Original Article

Clinicopathological profile of papillary carcinoma of thyroid: A 10-year experience in a tertiary care institute in North Karnataka, India

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Abstract

CONTEXT: Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy accounting for 80% of the thyroid cancers. Many histopathologic variants of PTC have been recognized, and few of these are of prognostic significance. The studies on clinicopathological features of PTC and its variants are so far seldom reported in India. **AIM:** The aim of the study was to study the percentage distribution of PTC among total thyroid specimens, the age and sex distribution of PTC, its histopathological features including frequency of nuclear findings, and various histological subtypes are also studied in detail. **METHODS:** All cases of PTC diagnosed in our department from April 2003 to March 2013 formed the material for the study. The tissues were routinely processed and stained. On microscopic examination, tumors were classified according to 2004 WHO classification. **RESULTS:** PTC formed the predominant type of malignancy accounting to 71% of the total cases. Of these, about 75% of patients were in the second to fifth decade. Male to female ratio was 1:5.4. Other than the usual classic variant and follicular variant, we also found rare types such as clear cell variant, tall cell type, oncocytic type, and macrofollicular variant. Microscopically, nuclear overcrowding and ground glass nuclei were seen in more than 90% of cases. Nodular goiter, Hashimoto's thyroiditis, and follicular adenoma were associated lesions in some cases. **CONCLUSION:** PTC is the most common thyroid malignancy, and it can affect any age group though it presents mostly in the third to fourth decade of life. Recognition of histological subtype is crucial in patient prognosis.

Key Words: Carcinoma, papillary, thyroid

Introduction

Thyroid cancer is the most common endocrine malignancy with higher mortality rates compared to all other endocrine malignancies.[1] The recent data from National Cancer Registry Program show that thyroid cancer constitutes 3.96% of total cancers.[2] Papillary thyroid carcinoma (PTC) being the most common represents 80%–85% of thyroid cancers.[3] Many histopathologic variants of papillary carcinoma have been recognized; few of these are of prognostic significance. The studies on clinicopathological features of papillary carcinoma and its variants are so far seldom reported in India.

Aim

Our study aimed to study the percentage prevalence of papillary carcinoma of thyroid among total thyroid specimens received over 10 years in our institute. The age and sex distribution of PTC, its histopathological features including frequency of nuclear findings, and its various histological subtypes were also studied in detail.

Methods

This was a partly retrospective (8-1/2 years) and partly prospective (1-1/2 years) study. All cases of PTCs diagnosed in our department from April 2003 to March 2013 formed the material for the study (Karnataka Institute of Medical Sciences, Hubli). Clinical details for the retrospective study were obtained from the files in the department. Paraffin blocks of sections were sorted out; sections were cut and stained with hematoxylin and eosin for histopathological study. For a prospective study on receiving the specimens, the gross features were noted, and the tissues were fixed in 10% formalin for 24 h. After formalin fixation, multiple bits were taken from representative sites. They were processed for histopathological examination, and paraffin blocks were made. A detailed microscopic examination of the tumors was done to arrive at an accurate diagnosis. Tumors were classified according to 2004 WHO classification. The data compiled were analyzed for various parameters such as age, sex, and incidence of different histological types. Statistical methods were employed.

Results

Age and sex distribution

We received 798 thyroid specimens in 10-year period, of which 204 (25.56%) were neoplastic lesions. Of the neoplastic lesions, 104 (50.9%) were benign and 100 (49.01%) were malignant [Figure 1]. Papillary carcinoma formed the predominant type of malignancy accounting for 71% of the total cases. Of these, about 75% of patients were in their second to fifth decade [Table 1]. Classical papillary carcinoma were the predominant type in these age groups, followed by follicular variant. The youngest patient was 8 years old and he had a macrofollicular variant of papillary carcinoma, and the oldest patient was 78 years old and he had follicular variant of papillary carcinoma. There were 60 female and 11 male patients forming the male-to-female ratio of 1:5. Classic variant followed by follicular variant is the most common types in females.

Pathological features

Grossly, most of the tumors were unifocal (92%) and well circumscribed. Cut section of the tumors showed solid gray

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Table 1: Age distribution of histopathologic variants of papillary carcinoma in the present study

Types	1-9 years	10-19 years	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years
Classic	-	1	9	9	14	7	2	-
Folli	-	1	4	9	2	1	4	1
Macro	1	-	-	-	-	-	-	-
Onco	-	-	1	-	-	1	-	-
Clear	-	-	-	1	-	-	-	-
Tall	-	-	1	-	-	-	-	-
Micro	-	-	1	1	-	-	-	-
Total	1	2	16	20	16	9	6	1

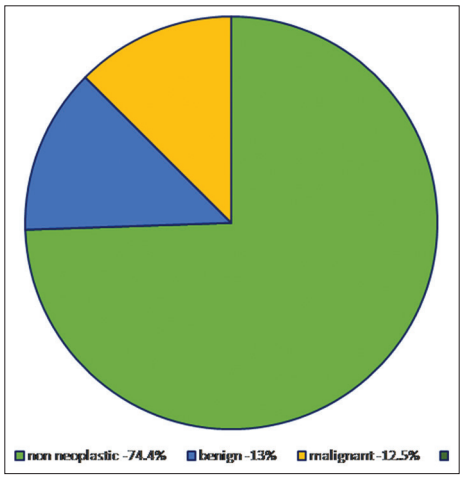

Figure 1: Percentage distribution of thyroid lesions

white tumor with papillary projections [Figure 2a]. Few cases (8%) had multifocal tumor with involvement of both the lobes.

Microscopic details

The percentage distribution of various microscopic types is listed in Table 2. Classic variant formed the predominant group accounting for 59% of the papillary carcinomas. This is followed by follicular variant (31%). Microscopically, we assessed the tumors for the presence of the parameters such as nuclear overcrowding, ground glass nuclei, arborizing papillary processes, nuclear grooves, and nuclear inclusions [Figure 2]. The percentage distribution of which is described in Table 3. Psammoma bodies were found in 32.39% of cases [Table 3 and Figure 3a]. We found two cases of papillary microcarcinoma (PMC) [Figure 4a].

Cervical lymph node metastasis was seen in 17 (23.9%) cases of papillary carcinoma. Of 17 cases, 15 were classic variants of papillary carcinoma and two were follicular variants of papillary carcinoma.

Associated lesions

Of 71 cases, 18 cases had associated lesions in the thyroid gland apart from the primary tumor. Nodular goiter was the most common associated condition accounting for 50% of the associated lesions. This was followed by Hashimoto's thyroiditis and follicular adenoma each accounting for 44.4% and 5.5% of the associated lesions, respectively.

Collision tumor

One case of minimally invasive follicular carcinoma had foci of PMC in the same lobe. Patient was 35-year-old female [Figure 4d].

Table 2: Distribution of various microscopic variants of papillary carcinoma in the present study

Microscopic variants	Number of cases (%)
Classic	42 (59.15)
Follicular variant	22 (30.98)
Macrofollicular	1 (1.4)
Oncocytic	2 (2.8)
Clear cell	1 (1.4)
Tall cell	1 (1.4)
Micropapillary	2 (2.8)
Total	71 (100)

Table 3: Microscopic features of papillary carcinoma in the present study

Microscopic features	Number of cases (%)
Arborizing papillae	46 (64.7)
Nuclear overcrowding	65 (91.54)
Ground glass nuclei	64 (90.14)
Nuclear grooves	62 (87.32)
Nuclear inclusions	32 (45.07)
Psammoma bodies	23 (32.39)

Discussion

PTC is the most common malignant tumor among all thyroid cancers, comprising an estimated 80% of thyroid cancers.[4] Papillary carcinoma is a malignant epithelial tumor showing follicular cell differentiation and characterized by distinctive nuclear features.[5] In the present study, papillary carcinoma accounts for 71% of the total thyroid malignancies. Othman *et al.*[6] and Gole *et al.*[7] also observed the incidence of papillary carcinoma to be 76.6% and 78.56%, respectively.

It occurs in a relatively younger age group than follicular carcinoma. Youngest patient in the present study was 8 years old. Radiation exposure is one of the well-known risk factors for PTC. Other risk factors include genetic factors, preexisting nodular disease, and association with genetic syndromes such as familial adenomatous polyposis syndrome.[4] In the present study, a maximum number of patients with PTC were in the third to sixth decade of life. Frazell and Foote[8] observed the maximum incidence of papillary carcinoma in the third to sixth decade of life. Carcangiu *et al.*[9] also observed the highest incidence of papillary cancer in the third to sixth decade of life.

In the present study, females predominate over males with a ratio of 5:1. Frazell and Foote[8] and Carcangiu *et al.*[9]

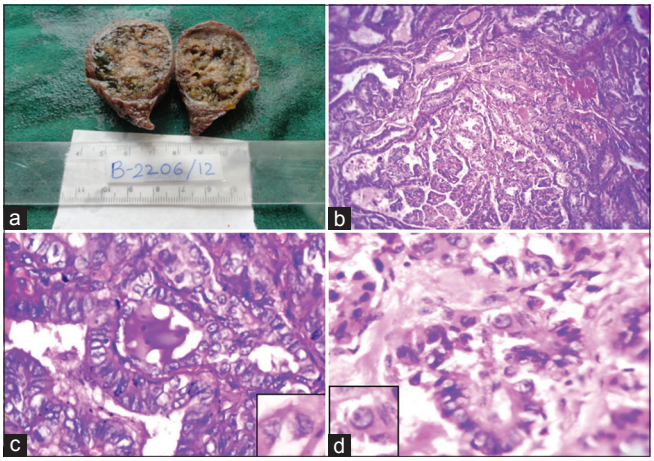

Figure 2: (a) Papillary carcinoma classic variant showing gray white tumor with papillary projections. (b) Microscopy of the classic variant showing arborizing papillary process. (c) Ground glass nuclei with nuclear grooves (inset). (d) Intranuclear inclusions in papillary carcinoma

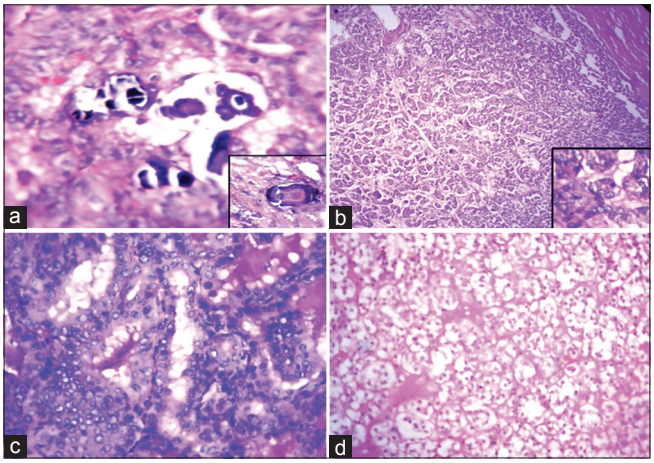

Figure 3: (a) Psammoma bodies in papillary carcinoma. (b) Follicular variant showing capsular invasion with nuclear features of papillary cancer (inset). (c) Oncocytic variant of papillary carcinoma. (d) Clear cell variant of papillary carcinoma

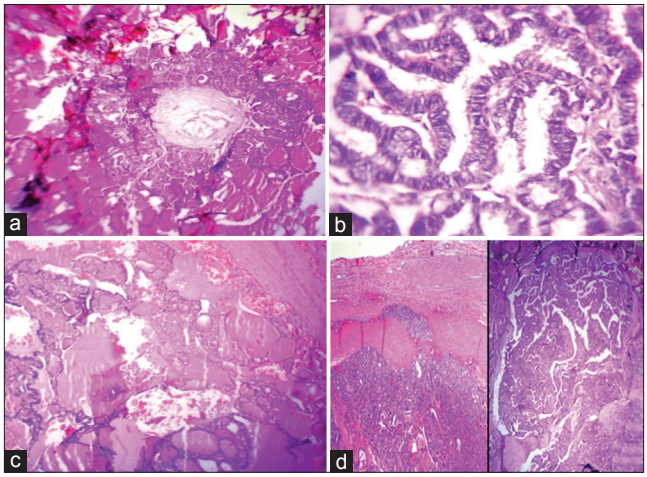

Figure 4: (a) Papillary microcarcinoma. (b) Tall cell variant of papillary carcinoma. (c) Macrofollicular variant of papillary carcinoma. (d) Collision tumor showing foci of follicular carcinoma and papillary microcarcinoma in the same lobe

observed female predominance in their studies with female to male ratio of 2.47:1 and 2.6:1, respectively. Heitz *et al.*[10] also observed female to male ratio of 3.1:1.

Papillary carcinoma has different macroscopic morphologies. The classic variant can be solid or cystic with papillary excrescences. Tumors are usually of tan color and are firm in consistency. The oncocytic variant has brown-to-mahogany color. Degenerative changes may be seen focally which may be the result of previous fine-needle aspiration cytology (FNAC) or develop spontaneously. These changes include cystic formation, hemorrhage, and necrosis. Papillary carcinoma can be unifocal or multifocal. In our study, 8% of the cases had multifocal tumor with the involvement of bilateral lobes. Occasionally, tumor may arise in thyroglossal duct cyst.

Papillary carcinomas are diagnosed by the characteristic nuclear features. These include optically clear nuclei also known as "orphan annie" nuclei, nuclear grooves, intranuclear inclusions, and nuclear overcrowding. These features are enough to suggest papillary carcinoma even if the papillary pattern is absent in the tumor.[11] In our study, all classic variants and one case of columnar and oncocytic variant showed arborizing papillary processes with fibrovascular core. The papillae in PTC are covered by epithelium with disturbed polarity and pale eosinophilic cytoplasm.[4] Papillary structures may also be seen in nodular goiter, follicular adenoma, or in diffuse hyperplasia because of the infolding of the epithelium. The important distinguishing feature here is the classic nuclear features of PTC which are absent in these benign conditions.[4] Ground glass nuclei were seen in 90.14% cases [Table 3] This is similarly seen in a study conducted by Hapke *et al.*[12] and Chan *et al.*,[13] who observed them in 83% and 84.3% of papillary carcinoma, respectively. Nuclear grooves were seen in 87.88% of cases which is in concurrence with the study by Chan *et al.*,[13] who observed it in almost all the cases he studied. In the present study, nuclear pseudoinclusions were seen in 45.07% of cases. Chan[13] in his study also observed nuclear pseudoinclusions in 46% of the cases.

Psammoma bodies are rounded concentrically laminated calcifications which must be distinguished from psammoma-like bodies which may be present within the colloid.[5] The present study shows psammomatous calcifications in 32.39% of papillary carcinomas. Klink *et al.*[14] found psammoma bodies in 43% of cases of papillary carcinomas and only once in a review of 2153 benign thyroid lesions; thus, they represent a very important clue to diagnosis.

Thyroid microcarcinoma is described as thyroid cancer with size less than 10 mm. The most common microcarcinoma, found incidentally, is papillary thyroid microcarcinoma.[9] In our study, we found two cases of PMCs accounting for 2.8% of papillary carcinomas. This is significantly less compared to study by Carcangiu *et al.*,[9] who reported 14.2% of PMC. Roti *et al.*[15] in a meta-analytical study observed an average incidence of 28.8% of PMCs among papillary cancers. In our case, these patients were in the second and third decade. One of the patients initially presented with swelling in right lateral side of the neck which turned out to be lymph node metastasis of papillary carcinoma on histopathology and this was later followed by thyroid resection. Preoperative ultrasound-guided FNAC of

the thyroid nodule was reported as colloid goiter with cystic change. Both the patients had nodular goiter in the adjacent thyroid. PMC presenting as lymph node metastasis is not uncommon.[16] Examination of cervical lymph nodes is very important as it may be the only presentation of the disease in such cases.[17] These tumors show RET/PTC arrangement as in usual thyroid cancer. These PMCs can also have BRAF mutations. The PMC with BRAF mutations is more aggressive and present with lymph node metastasis.[16]

In our study, 17 cases had lymph node metastasis accounting for 23.9% of the cases. Carcangiu *et al*.[9] and Shrikhande and Phadke[17] observed cervical lymph node metastasis in papillary carcinoma in 32.4% and 36.5% of cases, respectively.

Bhudaraja *et al*.[18] in his study of thyroid cancers observed 34% of the cases showing lymph node metastasis and all cases were papillary carcinoma metastasis. In a study of papillary carcinoma in 731 patients; 91 patients had metastasis outside the regional lymph nodes. The most common site was intrathoracic occurring in 73 out of the 91 patients.[19]

Associated lesions

In our study, 18 cases (25.3%) had associated lesions apart from the primary tumor. Nodular goiter was the most common lesion accounting for 50% of the lesions followed by Hashimoto's thyroiditis (44.4%) and follicular adenoma (5.5%). Gole *et al*.[7] in his study of 55 cases of papillary carcinoma, 21 cases (38.18%) had associated nonneoplastic lesions. Of associated lesions, 61.90% were nodular goiters, 19.04% were lymphocytic thyroiditis, and 19.04% were Hashimoto's thyroiditis. Madhavan and Othman[20] observed 34% of micropapillary carcinoma in patients underwent thyroidectomy for long-standing nodular goiter. Htwe *et al*.[21] in his study observed 6.7% incidence of thyroid cancers in goiterous thyroid lesions and papillary carcinoma was the most common accounting for 60% of cancers. Thus, it is imperative that thyroid specimens excised for benign conditions also demand a thorough gross examination to increase the yield of cancer detection.

Collision tumors

Collision tumors of thyroid are rare. In the literature, most are coexisting medullary and papillary cancer or metastatic carcinoma with papillary carcinoma. Follicular carcinoma and papillary carcinoma are very rare. Plauche *et al*.[22] reported a case report of coexisting papillary and follicular carcinoma in a 65-year-old female patient. In the present study, one female patient aged 35 years had minimally invasive follicular carcinoma and foci of PMC in the same lobe.

We had one case of clear cell variant [Figure 3d] which showed tumor cells having clear cytoplasm along with nuclear features of classical papillary carcinoma in more than 70% of the tumor tissue. In metastatic sites, recognition of this type may pose problem and application of immunostain for thyroglobulin and thyroid transcription factor-1 may be necessary.[5] We had one case of tall cell variant [Figure 4b]. We also had one case of macrofollicular variant [Figure 4c] and oncocytic variant [Figure 3c]. Recognition of these microscopic subtypes is important as the prognosis will vary. Tall cell variant is associated with more aggressive clinical behavior whereas macrofollicular type is known for good patient outcome.[5]

Conclusion

Papillary carcinoma is the most common thyroid malignancy. The disease can affect any age group though it presents mostly in the third to fourth decade of life. Females are more affected than males. Identifying the classical features of PTC and distinguishing PTC from other thyroid cancers as well as benign mimickers, recognition of various subtypes of PTC is crucial in the patient management. Despite advances in imaging techniques and molecular diagnostics, pathologists still play a very important role in the management of thyroid neoplasms and predicting the patient outcome and prognosis.

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Conflicts of interest

There are no conflicts of interest.

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