Profile Of Thyroid Neoplasms With Special Focus On Interesting Cases: A Hospital Based 12 Year Longitudinal Study

S Gole, V Satyanarayana, G Gole, T Ramamurti, M Hayath, A Deshpande, K Raghu, A Nirgude, S Tati

Citation

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Abstract

Introduction: The incidence of thyroid nodules increases throughout life. Benign neoplasms outnumber thyroid carcinomas by a ratio of nearly 10:1. The microscopic features of thyroid neoplasms have been described in world literature, together with their behavior and molecular biology. However, this retrospective longitudinal study aims to report a 12 year data about thyroid neoplasms encountered in a Medical college in a rural area of Andhra Pradesh, India. This study analyses the sociodemographic profile (age and sex data) associated with various types of benign and malignant tumors. Study also depicts few interesting, rare cases and cases posing diagnostic dilemma. Highlighting features of this study are few collision tumors and association of neoplasms with non-neoplastic lesions.

Materials and methods: The Hospital based longitudinal study includes cases gathered over a period of 12 years. During this period, 246 patients were diagnosed on histopathology as having thyroid neoplasms of different types either benign or malignant. In all the cases, thyroidectomy specimens were fixed in 10% neutral buffered formalin and stained with hematoxylin and eosin. For some cases special stain like Congo red was done for the confirmation of diagnosis. In few cases wherein there was a diagnostic dilemma, immunohistochemistry was performed.

Results: In our study a total of 246 thyroid neoplasms (n) were observed over a period of 12 years. The mean age was 35.50 years with (s.d.) of ± 13.608 years. Benign tumors were 176 (71.5%) and the malignant were 70 (28.5%). Out of total 246 cases, the highest number of cases 85 (34.6%) belonged to the age group of 21-30 years; of this 63 (74.11%) were benign and 22 (25.88%) malignant neoplasms, with female preponderance of 74 (87.05%) cases. Considering gender 205 (83.3%) occurred in the females and 41 (16.7%) in the males. Amongst benign tumors, 154 (87.5%) were females and 22 (12.5%) were the males. Amongst the malignant tumors, 51 (72.85%) were females and 19 (27.14%) were the males. Considering the benign tumor follicular adenoma and from malignant tumor papillary thyroid carcinoma (PTC) were the most common tumors.

Conclusion: Thyroid neoplasms though being very common neoplasms in routine practice can pose a diagnostic dilemma. Thorough observation and analysis of both gross and microscopic findings, deeper sections, cytochemistry, and the right use of immunohistochemistry are required in such cases. Awareness about Worrisome histologic alterations following Fine needle aspiration thyroid (WHAFFT) is needed to avoid misinterpretation. The technique of non-aspiration Fine needle aspiration (FNA) is significantly less traumatic. The association of thyroid neoplasms with the non-neoplastic lesions complicates still more if the Fine needle aspiration cytology (FNAC) is not suggestive of neoplasms.

INTRODUCTION

The microscopic features of thyroid neoplasms have been described in world literature, together with their behavior and molecular biology. However, this retrospective longitudinal study aims to report a 12 year data about thyroid neoplasms encountered in a Medical college in a rural area of Andhra Pradesh, India.

This study analyses the demographic profile (age and sex data) associated with various types of benign and malignant tumors. Study also depicts few interesting, rare cases and cases posing diagnostic dilemma. Highlighting features of this study are few collision tumors (two malignant tumors in the same case), and association of neoplasms with non-neoplastic lesions.
MATERIALS AND METHODS

The Hospital based longitudinal study includes cases gathered over a period of 12 years. During this period, 246 patients were diagnosed on histopathology as having thyroid neoplasm of different types either benign or malignant.

In all the cases thyroidectomy specimens were fixed in 10% neutral buffered formalin and stained with hematoxylin and eosin. For some cases special stain like Congo red was done for the confirmation of diagnosis. In few cases wherein there was a diagnostic dilemma, immunohistochemistry was performed.

RESULTS

In our study a total of 246 thyroid neoplasms (n) were observed over a period of 12 years. The data was compiled and analyzed using statistical package social sciences version 19. The results are expressed in percentages and proportions. Chi square test was used to find statistical significance. Table 1 shows the gender distribution as per the age group.

Table 1: Gender distribution as per the age group

<table>
<thead>
<tr>
<th>Age group (Years)</th>
<th>Female (%)</th>
<th>Male (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>3 (100)</td>
<td>-</td>
</tr>
<tr>
<td>11-20</td>
<td>27 (87.09)</td>
<td>4 (12.90)</td>
</tr>
<tr>
<td>21-30</td>
<td>74 (87.05)</td>
<td>11 (12.94)</td>
</tr>
<tr>
<td>31-40</td>
<td>45 (93.75)</td>
<td>3 (6.25)</td>
</tr>
<tr>
<td>41-50</td>
<td>39 (84.78)</td>
<td>7 (15.21)</td>
</tr>
<tr>
<td>51-60</td>
<td>16 (72.72)</td>
<td>6 (27.27)</td>
</tr>
<tr>
<td>61-70</td>
<td>3 (33.33)</td>
<td>6 (66.66)</td>
</tr>
<tr>
<td>71-80</td>
<td>1 (50)</td>
<td>1 (50)</td>
</tr>
</tbody>
</table>

Total 205 (83.3)  41 (16.7)

The mean age was 35.50 years with (S.D.) of ± 13.608 years. Out of total 246 cases, 205 (83.3%) occurred in the females and 41 (16.7%) in the males. For all the benign and malignant tumors together largest numbers of cases (85) were in the age group of 21-30 years along with female preponderance 74 (87.05%) cases in the same age group.

Table 2 depicts the sex incidence in the benign and malignant tumors.

Table 2: Gender distribution as per the tumor nature

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Female (%)</th>
<th>Male (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>154 (87.5)</td>
<td>22 (12.5)</td>
<td>176 (71.54)</td>
</tr>
<tr>
<td>Malignant</td>
<td>51 (72.85)</td>
<td>19 (27.14)</td>
<td>70 (28.45)</td>
</tr>
</tbody>
</table>

Total 205 (83.3)  41 (16.7) 246 (100)

Chi-Square = 7.731; df = 1; p value < 0.005 (Highly significant)

Considering gender, for benign tumors females were 154 (87.5%) and males were 22 (12.5%). Among the malignant tumors, 51 (72.85%) were females and 19 (27.14%) were the males. There is a significant difference between nature of tumor and gender of the cases, and this difference is statistically significant (p<0.05).

Table 3: Age group and tumor nature distribution of cases (N=246)

<table>
<thead>
<tr>
<th>Age group (Years)</th>
<th>Number of cases (%)</th>
<th>Tumor nature*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benign (%)</td>
<td>Malignant (%)</td>
</tr>
<tr>
<td>0-10</td>
<td>3 (1.2)</td>
<td>1 (33.33)</td>
</tr>
<tr>
<td>11-20</td>
<td>3 (12.6)</td>
<td>23 (74.59)</td>
</tr>
<tr>
<td>21-30</td>
<td>85 (24.56)</td>
<td>63 (74.21)</td>
</tr>
<tr>
<td>31-40</td>
<td>48 (19.5)</td>
<td>34 (70.83)</td>
</tr>
<tr>
<td>41-50</td>
<td>46 (16.7)</td>
<td>35 (76.8)</td>
</tr>
<tr>
<td>51-60</td>
<td>22 (8.9)</td>
<td>13 (59.09)</td>
</tr>
<tr>
<td>61-70</td>
<td>9 (3.7)</td>
<td>6 (66.66)</td>
</tr>
<tr>
<td>71-80</td>
<td>2 (0.8)</td>
<td>1 (50)</td>
</tr>
</tbody>
</table>

Total 246 (100) 176 (71.54) 70 (28.45)

*Chi-Square = 5.25; df = 7; p value > 0.05 (Not significant)

Out of total 246 cases, the highest number of cases 85 (34.6%) belonged to the age group of 21-30 years; of this 63 (74.11%) were benign and 22 (25.88%) malignant neoplasms. Benign tumors were 176 (71.54%) and the malignant were 70 (28.45%). There is no significant difference between age group and tumor type (p>0.05).

The distribution of 176 benign tumors with gender preponderance is shown in Table 4.
Figure 4
Table 4: Distribution of benign tumors with gender preponderance

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Number of cases (%)</th>
<th>Gender (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>170 (96.59)</td>
<td>19 (8.74)</td>
</tr>
<tr>
<td>Hürthle cell adenoma</td>
<td>6 (3.40)</td>
<td>5 (33.33)</td>
</tr>
</tbody>
</table>

The distribution of 70 malignant tumors with gender preponderance is shown in Table 5.

Figure 5
Table 5: Distribution of malignant tumors with gender preponderance

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Number of cases (%)</th>
<th>Gender (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>PTC</td>
<td>43 (61.42)</td>
<td>31 (72.09)</td>
</tr>
<tr>
<td>FVPTC</td>
<td>22 (17.14)</td>
<td>8 (66.66)</td>
</tr>
<tr>
<td>FTC</td>
<td>9 (12.85)</td>
<td>9 (100)</td>
</tr>
<tr>
<td>MTC</td>
<td>3 (4.28)</td>
<td>1 (33.33)</td>
</tr>
<tr>
<td>FNUMP</td>
<td>1 (1.42)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Mixed MTC and PTC</td>
<td>1 (1.42)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>SETTLE</td>
<td>1 (1.42)</td>
<td>1 (100)</td>
</tr>
</tbody>
</table>

PT: Papillary thyroid carcinoma; FVPTC: Follicular variant of papillary thyroid carcinoma; FTC: Follicular thyroid carcinoma; MTC: Medullary thyroid carcinoma; FNUMP: Follicular neoplasm of undetermined malignant; Mixed MTC and PTC: Mixed medullary thyroid carcinoma and papillary thyroid carcinoma; SETTLE: Spindle epithelial tumor with thymus like elements.

Though FVPTC being a variant of PTC, considering the large number of cases we have grouped them separately.

Amongst the benign tumors the most common tumor was follicular adenoma; and

PTC was the most common malignant tumor.

Our study includes the major thyroid neoplasms, including adenoma and carcinoma in its various forms.

Though the morphological features of thyroid neoplasms are well known worldwide, we are discussing few neoplasms which are rare. Some of the cases posing a diagnostic dilemma were resolved with the help of cytochemistry and immunohistochemistry.

Considering the malignant tumors, our study had 1 rare case of spindle epithelial cell tumor with thymus like elements (SETTLE) which occurred in a 13-year-old boy (Figures 1, 2).

Figure 6
Figure 1: Photomicrograph (10X) showing biphasic cell pattern (epithelial and spindle cells) separated into lobules by fibrosis.

Figure 7
Figure 2: Photomicrograph (10X) showing polygonal epithelial cells arranged in glands, trabeculae and sheets and the glandular lumina filled with mucin.

On histopathology, the differential diagnoses were SETTLE and MTC. Immunohistochemistry was done with Cytokeratin (CK), High Molecular Weight Keratin (HMWK), thyroglobulin, calcitonin, and Smooth Muscle Actin (SMA). Spindle and epithelial cells were positive for CK and HMWK. The cells were negative for thyroglobulin, calcitonin, and SMA (Figures 3-6).
Amongst the 43 PTC in this study, 1 case in a 70-year-old male posed a diagnostic difficulty. The microscopic features were suggestive of Composite Hemangioendothelioma. On serial and regrossed sections, we observed a few hyalinized papillary structures without classical nuclear features of PTC (Figures 7-9).
Figure 12
Figure 7: Photomicrograph (10X) showing increased vascularity and blood vessels with proliferation of endothelial cells.

Figure 13
Figure 8: Photomicrograph (10X) showing vascular proliferation with congestion.

Figure 14
Figure 9: Photomicrograph (10X) showing focal areas with papillary structures having dense hyaline core.

Immunohistochemistry showed thyroglobulin positive and CD31, CD34 negative (Figures 10-12).

Figure 15
Figure 10: Photomicrograph (4X) showing thyroglobulin positive.
Other rare variants of PTC encountered in this study were 2 cases of PTC; 1 case of mixed columnar and tall cell features and the other case with mixed features of Tall cell, Oncocytic and Warthin like with Hashimoto’s thyroiditis in the surrounding uninvolved thyroid parenchyma (Figures 13, 14).

In the present study, 3 cases of MTC were observed out of which, 1 case showed extensive amyloid deposition. Congo red stain demonstrated the abundant amyloid under the polarizing microscope (Figures 15, 16).
Amongst the benign tumors, follicular adenoma was the most common tumor (n=170). Two cases of follicular adenoma posed a diagnostic difficulty because of their histological appearance. A solitary thyroid nodule in a 27-year-old male having massive total infarction/cystic degeneration, posed difficulty to render diagnosis (Figure 17).

There was history of previous FNAC. Regrossed and further sections explored the viable tumor tissue showing features of follicular adenoma (Figure 18). The final diagnosis was made as Follicular adenoma with massive infarction.

The second case of Follicular adenoma was of a 54-year-old female. On histopathology, sections showed a well

Figure 15: Photomicrograph (4X) showing extensive amyloid deposition (arrows) with intermingled tumor cell clusters and surrounding normal thyroid tissue in the periphery.

Figure 16: Extensive amyloid deposition showing apple green birefringence under polarizing microscope (Congo red stain).

Figure 17: Lobectomy specimen showing encapsulated, grey brown lesion with areas of infarction, hemorrhage and compressed normal thyroid tissue in the periphery.

Figure 18: Photomicrograph (4X) showing compressed encapsulated tumor tissue with extensive infarction and normal thyroid tissue in the periphery.

Figure 19: Photomicrograph (4X) showing compressed capsulated tumor tissue with extensive infarction and normal thyroid tissue in the periphery.
encapsulated tumor tissue comprising of disrupted follicles due to edema, hemorrhage, and hyalinization. Few well defined micro- and macrofollicles were observed. There were scattered cells exhibiting moderate pleomorphism and hyperchromatism. Surrounding compressed normal thyroid tissue was seen. The differential diagnoses were Atypical Follicular Adenoma and Exuberant vascular proliferation in follicular adenoma with atypical features following FNAC (Figures 19, 20).

Figure 24
Figure 19: Photomicrograph (10X) showing compressed capsulated tumor tissue with normal thyroid tissue in the periphery.

Figure 25
Figure 20: Photomicrograph (40X) showing atypical tumor cells (arrow) with extensive hemorrhage and vascular proliferation.

In our study we observed out of 246 cases, few neoplasms (39) were associated with non-neoplastic lesions (Table 6).

Figure 26
Table 6: Various thyroid neoplasms associated with non-neoplastic lesions

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Associated non-neoplastic lesions (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nodular goiter</td>
<td>Lymphocytic thyroiditis</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>5 (29.41)</td>
<td>9 (52.94)</td>
</tr>
<tr>
<td>Hurthle cell adenoma</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PTC</td>
<td>10 (62.5)</td>
<td>3 (18.75)</td>
</tr>
<tr>
<td>FVPTC</td>
<td>3 (60)</td>
<td>1 (20)</td>
</tr>
</tbody>
</table>

DISCUSSION

The solitary thyroid nodule is a palpably discrete swelling within an otherwise apparently normal thyroid gland. Single nodules are about four times more common in women than in men. The incidence of thyroid nodules increases throughout life.

From a clinical standpoint, the possibility of neoplastic disease is of major concern in persons who present with thyroid nodules. Majority of clinically apparent thyroid neoplasms are primary and epithelial origin. Traditionally, they have been divided into adenomas and carcinomas, the latter group incorporating the medullary carcinomas together with the more common lesions composed of follicular cells. From a histogenetic standpoint, thyroid neoplasms are divided into three major categories, depending on the cell types involved, and subdivided them into the various benign and malignant categories such as; tumors exhibiting follicular cell differentiation (95%), tumors exhibiting C-cell differentiation, and tumors exhibiting follicular and C-cell differentiation. Lesions in the later two categories comprise about 5% of tumors.

Fortunately, the overwhelming majority of solitary nodules of the thyroid prove to be localized, non-neoplastic conditions or benign neoplasms such as follicular adenomas. In fact, benign neoplasms outnumber thyroid carcinomas by a ratio of nearly 10:1. While under 1% of solitary thyroid nodules are malignant.

Our study includes the major thyroid neoplasms, including adenoma and carcinoma in its various forms. This article depicts the sociodemographic profile of thyroid neoplasms considering the age and gender preponderance.

Though the morphological features of thyroid neoplasms are well known worldwide, we are presenting few neoplasms which are rare. Some of the cases posing a diagnostic dilemma were resolved with the help of cytochemistry and
imunohistochemistry.

Thyroid cancer incidence rates have increased worldwide for decades, although more for PTC than other types and more for females than males. The National Cancer Institute’s Surveillance, Epidemiology, and End Results 9 Registries Database for cases diagnosed during 1976-2005 to develop etiological clues regarding gender-related differences in PTC incidence had shown that PTC incidence rate among females was 2.6 times that among males (9.2 versus 3.6 per 100,000 person-years, respectively), with a widening gender gap over time. Age-specific rates were higher among women than men across all age groups, and the female-to-male rate ratio declined quite consistently from more than 5 at ages 20-24 to 3.4 at ages 35-44 and approached 1 at ages more than 80. APC models for papillary thyroid cancers confirmed statistically different age-specific effects among women and men (P < 0.001 for the null hypothesis of no difference by gender), adjusted for calendar-period and birth-cohort effects. Gender was an age-specific effect modifier for papillary thyroid cancer incidence. In our study significant difference between nature of tumor and gender of the cases was observed (p<0.05).

According to data from the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute thyroid carcinomas with follicular phenotype have demonstrated changing patterns over 30 years (1973–2003). PTC has significantly increased. They accounted for 74% of all cases of thyroid cancers in 1973 and 87% in 2003. During this period, the incidence rate of PTC (including the FVPTC) increased by 189%, the rate of FTC remained stable, and the rate of anaplastic carcinoma decreased by 22%. The rate of FVPTC alone increased by 173%. Our study also revealed that FVPTC was the second most common malignant tumor after PTC. Thyroid cancer was more common in females than in males. The present study also showed the same results. PTC rapidly increased during adolescence and reached a peak around age 52–56, then declined. In our study the maximum number of cases (16 out of total 43) belonged to the age group of 21-30 years. In our study significant difference between nature of tumor and gender of the cases was observed (p<0.05).

SETTLE is a very rare neoplasm related to the thyroid of young individuals. According to the US National Center for Biotechnology Research (PubMed database), the term SETTLE has been reported only 26 times in the English literature until July of 2010. In 1991, Chan and Rosai unified the concept of SETTLE when they described 8 neoplasms situated in the neck and thyroid of children and young adults, previously diagnosed as malignant teratoma of the thyroid, thyroid spindle cell tumor with mucous cysts or thyroid thymoma. SETTLE is a distinct low-grade neoplasm, believed to be derived from branchial pouch or thymic remnants, with only 1 case report showing association with epithelium-lined cysts of possible branchial pouch derivation. It belongs to a group of cervical lesions that includes ectopic cervical thymoma, ectopic hamartomatous thymoma and carcinoma with thymus-like element (CASTLE). This tumor is composed predominantly of spindle and epithelioid cells with glandular or ductular structures lined by a mucinous or respiratory epithelium. Inspite of indolent growth, SETTLE may give metastases many years after the diagnosis. Therefore, a long-term follow-up is required. This rare tumor occurs in young individuals with a mean age of 17.9 years at presentation (ranging from 2 to 59 years), with a male-to-female ratio of 1.1. The hallmark feature is a biphasic pattern composed of a predominant component of spindle cells and a minor glandular mucous component (Figures 1, 2). The two components of SETTLE are always negative for thyroglobulin, calcitonin, chromogranin A, synaptophysin, carcinoembryonic antigen (CEA), desmin and S-100 protein.

Differential diagnosis includes many epithelial and biphasic spindle cell tumors of the head and neck such as spindle cell variant of MTC that can also occur in the same age group, thymoma, spindle cell variant of anaplastic thyroid carcinoma, and synovial sarcoma.

Amongst the 43 PTC in this study, 1 case posed a diagnostic difficulty. The microscopic features were suggestive of Composite Hemangioendothelioma and PTC. Two rare variants of PTC were encountered in this study; 1 case of mixed columnar and tall cell features and the other with mixed features of Tall cell, Oncocytic and Warthin like with Hashimoto’s thyroiditis in the surrounding uninvolved thyroid parenchyma. Lee J et al reported a case with histological findings of a rare oncocytic variant of PTC with concurrent Hashimoto's thyroiditis. Tall cell carcinoma is an aggressive form of differentiated follicular-derived thyroid carcinomas. Berho et al studied 15 cases of thyroid tumors composed of oncocytic cells with nuclear features of PTC. In 13 cases, the tumors showed the features of Hashimoto's or lymphocytic thyroiditis in the surrounding, uninvolved thyroid parenchyma. Oncocytic PTC represents a distinctive
morphological variant of carcinoma of thyroid that does not appear to behave more aggressively than conventional PTC. Association of these tumors with autoimmune thyroiditis raises the possibility that the oncocytic changes may be pathogenetically related with the autoimmune thyroiditis. Ozaki et al.\(^4\) presented 13 cases of tall cell variant of PTC showing extensive lymphocytic and plasma cell infiltration and exhibiting histologic features of chronic thyroiditis. Immunohistochemically, the lymphocytes infiltrating the carcinoma focus were CD20+, CD45+, CD45 RO+ cells, which are same as those found in chronic thyroiditis. Follow up results suggested that the tall cell variant of PTC with extensive lymphocytic infiltration are less aggressive and have a favourable prognosis.

HAZARD ET AL.\(^9\) FIRST DESCRIBED MTC. DESAI ET AL.\(^10\) STUDY SHOWED MTC TO BE TWICE AS COMMON IN MEN AS IN WOMEN AND OCCURRED 10 YEARS EARLIER IN WOMEN. IN THEIR STUDY ABOUT 19% CASES, THE THYROID ADJACENT TO MTC SHOWED OPTICALLY CLEAR NUCLEI IN THE FOLLICLES CLOSE TO THE TUMOR CELLS, SAME AS THOSE FOUND IN PTC. IN OUR STUDY WE HAD 2 CASES OF MALES AND 1 CASE OF FEMALE. OUR STUDY HAD 1 CASE WITH HISTOLOGICAL FEATURES OF MIXED MTC AND PTC. THE OCCASIONAL CONCURRENT OCCURRENCE OF THESE TWO TUMORS AND THE INVOLVEMENT OF THE RET GENE IN BOTH MTC AND PTC, MAY BE THE POSSIBLE EXPLANATION FOR THE COLLISION OF THESE TWO TUMORS TOGETHER. LAX ET AL.\(^11\) PRESENTED 3 THYROID CARCINOMAS DISPLAYING MEDULLARY AND PAPILLARY COMPONENTS.

Collision tumors of the thyroid gland are a rare entity. These tumors pose a diagnostic as well as therapeutic challenge and reported cases have mixed histologies of follicular or papillary and medullary carcinomas. The term “collision tumor” refers to coexistent but independent tumors that are histologically distinct. Collision tumors can occur within the same organ or adjacent organs or in conjunction with a systemic malignancy or as a metastatic phenomenon. Various mechanisms have been proposed for collision tumors. The first, is a “chance accidental meeting” of two primary tumors. Another hypothesis suggests that the presence of the first tumor alters the microenvironment facilitating the development of the second primary tumor or seeding of metastatic tumor cells. The third theory suggests a common stem cell of origin for the two tumors.

Multicentricity of thyroid carcinoma especially PTC is not a rare event, occurring in a range of 18% to 22% of thyroid neoplasms. However, the presence of morphologically and histogenetically dissimilar primary neoplasia within the thyroid gland is very unusual. Collision tumors of the thyroid must be differentiated from mixed and composite tumors which show parafollicular and follicular derived cellular elements. Mixed tumors have a common cell of origin; tumor cells show expression of both thyroglobulin and calcitonin. Composite tumors on the other hand, have two discrete cellular populations – thyroglobulin positive and calcitonin positive.\(^12\)

The simultaneous occurrence of two distinct neoplasms derived from different cells of origin is a recognized, although rare, entity. In the thyroid, such lesions could consist of MTC composed of parafollicular C cells and well-differentiated carcinoma showing follicular epithelial cell differentiation. Given the high incidence of papillary carcinoma, the occurrence of the two tumors may be a coincidence. Alternatively, a common tumorigenic stimulus triggering neoplastic transformation of both parafollicular C cells and follicular epithelial cells is a plausible explanation for such a phenomenon.\(^13\)

Gosain et al.\(^14\) reported 3 cases of Hürthle cell adenomas coexisting with PTC. In our study we had 1 case of Hürthle cell adenoma with a micropapillary thyroid carcinoma.

Baloch et al.\(^15\) in their study of FVPTC reported 3 encapsulated lesions that had vascular invasion. Our study had 1 FVPTC with vascular invasion alongwith capsular invasion.

In our study 5 cases of micropapillary PTC amongst the total 43 PTC were observed. From total 9 cases of FTC, 8 were minimally invasive and 1 case was widely invasive.

Thyroid neoplasms at times may pose diagnostic difficulty because of their histological appearance (morphological changes) attributable to FNA. In the present study due to FNA, diagnostic difficulty occurred in follicular adenoma (Figures 17-20). Hemorrhage, necrosis or infarction caused by FNA may occasionally obscure the histological pattern of thyroid neoplasms.\(^16\) The granulation tissue organizing hematoma or necrosis can be highly cellular and vascular and mimic a sarcoma or an angiomatosus tumor. Damage to the capsule of an adenoma by needleling may stimulate
capsular invasion. Awareness about Worrisome histologic alterations following FNA thyroid (WHAFFT) is needed to avoid misinterpretation. The technique of non-aspiration FNA (needling) is significantly less traumatic. An increase in FNAs or size of needle results in more severe WHAFFT changes.

In our study there were few cases of neoplasms associated with non-neoplastic lesions (Table 6).

These coexistent lesions were defined only if they had occurred in a normal region of the thyroid gland, distinct from the site of the thyroid neoplasm. Peritumoral inflammatory response was not designated as Hashimoto’s thyroiditis and lymphocytic thyroiditis.

The association between Hashimoto’s thyroiditis with PTC,[17-29] and FVPTC[23,30,31] has been described widely in literature.

Although the link between chronic inflammation and cancer is well established, the association between Hashimoto’s thyroiditis and PTC has been controversial in medical bibliography since its initial description by Dailey et al in 1955.[17]

Ott RA et al[32] study showed 38% incidence of thyroid carcinoma coexistent with Hashimoto’s thyroiditis. The high incidence of carcinoma thyroid in Hashimoto’s thyroiditis lends credence to the hypothesis that Hashimoto’s thyroiditis is a predisposing factor in the development of thyroid carcinoma. Patil PV et al[22] reported frequency of carcinoma in Hashimoto’s thyroiditis varies between 0.5%-23.7%.

Kollur SM et al[31] study showed the incidence rates of Hashimoto’s thyroiditis coexistent with thyroid neoplasm as 15%. Pasquale MD et al[26] study revealed that atypical nodules may represent a precursor lesion of PTC in patients with Hashimoto’s thyroiditis. Prasad ML et al[29] observed focal papillary carcinoma–like immunophenotypic changes in Hashimoto’s thyroiditis and put forward the possibility of early focal premalignant transformation in some cases of Hashimoto’s thyroiditis.

Prognosis of patients with Hashimoto’s thyroiditis and carcinoma thyroid is far better than that of thyroid carcinoma alone, probably due to the presence of the chronic inflammatory reaction which suppresses growth and metastatic dissemination of the coexistent neoplasm of the thyroid gland.[17-19,24] Thyroid carcinoma stimulates the development of Hashimoto’s thyroiditis in some patients and presence of the autoimmune inflammatory reaction and circulating antibodies retard growth and dissemination of carcinoma thyroid.[19]

The review of literature reveals the association between Hashimoto’s thyroiditis with Hurthle cell tumor,[23,26,30] FTC,[18,19,26,28] and MTC.[19]

The coexistence between Hashimoto’s thyroiditis and Follicular adenoma has been widely described in literature.[21,24,30] The present study had 3 cases of such coexistence.

Tamimi et al in their study found the association between lymphocytic thyroiditis and thyroid tumors such as PTC, FTC, and follicular adenoma. The prevalence of lymphocytic infiltrate was indicative of autoimmune thyroiditis which was significantly higher in PTC (58%), FTC (20%), and follicular adenoma (14%). Their study revealed that there is possibility of an immunologic mechanism involved in the pathogenesis of PTC which stimulates lymphocytic infiltration in the thyroid tissue through an autoimmune mechanism.[20] In our study there were 9 cases of follicular adenoma coexistent with lymphocytic thyroiditis.

Lerma E et al study showed 4 cases of lymphocytic thyroiditis associated with neoplasms (2 PTC, 1 FTC, and 1 oncocytic adenoma).[23] Our study had 3 cases of PTC, and 1 case of FVPTC coexistent with lymphocytic thyroiditis. There was also 1 case of Hurthle cell adenoma with granulomatous thyroiditis.

**CONCLUSION**

Thyroid neoplasms though being very common neoplasms in routine practice can pose a diagnostic dilemma. Thorough observation and analysis of both gross and microscopic findings, deeper sections, cytochemistry, and the right use of immunohistochemistry are required in such cases. Hemorrhage, necrosis or infarction caused by FNA may occasionally obscure the histological pattern of thyroid neoplasms. Awareness about WHAFFT is needed to avoid misinterpretation. The technique of non-aspiration FNA (needling) is significantly less traumatic. The association of thyroid neoplasms with the non-neoplastic lesions complicates still more if the FNAC are not suggestive of neoplasms.
References


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