

Papillary Thyroid Carcinoma- Variants and Associated Disorders

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ABSTRACT

Introduction: Papillary Thyroid Carcinoma (PTC) is a malignant epithelial tumour. It is the most common form of thyroid cancer. Several variants have been described like classic, follicular, tall cell, diffuse sclerosing, papillary microcarcinoma and others.

Aim: To study the variants of PTC and to evaluate the presence of associated disorders.

Materials and Methods: In this retrospective study, total of 41 cases of PTC were studied from January 2016 to December 2018 in the Department of Pathology, Kempegowda Institute of Medical Sciences, Bengaluru, Karnataka, India. Demographic data and clinical findings were retrieved from case files. The histopathological slides were studied and the results were analysed using Fischer's-exact test using R (Robert Gentleman and Ross Ihaka) Statistical Software version 4.0.0.

Results: Total data of 41 cases of PTC was collected and analysed. The patient age range between 20-70 years with mean age of 47 years. Female preponderance was noted. Among 41 cases, most were classic variant (31, 75.6%) followed by follicular variant (6, 14.6%), papillary microcarcinoma (3, 7.31%) and diffuse sclerosing variant (1, 2.4%). Multinodular goitre was associated with 8 cases of PTC and Hashimoto's thyroiditis was associated with 5 cases of PTC. Among 13 cases of associated disorders, only six had preoperative diagnosis of PTC and remaining seven cases were diagnosed on histopathological examination.

Conclusion: Classic variant is the most common type of PTC. All thyroidectomies done for multinodular goitre and Hashimoto's thyroiditis should be screened thoroughly for PTC especially microcarcinoma.

Keywords: Classic variant, Diffuse sclerosing, Follicular, Hashimoto's thyroiditis, Multinodular goitre

INTRODUCTION

The PTC is a malignant epithelial tumour. Follicular cell differentiation is shown by the tumour with characteristic nuclear features [1]. The mean age of occurrence is 43 years [2]. The authors noted mean age of 47 years (20 to 75 years) with PTC known to have female preponderance [1]. Several variants have been described like classic, follicular, tall cell, diffuse sclerosing, encapsulated, microfollicular, oncocytic, columnar cell and papillary microcarcinoma. Most common variant is classic variant which exhibits classic nuclear features like ground glass nuclei, nuclear grooves and psammoma bodies. The second common variant was follicular variant. Follicular variant is also known as Lindsay tumour [2] and it is composed of follicles with PTC type nuclei. Tall cell variant is composed of papillae lined by cells where height is two or three times the width size. Diffuse sclerosing variant is characterised by sclerosis, psammoma bodies, extensive lymphocytic infiltration and squamous metaplasia. Most of the time papillary microcarcinoma is diagnosed incidentally. Here, the size is 1 cm or less than that. The Encapsulated variant is completely surrounded by capsule and has better prognosis [2]. PTC is studied exclusively for precursor lesion and researchers have found association between Hashimoto's thyroiditis and PTC [3-6]. Patients with Hashimoto's thyroiditis have an increase risk of developing thyroid carcinoma most commonly PTC [5]. Hashimoto's thyroiditis is associated with a small but real risk of developing PTC by providing a biological link between the two that is RET/PTC rearrangement [1].

Meta-analysis by Lee JH et al., showed that PTC has significant association with Hashimoto's thyroiditis and suggested careful monitoring of these patients with HT for the development of carcinoma. Thyroid cancer is predominantly of papillary type [3]. Molnar C et al., showed that thyroid gland affected by Hashimoto's thyroiditis have increased likelihood of developing PTC. They also confirmed that Hashimoto's thyroiditis can be considered as a

precondition for PTC. In their study, classical variant of PTC was the most common variant associated than the follicular and other variants [4]. Zhang Y et al., in their study evidenced that PTC with Hashimoto's thyroiditis has a greater incidence and 29.4% is accounted by it [5]. They concluded that Hashimoto's thyroiditis is associated with PTC in a significant risk manner.

Konturek A et al., in their study showed that PTC is associated with Hashimoto's thyroiditis which has increased by three fold. They have concluded that association between Hashimoto's thyroiditis and PTC is more than what is previously believed [6]. The present study was conducted with the aim to analyse the variants of PTC and to evaluate the presence of associated lesions.

MATERIALS AND METHODS

This was a retrospective study conducted on 41 cases of PTC from January 2016 to December 2018 in the Department of Pathology, Kempegowda Institute of Medical Sciences, Bengaluru, Karnataka, India. The demographic data and clinical findings were retrieved from the case files. The study was approved by Institutional Ethical Committee (KIMS/IEC/A42-2019).

All the cases reported to KIMS hospital during January 2016 to December 2018 were included in the study. There were 41 cases of PTC during the study period.

Inclusion criteria: All thyroid carcinoma diagnosed as PTC were included in the study.

Exclusion criteria: Thyroid carcinomas other than PTC were excluded from the study.

Specimens of thyroidectomies were received with request forms containing relevant clinical details and preoperative diagnosis. The specimens were examined, grossed and processed as per routine histopathology processing. Slides were stained with Haematoxylin and Eosin stain (H&E). The slides were studied under light microscope.

STATISTICAL ANALYSIS

The results were analysed by calculating frequency (n) and percentages (%). The Fischer's-exact test using R Statistical Software v 4.0.0 was used for association between PTC and disorders.

RESULTS

The present study included 41 cases of PTC. The patient's age ranged from 20-70 years with a mean age of 47 years. Majority of the patients were females (30/41).

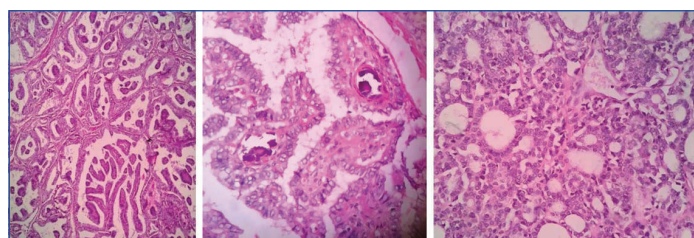
Gross features in the thyroidectomy specimens varied from tiny grey white lesions [Table/Fig-1a] to large irregular mass [Table/Fig-1b]. Some of them appeared granular. Multiple nodules and cystic areas noted in few. The most common type of PTC was classic variant (31/41, 75.6%) [Table/Fig-2]. Classic variant showed papillary structures lined by cells having ground glass nuclei, nuclear crowding, nuclear grooves and pseudoinclusions [Table/Fig-3]. Psammoma bodies were seen in eight cases [Table/Fig-4]. The second common type was follicular variant which showed follicular arrangement of cells with characteristics PTC nuclear features as described above [Table/Fig-5]. There were three cases of papillary microcarcinomas. All of them measured 1 cm or less in diameter and showed characteristic nuclear features.



[Table/Fig-1]: a) Papillary thyroid carcinoma-grey white lesions; b) Papillary thyroid carcinoma-large irregular mass.

Variants	Numbers	Percentage
Classic variant of PTC	31	75.60%
Follicular variant of PTC	6	14.63%
Papillary microcarcinoma	3	7.31%
Diffuse sclerosing variant of PTC	1	2.43%

[Table/Fig-2]: Distribution of PTC Variants.
PTC: Papillary thyroid carcinoma



[Table/Fig-3]: Classic variant of PTC (H&E, 100X).

[Table/Fig-4]: Classic variant of PTC showing psammoma bodies (H&E, 400X).

[Table/Fig-5]: Follicular variant of PTC (H&E, 100X). (Images from left to right)

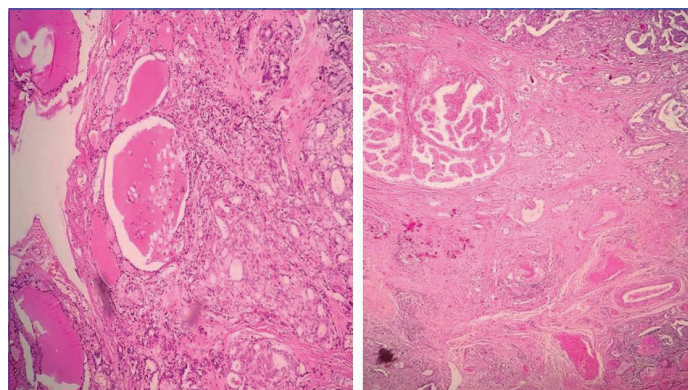
One case of diffuse sclerosing variant was noted where there was diffuse fibrosis throughout the tumour and the cells showed characteristic nuclear features. The slides of thyroidectomy specimens were studied to identify the associated diseases with PTC. Of 41 cases of PTC, 13 cases had associated disorders in thyroid [Table/Fig-6].

In these 13 cases, preoperative diagnosis of PTC was available in six cases and in the remaining seven cases PTC was diagnosed on histopathological examination. Multinodular goitre was noted in eight cases [Table/Fig-7], seven cases of them were associated with classic variant and one case was a papillary microcarcinoma. Among these eight cases, only two cases had preoperative

Variant of PTC	Associated disorders	
	Multinodular goitre	Hashimoto's thyroiditis
Classic variant of PTC	7 (17.07%)	3 (7.3%)
Follicular variant of PTC	0	1 (2.43%)
Papillary microcarcinoma	1 (2.43%)	1 (2.43%)
Diffuse sclerosing variant of PTC	0	0

[Table/Fig-6]: PTC variants and associated disorders.

diagnosis of PTC. In the remaining six cases, PTC was discovered on histopathological examination of thyroidectomy specimen for multinodular goitre. Association between PTC and multinodular goitre is not statistically significant (p -value=0.45). Hashimoto's thyroiditis was associated in five cases of PTC [Table/Fig-8]. Of these three cases were classic variant, one was follicular variant and other was papillary microcarcinoma.



[Table/Fig-7]: PTC associated with Multinodular goitre (H&E, 100X).

[Table/Fig-8]: PTC associated with Hashimoto's thyroiditis (H&E, 100X). (Images from left to right)

In these five cases of Hashimoto's thyroiditis, four cases had preoperative diagnosis of PTC and only one case was incidental which was a papillary microcarcinoma. Association between PTC and Hashimoto's thyroiditis is not statistically significant (p -value 0.45).

DISCUSSION

In total data of 41 thyroidectomies of the present study, 30 were female patients. In the present study, of 41 cases we found 31 were classic variant, 6 were follicular variant, 3 were papillary microcarcinoma and single case of diffuse sclerosing variant.

Anand A et al., study showed that PTC with Hashimoto's thyroiditis cases are less aggressive, presents earlier and less incidence of lymph node metastasis and extra thyroidal extension [7]. They also showed PTC with Hashimoto's thyroiditis patients have better prognosis, low recurrence and reduced mortality. They concluded that it is prudent to exclude malignancy in Hashimoto's thyroiditis.

We have found Hashimoto's thyroiditis associated with five cases of PTC of which three were classic variant, one was follicular variant and one was papillary microcarcinoma. [Table/Fig-9] depicts this in comparison to other studies [4,6]. The papillary microcarcinoma was diagnosed incidentally on histopathological examination of thyroidectomy specimen. Study by Resende de Paiva C et al., showed that an association was found between Hashimoto's thyroiditis and thyroid lymphoma [8].

Comparative analysis	Association of Hashimoto's thyroiditis with papillary thyroid carcinoma
Present study	5/41 (12.19%)
Molnar C et al [4] Hungary, 2019	43/262 (16.4%)
Konturek A et al [6] Poland, 2012	40/43 (93.0%)

[Table/Fig-9]: Comparison with other studies regarding association of Hashimoto's thyroiditis and PTC [4,6].

Moon S et al., in their meta-analysis showed that prognosis of patients is improved when Hashimoto's thyroiditis is co-existed with PTC. And also noted that lymph node metastasis, extrathyroidal extension is reduced and recurrence free survival duration is increased in comparison to other patients who did not have associated Hashimoto's thyroiditis. They concluded that association of Hashimoto's thyroiditis with PTC could be used to assess the prognosis of PTC [9]. Loh KC et al., and Yoon YH et al., had similar findings [10,11].

Graceffa G et al., showed that there is decreased tumour aggressiveness and recurrence of pathology is diminished with association of Hashimoto's thyroiditis and papillary thyroid carcinoma [12]. Rajkumar B et al., showed in their study that incidence of PTC with multinodular goitre was 25% when surgery was undertaken in the absence of any aetiological or risk factors [13]. Nadeem k et al., showed incidence of 14.9% and Hanumanthappa MB et al., found 10% incidence of PTC with multinodular goitre [14,15].

Fama F et al., showed a 12% risk of harbouring preoperatively unsuspected PTC, some even with capsular invasion in multinodular goitres [16]. Botrugna I et al., found in their study of 462 thyroidectomies for MNG, around 10% showing incidental thyroid carcinomas, most of which were PTC [17]. We have found eight cases of PTC associated with multinodular goitre, out of which seven were with classic variant and one was papillary microcarcinoma. Of the 8 cases 6 were incidental, unsuspected preoperatively.

Limitation(s)

It is a retrospective study, probably a prospective study would allow more detailed gross examination. Smaller sample size is a limitation.

CONCLUSION(S)

Classic variant is the most common type of PTC. All thyroidectomies done for multinodular goitre and Hashimoto's thyroiditis should be screened thoroughly for PTC especially microcarcinoma. Clinical importance between PTC and associated disorders has been found which has different line of management and follow-up. The present study did not show statistical significance between these disorders although. Further larger and multicentre study is required.

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