki; The patient subscribed the informed for research

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