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A Rare Entity of Papillary Carcinoma of Thyroid with Squamous Cell Carinoma Component: Case Report

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Abstract **Case Report**

While squamous metaplasia is a well-known phenomenon in papillary thyroid carcinoma (PTC), diagnosing a PTC with squamous differentiation (PTC-SD), especially in a young patient, is extremely rare, thereby posing a diagnostic challenge given its broad histopathological differential diagnosis. We present a rare case of PTC-SD diagnosed in a solitary thyroid nodule (STN) in a 45-year-old man with a family history of thyroid cancer. Indeed, detection of the squamous cell carcinoma component might not be feasible by fine-needle aspiration cytology or frozen sections, whereas permanent paraffin sections and immunohistochemistry (if necessary) usually allow its identification. Due to their diverse clinical and biological behaviors, it is important to differentiate PTC-SD from other conditions in which a thyroid specimen contains squamous epithelium.

Keywords: Papillary, thyroid, carcinoma, Squamous, Surgey, Immunohistochimic.

INTRODUCTION

Classic squamous cell carcinoma of the thyroid remains an extremely rare entity, because the normal thyroid gland does not contain a squamous-type epithelium which can be the origin of this entity [1]. The incidence of this tumor is 0.7 to 3%, and fewer than 50 cases have been reported in the literature. However, papillary carcinoma associated with a squamous cell component is a less rare tumor than the previous entity but remains exceptional and presents at the same time clinical and immunological symptoms characteristic of both components [1].

Although papillary thyroid carcinoma (PTC) is known to be associated with focal or extensive squamous metaplasia in 20 to 40% of cases [2], it remains extremely rare to diagnose PTC with squamous differentiation (PTC-SD) in a primary thyroid cancer while it is more common to find a squamous component in a secondary lymph node (LN) or in a distant metastasis, or even in the case of late tumor recurrence [3, 4] particularly in a young patient [6].

CASE PRESENTATION

Our 45-year-old patient presented to our structure with a painless cervical mass, fixed in relation to the superficial plane and mobile in relation to the deep plane. Ultrasound shows a right thyroid nodule of 6 cm long axis classified EUTIRADS 5.

The fine aspiration performed shows rigid clusters showing papillary-type cytonuclear atypia classified category 5 (suspicious of papillary carcinoma) according to the Bethesda 2023 system.

A decision for total thyroidectomy was made and the surgical specimen was received at our laboratory with a well-respected macroscopic protocol.

The histological study of the tumor identified macroscopically shows the presence of an invasive non-encapsulated proliferation respecting the thyroid capsule made of two components: follicular oncocytic showing papillary nuclear characteristics (Figure 1) and squamous cell showing well-defined squamous differentiation criteria (Figure 2).

An immunohistochemical study was carried out which shows the positivity of the follicular component for thyroglobulin (Figure 3) and TTF1 (Figure 4) which remain negative at the level of the squamous component. The latter is positive for cytokeratin 5/6 (Figure 5).

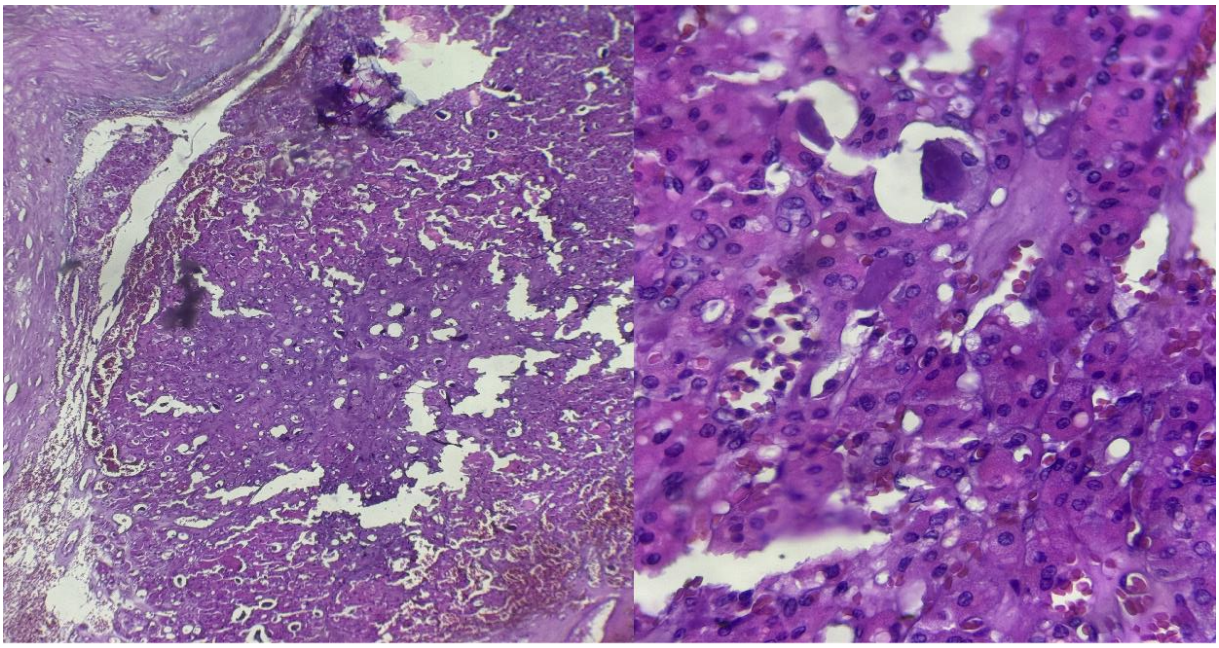

Figure 1: Histological image showing invasive oncocytic follicular tumor proliferation showing papillary-like nuclear features

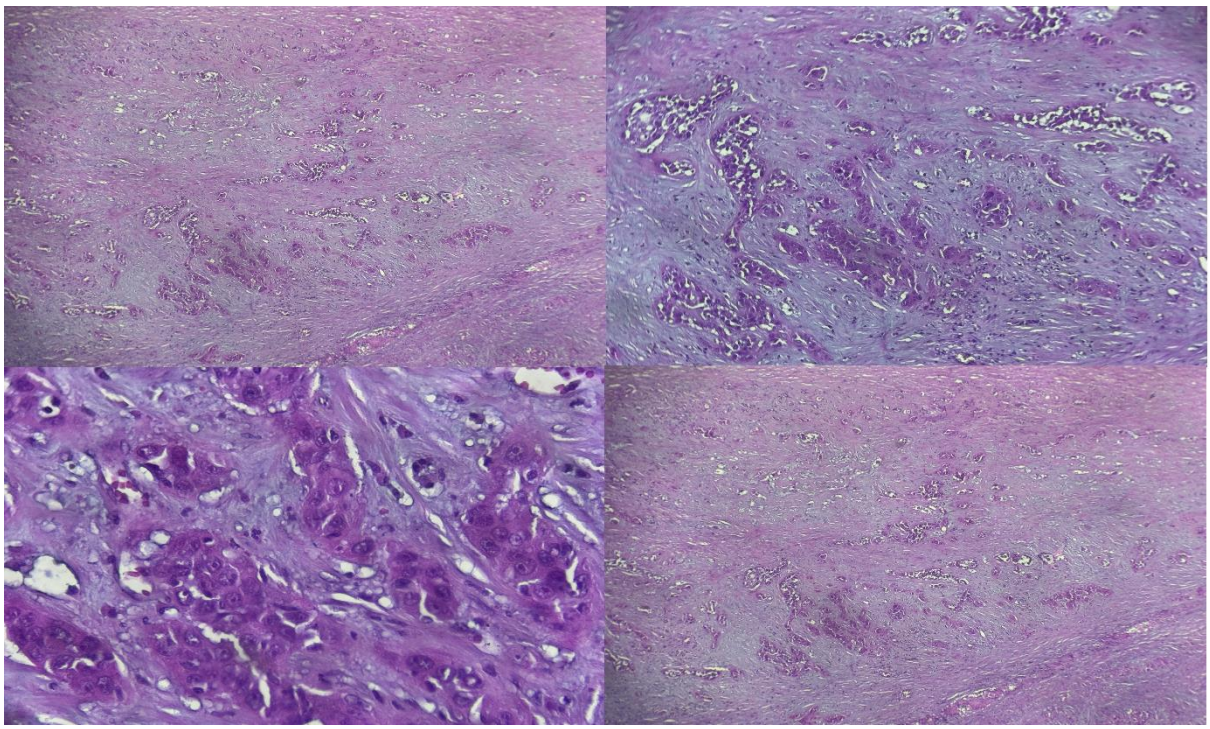

Figure 2: Histological image showing tumor proliferation of poorly differentiated and invasive squamous differentiation

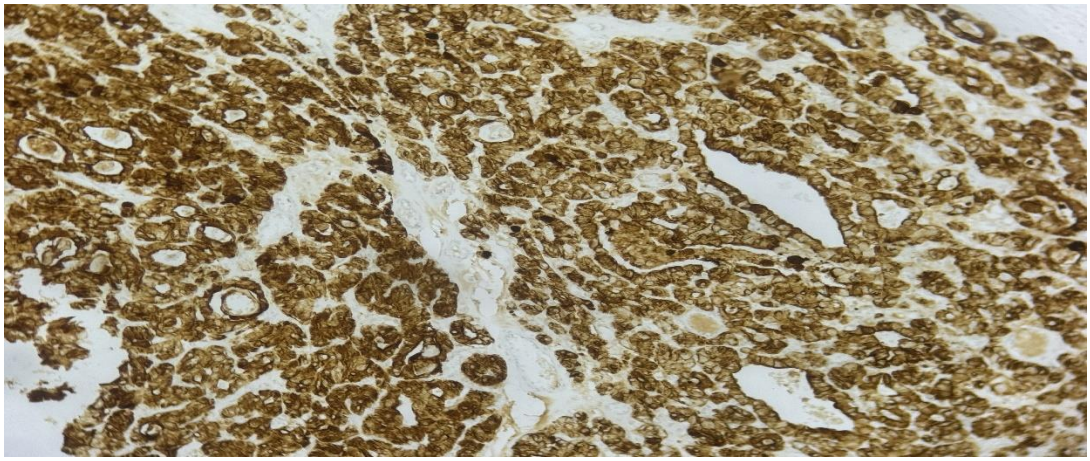

Figure 3: Immunohistochemical marking by thyroglobulin at the level of the follicular component

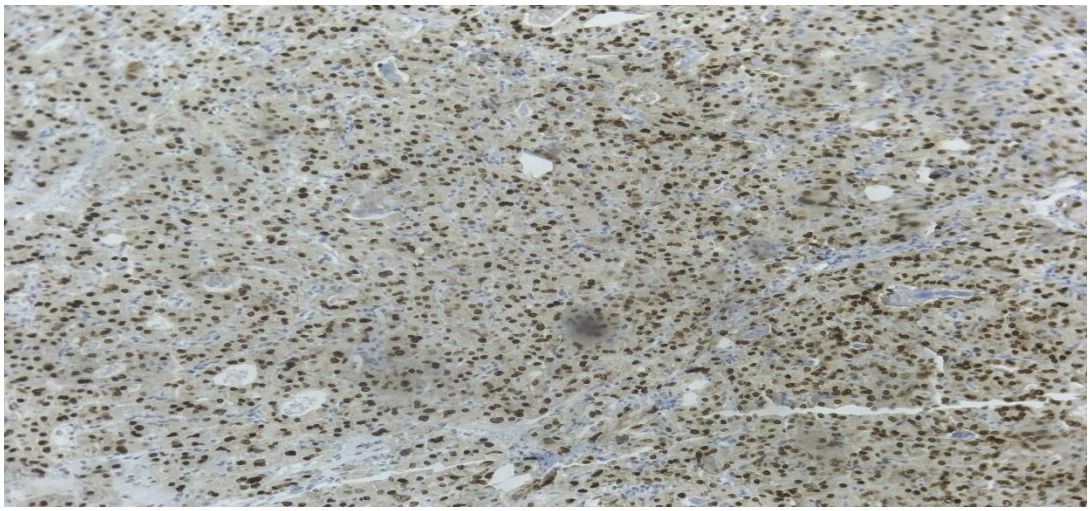

Figure 4: Immunohistochemical staining by TTF1 at the level of the follicular component

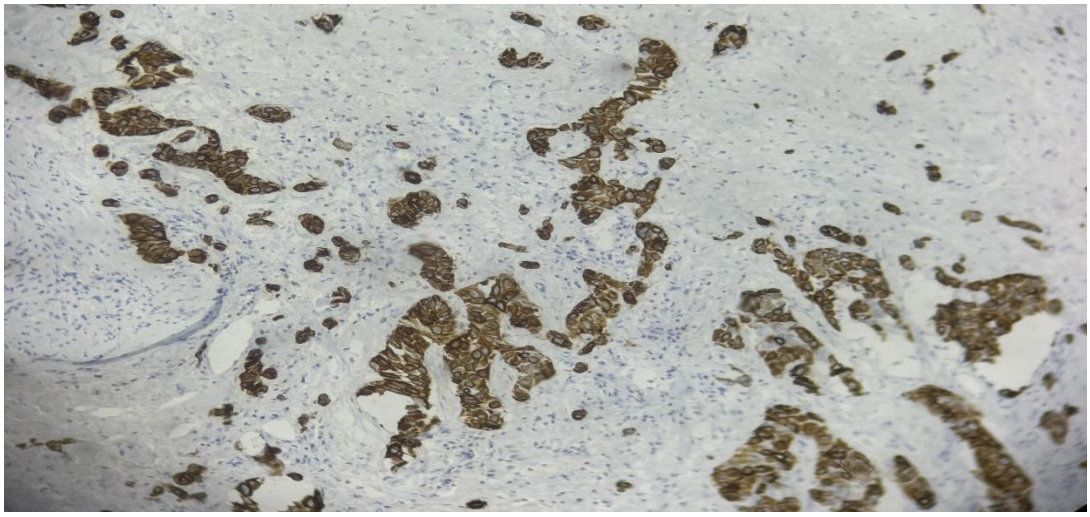

Figure 5: Immunohistochemical staining by CK 5/6 at the level of the squamous component

DISCUSSION

In a thyroid tumor, squamous differentiation is defined as a component of squamous cell carcinoma associated with well-differentiated thyroid cancer without anaplasia or poorly differentiated areas [3]. Normally, squamous epithelium does not form a histological component of the thyroid gland. Once present, this would raise one of the following possibilities: 1- well-differentiated squamous metaplasia in a non-neoplastic patient (nodular and lymphocytic goiter or thyroiditis) or neoplastic lesion of the thyroid [5, 2], 2- primary SCCa of the thyroid [7, 8], 3- metastatic SCCa originating from another site, 4- carcinoma with

thymic differentiation [5], 5- and finally a squamous cell component in a typical primary papillary carcinoma [3], which exists in our case. To make this diagnosis, it is necessary to base oneself on the following criteria: (1) the precision of the squamous epithelium and whether it is benign or malignant, (2) the knowledge of thyroid neoplasia and its old histological type, (3) the presence or the absence of other malignant components such as high-grade PTC or anaplastic carcinoma, (4) the existence of squamous cell carcinoma in other sites particularly in the head and neck region, and (5) the clinical interpretation of a recurrence or metastasis from an old thyroid carcinoma. In addition, IHC using squamous and thyroid differentiation antibodies can provide diagnostic assistance to demonstrate the biphasic pattern of the squamous component mixed with the follicular component of thyroid origin [6].

On the etio-pathogenetic level, the intrathyroidal metaplastic squamous component derives according to the hypotheses either from the thyroglossal duct, the thymic parenchyma or the branchial vestiges or can be caused by scars due to thyroiditis, and therefore patients suffering from this metaplasia carry the same risk of transformation either pure squamous cell carcinoma, or squamous cell component in follicular thyroid carcinomas. Although PTC has a good prognosis with a survival rate of more than 90% at 20 years, certain factors modify the prognosis, such as age greater than 45 years at the time of diagnosis, a larger tumor, incomplete excision, metastasis stage, extrathyroidal extension, certain histopathological variants such as the sclerosing, diffuse tall cell variant, and the presence of local capsular invasion. Reported adverse molecular prognostic factors include TERT promoter mutations and multiple simultaneous mutations, but the BRAFV600E mutation is controversial [5].

In the largest series of PTC-SD cases, Beninato *et al*., [3] considered this phenomenon as a step in the progression toward PTC dedifferentiation. Among the designated limited cases, PTC-SD has demonstrated aggressive clinicopathologic features, including the ability to spread outside the thyroid capsule, metastasize to lymph nodes or distant organs, and invade loco-regional structures, leading to poor long-term outcomes. Accordingly, the previous study recommended that PTC-SD cases should be treated according to evidence-based guidelines for high-risk thyroid cancers.

The average age at diagnosis of patients with this entity ranges from the fifth to the sixth decade, but the disease can occur at any age. Most cases have been reported in women [10]. Patients typically present with a rapidly growing neck mass, obstructive symptoms, and dysphonia. Lymph node metastases and invasion of local structures such as the trachea and esophagus are common at diagnosis. Thyroid cytology with a microbiopsy is important for the diagnosis, but surgical samples retain their place for diagnostic confirmation. The final diagnosis reported by the pathological study is crucial because the treatment and prognosis differ from other types of thyroid tumors [11]. In immunohistochemistry, the squamous component is positive for cytokeratin5/6 and P40, but not for thyroglobulin [9].

Surgery alone, chemotherapy or radiotherapy alone are ineffective [10] because there is a high probability of recurrence and local invasion. The only option for survival is extensive surgery to remove all tumor tissue, leaving healthy surgical margins. This is possible if the tumor is diagnosed at an early stage. In advanced stages, infiltration by the epidermoid component makes total resection of tumor tissue virtually impossible [10].

Concerning adjuvant treatment, the administration of iodine 131 is not useful because the squamous cells do not present follicular differentiation and do not absorb iodine. Combined treatment with surgery and postoperative radiotherapy decreases local recurrence, and some patients treated with this regimen have survived longer [12]. Other treatment options include combining surgery with postoperative radiotherapy and chemotherapy. This option is recommended because it reduces local recurrence of the disease. Several clinical trials with adriamycin, bleomycin, cisplatin, vincristine, doxorubicin, and cyclophosphamide have found no benefit in any of them [10] Thyroid squamous cells may have EGFR gene polymorphisms and increased expression of EGFR protein, which may represent a therapeutic target [13].

CONCLUSION

PTC-SD is a rarely encountered entity of thyroid cancer. Detection of the SCCa component may not be feasible by fine-needle aspiration cytology or frozen section examinations, while permanent paraffin sections and IHC (if necessary) usually allow such identification. Due to their diverse clinical and biological behaviors, it is important to differentiate PTC-SD from other conditions in which a thyroid sample contains squamous epithelium.

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