



Research Article

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Columnar Cell Variant of Papillary Thyroid Carcinoma: Cytological and Histopathologic Correlation

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Abstract

Of all primary thyroid neoplasm, papillary thyroid carcinoma (PTC) is the commonest one. Beside the conventional PTC, there are various histological variants, among them columnar cell variant of papillary thyroid carcinoma (PTC-CCV), which is a rare entity that demonstrates a more aggressive clinical course compared with the other variants of PTC. Cytologically, its diagnosis is by exclusion of any cellular papillary fragments whereas, histologically by its unique features.

Methods: A total of twelve thyroidectomies mainly of PTC-CCV with their preoperative FNAC were included and collected over a 5-year period. All the aspirated materials were stained previously by H&E stains.

Results: All cases were demonstrating the presence of papillary malignant structures. Majority of the studied cases FNAC was revealing hypercellularity with variable superposition in association with paucity of nuclear pseudoinclusions and grooves.

Keywords

PTC, PTC-CCV, FNAC, Histopathology

Introduction

Thyroid cancer is considered the most common endocrine malignancy, PTC is the commonest malignancy involving the thyroid gland and represents up to 80% [1]. Thyroid carcinoma are classified into; differentiated thyroid carcinoma (DTC) that included papillary, follicular, Hürthle cell, and medullary thyroid carcinoma (MTC), and anaplastic thyroid carcinoma (ATC), PTC is the most common type whereas, ATC is the least one [2,3]. Histologically, there are many subtypes of PTC, one of them is PTC-CCV which is initially mentioned by Evans et al in 1986, It is a rare entity and accounts up to 0.4% of all PTC cases [4-6]. PTC-CCV is characterized by some unique features as rapid growth rate, local invasion and early development of lymph node metastasis, and has a high rate of recurrence with bad response to radioactive iodine therapy [7,8]. The latest WHO classification of endocrine neoplasm defined this variant as hypercellular neoplasm exhibiting thin papillae or glandular-like spaces lined by pseudostratified epithelium. The cells may show occasional sub-nuclear vacuolization or even clear cytoplasm [9]. This article is focused on previously done FNAC of thyroid nodules and their received surgical specimens with correlation of the cytologic and Histological

findings (Table 1) [10].

Material and Methods

The present study was performed on selected twelve patients all underwent preoperative US-guided fine needle aspiration cytology (FNAC). Prepared smear slides were fixed in Cablin's jar with 90% alcohol, stained by H&E and examined. All patients underwent total thyroidectomy. All the specimens were performed in the surgical departments, ten sent to the Department of Histopathology, Northern zone, KSA, through the period from December 2015 through January 2020. All the clinical findings of the patients including

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age, gender, and clinical complaints were obtained from patient's medical records and referral enclosed requests. All the surgical specimens were received fixed in 10% neutral buffered formalin solution, then processed and paraffin-embedded blocks were prepared, and were cut into 3 micron-thick tissue sections. The preformed paraffin sections were stained by Hematoxylin and Eosin stains (H&E). All the stained sections examined microscopically (by 2 experienced pathologists).

Results

The clinical features of all the studied cases of PTC-CCV were summarized in Table 2, majority of them were seen in females and representing 75% as well as, majority of cases were suffering from neck swelling that was observed in 66.5%. The Ultrasonographical findings were mentioned in Table 3, the left thyroid lobe was harboring majority of the nodules that were selected in this study. Additionally

suspicious thyroid nodules were seen in nine cases (75%) and described as TRI-RADS 5. In regard to the U/S majority of lymph nodes were reactive and presented by intact hilum whereas one lymph node showed signs of involvement by malignant deposits as ovoid shape and lost hilum. In regard to FNAC (Table 4), majority of the cases were follicular neoplasm Bethesda category V according to the update Bethesda Reporting 2017 of thyroid neoplasm, all the cases revealing cellular fragment with pseudostratified lining epithelia (Figure 1, Figure 2, Figure 3 and Table 5). Additionally, nuclear pseudoinclusions or any calcified bodies or mitosis or necrosis were not observed among all selected cases (Table 5). The histological findings were summarized in Table 6, Papillary structures lined by pseudostratified cells were detected in 9 cases (75%) among all cases (Figure 4) whereas each extra-capsular invasion and lymph node was seen in one case for both parameters (Figure 5).

Table 1: According to a recent publication by Andre’s, et al., 2020, PTC-CCV is histologically characterized by these features [10].

Clinical features	Histological features	Molecular features
Infiltrative form with extrathyroid extension: Rapid growth rate Local invasion Early lymph node metastasis High rate of recurrences 5 th -6 th decade of life Encapsulated form minimally invasive: high cure rate	Columnar cells with pseudostratified nuclei and no eosinophilic cytoplasm Hypercellular neoplasm with thin papillae and glandular structures Nuclear features of papillary carcinoma not as well developed as classic PTC Occasional subnuclear vacuolization or even clear cytoplasm	BRAFV600E (33%)

Table 2: Clinical findings of all cases of PTC-CCV.

Age	No	Gender		Clinical manifestations	Total
		Male	Females		
20	2	3	9	Neck swelling	8
25	1			Weight loss	2
30	3			Pressure symptoms	1
35	4			Voice troubles	1
50	2				
Total	12				12

Table 3: Ultrasonogical Findings.

Tumor size (cm)	Location	Nodules (US)		Cervical LN status
		Benign	Suspicious	
1-1.5	LT Lobe.	3	9	Reactive
01-Feb	LT. Lobe			Reactive
02-Mar	LT. Lobe			Reactive
02-Apr	LT. Lobe			Suspicious
02-May	RT. Lobe.			Suspicious
03-May	RT. Lobe			Suspicious
05-Jun	LT. Lobe			Involved
7	LT. Lobe			Reactive

Discussion

Among the aggressive variants of classic PTC is columnar cell variant, which is the most misdiagnosed and under recognized entity at cytohistological levels. Clinically it is presenting by an asymptomatic enlarging neck mass [11]. Regarding the diagnosis of this variant, there is no clear consensus describing the minimal percentage of columnar cells that confers a diagnosis of PTC-CCV, with reported series varying from 30% to 80% [12]. Additionally, in comparison with the classic PTC, CCV is more lethalwith more invasion potentiality. These findings have an important implication for risk stratification and therefore therapy as well as, the encapsulation rather than the columnar cells is attributable

Table 4: Preoperative FNAC diagnosis of all studied cases.

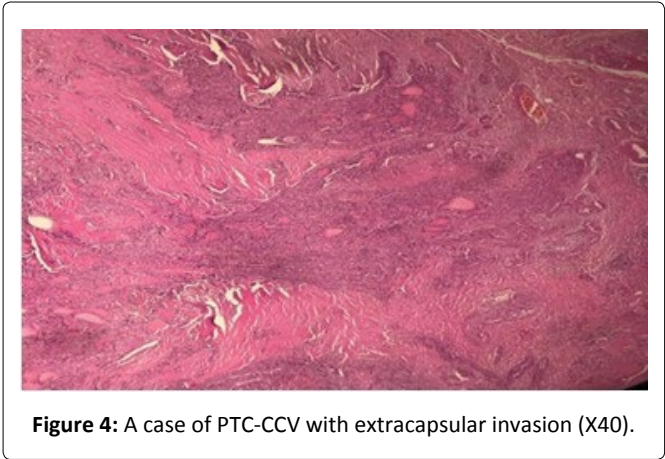
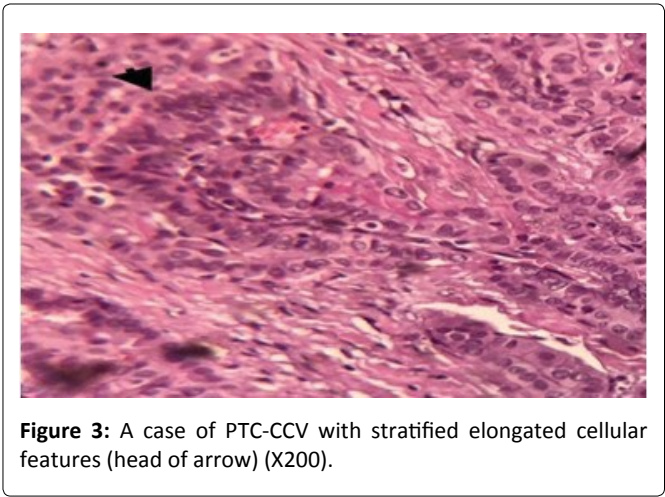
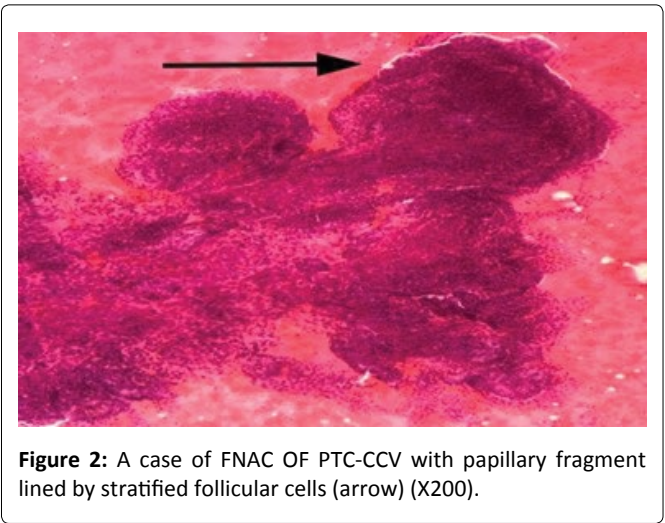
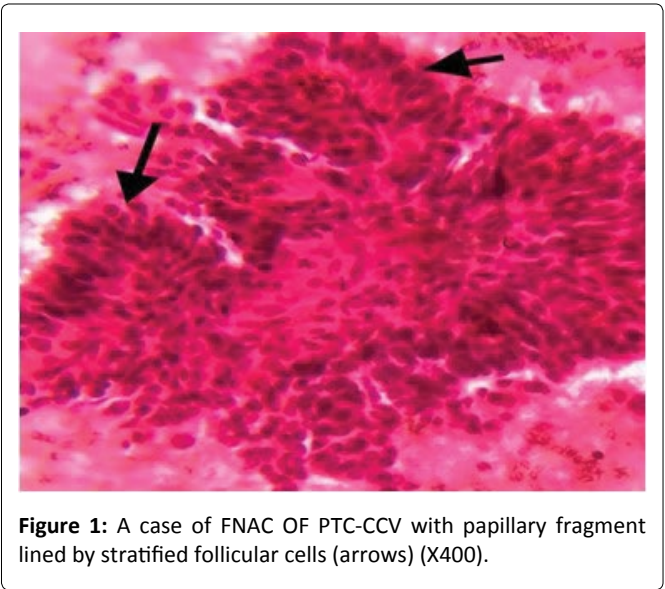
PTC	Follicular neoplasm	Hurchle cell neoplasm	Adenomatoid nodule	Follicular lesion	Total
1	7	1	2	1	12

Table 5: Cytological Features of PTC-CCV in all FNAC examined cases.

Architectural	Cellular	Nuclear	No. (%)
Cellularity (hyper.)	Size (medium/large)	Chromatin (dark/densely)	11 (91.7%)
Papillae	Giant	Pseudoinclusions	0 (0%)
Psammoma bodies	Polygonal	Mitosis	0 (0%)
Colloid	Elongated	Pseudostratification	12 (100%)
Necrosis (0; 0%)	Single cells	Grooves	10 (83.3%)
		Atypia	9 (75%)
		Nucleoli	8 (66.7%)

Table 6: Histopathological diagnosis of all studied cases.

Stratified lined Papillae	Follicles	Psammoma bodies	LN	Extra-capsular involvement	Total
9	1	0	1	1	12



to the outcome of PTC-CCV [10]. Histopathologically, PTC-CCV may resemble many malignant entities includes PTC-tall cell variant (TCV), carcinoid tumor, and metastatic carcinoma, particularly from adenocarcinoma of the colon, lung, or endometrium. The application of WHO histological criteria

is helping in the differential diagnosis between PTC-CCV and PTC-TCV. Additional immunohistochemical evaluation can differentiate between PTC-CCV and the other cancerous entities [6,11,13,14].

The cytological diagnosis of PTC-CCV based on FNAC may be challenging because of the lack of standardized criteria applicable to these features according the update Bethesda Reporting for thyroid diagnosis in contrast to the classic PTC [4,14]. A recent study mentioned that the encapsulated

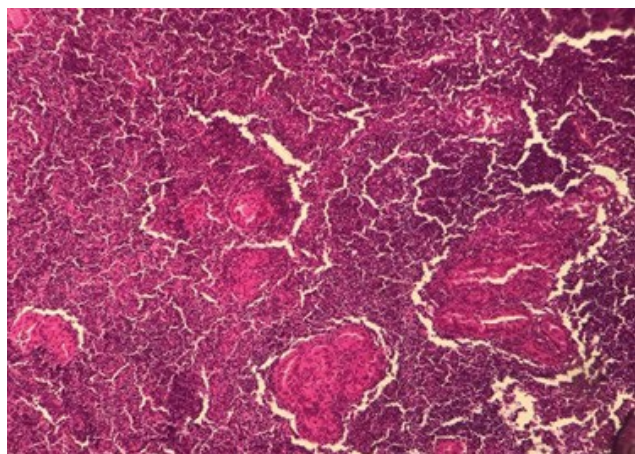


Figure 5: A case of PTC-CCV with lymph node invasion (X40).

CCPTC is associated with better outcomes after complete surgical removal than the conventional not encapsulated PTC-CCV [15].

In this study majority of the cases were seen in younger female and they are encapsulated and limited to the thyroid gland. These findings were similar to a study discussed that, encapsulated PTC-CCV occurred mostly in young female patients while the infiltrative ones in older patients with an almost equal male to female ratio. Additionally, this study mentioned minimally invasive CCV behaved in a very indolent fashion while the widely infiltrative tumors had a very poor outcome. As well as this study demonstrates that columnar cell variant when encapsulated and confined to the thyroid has an outcome similar to classic PTC.

As papillary thyroid carcinoma is the most common malignant tumors of the thyroid gland, it carries an indolent malignant tumor with an excellent prognosis and has an overall mortality rate of 1% per year [16,17]. Basically, there is no data mentioned the percentage of columnar cells required for diagnosis of PTC-CCV. Some suggested proportion of cells ranged from 30% to 80% to fulfill criteria for this diagnosis. Others listed additional characteristics seen in more than 50% of PTC-CCV cases including, colloid, elongated cells, dark or densely packed chromatin, absent or mild nuclear atypia, inconspicuous nucleoli, and the absence of intra-nuclear pseudoinclusions [13,14]. The revised American Thyroid Association guidelines recently categorized the PTC and its variants according to the biological behavior and PTC-CCV as an aggressive subtype. Additionally, some authors have reported a better prognosis for encapsulated tumors [18,19]. Andre's, et al., 2020 are discussing that PTC-CCV is considered the rarest subtypes of aggressive forms of PTC and the capsule if found is an important prognostic factor. A study by Wenig, et al., 1998, mentioned that the encapsulated form of this variant is an indolent yet, the widely infiltrative form is very aggressive. So, in PTC-CCV encapsulation rather than the columnar cells is an essential for prediction of outcome among this variant of thyroid cancer [10]. Update study by Limberg, et al., 2019 [18] discussing data from the National Cancer Database and showed that in the absence of invasive

features, PTC-CCV, PTC-TCV, and PTC-DSV have similar overall survival to that of classic PTC [19].

Conclusion

Papillary thyroid cancer, Columnar variant (PTC-CCV) is lined to more aggressive behavior, higher rates of recurrence, and metastasis so, its accurate histological diagnosis is essential for the therapy and prognosis of patients.

Disclosure

The authors report no conflicts of interest in this work.

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