Section: Pathology

Original Research Article

HISTOPATHOLOGICAL EVALUATION OF THYROID LESION AND DECODING THE GREY ZONE IN FOLLICULAR PATTERNED LOW RISK THYROID NEOPLASMS: A RETROSPECTIVE STUDY IN TERTIARY CARE CENTER, RAMANATHAPURAM

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ABSTRACT

Background: Thyroid gland is unique among the endocrine organs. It can be affected by wide variety of diseases from autoimmune diseases to malignant lesions. The aim and objective is to determine histopathological spectrum of thyroid lesions with diagnostically challenging cases among thyroid surgical specimens. **Materials and Methods:** Patients who had undergone thyroidectomy procedures for both non-neoplastic and neoplastic thyroid lesions were enrolled in this study. Study conducted at department of Pathology, Government medical college, Ramanathapuram for a period of two years from November 2023 to October 2025. **Result:** 46 thyroidectomy specimens were included in our study. Commonest age group of presentation is 4th decade with female preponderance. Out of 46 cases, 33 cases were non neoplastic (71%), 13 cases were neoplastic (29%). Most common non neoplastic lesion is thyroid follicular nodular disease accounting for 19 cases out of 33 cases followed by thyroid follicular nodular disease with associated Hashimoto's thyroiditis which account for 10 out of 33case. Common neoplastic lesions are well differentiated thyroid tumour of uncertain malignant potential and papillary carcinoma each accounting for 5 cases out of 13 cases. Followed by follicular adenoma which constitutes 3 out of 13 cases. **Conclusion:** In our study, we emphasize the importance of recognizing the various macroscopic and microscopic features of Well differentiated thyroid tumor of uncertain malignant potential for making prompt diagnosis, appropriate clinical management and prognostication.

INTRODUCTION

Thyroid is the largest and most important endocrine gland which secretes T3, T4 and calcitonin. It's a H shaped gland composed of right lobe, left lobe and isthmus, located in front of C5-T1 vertebra.[1] Burden of thyroid disease in India is high-approximately 42 million people are affected.[2] Common thyroid diseases are Iodine deficiency diseases, goitre, autoimmune thyroiditis and thyroid neoplasms.[3]

According to WHO, 7% of the world population is suffering from clinically apparent goiter. Majority of these patients are from developing countries where the disease is attributed to iodine deficiency.[4] Prevailing in Female gender and 1-2% in children.[5] Patient may manifest either as hypothyroid, hyperthyroid or euthyroid.[6] Causes of hypothyroidism includes Iodine deficiency, Hashimoto's thyroiditis, radiation and medications. Causes of hyperthyroidism are graves' disease, toxic multinodular goitre and thyroiditis.[7]

Coastal states like Gujarat, Goa, Kerala and hilly areas like Himalayan regions are endemic for thyroid lesions in India.[4]

Aim: To analyse the histopathological spectrum of thyroid lesions with diagnostically challenging cases among thyroidectomy specimens and relationship with age of the patient.

MATERIALS AND METHODS

This is a retrospective study of 2 years from November 2023 to October 2025period done in the

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Department of Pathology, Government medical college, Ramanathapuram. Patient details, clinical history and laboratory investigations were collected along with the received hemithyroidectomy and total thyroidectomy specimens. Specimen was received in 10% formalin. After overnight fixation, representative bits were taken for processing and stained with hematoxylin and eosin stain for histopathological examination.

RESULTS

Over two years period totally 46 hemithyroidectomy and total thyroidectomy specimens were received. Age distribution ranged from 15 - 70 years with peak incidence in the third decade between 31 - 40 years of age. Our study showed female preponderance.

Out of 46 cases, 33 (71%) cases were non neoplastic, 13 (29%) cases were neoplastic lesions.

Most common non neoplastic lesion is thyroid follicular nodular disease accounting for 19 cases (58%) out of 33 cases.

Other non neoplastic lesions include thyroid follicular nodular disease associated with features of Hashimoto's thyroiditis - 10 cases (30%) and Hashimoto's thyroiditis - 4 cases (12%)

Common neoplastic lesion are well differentiated thyroid tumour of uncertain malignant potential (WDT-UMP) – 5 (38%), Papillary carcinoma thyroid - 5 cases (38%) and follicular adenoma accounting for 3 cases (24%) out of 13 cases.

After extensive histopathological examination of thyroid specimens, diagnostically challenging various histomorphological pattern were noted in both neoplastic and non neoplastic thyroid lesions and also in the thyroid tissue surrounding the tumours. 10 cases of thyroid follicular nodular disease showed features of Hashimoto's thyroiditis in the surrounding thyroid tissue. One case of papillary carcinoma showed features of Hashimoto's thyroiditis in the surrounding thyroid parenchyma. Five cases of follicular patterned thyroid tumours showed papillary like nuclear features with a nuclear score of 2 and is termed as well differentiated tumor of uncertain malignant potential.

Table 1: Age wise incidence of thyroid lesions

S.No	Age	No of cases
1	<10 years	0
2	11-20 years	1 (2%)
3	21-30 years	1 (2%)
4	31-40 years	15 (33%)
5	41-50 years	13 (28%)
6	51-60 years	13 (28%)
7	61-70 years	3 (7%)

Table 2: Histomorphological patterns of non neoplastic thyroid lesions

S. No	Types	No of cases
1	Thyroid follicular nodular disease	19 (58%)
2	Thyroid follicular nodular disease with Hashimoto thyroiditis	10 (30%)
3	Hashimoto's thyroiditis	4 (12%)

Table 3: Histomorphological types of neoplastic thyroid lesions

S.No	Category	Types	No of cases
1	Benign	Follicular adenoma	3 (24%)
2	Follicular pattern thyroid tumors of uncertain malignant Potential	Well differentiated thyroid tumour of uncertain malignant potential	5 (38%)
3	Malignant	Papillary carcinoma, classic subtype	4 (31%)
		Follicular variant of papillary carcinoma thyroid (FVPTC)	1 (7%)

DISCUSSION

Thyroid is the most important endocrine gland composed of follicles lined by thyroid follicular epithelial cells and filled with colloid.[8] Colloid is scalloped in active secretion of thyroid hormones. The 'C' cells are present in stroma between follicles which constitutes 0.1% of the entire gland.[9] Stimulus for thyroid hormone synthesis is thyroid stimulating hormone from the pituitary.[10] Thyroid follicular cells synthesize thyroglobulin which further undergoes iodination and coupling with the help of thyroid peroxidase forming T3 and T4 which is stored as colloid.[11]

WHO Classification of thyroid tumours - 5th edition has categorized follicular cell derived neoplasms as benign, low risk neoplasm and malignant neoplasm.

The terms "Thyroid follicular nodular disease" and "Differentiated high grade thyroid carcinomas" has been introduced recently.[12] Follicular patterned thyroid neoplasm with presence of papillary like nuclearfeatures and absent vascular invasion or capsular invasion is termed as Non invasive follicular thyroid neoplasm with papillary like nuclear features (NIFTP). Follicular patterned thyroid tumours with presence of papillary like nuclear features and questionable vascular invasion or capsular invasion is termed well differentiated thyroid tumour of uncertain malignant potential (WDT-UMP). Follicular patterned thyroid tumour with absent papillary like nuclear features and questionable vascular invasion or capsular invasion is termed as follicular tumour of uncertain malignant potential.[12]

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Most common age group affected by neoplastic thyroid lesion in our study is 41-50 yrs. Most common age group affected by non neoplastic thyroid lesion in our study is 31-40 yrs.[13,14] Similar findings were found in the study of Divya et al (30-40 yrs),Ayesha et al (30-40yrs), Padmavathi et al (40 yrs). All studies showed female preponderance.[1,2,3]

Percentage of neoplastic lesions in our case(29%) and non neoplastic lesions is (71%),well correlated with findings of divya et al (neoplastic-22%,non neoplastic-78%), Ayesha et al(neoplastic-16%,non neoplastic-84%) and Padmavathi et al (neoplastic-30%,non neoplastic-70%).[1,2,3]

Incidence of benign lesions were more compared to malignant lesions in our study.

Diagnostically Challenging Cases: Navigating The Grey Zones of Thyroid Pathology

Case 1: 45 years /Female complaints of swelling in the anterior aspect of neck involving the left lobe of thyroid. Left hemithyroidectomy done.

Macroscopy [Figure 1]: Received one lobe of thyroid measuring 5x4x2.5cm. External surface – capsule appears to be intact. Cut surface - shows questionable encapsulated fairly circumscribed solid and cystic neoplasm, cyst measuring 3x2.5x2cm filled with brownish fluid surrounded by grey white to grey tan solid area measuring 5x2.3x1cm. Adjacent normal thyroid parenchyma made out.

Case 2: 57years /Female, came with a complaints of swelling in front of neck

Macroscopy [Figure 2]: Received specimen of total thyroidectomy, larger lobe measuring 6.5x5x3.8cm, smaller lobe measuring 3.2x1.5x0.9cm and isthmus measuring 3x0.8x0.4cm. External surface – capsule intact. Cut surface of larger lobe shows a fairly circumscribed, ? encapsulated nodule measuring 2.5x1.5x1cm with surrounding thyroid parenchyma. Nodule appears grey tan, grey brown with focal grey white area. Cut surface of smaller lobe and isthmus – unremarkable

Case 3: 48years / Female, came with complaints of weight gain and difficulty in swallowing, on examination found to have thyroid gland enlargement and further evaluation was done

Macroscopy [Figure 3]: Received specimen of total thyroidectomy, right lobe measuring 4.5x3.5x2.5cm, left lobe measuring 4x2x0.5cm and isthmus measuring 1.8x1.5cm. External surface - capsule intact. Cut surface of right lobe-fairly circumscribed, encapsulated, vaguely nodular grey white lesion measuring 3x2.5x2cm, surrounded by rim of normal thyroid parenchyma. Cut surface of left lobe-grey white single nodule measuring 1.2x1x0.8cm,surrounded by normal thyroid parenchyma. Cut surface of isthmus-unremarkable.

Case 4: 42 years/Female, known case of hypothyroidism on treatment for 8 years, on follow up USG showed a TIRADS - IV nodular lesion, total thyroidectomy done.

Macroscopy [Figure 4]: Received specimen of total thyroidectomy in two fragments, larger lobe measuring 3.5x3x3cm, left lobe measuring 4x2x0.5cm and isthmus measuring 1x1cm. External surface – capsule intact. Cut surface of the larger lobe shows a fairly circumscribed, encapsulated, grey tan to grey white firm nodule measuring 3x3x3cm, focally surrounded by compressed thyroid parenchyma. Cut surface of smaller lobe shows multiple grey tan nodules filled with colloid, gritty to cut. Cut surface of isthmus – grey brown.

Case 5: 47years /Female, complaints of swelling in front of neck

Macroscopy [Figure 5]: Received hemithyroidectomy as two fragments, larger fragment measuring 4.5x4x2.5cm, smaller fragment measuring 2.5x2x1cm. Cut surface of larger fragment shows a questionable encapsulated, grey tan firm solid area measuring 3x1.5x1cm and showing one tiny cyst measuring 0.5cm in diameter, filled with brownish fluid. Cut surface of smaller fragment – grey white, grey brown and shows a cyst measuring 0.3cm in diameter.

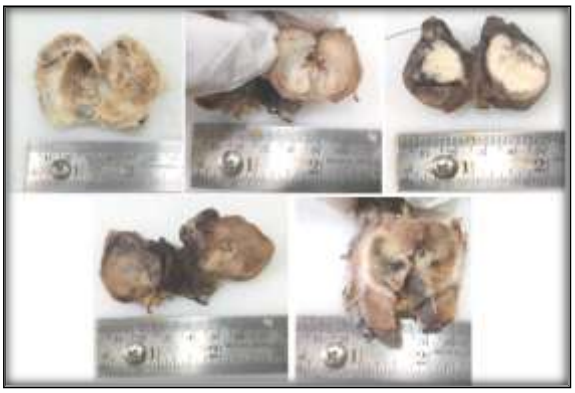

Figure 1: Histopathology: (Fig A, B, C, D) Section studied shows well circumscribed encapsulated solid and cystic neoplasm composed of closely packed microfollicles and few macrofollicles filled with colloid. Predominant areas show follicles with well developed nuclear features like nuclear enlargement, overlapping, membrane irregularity, chromatin margination and clearing. Foci of suspicious capsular invasion also noted.

Case were reported as Well differentiated thyroid tumour of uncertain malignant potential (WDT-UMP)

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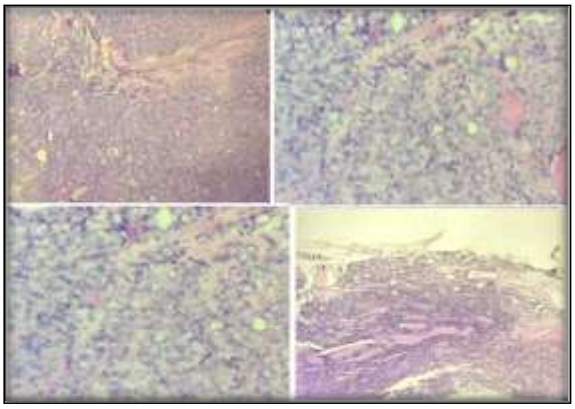

Figure 2: A: Histopathological image of Follicular patterned low risk thyroid neoplasm [Well differentiated thyroid tumour of uncertain malignant potential (WDT-UMP)] (H&E stain, magnification x100)
B, C: Histopathological image of Well differentiated thyroid tumour of uncertain malignant potential showing papillary carcinoma like nuclear features (WDT-UMP) (H&E stain, magnification x400)
D:Histopathological image of Well differentiated thyroid tumour of uncertain malignant potential (WDT-UMP) showing questionable capsular invasion (H&E stain, magnification x100)

Variable gross characteristics of Well differentiated thyroid tumour of uncertain malignant potential: As per WHO 2022, WDT-UMP can usually present as single thyroid nodule with size ranging from 1 to 3cm, in few cases lymphocytic thyroiditis and hyperplastic nodules have been reported in the surrounding thyroid parenchyma. Several studies have documented diverse gross morphology like solid or solid and cystic or cystic lesion which is well circumscribed, encapsulated, grey white, grey tan tumour associated with secondary changes such as haemorrhage, fibrosis, cystic degeneration and calcification.[12,13] The cases in our study were concordant with other similar articles.

Assessment of nuclear morphology and architecture lead to interobserver variations in the diagnosis of follicular variant of papillary thyroid carcinoma.[12] Hence, the term "Well differentiated thyroid tumour of uncertain malignant potential" has been coined by Chernobyl pathologist group for appropriate acknowledgement of encapsulated tumour with follicular architecture and incompletely developed papillary carcinoma like nuclear features. This terminology was introduced to avoid the extensive surgical approach and aggressive treatment including radiotherapy. These tumours have indolent course with the risk of recurrence and metastasis being very low.[12,13]

CASE 6

Beyond The Margin: Morphological Alterations In Surrounding Parenchyma Of Thyroid Lesions40 years/ Female complaints of swelling in the anterior aspect of neck for 2 years involving the right lobe of thyroid. Right Hemithyroidectomy done

Macroscopy [Figure 6.1]: Received one lobe of thyroid measuring 7X3.5X3cm.External surface - nodular, capsule intact. Cut surface- shows multiple colloid filled nodules ranging in size from 0.2-2.5cm.Foci of gray tan area and calcification made out.

Histopathology [Figure 6.2]: Sections studied from one lobe of thyroid shows nodular configuration of thyroid follicles of varying sizes filled with colloid lined by cuboidal epithelial cells. There are few areas showing degenerated thyroid follicular epithelial cells and oncocytic cells with dense lymphoid aggregates and germinal centre formation. Focal area of calcification also seen.

Case was reported as Thyroid follicular nodular disease with associated Hashimoto thyroiditis

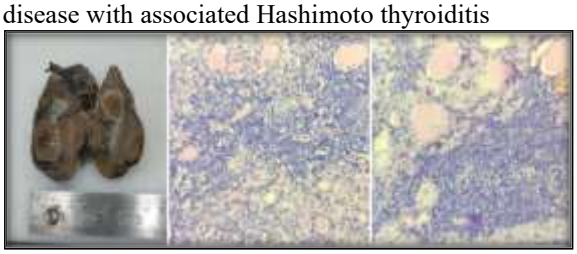

Figure 6.1: Gross image of Thyroid follicular nodular disease with associated Hashimoto thyroiditis
Figure 6.2: Histopathological image of Thyroid follicular nodular disease with associated Hashimoto thyroiditis (H&E stain, magnification x100 & x400)

Case 7: 17 years /Female –Complaints of swelling in the anterior aspect of neck for past 1 year -Total thyroidectomy done.

Macroscopy [Figure 7.1]: Received total thyroidectomy specimen,left lobe measuring 6X4X3cm,right lobe measuring 2x2x1cm,isthmus measuring 2x2x1cm.External surface- Capsule intact.Cut surface- solid grey tan infiltrating growth involving right lobe,left lobe and isthmus with papillary excresences measuring 5.8x4.5x3cm surrounded by tiny rim of thyroid parenchyma.Skeletal muscle attached to left lobe of thyroid is grossly uninvolved by tumour.

Histopathology [Figure 7.2]: Sections studied shows malignant thyroid neoplasm composed of branching papillae with fibrovascular core lined by follicular epithelial cells . The neoplastic cells are round to oval with scant cytoplasm exhibiting nuclear enlargement, crowding,overlapping,grooving and chromatin clearing. Surrounding thyroid parenchyma shows features of Hashimoto thyroiditis and foci of psammomatous calcification.

Case was reported as Papillary carcinoma, classic subtype with associated hasimoto thyroiditis

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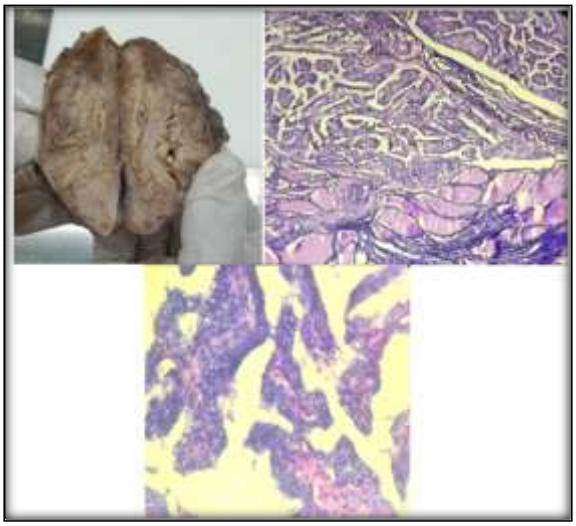

Figure 6.1: Gross image of Papillary carcinoma, classic subtype with associated hasimoto thyroiditis
Fig 6.2: Histopathological image of Papillary carcinoma, classic subtype with associated hasimoto thyroiditis (H&E stain, magnification x100 & x400)

CONCLUSION

Thyroid diseases are one of the common endocrine diseases with female preponderance. Commonly neoplastic lesions encountered in 4th decade and non neoplastic lesions in 3rd decade. Though Fine needle aspiration cytology is a simple diagnostic modality, histopathological examination is required for definitive diagnosis. Most common thyroid disorder is non neoplastic lesion (Thyroid follicular nodular disease). Categorization of thyroid lesions according to WHO guidelines and standardized reporting is essential to aid and assist the clinician for tailored treatment and prognostication.

In our study, we emphasize the importance of recognizing the various macroscopic and microscopic features of Well differentiated thyroid tumor of uncertain malignant potential for making prompt diagnosis, appropriate clinical management and prognostication. Since these tumors generally exhibit an indolent course with low risk of metastasis and recurrence, correct categorization helps to avoid unnecessary aggressive treatment, ultimately benefiting patient care and safeguarding patient well being.

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