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CASE REPORT

Spindle Cell Papillary Thyroid Carcinoma (SC-PTC): A Rare and Challenging Case in Thyroid Pathology

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Abstract

Spindle cell PTC (SC-PTC) is an exceedingly rare PTC subtype believed to have a favorable prognosis. However, a clear and precise definition of SC-PTC is still lacking. Currently, spindle cells in SC-PTC are regarded as a form of metaplasia, wherein follicular carcinomatous cells transform into mesenchymal-like cells devoid of papillary nuclear features. We report the case of a 45-year-old woman diagnosed with spindle cell PTC. The patient presented cervical swelling that progressed gradually over a span of 2-years without causing compressive symptoms. Clinical examination revealed a multinodular goiter, while neck ultrasonography identified a hypoechogenic nodule measuring 4 cm in length in the right lobe [Tirads 4]. Fine needle aspiration (FNA) of this nodule showed follicular neoplasm or suspicion for follicular neoplasm (FN/SFN) [Category IV]. Subsequently, the patient underwent a total thyroidectomy. Following the histological examination of the specimen complemented by immunohistochemical study, a diagnosis of Spindle cell PTC was made. Therefore, we aim to present this uncommon occurrence, which occasionally manifests in papillary thyroid carcinoma.

Keywords

Papillary thyroid carcinoma, Spindle-cell carcinoma, Immunohistochemistry, Metaplasia, Pathology

Abbreviations

SC-PTC: Spindle Cell Papillary Thyroid Carcinoma; PTC: Papillary Thyroid Carcinoma; FNA: Fine Needle Aspiration; MTC: Medullary Thyroid Carcinoma; PSCNT: Post-Fine Needle Aspiration Spindle Cell Nodule of Thyroid; MMPC: Mixed Medullary Papillary Carcinoma; ATC: Anaplastic Thyroid Carcinoma; H&E: Hematoxylin and Eosin Main Text

Introduction

Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy, accounting for 80% to 90% of thyroid carcinomas [1]. Classic PTC and infiltrative follicular variant PTC are the most common PTC subtypes [1]. The 5-year survival rate generally exceeds 90% [2,3]. Conversely, rare PTC subtypes, such as tall cell PTC or columnar cell PTC, are associated with aggressive behavior and thus a poorer prognosis [2,4]. Spindle cell PTC (SC-PTC) is an extremely rare and poorly defined PTC subtype described as PTC with an area of spindle cell pattern that expresses follicular markers [5]. Currently, it is recognized that SC-PTC has a good prognosis [4,6]. Diagnosis of SC-PTC is challenging for pathologists due to its rarity and the multitude of its differential diagnoses [5,6]. Some thyroid neoplasms with worse prognoses can also display a spindle cell pattern [5,6]. Additionally, spindle cell patterns are observed in some benign neoplasms and inflammatory thyroid pathologies [5,6]. Correct diagnosis is crucial due to its implications for prognosis and therapy [5,6].

We report here a singular and the only case of SC-PTC diagnosed in our institution. Firstly, we aim to address the clinicopathological features of this PTC subtype. Secondly, we aim to discuss differential diagnoses to consider here, as well as the wide spectrum of spindle cell lesions of the thyroid. At the end of this paper, we will briefly discuss the pathological approach to thyroid lesions with a spindle cell pattern.

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Case Description

A 45-year-old woman presented with cervical swelling that progressed gradually over a span of 2 years without pain or causing compressive symptoms. She had no significant personal or familial medical history. Clinical examination revealed a multinodular goiter, with no signs of dysthyroidism or neuroendocrine manifestations.

Neck ultrasonography revealed a slightly hypoechogenic nodule measuring 4cm in length in the right lobe, with no enlargement of neck lymph nodes [Tirads 4].

The fine needle aspiration (FNA) of this nodule showed follicular neoplasm or suspicion for follicular neoplasm (FN/SFN) [category IV]. Subsequently, she underwent a total thyroidectomy. The total thyroidectomy specimen was submitted for histopathological examination.

Gross examination of the specimen revealed a bilobed, white-tan nodule measuring 3.6 cm in the right lobe (Figure 1). There was no evidence of extra thyroidal extension.

Microscopically, this nodule corresponded to a neoplasm with a double component. The two components were adjacent, with each occupying 50% of the overall tumor volume (Figure 2):

- The first component was an infiltrative follicular variant of PTC with 2 mitoses/mm2, capsular invasion and angioinvasion.

- The second component was an un encapsulated, non-infiltrative spindle cell lesion. Cells were uniform and arranged in short fascicles. They exhibited eosinophilic cytoplasm, indistinct borders, and single nuclei with fine granular chromatin and no nucleoli. There was no mitotic activity, necrosis, or inflammation. The stroma was collagenous with numerous thin-walled vessels and the presence of amyloid elements that tested negative for "Red-Congo" staining.

Immunohistochemistry led to a diagnosis of SC-PTC (Figure 3). It showed diffuse expression of thyroglobulin and CKAE1/AE3 by both components, without expression of calcitonin.

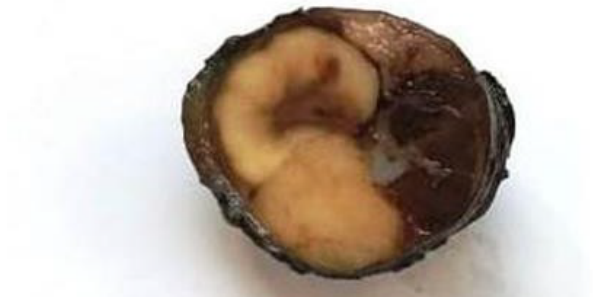

Figure 1: Macroscopic appearance of the nodule.

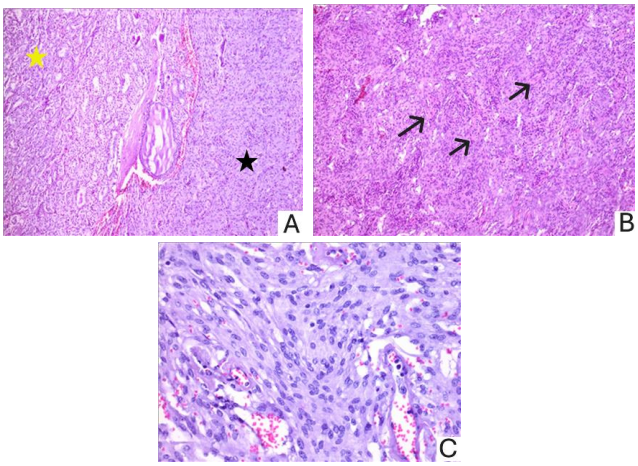

Figure 2: Histological features of the lesion. (A) Adjacent infiltrative follicular variant PTC [yellow star] and spindle cell lesion [Black star] (H&E stain, ×40). (B) Spindle cells arranged in short fascicles and stroma contained pseudo amyloid deposit [Arrows] (H&E stain, ×100). (C) Uniform spindle cells with an eosinophilic cytoplasm, indistinct borders and fine granular chromatin nuclei (H&E stain, ×400).

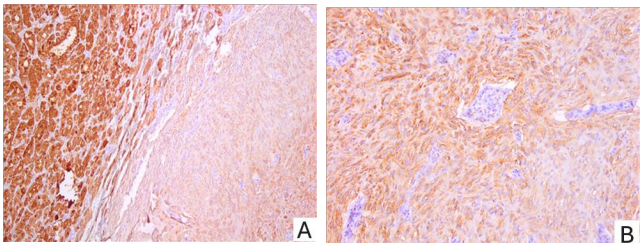

Figure 3: Immunohistochemistry findings. (A) Diffuse expression of thyroglobulin by the both components (×100). Expression of thyroglobulin by the spindle cell component (×200).

Discussion

SC-PTC is predominantly observed among adult women [5,6]. Leong, et al. found a female-to male ratio of 9:4 and a wide age range from 25 to 67-years-old [5]. SC-PTC can arise in any thyroid lobe as a nodule without a specific appearance [5,6]. The nodule size can vary from 3 mm to 50 mm [5]. Histopathologically, it consists of elongated-shaped cells with an eosinophilic cytoplasm, indistinct borders, and fine granular chromatin nuclei [5,6]. There are no papillary nuclear features or significant nuclear atypia [5,6]. Mitoses are rarely seen [5,6].

These spindle cells are arranged in a nodular or diffuse pattern [5,6]. There is no inflammation or necrosis [5,6]. The spindle cell component usually occurs in conjunction with a classic or infiltrative follicular PTC and can involve 1% to 95% of the tumor [5,6]. The spindle cell component expresses follicular markers including thyroglobulin, TTF-1, and TTF-2 [5-7]. Spindle cell component in SC-PTC can now be characterized as a metaplasia in which follicular carcinomatous cells transform into mesenchymal-like cells devoid of papillary nuclear features or any other significant atypical [5,8,9]. The pathophysiology of this metaplasia remains unclear [5,8,9].

Spindle cells are not commonly encountered in thyroid pathology [10,11]. They can appear in association with various reactive, hyperplastic, and neoplastic processes, including post-fine needle aspiration spindle cell nodule of the thyroid, multinodular goiter, follicular adenoma, and a subset of PTC [5,7,11]. Immunohistochemistry is essential for the accurate diagnosis [5,7,12]. In our case, we primarily suspected essentially SC-PCT, mixed medullary-papillary carcinoma (MMPC), anaplastic transformation of PTC and post-fine needle aspiration spindle cell nodule of thyroid (PSCNT).

Medullary thyroid carcinoma (MTC) with spindle cell morphology presents a similar appearance to SC-PTC [5,7,13]. The distinguishing histological feature here is the presence of an amyloid stroma [13]. MTC typically expresses parafollicular markers such as calcitonin and neuroendocrine markers [7,13]. In our case, the presence of pseudo amyloid deposits in the stroma, along with the coexistence of infiltrative follicular PTC and a spindle cell pattern, initially led us to suggest MMPC. However, this diagnosis was ruled out due to the positivity of thyroglobulin and negativity of the "Congo-red" stain and calcitonin. Additionally, clinical and biological signs suggestive of MTC were absent in our case, including a familial history of MTC, personal or familial history of NEM2, neuroendocrine manifestations such as diarrhea and flushing, and elevated levels of serum calcitonin and serum CEA [13].

PSCNT typically manifests as a small nodule, usually ranging from 1 mm to 7 mm in size [5,7,14]. This reactive myofibroblastic proliferation must be considered in the context of fine needle aspiration (FNA) [5,7,14]. Histopathologically, it presents as a non-encapsulated and relatively well-circumscribed spindle cell proliferation, located at the center of a pre-existing lesion. The spindle cells exhibit elongated nuclei with vesicular chromatin and inconspicuous nucleoli, with rare mitotic figures. The degree of inflammation can vary [5,7].

Immunohistochemistry typically shows SMA expression, supporting a myofibroblastic origin [5,7,14]. In our case, PSCNT was ruled out due to the expression of CK AE1/AE3 and thyroglobulin.

Anaplastic thyroid carcinoma (ATC) is a rare and highly aggressive thyroid malignancy, typically occurring in individuals over 60-years-old [15]. It is characterized by its large size, rapid growth, extra thyroidal extension, lymph node involvement, and distant metastasis [5,6,15]. Histopathologically, ATC exhibits marked pleomorphism, a very high mitotic index and high Ki67 expression, necrosis, and extensive vascular invasion [5,6,15]. A pure spindle cell pattern may also be observed in ATC, often with expression of cytokeratin and focal or no expression of follicular markers [5,6,15]. In our case, anaplastic transformation of PTC was excluded based on morphological findings and diffuse expression of thyroglobulin.

Spindle cell metaplasia is also described in other follicular thyroid lesions such as follicular carcinoma, follicular adenoma, and thyroid follicular nodular disease [8,9,16]. The spindle cell morphology is similar in all follicular-derived lesions, and immunohistochemistry is generally unhelpful in distinguishing between them [10,17]. Ma, et al. discussed this challenge by reporting a case in which the entire tumor displayed spindle cell morphology along with the expression of follicular markers [17]. The presence of an adjacent classic or infiltrative follicular PTC led to the diagnosis of SC-PTC, similar to our case.

Other thyroid neoplasms with a spindle cell pattern include [5,7,10]:

- Thymic tumors within the thyroid, such as thymoma and spindle epithelial tumour with thymus-like elements.

- Mesenchymal tumors like leiomyoma, peripheral nerve sheath tumours, solitary fibrous tumor, and sarcomas.

- Thyroid metastases including melanoma or sarcomas.

Some non-neoplastic disease can also display a spindle cell pattern, including Riedel's thyroiditis, the fibrous subtype of Hashimoto's thyroiditis, and De Quervain's granulomatous thyroiditis [9,10]. Clinical and morphological findings are usually sufficient to make the diagnosis [6,9].

It is currently recognized that the prognosis for SC-PTC is generally favourable [4,6]. In the fifth edition of the World Health Organization (WHO) classification of thyroid tumors, high grade PTC is defined by a mitotic count of ≥ 5 mitoses/mm 2 and the presence of necrosis [18]. In SC-PTC, such as in our case, mitoses are rare and necrosis is typically absent. Additionally, the index of proliferation Ki67 is typically <2% in SC-PTC [5,6]. However, further investigations may still be necessary for a comprehensive evaluation.

Spindle cell pattern thyroid lesions are rare and pose a challenge for pathologists [5,12]. Currently, there are no standard pathological guidelines established for them. Accurate diagnosis is crucial for prognosis and treatment planning [5,6]. Immunohistochemistry is often necessary, but it must be complemented with correlation with clinical and morphological findings to determine the appropriate markers [5,9].

Conclusion

SC-PTC is a rare and poorly defined PTC subtype. Diagnosis of SC-PTC presents a challenge for pathologists due to its rarity and the various thyroid pathologies that may exhibit a spindle cell pattern. Achieving an accurate

diagnosis necessitates the use of immunohistochemistry study.

Conflicts of Interest

Authors declare no conflicts of interest.

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