A STUDY ON PAPILLARY THYROID CARCINOMA- HISTOPATHOLOGICAL VARIANTS AND PATTERNS

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ABSTRACT

BACKGROUND

Papillary carcinoma is a frequently reported thyroid malignancy. Diagnosis is based on the microscopic architecture and the characteristic nuclear features such as nuclear clearing, grooves and pseudo inclusions which can be seen on routine haematoxylin and eosin stained sections. Many morphological variants of this entity have been reported in the literature, classical papillary thyroid carcinoma (PTC) being the most common variant. Follicular, solid, tall cell, columnar etc., are the other variants. Some of these variants cause diagnostic difficulties on histopathological examination and also they have varied prognostic implications.

METHODS

This is a retrospective descriptive study which included 44 cases of papillary thyroid carcinoma diagnosed on histopathology over a period of 3 years.

RESULTS

Classical PTC was the most common variant (52.3%), followed by papillary micro carcinoma (13.6%), follicular variant (11.4%), mixed type that had features of both papillary and follicular (9.1%), tall cell and solid variants (4.5% each); and encapsulated, Warthin-like variants (2.3% each). Associated Hashimoto's thyroiditis was seen in 20.4% cases (n=9/44).

CONCLUSIONS

Papillary thyroid carcinomas showed a female sex predilection. Though seen within a wide age range, they were more common in the third decade. Classical papillary thyroid carcinoma was the most common variant followed by micro papillary carcinoma and follicular carcinoma. Rare variants found in the study were tall cell and Warthin like variants. Nodular goitre and Hashimoto thyroiditis were the common lesions associated with PTC. Histological variations and patterns in papillary thyroid carcinoma have prognostic implications, so it is important to identify and report them whenever present.

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BACKGROUND

Papillary carcinoma of thyroid (PTC) is the most common thyroid malignancy. Many morphological variants of this tumour have been described based on various characteristics like size (micro papillary carcinoma), circumscription (encapsulated variant), architecture (classical, follicular, solid, micro papillary, Warthin like) and based on the cell size and type (columnar, tall cell).[1-4] It is important to be aware of these variants as some of them pose diagnostic challenges and also because of the prognostic implications of certain variants. Tall cell variant (TCV) is considered an aggressive variant and is associated with old age, large tumour size, multifocality, extrathyroidal and lymph node involvement.[2] Warthin like variant can be mistaken for a lymphoepithelial lesion, Hurthle cell tumour or a tall cell variant both on cytology and histopathology.[3]

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Incidence of PTC was found to be high in patients with chronic lymphocytic thyroiditis. However, relationship between both these lesions could not be explained convincingly even in long term studies. Some of the molecular studies indicate that in few cases of Hashimoto's thyroiditis follicular cells show genetic changes similar to those cells in PTC.[5,6] However, few recent studies contradict this as it was found that BRAF gene mutation which is specific for PTC is not present in Hashimoto's thyroiditis.[7] Even though association of HT with PTC is not well established, histologically and cytologically the reactive nuclear changes that occur in a background of HT pose a diagnostic challenge in differentiation from PTC. Nuclear clearing, grooves, nuclear membrane thickening and intranuclear inclusions which are features of PTC can be seen in reactive follicular cells of HT too.[2,4,5] Different histopathological patterns and variants of PTC have been reported to influence the prognosis of patients and for predicting cancer recurrence.[8,9]

METHODS

This was a retrospective descriptive study done in the pathology department of a tertiary care hospital. Duration of study was three years. Forty two cases of papillary thyroid carcinoma diagnosed during this time were included in the study. Slides retrieved from the files were reviewed and various histological findings were noted. Clinical and gross findings of the biopsies in these cases were collected from the files and recorded.

RESULTS

Forty four cases of papillary thyroid carcinoma were diagnosed during the study period of three years. As per the clinical details given in the histopathology request forms there were 39 females and 5 males with a male to female ratio (M:F) of 1:7.8. Maximum numbers of cases were seen in the third decade. Biopsies received were either hemi -, subtotal- or total thyroidectomy specimens. Total thyroidectomy specimens were 30, right-, left-hemithyroidectomy and subtotal thyroidectomy specimens were 8, 5 and 1 respectively. Along with the thyroidectomy specimen lymph nodes were also received in thirteen cases. On gross examination single nodular lesions were identified in 12 cases (27.2%), focal lesions in both lobes (multicentric) in 7 cases (15.9%) and, more than one lesion in the same lobe (multifocal) in 11 cases (25%). Seven cases were papillary micro carcinomas, out of which in one case lesion was identified grossly as less than 1cm nodule; also included in single nodular lesions group. In rest of the cases no definite lesion was identified on gross examination.

Based on the microscopic features these lesions were classified into variants. Maximum numbers of cases were of classical PTC, 23 cases. There were 6 cases of papillary micro carcinoma, 5 cases of follicular variant, 4 cases of mixed papillary and follicular, 2 cases each of tall cell variant and solid variant and a single case each of Warthin like variant and encapsulated variant (Table 1).

Variants	Number of Cases (%)
Classical	23 (52.3)
Follicular	05 (11.4)
Papillary microcarcinoma	06 (13.6)
Solid	02 (4.5)
Tall cell	02 (4.5)
Encapsulated	01 (2.3)
Warthin-like	01 (2.3)
Mixed papillary and follicular	04 (9.1)
Total	**44**

Table 1. Morphological Variants of Papillary Carcinoma (n=44)

Associated Features	Number of Cases	% (Out of a Total of 44 Cases)
Hashimoto's thyroiditis	09	20.4 %
Multinodular goitre	13	29.5 %
Capsular invasion	05	11.4 %
Vascular invasion	02	4.5 %
Perineural invasion	01	2.3 %
Follicular adenoma	01	2.3

Table 2. Various Other Associated Morphological Features Seen in Papillary Thyroid Carcinoma

Variants	Name of The Study (Number of Cases and Percentage)			
	Qureshi A et al[1] (115 Cases)	Srinivasan G et al[12] (108 Cases)	Anupama Raj K et al[13] (70 Cases)	Present study (44 Cases)
Classical	44(38%)	79(73%)	39 (55.7%)	23 (52.3%)
Papillary microcarcinoma	30(26%)	3(3%)	12 (17.1%)	06 (13.6%)
Follicular	18(15.6%)	17(16%)	11(15.7%)	05 (11.4%)
Encapsulated	-	5(4%)	-	01 (2.3%)
Solid	-		-	02 (4.5%)
Tall cell	2(1.9%)		1(1.4%)	02 (4.5%)
Sclerosing	1(0.9%)	1(1%)	-	-
Warthin-like	-		3(4.2%)	01 (2.3%)
Cribriform and morular	-	1(1%)	-	-
Mixed	20(17.5%)		4 (5.7%)	04 (9.1%)
Columnar cell	-		-	-

Table 3. Morphological Variants of Papillary Thyroid Carcinoma. Comparison Between Present Study and Other Studies

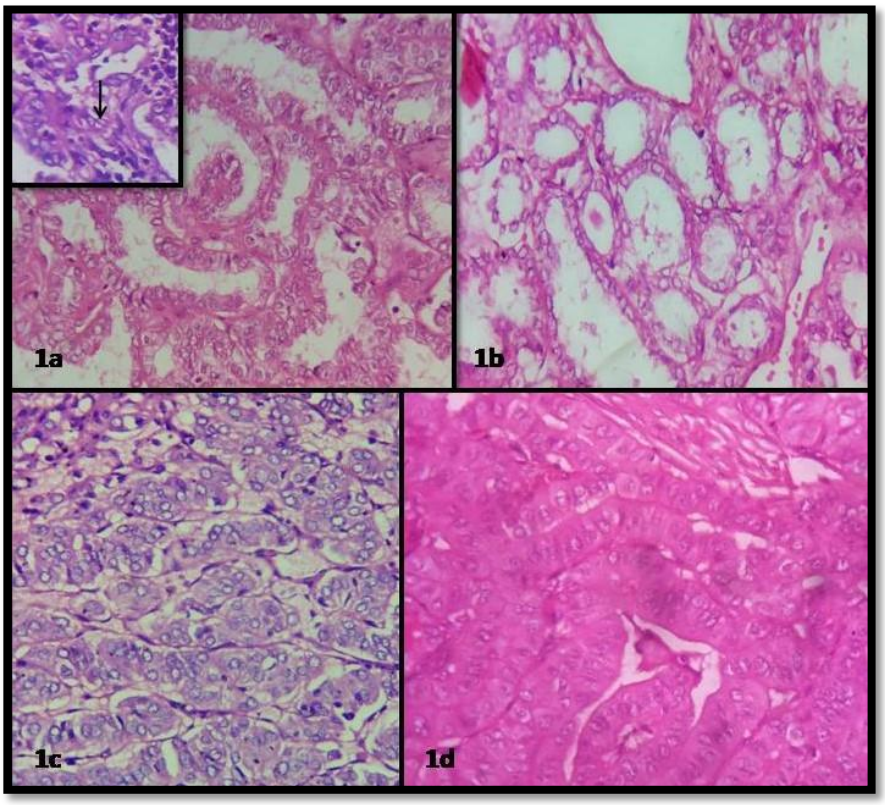

Figure 1. Papillary Thyroid Carcinoma (H & E) 1a. Classical Type Showing Papillae Lined by Cuboidal Cells Showing Crowding. Inset Showing Cells with Round Clear Nuclei, Some Showing Nuclear Grooves (Arrow) 1b. Follicular Variant: Tumour Cells in Arranged in Follicles, 1c. Solid Variant, 1d. Tall Cell Variant

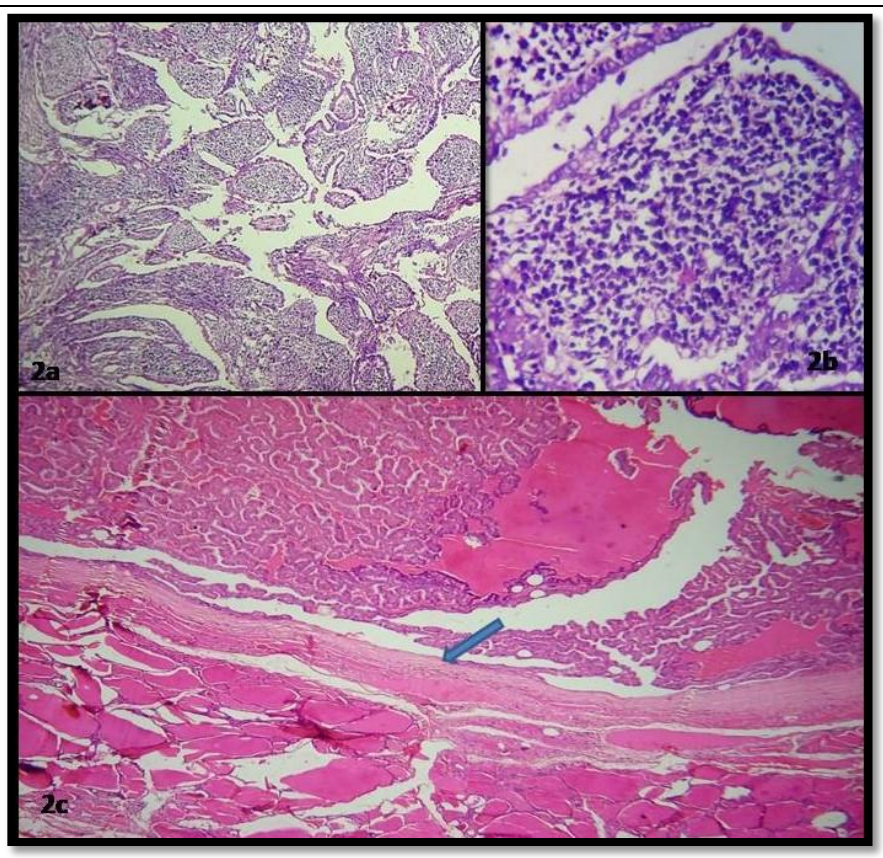

Figure 2. Papillary Thyroid Carcinoma (H&E) 2a Warthin's Variant, Cores of Papillae Expanded by Lymphoid Aggregates (10x) 2b. High Power (40x). 2c: Encapsulated Variant- Fibrous Capsule Noted at The Periphery of the Papillary Thyroid Carcinoma (Arrow)

All the cases were diagnosed on the basis of nuclear features such as optically clear nuclei, grooves, pseudo inclusions nucleoli, peripheral condensation of chromatin and nuclear crowding. In addition based on the patterns they were further classified into variants. Papillae with fibro vascular cores were the predominant pattern in all classical PTCs (Figure 1a). Follicular variants were almost entirely made up of follicles but having the characteristic nuclear features and showed invasive growth pattern (Figure 1b).

Solid variant showed predominantly nests and sheets of tumour cells and focal areas of classical papillary carcinoma (Figure 1c).

Cases showing papillae lined by tall cells with height three times the width were diagnosed as tall cell variant (Figure 1d). A single case showed papillae with cells having oncocytic appearance and nuclear features of PTC. The cores of these were broadened due to lymphocytic collections forming nodules, resembling Warthin's tumour of salivary gland origin (Figure 2a, 2b). This was diagnosed as Warthin like variant of PTC.

Encapsulated variant was lesion with features of papillary carcinoma completely circumscribed by a thick capsule (Figure 2c). Lymph nodes were received in 13 cases out of which seven cases showed tumour deposits. Capsular, vascular and perineural invasion was present in 5, 2 and 1 cases respectively. Extensive sclerosis was seen in 5 cases. A background of Hashimoto's thyroiditis and multinodular goitre were present in 9 and 13 cases respectively (Table 2).

Papillary microcarcinomas were incidental findings except in a single case where thyroidectomy followed a diagnosis of PTC on cytology. In four (57.1%) cases background was multinodular goitre, two cases (28.4%) showed Hashimoto's thyroiditis and in one case (14.2%) follicular adenoma was seen in the other lobe.

DISCUSSION

Papillary thyroid carcinoma shows a female preponderance and is commonly seen in the age group of 20 to 50 years.[1] Present study showed similar findings, male to female ratio was 1:7.8 and maximum number of cases were seen in third and fourth decades of life. Female predominance was also noted in various other studies with a male to female ratio ranging from 1: 2.5 to 5.[10,11] Rao R et al and in various other studies maximum number of papillary carcinomas were seen in third to sixth decade of life.[11]

Papillary carcinoma can be unifocal, multifocal or multicentric. In present study single nodular lesions were identified in 12 cases (27.2%), more than one lesion in the same lobe (multifocal) in 11 cases (25%) and focal lesions in both lobes (multicentric) in 7 cases (15.9%). Rao R et al in their study found 8% of the cases having multifocal tumour with the involvement of bilateral lobes.[11] Over 30% of PTCs were found to be multicentric and most of them associated with papillary microcarcinomas.[12] Multicentric PTC presents with high recurrence rates and advanced TNM staging compared with unifocal PTC.[13] In these studies multiple foci of tumour present in the same lobe or both the lobes and isthmus were considered as multicentric lesions. In another study lesions were considered multifocal when two or more lesion seen in the same lobe and multicentric when more than one tumour foci present in different lobe, which had been followed in the present study.[14]

Different histopathological patterns and variants of PTC have been reported to influence the prognosis of patients and for predicting cancer recurrence.[9,10] Various morphological variants of papillary thyroid carcinoma had been reported, of which classical variant is the most common one followed by papillary micro carcinoma and follicular variant. Similar findings were noted in this study. Other variants included in the study were encapsulated, tall-cell, Warthin-like and mixed papillary and follicular (Table 3). The incidence of morphological variants of papillary thyroid carcinoma as seen in different studies and present study was represented in the following table (Table 3).

Papillary carcinoma of thyroid of size less than 1cm is called papillary micro carcinoma. Most of them are occult malignancies found incidentally in thyroidectomy specimens, removed for other causes. In this study papillary micro carcinomas account for 13.6 % of the PTCs. Out of which one was diagnosed initially on fine needle aspiration cytology and the rest were incidental findings. In our study, we found 6 cases of PMCs accounting for 13.6% of papillary carcinomas. This is in correlation with the findings in Carcangiu et al., study who reported 14.2% of PMC.[14]

Follicular variant is a common variant of PTC comprising about 20-30 % of all papillary carcinomas. It is composed predominantly or almost entirely of follicles lined by cells showing nuclear features of papillary carcinoma. [2,15] In this study they constituted to 11.4% of cases. In the present study we have encountered some of the rare variants like tall cell and Warthin like variants. Warthin like variant can be mistaken for a lymphoepithelial lesion, Hurthle cell tumour or a tall cell variant both on cytology and histopathology. Recognition of these microscopic subtypes is important due to the prognostic significance. Tall cell variant is known to be aggressive in its clinical behaviour whereas macro follicular type has good outcome.[2] Solid variant of PTC is dominated by solid sheets of tumour cells. This variant is more common among children. It is difficult to differentiate this tumour from poorly differentiated carcinoma due to architectural resemblance, however nuclear features are the clue for diagnosis.[2] We had two case of this variant, both seen in adults. Encapsulated variant of papillary carcinoma of thyroid accounts for 4 to 12 % cases. A single case was encounters in this study.

Nodular goiter and Hashimoto's thyroiditis were the common lesions associated with papillary thyroid carcinoma in our study. A single case showed a coexisting follicular adenoma and micropapillary carcinoma. Rao R et al reported nodular goiter as the most common lesion seen in association with PTC. Of the associated lesions 50% were nodular goitres followed by Hashimoto's thyroiditis (44.4%) and follicular adenoma (5.5%). In Gole et al study out of 55 cases of papillary carcinoma 21 cases (38.18%) had associated non neoplastic lesions, of which 61.90% were nodular goiters, 19.04% were lymphocytic thyroiditis, and 19.04% were Hashimoto's thyroiditis.[11,16] Studies suggest that PTC in a background of Hashimoto's thyroiditis is associated with better prognosis.[17,18]

In present study lymph nodes were submitted in 13 cases and 53.8% of these cases showed metastatic deposits. In Rao R et al study, 17 cases had lymph node metastasis accounting for 23.9% of the cases.[11] PTCs associated with lymph node metastasis had higher recurrence rates.[19]

CONCLUSIONS

Papillary thyroid carcinomas show a female sex predilection. Even though seen within a wide age range they were more common in the third decade. Classical papillary thyroid carcinoma was the most common variant followed by micro papillary carcinoma and follicular carcinoma. Rare variants found in the study were tall cell and Warthin like variant. Nodular goiter and Hashimoto's thyroiditis were the common lesions associated with PTC. A rare case showed coexisting papillary micro carcinoma and follicular adenoma.

Histological variations in papillary thyroid carcinoma and its association with other histological patterns like association with Hashimoto's thyroiditis have prognostic implications, so it is important to identify and report them whenever present.

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