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Classical Papillary Thyroid Carcinoma and its Histopathological Variants.

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ABSTRACT

Papillary carcinoma of the thyroid was regarded previously as a single group with indolent clinical course and excellent prognosis. This view has changed. Recent histopathological reports emphasize that papillary carcinoma should be further classified into its variants because of the prognostic implications. We report its incidence, clinical behaviour and outcome of variants of papillary thyroid cancers at Narayana Medical College, Nellore. To study the incidence, age and gender of variants of papillary thyroid carcinoma and to analyze the results with published data. These cases were received in the surgical pathology laboratory of Narayana Medical College, Nellore from July 2006- June 2008. We have reviewed clinical case sheets, microscopic slides and histopathological reports of these carcinomas. Accordingly we report our experience of different variants, a series of 37 papillary carcinoma. The following results have been obtained:19 cases were Classical (usual) papillary carcinoma, 8 Follicular variant, 4 Diffuse sclerosing variant, 3 Encapsulated variant, 2 Mixed tall cell columnar cell variant and 1 Tall cell variant**.** These variants differ from each other not only on a morphologic basis, but also in clinical behavior and prognosis. Rightly subtyped histopathological report will help the clinicians for its management and prognostic implications.

Keywords: Papillary carcinoma of Thyroid, Follicular variant of Papillary Thyroid Carcinoma, Tall Cell Variant.

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INTRODUCTION

Tumours of the thyroid account for 1% of the overall human cancer burden,they represent the most common malignancies of the endocrine system and pose a significant challenge to pathologists, surgeons and oncologists. Thyroid cancer occurs primarily in young and middle aged adults, with approximately 1,22,000 new cases per year worldwide[1]. Despite the increase in incidence, the mortality rate is declining. Thyroid carcinomas can be caused by environmental, genetic and hormonal factors. Because of the thyroid dependence on environmental iodine, it is particularly vulnerable to the genotoxic effects of radioactive iodine and to the nongenotoxic effects (TSH stimulation) resulting from iodine deficiency. Thyroid carcinoma in a population can be compared to an iceberg-partly visible (clinically evident tumours) but mostly hidden tumours (occult tumours) [2].

Papillary carcinoma is most closely linked to radiation, with young children being particularly susceptible. Papillary carcinoma is the commonest of thyroid malignancies[3] and it is well-differentiated malignant thyroid neoplasm [4]. In adults, the male: female ratio of papillary carcinoma of the thyroid is 1:3 while in children, the tumour is distributed in both sexes equally. Papillary thyroid carcinoma (PTC) was regarded previously as a single group with indolent clinical course and excellent prognosis. This view has changed. Recent reports emphasize that papillary carcinoma should be further classified into its variants because of prognostic implications [4].

Objectives

To study the incidence of variants of papillary thyroid carcinoma Age & Gender incidence of each variants of papillary thyroid carcinoma and to analyze the results with published data.

METHODOLOGY

The material for the study included resected biopsy specimens of the thyroid lesions, submitted to the Department of Pathology, Narayana Medical College Hospital, Nellore, between August 2006 to July 2009.The details of each case were obtained from the clinical records. The Specimens were fixed in 10% formalin for 24 hours after recording the gross morphological features. Depending on the size and appearance of the tumour, appropriate number of 5mm thick bits were cut from the lesion and submitted for processing, 4 – 5 micron thick sections were cut with a microtome and stained with Haematoxylin and Eosin stain (H&E). The diagnosis of thyroid malignancy was made on the basis of gross morphology, microscopic features of H & E sections and with clinical correlation.

OBSERVATION AND RESULTS

The study conducted from August 2006 to July 2009 included a total number of 146 Surgically excised specimen received in the department of Pathology, Narayana Medical College

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Hospital, Nellore, and Andhra Pradesh. Out of 146 specimens 71 were non-neoplastic lesions and 75 were neoplastic lesions.

Papillary carcinoma of thyroid presents with various clinical features. Solitary nodule is the common finding of any thyroid lesion, and the other symptoms are dysphagia, cough and least being dyspnoea. All these symptoms occur to a greater extent in neoplastic lesions rather than in non-neoplastic lesions. The various presenting signs in neoplastic thyroid swelling are hoarseness of voice, loss of weight, sleepless nights, excessive sweating, palpitation, irritability and enlargement of cervical lymphnodes.

Table 1: Frequency of Histologically confirmed thyroid lesions – (146cases)

S.no	Thyroid lesions	No of cases	Percentage
1.	Colloid goiter	2	1.36%
2.	Multinodular goiter	31	21.23%
3.	Adenomatous goiter	12	8.21%
4.	Autoimmune thyroiditis	24	16.43%
5.	Thyroglossal cyst	2	1.36%
6.	Follicular adenoma	34	23.28%
7.	Papillary carcinoma	37	25.34%
8.	Follicular carcinoma	4	2.73%
9.	Medullary carcinoma	-	-
10.	Anaplastic carcinoma	-	-
Total		146	

Table – 1 shows frequency of thyroid lesions diagnosed histologically. Out of 146 cases, multinodular goitre were more in number in non-neoplastic lesions followed by auto immune thyroiditis, adenomatous goitre and colloid goiter.In neoplastic lesions 37 cases were reported as Papillary carcinoma followed by 34 as Follicular adenoma and 4 as Follicular carcinoma.

Table 2: Histologic Follow - up of patients in whom the retrospective diagnosis was discordant with the official diagnosis.

Previous FNA Diagnosis (no)	Histopathological Diagnosis (no)
Colloid goitre (1)	Classical Papillary thyroid carcinoma (1)
Multinodular goitre (1)	Classical Papillary thyroid Carcinoma (1)
Adenomatous goitre (2)	Follicular Variant of Papillary Thyroid Carcinoma (2)

Table – 2 shows FNAC diagnosis with the official histopathologic diagnosis. One case of colloid goitre in FNAC was reported as Classical Papillary Thyroid carcinoma in histopathology. One case of multinodular goitre and two cases of adenomatous goitre were reported as Classical PTC and Follicular variant of Papillary Thyroid carcinoma respectively.

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Table 3: Age, gender and distribution of histological variants of papillary thyroid carcinoma (37 cases)

S.no	Classic PTC and its Variants	NO:	Gender		Age Distribution (Yrs)			
			Female	Male	20-30	30-40	40-50	50-60
1.	Classic	19	13	6	5	4	7	3
2.	Follicular	8	5	3	-	2	3	3
3.	Encapsulated	3	2	1	-	3	-	-
4.	Tall cell variant	1	1	-	-	-	1	-
5.	MTCCCV	2	2	-	-	-	1	1
6.	Diffuse Sclerosing	4	2	2	-	1	1	2
Total		37	25	12	5	7	15	10

MTCCCV- Mixed Tall Cell Columnar Cell variant

Table – 3 shows histologically proven variants of papillary thyroid carcinoma. Out of 37 cases, 19 were reported as Classical PTC, next Follicular variant; 8, followed by Diffuse sclerosing variant; 4, Encapsulated variant; 3, Mixed Tall cell Columnar cell variant; 2 and Tall cell variant;1. 25 were females, 12 were males, the ratio being 2:1approximately. It is obvious from the table that female preponderance is seen all variants of papillary thyroid carcinoma.

Table 4: Involvement of lymph nodes: out of 37 cases of papillary carcinoma 7 shows secondary deposits.

S.no	Age	Sex	Histological Diagnosis	No of lymph nodes
1.	40	M	Classic PTC	12
2.	35	F	Classic PTC	4
3.	43	F	Classic PTC	4
4.	52	F	Follicular Variant	3
5.	46	M	MTCCCV	5
6.	59	M	Tall cell variant	4
7.	48	F	Diffuse Sclerosing Variant	2

MTCCCV- Mixed Tall Cell Columnar Cell varian

Table – 4 shows involvement of lymph nodes by classical papillary carcinoma and its variants. 6 of 37 cases show secondary deposits in the lymph nodes by the same tumor. Although females show more predilection for thyroid lesions, lymph nodes involvement was less. Current study depicts the same, carcinoma of thyroid when it occurs in males shows more aggressive behaviour than females. (Table:4)

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GROSS AND MICROSCOPIC PICTURES OF CLASSICAL PTC AND ITS VARIANTS

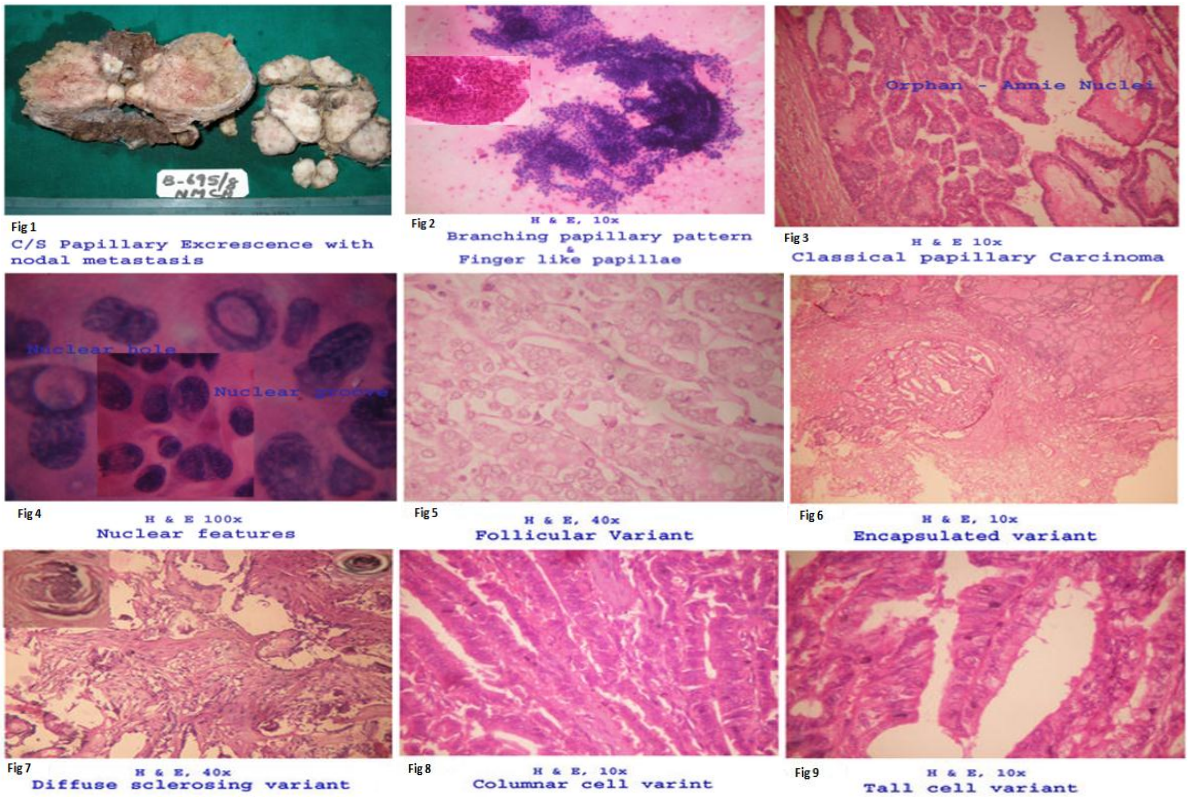

Figure 1: shows cut-section of thyroid comprising of papillary excrescences along with enlarged lymphnodes,which also exhibits papillary excrescences.
Figure 2: shows branching papillary pattern and inset shows finger like papillae.
Figure 3: shows papillae in arborizing pattern with Orphan- Annie eye nuclei. Few foci shows papillae with broad, edematous and hyalinised tissue.
Figure 4: shows nuclear grooves and intranuclear cytoplasmic inclusion.
Figure 5: shows small to medium sized follicles with virtually no papillary structures. The cells lining the follicles contain large clear nuclei.
Figure 6: shows a fibrous capsule and focal infiltration by tumour growth.
Figure7: shows psammoma bodies and stromal fibrosis.
Figure 8: shows pseudostratified columnar cells, some of the cells exhibits hyperchromatic nuclei.
Figure 9: shows cells whose heights are atleast three times their width.

DISCUSSION

Thyroid nodules are seen commonly in clinical practice, the majority of these lesions are benign. Infact, thyroid malignancy is found in less than 5 to 10% of hypofunctioning thyroid nodules. Interestingly, the biology of thyroid malignancy represents a spectrum of characteristics ranging from well-differentiated lesions which has excellent prognosis to anaplastic carcinoma which is almost uniformly fatal. De Lellis R et al [5] depicted that carcinoma of thyroid gland was relatively rare disease and constitutes < 1% of all malignancies. Infact benign neoplasms outnumber thyroid carcinomas by a ratio of nearly 10:1. We observed 37 malignant lesions in our study,in which 32 cases were above 30 years and 5 cases were in

between 20 – 30 years. Similar finding were observed by Andersons et al.[6] However DeLellis R et al [5] observed maximum number of thyroid malignancies in 4th, 5th and 6th decade as compared to 3rd decade.

Papillary carcinoma

The present study depicts 37 cases of papillary thyroid carcinoma which comprised 25.34% of the total 146 cases and it is correlated with the study of Gupta S et al [7] and Khan A et al. [8] Maximum cases were observed in the age group of 30 – 50 years. The average age group for papillary carcinoma to occur was between 30-50 years, herewith our findings were comparable to Gillespie M et al [9] and Khan A et al.[8] Female preponderance was observed in all lesions of thyroid with F: M ratio = 2:1, this might be due to geographical variations and the different etiological factors, which correlated with the study of Rosai et al [10] and De groot et al.[11]

Classic Papillary Thyroid Carcinoma and its Histopathological Variants

Classical Papillary Carcinoma is characterized by 5 well-known histopathological features: ie, papillae; empty-looking nuclei; nuclear grooves; nuclear pseudo inclusions and psammoma bodies. Khan A et al [8] in his study of 35 cases, 20 are classical papillary carcinoma (5.71%). Similar findings observed in our study, there were 19 cases (18.62%) of classical papillary thyroid carcinoma out of 37 cases (Fig:2-4). Among 19 cases, one case was showing secondary deposits in 12 lymph nodes and 2 cases were showing secondary deposits in 4 lymph nodes by the same tumour.

Follicular Variant

They are composed of small to medium sized follicles with virtually no papillary structures. A variable amount of colloid, which may appear hypereosinophilic and scalloped, was seen in the follicles. The majority of cells lining the follicles contain large clear nuclei with grooves and nuclear pseudoinclusion. Aron M et al [12] in his study of 59 cases, 33 were FVPTC (55.93%). Current study shows 4 cases of FVPTC (10.81%) (Fig 5). Fortunately, the prognosis of both of these classic and follicular variant are good.

Encapsulated Variant

This variant constitutes 4-14% of all papillary carcinomas. The Patient tend to be younger with excellent prognosis. Papillary carcinoma that is totally surrounded by a fibrous capsule that may be intact or focally infiltrated by tumour growth. We report three cases of encapsulated variant (8.1%), all were in younger age group.(Fig:6).

Diffuse Sclerosing Papillary Carcinoma

Khan A et al studied one case of Diffuse sclerosing variant of papillary thyroid carcinoma which occured in a middle aged man. Vickery et al [16], Hedinger et al.[17] and Rosai et al [9] described diffuse sclerosing papillary carcinoma as aggressive behaviour which occurs in a middle aged man. Isarangkul et al [18] recorded dense focal fibrosis within tumor masses in 89% of his 37 cases of papillary carcinoma. Present study depicts four cases of diffuse sclerosing papillary carcinoma (10.81%), occurred in young adults and middle age (Fig:7). The tumour had spread widely in the thyroid parenchyma and also had extended outside the capsule. There was patchy lymphocytic infiltrate and numerous psammoma bodies.

Tall Cell Variant

The Tall cell variant of papillary carcinoma was first described by Hawk & Hazard [13] in1976. This is a rare tumour and is seen in approximately 10% of cases of papillary carcinomas. This pattern is seen in the older age group, and behaves more aggressively, when compared with the classical group. It is composed of cells whose height are atleast three times their width. The neoplastic cells have abundant eosinophilic cytoplasm. Nuclear grooves and pseudoinclusion tend to be abundant. Gupta S et al [7] in his study, reported 7 cases as tall cell variant (4.43%). In our study, we report a case of Tall cell variant of papillary thyroid carcinoma (2.70%). (Fig:9)

Mixed Tall Cell Columnar Cell variant

A tumor closely related to the tall cell was later described by Evans et al [14] as the columnar cell variant of papillary carcinoma. The tumor has the same aggressive behaviour as the tall cell variant. Generally both these variants are lumped together as the tall cell/ columnar cell variant. Akslen et al [15] have also described a case in which tall cell carcinoma and columnar cell carcinoma co-existed. This rare variant is composed of pseudostratified columnar cells some of which may contain supranuclear and subnuclear cytoplasmic vacuoles reminiscent of early secretory endometrium. Hyperchromatic nuclei may predominate. The follicles may appear elongated and empty resembling tubular glands. Khan A et al [8] in his study of 35 cases 3 cases showed mixed tall cell columnar variant 8.57%. Similarly our study depicts 2 cases of mixed tall cell columnar variant (5.40 %), out of 37 cases of papillary carcinoma (Fig 8).

CONCLUSION

We emphasize that a histopathological report of papillary carcinoma of the thyroid should indicate whether the tumour is of the usual type or belongs to the unusual variants which may have an adverse prognosis. This will help the surgeon in deciding the treatment modality of these neoplasms. Some of the subtypes have a worse prognosis than the classic type, such as the tall cell variant. It is of prime importance to report the variants of papillary thyroid carcinoma.

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REFERENCES

[1] Stewart BW, Kleihues P. 2003, World Cancer Report: Lyon IARC Press.
[2] Key C R. Human Pathol 1971;2(4):521-523.
[3] Gharib H, Goellner JR. Ann Intern Med 1993;118:282-289.
[4] Chin JK. Histopathol 1990; 5:241-257
[5] De Lellis RA and Lloyd RV. 2002: 59-64.
[6] Anderson's, Ivan Danjanov, James Linder: Thyroid gland Anderson's pathology, 10th edition, 1996:p 1943-1972.
[7] Gupta S and Sodhani P. Acta Cytologica 2004: 795 – 801.
[8] Khan A.R and Abu-eshy SA. Am J Clin Pathol 1996: 1-9.
[9] Gillespie MB. J Head Neck Surg 2006:1-3.
[10] Juan Rosai MD, Maria Luisa, Careangiu MD, Ronald A, Delellis MD : Atlas of tumour pathology, tumour of thyroid gland. Washington DC 1990, Third series fascide 5 AFIP.
[11] De Groot Leslie J : thyroid and its disease, 5th edition 1984: p756-331.
[12] Aron M, Mallik A and Verma K. Acta Cytolog 2005: 6632-6637.
[13] Hawk WA, Hazard JB. Am J Clin Pathol 1996: 1-9.
[14] HL. Am J Surg Pathol 1987;11: 592-597.
[15] Akslen LA, Varhaug JE. Am J Clin Pathol 1996: 1-9.
[16] Vikery AL, Carcangiu M, Johnnessen JV, Sorbrinho – Simoes M. Am J Clin Pathol, 1996: 1-9.
[17] Hedinger C, et al. Am J Clin Pathol, 1996: 1-9.
[18] Isarangkul W. Am J Clin Pathol 1996:1-9.