International Journal of Clinical and Diagnostic Pathology

ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2020; 3(2): 167-171
Received: 25-02-2020
Accepted: 28-03-2020

Namrata Rao
Assistant Professor, Department of Pathology, Melaka Manipal Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India

Pavithra P
Associate Professor, Department of Pathology, Melaka Manipal Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India

Varun Kumar Singh
Assistant Professor, Department of Pathology, Melaka Manipal Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India

Brij Mohan Kumar Singh
Associate Professor, Department of Pathology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India

Rashmi Shetty
Assistant Professor, Department of Pathology, Melaka Manipal Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India

Corresponding Author:
Pavithra P
Associate Professor, Department of Pathology, Melaka Manipal Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India

Thyroid revisited-histopathological spectrum of thyroid carcinomas with cytological correlation

Namrata Rao, Pavithra P, Varun Kumar Singh, Brij Mohan Kumar Singh and Rashmi Shetty

DOI: https://doi.org/ 10.33545/pathol.2020.v3.i2c.248

Abstract
Introduction: Thyroid carcinomas are common malignancies encountered in routine diagnostics
Aim: Aim of this study was to analyse the histopathological spectrum of thyroid malignancy with papillary carcinoma subtyping and to assess the cytological and histopathological correlation of thyroid malignancies.
Methods and materials: Carcinoma thyroid cases diagnosed between January 2016 and January 2020 were retrieved. Demography, histopathological spectrum and cytology-histopathology correlation were assessed and in case of discrepancy the cause was analysed.
Results: A total of 102 cases of carcinoma thyroid were found, majority being in the fourth decade with female preponderance. Most patients were euthyroid at diagnosis and presented with thyroid nodule. On histopathology, majority were papillary carcinomas with classical type being the commonest. On cytological correlation discrepancy was seen in 13 cases.
Conclusion: It is vital to be aware of their morphology to avoid misdiagnosis. Cytology is an effective way of determining the type of lesion before excision.

Keywords: carcinoma, papillary, subtypes, thyroid

Introduction
Thyroid is distinct as it is the earliest endocrine organ to develop in fetal life and is also the largest [1]. It can be affected by a wide spectrum of disorders ranging from developmental, inflammatory, hyperplastic to neoplastic lesions. Although thyroid malignancy accounts for only 1.5% of all cancers, it is still the commonest endocrine malignancy [2]. They present as mass lesions for which fine needle aspiration cytology and histopathology play a crucial role. The aim of this study was to analyse the histopathological spectrum of thyroid malignancy with papillary carcinoma subtyping and to assess the cytological and histopathological correlation of thyroid malignancies.

Materials and methods
This is a retrospective study conducted in the department of pathology of a tertiary hospital. Cases of carcinoma thyroid diagnosed between January 2016 and January 2020 were retrieved from the laboratory information system. The cases of carcinoma thyroid were classified according to the WHO classification-2017 based on their histological subtype. The age, sex and fine needle aspiration cytology report of the above cases were retrieved. The age incidence, sex prevalence and cytology-histopathology correlation were assessed. The cause of discrepancy in cases with no cytology histology correlation was analysed. The distribution of cases of carcinoma thyroid and the variants of papillary carcinoma were tabulated.
Inclusion Criteria: Cases of carcinoma of thyroid diagnosed between January 2016 and January 2020.
Exclusion criteria: Benign lesions and non-neoplastic lesions of the thyroid were excluded from the study.

Results
During the five year study period, a total of 102 cases of thyroid were found. Majority of the patients were in the fourth decade. The age distribution of thyroid carcinomas is shown in

Table 1 Among all the cases, 65 were females and 37 were males. There was a female preponderance with female: male ratio being 1.7:1.

Table 1: Age distribution of thyroid carcinomas

Age	Number of cases
10-20	4
20-30	7
30-40	28
40-50	33
50-60	12
60-70	13
70-80	4
80-90	1

Sixty seven patients were euthyroid at diagnosis, 3 were hyperthyroid, 2 were hypothyroid and thyroid profile was not done in 30 cases. Regarding the clinical presentation, 86 cases presented with nodule in the thyroid, one case of anaplastic carcinoma presented with a nodule and hoarseness of voice, five patients of papillary carcinoma presented with enlarged cervical lymph nodes and 10 cases of carcinoma were incidentally detected on histopathology.
On histopathology, majority were papillary carcinomas (79.4%) followed by follicular carcinoma (11.7%), medullary carcinoma (6.8%) and anaplastic carcinoma (2.9%). One case had both follicular carcinoma and anaplastic carcinoma in different lobes of the thyroid. (Table 2)

Table 2: Histological subtypes of thyroid malignancies

Histological type	Total number of cases
Papillary carcinoma	81
Follicular carcinoma	12
Medullary carcinoma	7
Anaplastic carcinoma	3 (one case had follicular and anaplastic)
Total	102

The subtypes of papillary thyroid carcinoma are summarised in Table 3. With respect to this, the classical type was the commonest (70.3%) followed by follicular variant (17.2%). There were no cases belonging to diffuse sclerosing, hobnail, solid, spindle cell, clear cell and warthin like variant. Among the medullary carcinoma thyroid, two were spindle cell variants, one was mucinous variant, the rest being classical type. One sarcomatoid variant of anaplastic carcinoma was seen. Microscopic images of papillary carcinoma (classical type, follicular variant, hurthle cell variant), medullary carcinoma and anaplastic carcinoma is shown in figure 1, 2 and 3 respectively.

Table 3: Subtypes of Papillary thyroid carcinoma

Histological subtype of papillary thyroid carcinoma	Number
Classic	57
Microcarcinoma	4
Follicular variant of papillary carcinoma	14
Tall cell type	1
Cribriform morular type	1
Columnar cell type	1
Hurthle cell type	1
Macrofollicular type	1
Nodular fasciitis like stroma	1
Total	81

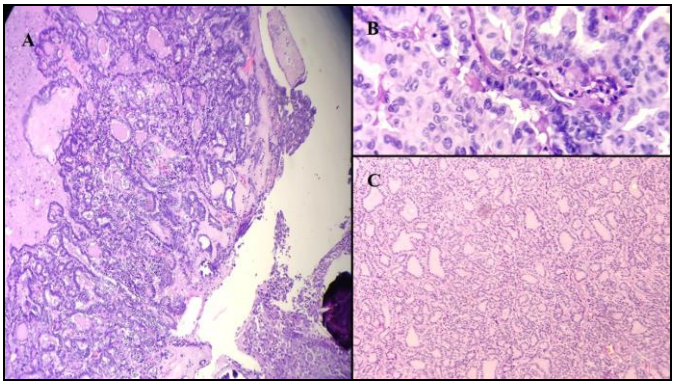

Fig 1: Papillary carcinoma-classical variant showing psammoma body (H&E, 100x). B: Hurthle cell variant of papillary carcinoma showing cells with abundant eosinophilic cytoplasm (H&E, 400x). C: Follicular variant of papillary carcinoma (H&E, 100x).

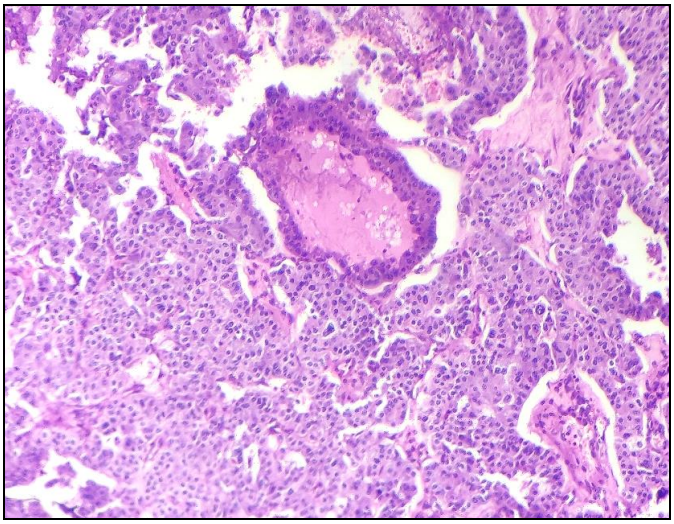

Fig 2: Microscopy showing features of medullary thyroid carcinoma with extracellular amyloid. (H&E, 100x).

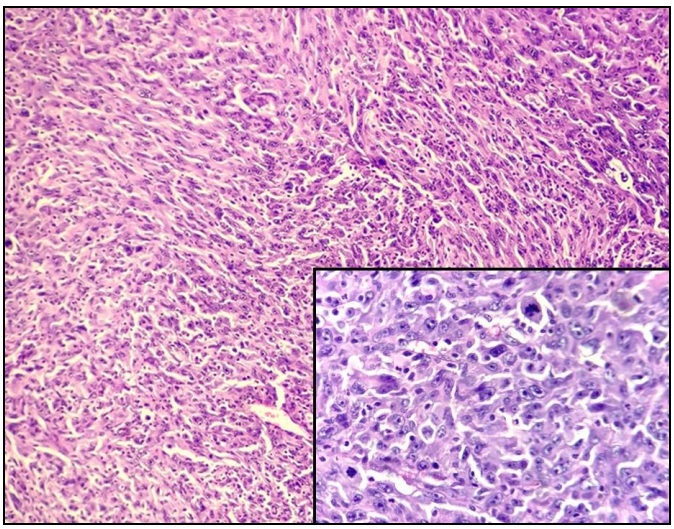

Fig 3: Microscopy showing features of anaplastic carcinoma (H&E, 100x). Inset shows bizzare tumour cells with atypical mitosis (H&E, 400x).

Cytology with histopathology correlation of the above cases were done. The diagnosis in both correlated in 66 cases. One case was diagnosed as medullary carcinoma on cytology, had features of papillary carcinoma on histopathology,

however the diagnosis of malignancy in this case was not missed. FNA was not done in 21 cases and the sample was inadequate in 2 cases. The diagnosis on cytology was given as colloid goiter in 9 cases and adenomatous nodule in 2 cases. Eight cases of colloid goiter on histopathology showed features of papillary carcinoma and one case showed features of follicular carcinoma. The two cases of adenomatous hyperplasia on histopathology showed papillary carcinoma and follicular carcinoma respectively. The case having synchronous follicular and anaplastic carcinoma was diagnosed as follicular neoplasm on cytology, however the anaplastic component was missed causing discrepancy.

Discussion

Thyroid carcinomas are more common in women as compared to men with female: male ratio in this study being 1.7:1. Female predominance dominated in all the studies with the ratio being 2.6:1 and 3.1:1 in studies done by Carcangiu *et al* [3] and Heitz *et al*. [4] respectively

The tumours were more common in fourth and fifth decades of life which is similar to that in the study conducted by Frazell and Foote [5]. Most of the patients were euthyroid at diagnosis and presented with nodule in the thyroid which are similar to the findings in the study conducted by Makazlieva *et al*. [6].

Based on histology the most common type was papillary carcinoma which in this study accounted for 79.4% of the cases and the least common was anaplastic carcinoma which accounted for 2.9% of the cases. These findings are consistent with the findings of Gole *et al*. [7], Othman *et al*. [8] and Rao.R *et al*. [9] in which the incidence of papillary carcinoma was 78.56%, 76.6% and 71% respectively. Diagnosis of papillary carcinoma is challenging since it has a number of variants each having varied morphology, however the most common variant was the conventional type followed by follicular variant. Brief discussion of morphology of thyroid carcinomas and variants of papillary shall be discussed to enable correct diagnosis.

Papillary carcinoma: The risk factors include genetic factors, prior exposure to ionising radiation and nodular lesions of the thyroid [10]. Most common presentation is nodule in the thyroid with few of them associated with cervical lymphadenopathy and hoarseness of voice due to injury to recurrent laryngeal nerve. Cystic degeneration is common in these tumours. Ultrasonography is a useful tool in identifying solid, cystic lesions and calcification. Papillary carcinomas present as cold nodule on nuclear scan. Morphology is crucial in arriving at a diagnosis. Subtyping of these tumours carry prognostic significance, hence morphological details are discussed below.

Classic/ conventional papillary carcinoma: The tumour cells are arranged in papillary pattern. The cells lining the papillae exhibit nuclear grooving, clearing and intranuclear inclusions with presence of psammoma bodies. The colloid is thick and can show scalloped appearance.

Follicular variant of papillary carcinoma (FVPC): Is a common variant accounting for 20-30% of papillary carcinomas. The histological features include follicular pattern of tumour cells with papillary like nuclear features which include intranuclear inclusion, nuclear grooving, psammoma bodies [11]. FVPC are commonly misdiagnosed as follicular adenomas due to circumscription on gross, follicular architecture and subtle nuclear features which is bound to have observer variation.

Hurthle cell variant: these tumour cells have abundant eosinophilic cytoplasm with the classic nuclear features. The eosinophilia is due to abundant mitochondria. Since hurthelisation is a common change which can be associated with non neoplastic and neoplastic conditions, importance lies in identifying the nuclear features [12].

Tall cell variant: Is diagnosed when the height of tumour cells is greater than three times the width. The tumour cells have their nucleus located basally which exhibit papillary like nuclear features and have abundant eosinophilic cytoplasm [13]. It is important to recognise and mention this variant even when it forms a minor component of tumours because it is associated with increased incidence of extrathyroidal disease, recurrence and metastasis. The tumour usually account for 10% of papillary carcinomas [14].

Columnar cell variant: The tumour cells are elongated exhibit pseudostratification with cytoplasmic vacuolations. However the tumour cells lack the classic nuclear features [15].

Papillary carcinoma with nodular fasciitis like stroma: As the name suggests the tumour has a nodular fasciitis like stroma which can mask the component of papillary carcinoma. In this the tumour cells exhibit the features of classic papillary carcinoma. This entity requires extensive sampling to avoid missing the actual tumour component and avoid mislabelling the tumour as a mesenchymal tumour.[16]

Macrofollicular variant: Tumour cells are arranged in macrofollicular pattern and have the characteristic papillary nuclear features [17].

Cribriform morular variant: The tumour cells are arranged in cribriform pattern and as squamous morules. Focally nuclear features of papillary carcinoma are present [18]. It is associated with familial adenomatous polyposis syndrome hence raising a possibility of underlying APC germline mutation [10].

Papillary microcarcinoma: Is an entity with tumour size less than 1 cms and exhibits all the features of classical papillary carcinoma [17]. Multiple microcarcinomas should suggest the possibility of a larger papillary thyroid carcinoma. These microcarcinomas would then be attributed as dissemination from the larger papillary carcinoma and should suggest the presence of an underlying RET/PTC germline mutation [10].

From the above discussion it can be inferred that diagnosis of papillary carcinoma and its variants requires careful examination of the nuclear features and the pattern of arrangements of tumour cells. Classic, follicular variant, oncocytic and clear cell variant carry no prognostic significance. Even focal presence of nuclear features is sufficient for the diagnosis. Presence of mere papillary architecture in the absence of nuclear features should be classified as benign papillary hyperplasia.

Follicular carcinoma: Tumour cells may be arranged in macrofollicular, normofollicular or microfollicular pattern. Diagnostic feature is presence of capsular invasion and/or vascular invasion. Invasion of vessels in capsule and beyond are considered. Follicular carcinomas have distant metastasis at diagnosis because of their affinity for the blood vessels [19].

Medullary carcinoma: The tumour cells can be plasmacytoid, spindle shaped, round with stippled nuclear chromatin and eosinophilic cytoplasm. Amyloid deposits are

present in the stroma. In medullary carcinoma, variants are not of any prognostic significance [20].

Anaplastic carcinoma: The tumour cells are highly pleomorphic with increased mitosis, necrosis and presence of giant cells. These are aggressive tumours with adverse prognosis [21]. The concurrence of follicular carcinoma and papillary carcinoma with anaplastic carcinoma is known to occur, in view of histogenesis from the follicular cell. Anaplastic carcinoma can also be due to dedifferentiation from a more differentiated carcinoma [22]. However in our case the synchronous presence of follicular and anaplastic carcinoma is two different lobes of the thyroid is due to the origin of these tumours from a common precursor cell.

FNA is a simple inexpensive technique of determining the nature of the lesion, thereby serving as an important method in guiding the management of the patient. However this technique is associated with pitfalls. Errors in judgement are usually due to the lesion not being sampled, wrong diagnosis and inadequacy of the samples [1]. Smears were categorised as satisfactory if it had five to six clusters of cells with each cluster comprising of 10 or more cells. In our study, smears were unsatisfactory in 2 cases. This study was done to also determine the accuracy of FNA in diagnosing thyroid carcinomas. Cytology with histopathology correlation was seen in 66 cases out of 81 cases for which FNA was done, accounting for 81.4% accuracy. Discrepancy was seen in 13 cases accounting for 16%. Seven cases of papillary carcinoma were misdiagnosed as colloid goitre on cytology. The probable reasons are frequent association with cystic change and tiny focus of malignancy in a multinodular goiter. One case of papillary carcinoma was reported as colloid goitre with papillary hyperplasia on cytology, however the subtle nuclear features were missed on cytology. One case of follicular variant of papillary carcinoma was diagnosed as adenomatous hyperplasia on cytology due to the presence of microfollicular pattern. The common differential diagnosis of microfollicular pattern in smears are FVPTC, follicular neoplasm and hyperplastic nodule, thereby accounting for the discrepancy in diagnosis.

Two cases of follicular carcinoma was misdiagnosed as colloid goitre and adenomatous hyperplasia respectively on cytology probably due to aspiration in colloid rich areas of thyroid. Also the representative features like nuclear overcrowding, overlapping, repeatitive microfollicles were missed on cytology due to abundance of colloid, adenomatous hyperplasia also presents with repeated microfollicular pattern. One case of papillary carcinoma was misdiagnosed as medullary on cytology, due to presence of nuclear inclusions which can occur in cases of medullary carcinoma. In such a case IHC for calcitonin and thyroglobulin or congo red stain for amyloid can be done.

One case of follicular neoplasm reported on cytology showed foci of follicular carcinoma and anaplastic carcinoma in separate lobes of thyroid. The discrepancy was due to the second lesion (anaplastic carcinoma) not being sampled. This can be minimised by multiple sampling since multiple lesions can involve the thyroid simultaneously. Findings on imaging also serve an adjunct to accurate diagnosis. Also cytology cannot differentiate between follicular adenoma and follicular carcinoma. Inadequacy of sampling was seen in two cases which can be minimised by ultrasound guided FNA technique.

Conclusion

Thyroid carcinomas are a common malignancy encountered in routine diagnostics. It is vital to be aware of their morphology including uncommon variants to avoid misdiagnosis. FNAC is an effective way of determining the type of lesion before excision, the efficacy of which can be improved by multiple sampling and by taking help of imaging modalities.

References

1. Pavithra P, Rashmi N. Utility of cytodiagnosis in the management of thyroid lesions. Int J Pharm Bio Sci. 2014; 5(4):(B)1173-1182.
2. Beigh A, Amin J, Junaid S, Wani L, Farooq S, Farooq S *et al*. Histopathological Study of Thyroid Neoplastic Lesions in a Tertiary Care Hospital - A 5 Year Study. International Journal of Contemporary Medical Research [IJCMR]. 2018; 5(4).
3. Carcangiu ML, Zampi G, Pupi A, Castagnoli A, Rosai J. Papillary carcinoma of the thyroid. A clinicopathologic study of 241 cases treated at the University of Florence, Italy. Cancer. 1985; 55:805-28.
4. Heitz P, Moser H, Staub JJ. Thyroid cancer: A study of 573 thyroid tumors and 161 autopsy cases observed over a thirty-year period. Cancer. 1976; 37:2329-37.
5. Frazell EL, Foote FW Jr. Papillary cancer of the thyroid; a review of 25 years of experience. Cancer. 1958; 11:895-922.
6. Makazlieva T, Vaskova O, Majstorov V, Stojanoski S, Manevska N, Jovanovic R *et al*. Demographic and Clinical Features of Thyroid Carcinomas in Republic of Macedonia (1999-2010). Open access Macedonian journal of medical sciences. 2017; 5(7):1005-1010.
7. Gole SG, Satyanarayana V, Gole GN, Ramamurti T, Hayath MS, Deshpande A *et al*. Profile of thyroid neoplasms with special focus on interesting cases: A hospital based 12 year longitudinal study. Internet J Pathol, 2013, 14.
8. Othman NH, Omar E, Naing NN. Spectrum of thyroid lesions in hospital Universiti Sains Malaysia over 11 years and a review of thyroid cancers in Malaysia. Asian Pac J Cancer Prev, 2009; 10:87-90.
9. Rao R, Giriyan SS, Rangappa PK. Clinicopathological profile of papillary carcinoma of thyroid: A 10-year experience in a tertiary care institute in North Karnataka, India. Indian J Cancer. 2017; 54:514-8.
10. Al-Brahim N, Asa S. Papillary thyroid carcinoma an overview. Arch Pathol Lab Med. 2006; 130:1057-1062.
11. Suster S. Thyroid tumors with a follicular growth pattern, problems in differential diagnosis. Arch Pathol Lab Med. 2006; 130:984-8.
12. Baloch ZW, Livolsi VA. Oncocytic lesions of the neuroendocrine system. Sem Diagn Path. 1999; 16(2):90-9.
13. Ghossein R, Livolsi VA. Papillary thyroid carcinoma tall cell variant. Thyroid. 2008; 18:1179–1181.
14. Hawk W, Hazard J. The many appearances of papillary carcinoma of the thyroid. Cleveland Clin Q. 1976; 43:207-216.
15. Boerner SL, Asa SL. Biopsy interpretation series: Biopsy interpretation of the thyroid. Epstein JI, editor. Philadelphia: Wolter Kluver /Lippincott Williams &Wilkins, 2009.

16. Na KY, Kim HS, Sung JY, Park WS, Kim YW. Papillary carcinoma of the thyroid gland with nodular fasciitis-like stroma. Korean J Pathol. 2013; 47:167-171.
17. Variants of Papillary Thyroid Carcinoma: Multiple Faces of a Familiar Tumor Serpil Dizbay Sak
18. Nikiforov YE, Ohori NP. Papillary carcinoma. In: Nikiforov YE, Biddinger PW, Thompson LDR editors. Diagnostic pathology and molecular genetics of the thyroid: A comprehensive guide for practicing thyroid pathology. 2nd edition. Philadelphia: Wolter Kluver /Lippincott Williams &Wilkins, 2012, 183-246.
19. Girardi FM, Barra MB, Zettler CG. Variants of papillary thyroid carcinoma: association with histopathological prognostic factors. Brazilian Journal of Otorhinolaryngology. 2013; 79(6):738-744. doi: 10.5935/1808-8694.20130135
20. Etit D, Faquin W, Gaz R, Randolph G, DeLellis R, Pilch B *et al*. Histopathologic and Clinical Features of Medullary Microcarcinoma and C-Cell Hyperplasia in Prophylactic Thyroidectomies for Medullary Carcinoma. Arch Pathol Lab Med. 2008; 132:1767-73
21. Ragazzi M, Ciarrocchi A, Sancisi V, Gandolfi G, Bisagni A, Piana S *et al*. Update on Anaplastic Thyroid Carcinoma: Morphological, Molecular, and Genetic Features of the Most Aggressive Thyroid Cancer. International Journal of Endocrinology, 2014, 1-13.
22. Ganguly R, Mitra S, Datta AK. Synchronous occurrence of anaplastic, follicular and papillary carcinomas with follicular adenoma in thyroid gland. Indian J Pathol Microbiol. 2010; 53:337-9