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Case Report

Identification of high-risk factors in papillary thyroid carcinoma diagnoses: a case report

Juekun Wu[1*], Ying Ruan[1*], Zhiyong Xiong[2], Lu Zhou[3], Zenan Huang[1], Yu Liu[1], Renbin Liu[1]

Departments of [1]Thyroid and Breast Surgery, [2]General Surgery, [3]Pathology, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China. [*]Equal contributors.

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Abstract: Papillary thyroid carcinoma (PTC) is a common malignancy with multiple variants, some of which are rarely encountered in routine surgical pathology practice. Here, we describe both gross and histopathological features of a rare variant of papillary thyroid carcinoma in a 58-year-old male with a literature review. The immunohistochemical results showed both anaplastic sarcomatoid and PTC components that were positive for CK19, galectin-3, and ki-67, thus supporting anaplastic transformation of PTC at the metastatic site. Given the rarity of this condition, the experience gained from the present case is a useful addition to the current knowledge on disease prognostication and management.

Keywords: Papillary thyroid carcinoma (PTC)

Introduction

The vast majority of thyroid tumors are primary epithelial tumors, including follicular adenoma, papillary carcinoma, and anaplastic carcinoma. Follicular carcinoma is the most common endocrine malignancy, and its diagnosis is relatively simple and straightforward, which may lead to the erroneous conclusion that the diagnosis of thyroid tumors is easy to master [1-3]. Papillary thyroid carcinoma (PTC) is poorly differentiated and follicular carcinoma is the most frequently cited to coexist with anaplastic thyroid carcinoma. The early diagnosis of thyroid carcinoma reduces the incidence of anaplastic thyroid carcinoma [4, 5], the prognosis for which is the worst for all types of thyroid cancer, with a 5-year survival rate of 5%~15%. Malignant large cell carcinoma, primary thyroid small cell carcinoma, squamous cell carcinoma, giant cell carcinoma, adenoid cystic carcinoma, mucinous adenocarcinoma, poorly differentiated papillary carcinoma, and follicular adenocarcinoma can all be categorized as anaplastic thyroid carcinomas. This report is to elucidate the understanding of the clinical characteristics of PTC and explore novel clinical indicators for differentiation and diagnosis [5].

In fact, the seemingly simple diagnosis of a thyroid tumor is actually accompanied by many details and diagnostic pitfalls, especially with papillary cancer and tumors with follicular growth patterns. With the auxiliary effects of associated bio-markers (HBME-1, CK19, Gal-3), PTC is an easily diagnosed type of thyroid cancer. Exceptions are not rare, however. For example, the bio-markers related to PTC could actually indicate the positive expression of follicular epithelium in Hashimoto's thyroiditis. It is difficult to distinguish between these two diseases by immunohistochemistry. So far, apart from the application of clonality analysis to identify adenoma and nodular hyperplasia, the value of molecular biology is limited in terms of the differential diagnosis of benign and malignant thyroid tumors, regardless of whether they are follicular or papillary carcinoma [6]. A correct diagnostic determination of thyroid tumors must begin with the recognition of these pitfalls. The first case of misdiagnosis of a thyroid tumor was described in 1989 and, since then, nearly 25 more have been reported [7]. We describe an additional case of PTC in a 58-year-old male.

Case report

Informed consent was given from the patient prior to his inclusion in this case study. A 58-year-old male presented with a right supraclavicular mass 6 months before being admitted. The mass gradually enlarged in size and was

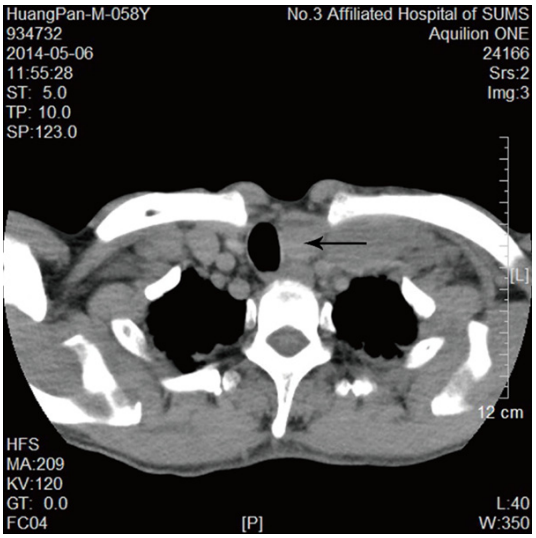

Figure 1. Cervical CT scans and gross view of thyroid tumors. A mass over the left thyroid lobe with lymphadenopathy and extension into the sternocleidomastoid muscle.

complicated by epigastric pain and nausea during the 2 months preceding his initial exam. Physical examination identified a firm mass less than 1.5 cm × 1.5 cm in size and located in the middle lower lobe of the thyroid, which moved with deglutition (**Figure 1**). His past medical history was unremarkable. Thyroid function tests were within the normal range. Ultrasonography identified that the left lobe of the thyroid was enlarged with a heterogeneous echotexture. This suggested a multinodular goiter by radiological diagnosis.

A fine-needle aspiration revealed cellular material showing follicles with nuclear features of papillary carcinoma and no lymphoid tissue. These findings suggest the follicular variant of papillary thyroid carcinoma. Both lobes underwent thyroidectomy and a dissection of the left-side lymph nodules was conducted.

On gross examination, the left lobe of the thyroid was enlarged and was measuring 2.5 × 2 cm, with a series of lymph nodules in left side of the neck. The left-side infrahyoid neuromusculature was dissociated (**Figure 2A**) and the left-side sternocleidomastoid muscle was pulled out (**Figure 3A**) to cut and ligature. We also detected multiple lymph nodes around the carotid artery sheath, which was covering the common carotid artery, internal jugular vein, and pneumogastric nerve. Since the internal jugular vein was severely covered, we removed all the visible lymph nodes and cleaned the first-, second-, third-, fourth-, fifth-, and sixth-order lymph node groups. The patient recovered well after surgery, but suffered some hoarseness. Based on the regular post-surgery pathological analysis, the diagnosis of papillary thyroid carcinoma was confirmed. The immunohistochemical results were TPO (-), CK19 (+), Gal-3 (+), MC (+), and Ki-67 (+). **Figures 2** and **3** show the HE staining of the tumor cells in the left-side infrahyoid neuro-musculature and the left-side sternocleidomastoid muscle. Metastatic cancer was identified in the 1/14 (third group), 3/8 (fourth group), and 2/5 (sixth group) on the left side of the lymph nodes. The repeat Rx-WBS revealed a region of slight radioactivity in the right thyroid, suggesting scanty thyroid tissue in the right lobe.

Discussion

It is commonly known that PTC has several morphologic variants and is a differentiated thyroid carcinoma originating from the thyroid parenchyma, which is the most common and the best prognosis. PTC is more common in children and young women [8]. The CT scans of PTC often show complications due to calcification or low-density masses, although significantly enhanced cystic degeneration of the papillary wall nodule is relatively rare, and easily invades the thyroid capsule [9]. Ultrastructural and immunohistochemical methods have identified that the spindle cells in the tumor stroma have certain characteristics of myofibroblasts.

Although the patterns of disease progression and the clinical outcome are still not clear because of the rarity of this variant, some evidence suggests that it may be more aggressive than classic PTC [10]. **Table 1** summarizes similar cases with clinicopathological features of thyroid carcinoma, but few reports have been published with pulmonary or skeletal metastasis at presentation. Most cases are managed by a similar surgical strategy as classic PTC [11]. The following findings would support a diagnosis of incidental anaplastic thyroid cancer: (i) final pathologic review of primary operative specimens, in which micro-focal malignant cells with slight differentiation were found in the typical papillary cancer area; (ii) a patient's primary symptom was a mass in the left supra-

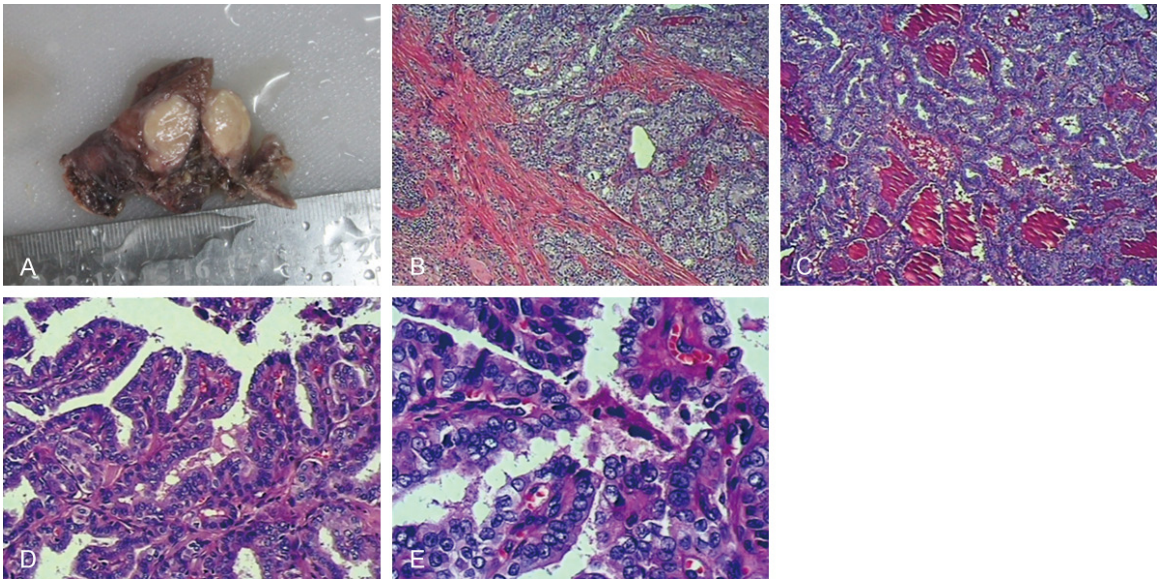

Figure 2. HE staining of the tumor cells in the left-side infrahyoid neuro-musculature. A. The left-side infrahyoid neuro-musculature. B. Tumor cells exhibit infiltrative growth, interstitial fibrosis, and lymphocyte and plasmocyte cell infiltration (×10). C. The follicular tumor structure is irregular, angular, and circuitous, occasionally with a micropapillary manifestation (×20). D. Typical papillary structure, complex, branching, disordered (×40). E. Large nuclear overlap, transparent nucleus (glassy), visible nuclear groove, and small nucleoli (×40).

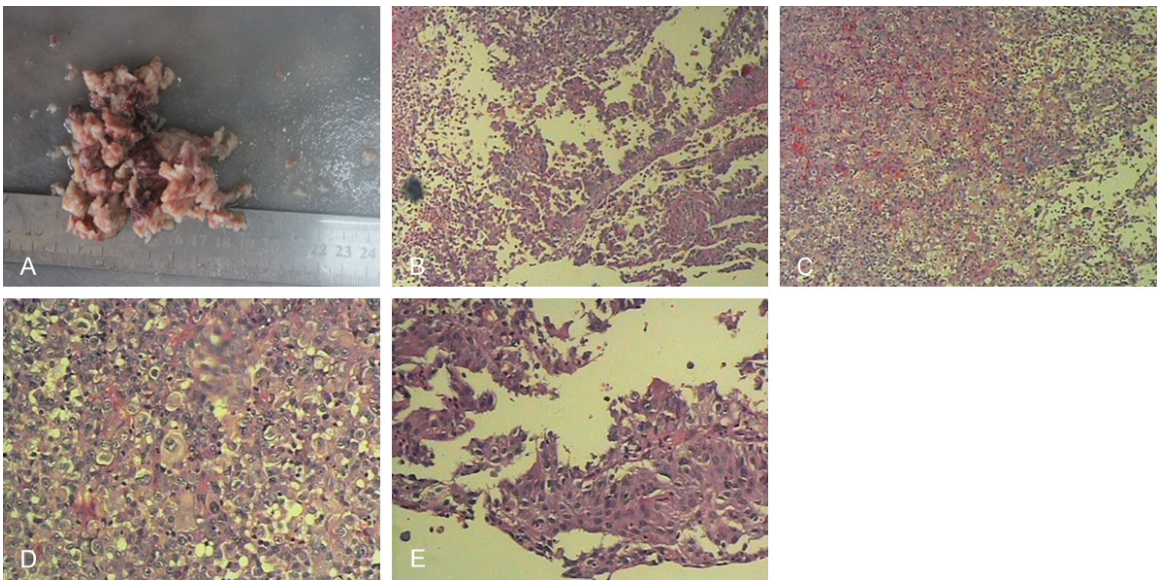

Figure 3. HE staining of the tumor cells in the left-side sternocleidomastoid muscle. A. The left-side sternocleidomastoid muscle. B. Infiltrative growth of tumor cells, unclear cell boundaries, and neutrophils and lymphocytes infiltration (×10). C. Cells are rich in cytoplasm, dichromatic, unclear boundaries (×20). D. Cell atypia is obvious, nuclear vacuolization, visible nucleolus (×40). E. Cells in the region are arranged in nests, and the adipocyte is rich in eosinophilic acid. The cell boundary is still clear (×40).

clavicular fossa, which would mean that the extracapsular invasion and lymph node metastasis had already existed before the initial diagnosis, thereby having lost the therapeutic window for a radical operation and causing uncontrollable disease progression; (iii) anaplastic cancer develops far faster than papillary thyroid cancer, suggesting that the focal anaplastic cancer associated with differentiated thyroid cancer is an early stage of ATC; when the

Table 1. Review of similar cases about clinicopathological features of thyroid carcinoma

Author	Age/Gender	Size	Location	Background	Immunohistochemical result	Treatment	Prognosis
Sato K, et al [3]	77/M	2.5	Right neck	Anaplastic	Cytokeratin (+), vimentin (+), α-SaMA (+), BAF47/INI1 (+), Thyroglobulin (-), calcitonin (-), CD15 (-), HBME-1 (-), TTF-1 (-), desmin (-), HHF35 (-), α-SMA (-)	Surgery	DOD, 6 months later
Abe T, et al [4]	61/M	-	Left-sided pleural effusion	Anaplastic	TTF-1 (+), thyroglobulin (-), surfactant apoprotein A (-)	Chemotherapy	DOD, 6 months later
Solomon JP, et al [5]	64/M	20	Left upper quadrant retroperitoneum	Anaplastic	AE1/AE3 (+), galectin-3 (+), PAX8 (+), vimentin (+), p53 (+), CK7 (+), CK19 (+), S100 (+), TTF-1 (+), Thyroglobulin (-), HBME-1 (-), CK20 (-), OCT3/4 (-), CD117 (-), CD45 (-), HMB45 (-)	Surgery	DOD, 3 weeks later
Carda C, et al [11]	59/M	-	Retrotracheal region	Anaplastic	Myogenin (+), MyoD1 (+), HHF35 (+), Thyroglobulin (-), calcitonin (-)	Surgery + radiation + chemotherapy	DOD, 15 months later
Carda C, et al [11]	62/M	-	Left anterior cervical	Anaplastic	Desmin (+), myogenin (+), smooth muscle actin (+), HHF35 (+), Thyroglobulin (-), calcitonin (-)	Surgery + radiation	-

M: male; α-SaMA: α-sarcomeric muscle actin; α-SMA: α-smooth muscle actin; DOD: died of disease; HHF35: muscle-specific actin; TTF-1: thyroid transcription factor-1.

anaplastic neoplastic foci quickly develops until it dominates and wholly replaces the component of papillary cancer, it will appear as a common anaplastic cancer, with poorer prognosis.

Diagnosis of papillary thyroid carcinoma requires a careful consideration of the clinical context. It is vital to recognize the distinct enhancement in papillary wall nodules with cystic degeneration as typical signs of PTC. Histologically, cystic degeneration in PTC may be associated with changes in the necrosis of the tumor emboli, and the papillary wall nodules are mainly related to the presence of residual solid tumors beneath the capsule or a small amount of normal thyroid tissue [12]. Based on the available literature, it does not seem to impact the clinical behavior and prognosis of otherwise conventional PTC, with a disease-free survival up to 5 years based on the longest follow up visit. According to the 2004 WHO classification, papillary carcinoma is a malignant epithelial tumor with distinctive cellular features and follicular cell differentiation [13]. If a thyroid tumor is characterized by extensive papillary carcinoma, papillary thyroid carcinoma should be diagnosed, even if there is no papillary structure. It is also noteworthy that clear nuclei can also be seen in some benign thyroid lesions, such as diffuse hyperplasia (Graves's disease) and Hashimoto's thyroiditis. The point of discrimination is that the nuclear changes are scattered throughout the thyroid gland, whereas the changes in the papillary nuclei are limited to the histologically identifiable nodules [14]. In the end, it is essential to note that, although PTC is most commonly restricted to these cases, it can also be found in the context of a benign thyroid lesion, thus providing additional support to its metaplastic nature. The seemingly simple diagnoses of thyroid tumors are subject to many pitfalls, especially for papillary carcinomas and tumors with follicular growth, which have received considerable attention [15].

Conclusion

This case is a sobering call to vigilance. Although most similar cases are papillary thyroid carcinomas with an ideal prognosis, clinicians also need to consider the possibility of undifferentiated carcinoma or focal changes in the background of the dedifferentiation of differentiated cancer, resulting in deterioration of the patient's condition and the rapid progression of disease. Therefore, proper use of imaging methods must be made, in order to closely observe suspicious malignant lesions and actively intervene within the ideal time window. Higher requirements should also be made for the pathological diagnosis of postoperative specimens.

Disclosure of conflict of interest

None.

Address correspondence to: Renbin Liu, Department of Thyroid and Breast Surgery, The Third Affiliated Hospital of Sun Yat-sen University, 600 Tianhe Road, Guangzhou 510630, China. Tel: +86-20-85252651; E-mail: liur@vip.163.com

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