Original Research Article

Histopathological spectrum of papillary carcinoma thyroid – a 4 year retrospective analysis

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Abstract

Introduction: Papillary carcinoma of thyroid is the most common malignant tumor constituting about 80% of all malignancies of thyroid. It has an indolent course with an excellent prognosis and numerous histological variants have been reported till date. Also various associated lesions are also being noted, of which has himotos thyroiditis is one of the common lesions. **Objective:**1)To analysevarious histopathological features of papillary carcinoma thyroid. 2) Toevaluate the presence or absence of has himotos thyroiditis in the background of papillary carcinoma. **Design**: Hospital based cross sectional study. **Subject**: Histopathologically diagnosed cases of papillary carcinoma thyroid in a 4 year period. **Methods:** Retrospective analysis of histopathologically diagnosed cases of papillary carcinoma thyroidhas been done. **Results:** Papillary carcinoma thyroid is more prevalent among females with most of thelesions showing conventional papillary pattern in 72.8% cases. Almost all the cases have the typical nuclear features described. Hashimotos thyroiditis is seen in 44.2% of the cases. Papillary micro carcinoma seen in 17.1% patients. Multifocality is seen in 28.5%. The association between papillary carcinoma and has himotos thyroiditis was evaluated using chi square test, p value= 0.001 and was found to be statistically significant. **Conclusion**: Our study has well correlated with the literature, with regards to epidemiological profile and the predominant histopathological pattern. Hashimotos thyroiditis is predominant associated lesion.

Keywords: Hashimotos Thyroiditis, Histopathology, Papillary Carcinoma Thyroid (PTC)

Introduction

Papillary carcinoma is the most common malignant tumor of thyroid gland and comprises about 80–85% of thyroid malignancies. They arebiologically indolent, with an excellent prognosis (survival rates of >95% at 25 years) [1]. Most tumors are diagnosed in patients in the third to fifth decades of life. Female – male ratio is 2:1 to 4:1 [2,3]. Small nodules of PTC or micro-carcinomas (less than 1 cm in size) are usually of no clinical significance especially in young patients (less than 40 years), since such individuals have a 20-year survival of greater than 98% even with palpable tumors.

The tumors invade lymphatics leading to multifocal lesions and to regional node metastases. Multifocal papillary carcinomas constitute 20-30% of cases reported[4] Microscopically, neoplastic papillae contain a central core of fibrovascular tissue lined by one or occasionally several layers of cells with crowded oval nuclei. Cytologically, the nuclei show characteristic crowding, overlapping, clearing, grooves and intra nuclear pink cytoplasmic inclusions. Of all the associated lesions, hashimotos thyroiditis occupy a special place. Its relation with papillary carcinoma thyroid isa long term debated topic in literature and till date, studies establish that there was coexistent thyroiditis and carcinoma in 11–36% of patients [5]. In the present study we have retrospectively analysed the slides reported as papillary carcinoma, with special reference to its various histopathological features, nuclear morphologies, uni/multi focality and looked for any significance in the association between hashimotos thyroiditis and papillary carcinoma thyroid.

Materials and Methods

The cross-sectionalstudy consists of retrospective histo-pathological analysis of papillary carcinoma thyroid, reported ina 4 year period in KMCT Medical College, Kozhikode. Multiple representative sections aretaken

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from these specimens, which were processed by formalin fixation, paraffin embedded and stained by standard H and E method. Five to ten sections of the tumorstudied in detail by two different pathologists and average of both observers was analyzed. Repeat deeper sections were taken from the respective blocks wherever necessary. Special mention has been given to neoplasms with hashimotos thyroiditis as the associated lesion and the association of the same with papillary carcinoma isevaluated using SPSS and Microsoft excel analysis. There is no specific inclusion or exclusion criteria inthis study.

Results

We had studied 70 cases of histopathologically confirmed papillary carcinoma thyroid over a span of 4 years in our institution. There were 616 cases of thyroidectomy specimens received in our department during this period, out of which, 70 cases were diagnosed as papillary carcinoma.

Of the 70 cases of papillary carcinoma, 59 were females and 11 males. Male: female ratio was 1:5.

53% of the cases were proven as neoplastic in FNAC samples, as per the Bethesda system of thyroid cytology reporting.

Among the papillary carcinoma cases, the conventional papillary pattern dominated (72.8%) which was followed by follicular variant of papillary carcinoma (15.7%) [Fig 2A]. There were 3 Warthin like variants [Fig 3A, 3B], 4 cases with combined papillary and follicular patterns and one tall cell subtype [TABLE-1]

Papillary microcarcinomas accounted to 12 out of 70 cases (17.1%) (Fig 2B). Among the studied cases, multifocality was noted in 20 cases (28.5%)

Almost all the cases showed the typical nuclear characteristics ofcrowding, overlapping, clearing, grooving and cytoplasmic pseudoinclusions, [Fig 1A, 1B] except for one case oftall cell variant of papillary carcinoma thyroid.

Psammoma bodies were noted in 50% of cases [Fig 1C], Lymphnode metastases were seen in only 9 cases.
Cystic papillary carcinomas accounted in 7 cases.

In the samples studied, there were different associated lesions in the adjacent thyroid tissue like, multi nodular goiter, adenomatous hyperplasia and even normal thyroid tissue. But among all, the most commonly noted associated lesion was hashimotos thyroiditis which was present in 31 out of 70 cases [Fig 3C]. In the four years of study, 84 cases of hashimotos thyroiditis were diagnosed. While looking for the association between these two lesions (hashimotos thyroiditis and papillary carcinoma thyroid), we found it was statistically significant, using chi square test, with a p value of 0.001.

Table-1: Histological variants of papillary carcinoma thyroid and their distribution.

Histological variants	Number of cases
Conventional papillary pattern	51
Follicular variant	11
Combined follicular + papillary pattern	4
Warthin cell variant	3
Tall cell variant	1

Table-2: Chi square test.

	Papillary carcinoma positive	Papillary carcinoma negative
Hashimotos thyroiditis positive	31	53
Hashimotos thyroiditis negative	39	532

P value =0.001 (statistically significant)

Discussion

The most common endocrine malignancy is thyroid cancer, which is more commonly seen in females. Among all the thyroid tumors, papillary carcinoma tops the position in its prevalence. In our study, we concentrate on the histopathological characteristics of the already diagnosed papillary carcinoma cases for a 4 year period, and evaluate any significance in the association between hashimotos thyroiditis and papillary carcinoma thyroid.

Based on recent data, thyroid cancer is the fifth most common cancer in womenwhich presents in 20-55 years of age [6]. Papillary carcinoma thyroidcan present as an asymptomatic thyroid nodule that presents as a neck mass [7]. According to the literature, early menarche, young parous women with recent pregnancy, all have an increased risk of this malignancy [8]. In our institution, among the malignant thyroid lesions of thyroid, papillary carcinoma is the commonest. For the last 4 years 70 cases of papillary carcinoma have been reported out of 616 thyroidectomy specimens. Females are commonly involved by this lesion (84.2%); male: female ratio being, 1:5.

Though, dietary iodine concentrations appear to influence the incidence of the papillary carcinomas, the most important relationship in regard to the etiology of papillary thyroid carcinoma is the association with radiation. In our study, Fine Needle Aspiration Cytology was done in a few cases, where 53% of cases were proven as neoplastic.

Papillary carcinomas will vary in its gross presentations.It can appear anywhere in the gland. The lesions are firm and usually white in color with invasive margins. Calcification is a common feature. In some lesions, cyst formation is seen. In fact, some lesions may be rarely almost completely cystic making diagnosis difficult [9].In our study, there were 7 cases with cystic component.

Microscopically, most of our cases had the typical papillary pattern, with the characteristic nuclearfeatures of nuclear crowding, overlapping, clearing, nuclear grooves and inclusions. There was a case of tall cell variant of papillary carcinoma, which showed less number of nuclear features.

Psammoma bodies are lamellations of calcifications produced by focal areas of infarction of the tips of papillae attracting calcium that is deposited on the dying cells [10,11]. Another proposed theory invokes the mechanism of intracellular accumulation of calcium by tumor cells that lead to their death and release of the calcium [12]. 50% of cases in this study showed psammoma bodies. Though, regional lymphnode metastasis is common in this lesion, our study reveals only 9 out of 70 cases with the same. Papillary carcinoma thyroid has numerous variants, of which the most important one is follicular variant of papillary carcinoma. We had 11 cases of follicular variant, which is thesecond most common subtype in this study. 72.8% of the cases had the typical conventional papillary pattern. We had one case of tall cell variant, and 3 cases of warth in like variant of papillary carcinoma.

Papillary microcarcinomas are those tumors which are less than 1cm in diameter. It is a very common incidental finding in autopsy studies (6-36%) and in thyroids removed for other reasons (5-24%)[13]. RET rearrangements are a frequent finding in papillary microcarcinoma and in a recent meta-analysis the prevalence of BRAFV600E mutation was reported as 47.48%[14,15]. The term ‘papillary microtumor’ has been proposed. This terminology excludes tumors in patients less than 19 years of age and tumors with metastases.12 out of 70 cases (17.1%) showed papillary microcarcinoma in our study.

Multifocal papillary thyroid carciniomas (mPTCs) comprise about 20% to 30% of all papillary thyroid carcinomas[16]. These foci may occur from intraglandular metastases from a single dominant tumor or arise independently as unrelated neoplastic clones from a distinct progenitor cell [17,18]. Thus the two theories ofde novo carcinogenesis and intrathyroidal metastasis are the prevalent explanations for the mutifocality. In this study, out of 70 cases, 20 had multifocal papillary carcinoma thyroid (28.5%).

Association of Hashimoto’s thyroiditis with papillary thyroid carcinoma was first put forwardby Dailey, et al. in 1955 [19]. Okayasu, et al. was the person who found out aclear association between these two diseases among patients of different ethnic origin [20]. In our study,out of, 616 cases of thyroidectomies, 84 cases were diagnosed as hashimotos thyroiditis (13.63%). Among these, 31 cases had associated papillary carcinoma thyroid. That is, incidence of cases with both papillary carcinoma and hashimotos thyroiditis is 44.2%. Thus, the association between these two lesions was calculatedusing chi square test, and was found to be significant (p value =0.001).

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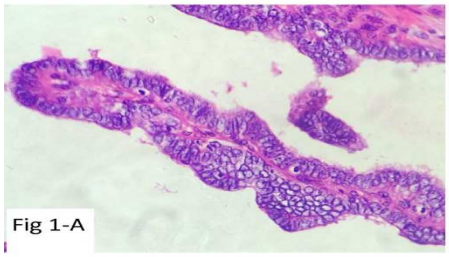
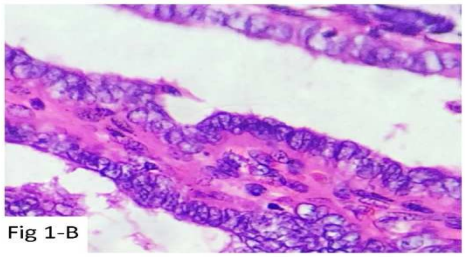
Seminal work by Fiore et al. on thyroiditis with papillary carcinoma showed high titers of thyroid antibodies ($p<0.001$) compared to hashimotos thyroiditis alone [21]. The sustained inflammatory response in hashimotos thyroiditis may act as carcinogen. Hashimotosoccasionally exhibits cytological alterations, nuclear modifications similar to those seen in carcinoma like RET/PTC rearrangement and BRAF mutations suggesting that the neoplastic and autoimmune disease share the same platform of molecular pathogenesis [22,23,24,25]. Thus explaining the possible relation between these two lesions.





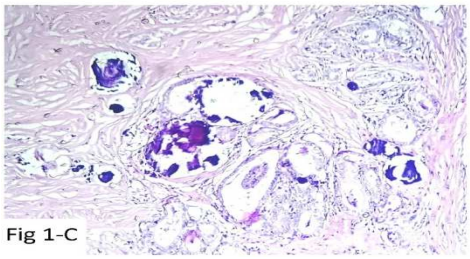


FIG1A & 1B– PHOTOMICROGRAPHS OF TYPICAL NUCLEAR FEATURES (CLEARING, CROWDING,OVERLAPPING, GROOVING) (H&E 40X)

FIG 1C– CONCENTRIC LAMELLATIONS OF CALCIFICATIONS FORMING PSAMMOMMA BODIES (H&E 5X)

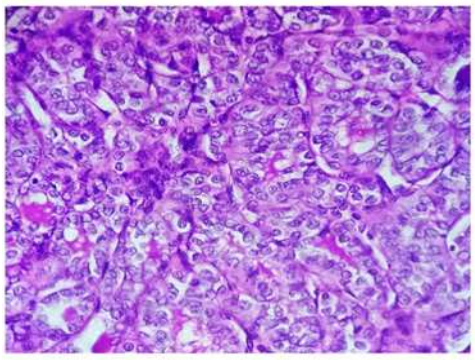


FIGURE 2-A

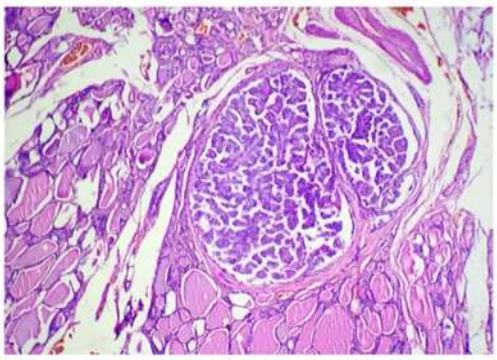
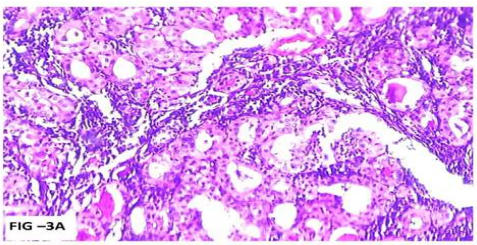
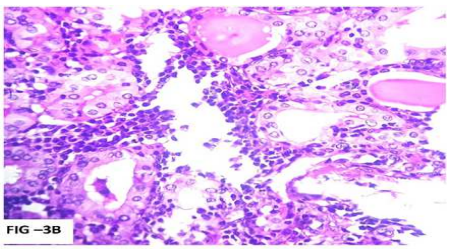


FIGURE 2-B

FIGURE 2A– H&E 40X—FOLLICULAR VARIANT OF PAPILLARY CARCINOMA THYROID

FIGURE 2B– H&E 5X– FOCUS OF PAPILLARY MICROCARCINOMA IN A MULTI NODULAR GOITRE.





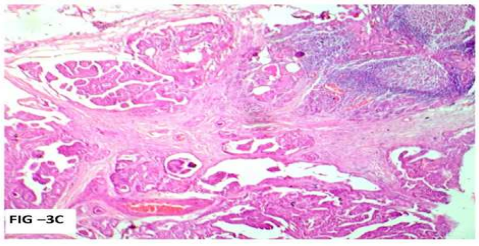


FIGURE 3A & 3B– WARTHIN LIKE VARIANT OF PAPILLARY CARCINOMA (H&E, 10X AND 40X)

FIGURE 3C– PAPILLARY CARCINOMA THYROID WITH HASHIMOTOS THYROIDITIS (H&E 5X)

Conclusion

1. Papillary carcinoma thyroid is the commonest malignancy of thyroid encountered in our department during the 4 year study period.
2. Females are more affected by this neoplasm, male: female ratio being, 1:5.
3. The most common histopathological pattern is the conventional papillary pattern, followed by follicular variant. Other rare variants like,warthin like variant and tall cell variants were reported in our study.
4. 17.14% of cases hadpapillary micro carcinomas and 28.5% of cases had multifocality which contributed to poor prognosis.
5. Among the associated lesions seen with the neoplasm, there was striking increase in hashimotos thyroiditis. Upon calculation of the p value by chi square test, it was found that the association between hashimotos and papillary carcinoma thyroid was significant, which correlated well with the previous literatures.

This study concludes that conventional papillary carcinoma thyroid is the most commonly encountered thyroid malignancy in Malabar region. Papillary thyroid carcinoma hada strong association with hashimotos thyroiditis.

Authors Contribution: Dr. Anupama Raj.K. has made the conception and design of the study and has been involved in drafting the manuscript. Dr. Benzy Paul has doneacquisition of data, analysis and interpretation of data. Dr. K. A Aisabi has given final approval of the version to be published.

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