



Research Article

CLINICAL AND HISTOPATHOLOGICAL ANALYSIS OF VARIANTS OF PAPILLARY CARCINOMA OF THYROID GLAND- REPORT FROM A TERTIARY CARE CENTER IN KERALA, SOUTH INDIA

Lakshmanan P. P¹, Anilakumari V. P² and Byjo V³

¹Department of Surgery Government Medical College, Kozhikode, Kerala

²Department of Nuclear Medicine Government Medical College, Kozhikode, Kerala

³Department of Neurosurgery: Government Medical College, Kozhikode, Kerala

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ABSTRACT

Introduction: Papillary carcinoma of thyroid (PTC) is the most common thyroid cancer and one among the most curable of all cancers. Recent reports emphasize that, it should be further sub-classified into its variants because of prognostic implication. The purpose of this study to assess the frequencies of different variants of papillary carcinoma thyroid from our patient population and study their association with clinical characteristics.

Methods: A total of 81 patients with post-operative diagnosis of PTC seen in our institution during 2014-2015 were included in the study.

Results: Out of the 81 patients, there were 65 (80.2%) females and 16 (19.8%) male patients. All patients had neck swelling at presentation. Forty four (54.3%) patients presented with thyroid swelling of less than six months duration. Seven variants of PTC were identified in our series- classical PTC (n=56; 69%), follicular variant (n=11; 14%), micropapillary variant (n=6; 7%), tall cell variant (n=4; 5%), encapsulated variant (n=2; 3%), and diffuse sclerosing and oncocytic variants (n=1 each; 1%) each. The AMES risk stratification did not differ across histological subtypes. Males were more likely to have high-risk disease when compared to females (62% vs. 33%; p<0.001).

Conclusions: Among patients with PTC about 80% patients are female and majority of male patients with PTC belongs to high risk group. Consistent with previous observations, classical PTC was most common followed by the follicular variant.

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INTRODUCTION

Papillary carcinoma (PTC) is the most common malignant tumor of thyroid gland, comprising 80% of all cases of thyroid malignancies. (1-4) PTC is usually diagnosed in patients in their third and fifth decades of life and women are affected more frequently than men with a ratio of 2 to 4:1. (5,6) PTC is one among the most curable of all cancers. Clinically, PTC behaves in an indolent fashion and carries an excellent prognosis. (7) There are about 15 histological variants of PTC of which classical PTC is the most common. (7,8) Histology of classical PTC shows a branching papillary architecture with a central fibrovascular core covered by cells with eosinophilic cytoplasm and enlarged oval nuclei with nuclear overlapping. (9) Sparse literature exists regarding the spectrum of variants of PTC seen in developing countries. In this study we aimed to review the histological variants of PTC seen at our center.

MATERIALS AND METHODS

The study was conducted in Govt. Medical College, Kozhikode, a tertiary care teaching hospital in South India. The hospital provides referral care to a population base of about one crore. Patients who underwent thyroidectomy and were found to have PTC in the thyroid or dissected lymph node(s) during a two-year period from January 2014 to December 2015 were included in the study. We enrolled patients retrospectively and prospectively during the period. Details regarding patient demographics, clinical presentation, basic laboratory tests, and thyroid function tests were collected by personal interview and examination for prospectively enrolled patients, and from the medical records for retrospectively enrolled patients.

Patients were categorized into high or low-risk groups using the AMES (age, metastases, and extent of primary cancer) classification. (10) Estimation of tri-iodothyronine (T3), tetraiodothyronine (T4) and thyroid stimulating hormone (TSH) were done using electrochemiluminescence assay (details of kits). The study was approved by the institutional review board. The collected data were subjected to statistical analysis using SPSS version 22.0. Continuous variables were

*Corresponding author: **Lakshmanan P. P**

Department of Surgery Government Medical College, Kozhikode, Kerala

summarized as median; categorical variables were summarized as proportions and compared between groups using Chi-square test.

RESULTS

A total of 81 patients were included in the analysis and 65 (80.2%) of them were female and 16 (19.8%) were male. The median age at diagnosis of PTC was 39 years (range, 17-67). All patients had neck swelling at presentation and 44 (54.3%) patients presented with thyroid swelling of less than 6 months duration. Majority of cases sought medical attention for an otherwise asymptomatic thyroid swelling (65.4%; n=53). Twenty eight (34.6%) patients had symptoms including recent enlargement of the swelling, vague pain or throat discomfort. Four (4.9%) patients presented with cervical lymph node enlargement alone. Thyroid hormone study was done in all patients. There were 7 (8.6%) cases of hyperthyroidism detected biochemically as well as clinically. Two patients were hypothyroid (2.5%). The remaining patients were euthyroid.

Seven variants of papillary carcinoma thyroid were identified in our series. The classical (69.1%) and follicular (13.6%) variants were the most common. The distribution of variants of PTC in our study population is shown in Table 1.

Table 1 Histological variants of papillary carcinoma of thyroid gland (n=81)

Histopathological variant	Frequency, n (%)
Papillary carcinoma classical variant	56 (69.1%)
Papillary carcinoma follicular variant	11 (13.6%)
Papillary carcinoma micropapillary	6 (7.4%)
Papillary tall cell variant	4 (4.9%)
Papillary encapsulated variant	2 (2.5%)
Papillary diffuse sclerosing variant	1 (1.2%)
Papillary oncocytic variant	1 (1.2%)
Total	81 (100%)

All the patients in the study were grouped into low risk and high risk groups, based on AMES risk stratification criteria. Each type were analyzed through the risk groups. Overall, 56(69%) cases were classified as low-risk and 25(31% cases under high-risk (Table 2).

Table 2 Distribution of AMES risk groups based on histological variants (n=81)

Histopathology	High-risk, n(%)	Low-risk, n(%)	Total
Classical variant	21 (37%)	35 (63%)	56
Follicular variant	1 (9%)	10 (91%)	11
Others	3 (21%)	11 (79%)	14
Micropapillary variant	0	6 (100%)	6
Tall cell variant	2 (50%)	2 (50%)	4
Encapsulated variant	0 (0%)	2 (100%)	2
Diffuse sclerosing variant	1 (100%)	0 (0%)	1
Oncocytic variant	0 (0%)	1 (100%)	1

Among the classical type, 35 (62.5%) were classified under low-risk group while 21 (37.6%) cases were in high-risk category. Majority of patients with follicular variant (90.9%) were in low-risk group. All of the 6 patients with micropapillary carcinoma and the 2 patients with encapsulated variants came under the low-risk category. However, there was no statistically significant difference in risk categories across the different variants [Chi-square= 3.18; P=0.20]. The AMES groups showed characteristic differences when compared between male and female patients. Out of 65 female patients, 50 (77%) were low-risk while among 16 male

patients only 6 (38%) came under low risk category. The males were more likely to have high-risk disease compared to females (62% vs. 33%) (Chi-square= 20.9; p<0.001).

We also compared the preoperative FNAC report with the postoperative HPR report. We found that only in 36 (44.4%) cases, pre-operative FNAC was consistent with PTC.

DISCUSSION

This study summarizes our experience with patients with PTC seen over a period two years. The median age at diagnosis was 39 years and most patients were female. Most common clinical presentation was with asymptomatic thyroid swelling. Classical and follicular variants were most common in our cohort. AMES high-risk disease was more common in males while the risk categorization did not vary across the histological subtypes. Only 44% patients with a post-operative diagnosis of PTC had a diagnostic FNAC pre-operatively.

As evidenced by the number of cases seen per year, our center is a high-volume center for treatment of PTC. Two centers have reported 40-80 cases per year(11,12) while most other centers have reported only 5-20 cases per year(13-16). The gender distribution of our cases is also consistent with most reports with about 20% of patients being male, (12,13,15,16) except one study which reported 50% of patients as being male (17). A large series from Japan reported a female to male ratio of 10:1. (1)

In our study the most common presentation was with thyroid swelling, consistent with previous reports. (11-17,1) About 30% of our patient had other symptoms, compared to a smaller proportion of patients (<10%) in another series. (17) About 10% of patients with PTC in our series had hyper- or hypothyroidism while only <3% patients had endocrine abnormalities in a similar series. (17)

Consistent with previous series, the classical variant was the most common histological sub-type identified in our series. (12-16,1) The follicular variant was the second most common. The follicular variant resembles follicular neoplasm on gross examination, but long term prognosis is similar to classical PTC. (1) Micropapillary, tall cell, encapsulated, diffuse sclerosing and oncocytic variants were also identified in our series. We did not encounter any patient with variants like macrofollicular, columnar, cribriform-morular, prominent hobnailing, insular, squamous or mucoepidermoid, solid, Wharthin-like variants or PTC with fascitis-like stroma.(8)

The AMES risk stratification did not differ across histological subtypes in our analysis; but the impact of rare variants in this analysis is hard to ascertain. Larger series incorporating more patients with these variants are necessary to define the risk stratification of patients with uncommon variants of PTC. Irrespective of the histological subtypes, males with PTC were more likely to have AMES high-risk disease.

In our study papillary micro carcinoma was found only in 6 patients (7.4%). This is comparable with most reports (12,14,16) while Girardi et al from Brazil and Lam *et al* from Australia have reported micropapillary carcinoma in 42.1% and 27.8% patients respectively in their series. (15,18) The lower occurrence of micro papillary carcinoma in our series may be due to lower detection resulting from reluctance to investigate non-palpable thyroid nodules or mild thyromegaly by means of newer imaging modalities including high

frequency ultrasound.

The demographic distribution of papillary carcinoma in our series is similar to previous reports. Classical PTC was most common, whereas frequency of more aggressive varieties like, diffuse sclerosing type, tall cell variant and oncocytic variant were very low. In view of prognostic implication is important to specify the variant of papillary cancer in the histological diagnosis. Multi-center studies with long-term follow-up are necessary to define the clinical behavior of the rare variants.

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