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DECODING NON-INVASIVE FOLLICULAR THYROID NEOPLASM WITH PAPILLARY-LIKE NUCLEAR FEATURES (NIFTP): INSIGHTS FROM A CASE SERIES

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ABSTRACT

Background: Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP) is a recently recognized entity that presents challenges in diagnosis due to its similarities with more aggressive thyroid neoplasms, particularly follicular variant papillary thyroid carcinoma (FVPTC). Proper recognition is crucial to avoid overtreatment. **Objective:** We present a case series of three cases of NIFTP diagnosed after hemi-thyroidectomy, focusing on the histopathological features that contributed to its diagnosis. **Findings:** All cases exhibited well encapsulated follicular growth patterns with PTC-like nuclear features but lacked invasion. None of the patients showed recurrence during follow-up. **Conclusion:** As the understanding of NIFTP continues to evolve, it is important for clinicians and pathologists to remain vigilant in distinguishing it from more aggressive thyroid neoplasms.

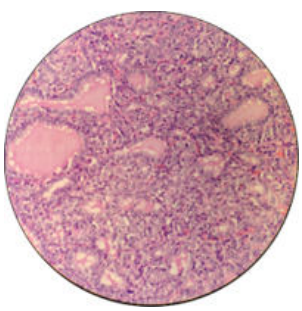
INTRODUCTION

Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP) was introduced as a distinct entity in the 2017 World Health Organization (WHO) classification of thyroid tumors.[1] This is a subset of encapsulated and noninvasive follicular variant papillary thyroid cancer, whose introduction had the intent of de-escalating treatment given its very low malignant potential, approaching to that of follicular adenomas.[2] The prevalence is 9.1% of all papillary thyroid cancers worldwide and Very rare in Asian population (1.6%) compared with Western series (13.3%).[2] NIFTP is considered to have an indolent behavior and an excellent prognosis, distinguishing it from FVPTC, which is typically more aggressive. However, the diagnostic challenges surrounding NIFTP necessitate a thorough understanding of its clinical, histopathological and molecular features.[3]

Case Series

Three cases were included in the study. All three of them were females (100%). The site of tumor was thyroid lobe. All the patients presented with painless, palpable nodule in thyroid lobe. Hemi-thyroidectomy was done in all three cases and the specimens were received in histopathology section in Pathology department.

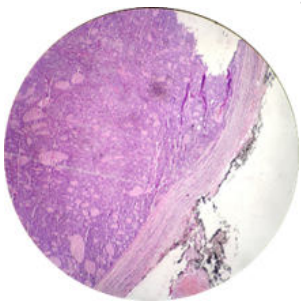
Case 1



A 22 year old female presented with Painless, palpable nodule in the right thyroid lobe, which had been growing over the past 2 months. The gross examination of hemi-thyroidectomy specimen revealed a well-circumscribed nodule with fibrous capsule confined to the thyroid gland without evidence of extra thyroidal extension. Microscopic examination revealed thyroid follicular cells arranged in micro/macro follicular pattern containing colloid, sheets and at places interspersed with larger follicles lined by normal appearing cells. The cells showed mild anisonucleosis having enlarged rounded nuclei, at many places optically clear nuclei, margination of chromatin, nuclear grooving, subtle irregular nuclear contour and inconspicuous nucleoli. Mitotic activity <2/10 HPF.

Case 2

A 31 year old female presented with Painless, palpable nodule in the left thyroid lobe, which had been slowly growing over the past 4-5 years. USG suggested possibility of benign lesion, TIRADS- II lesion. The gross examination of hemi-thyroidectomy specimen revealed a well-circumscribed nodule with fibrous capsule confined to the thyroid gland without evidence of extra thyroidal extension. Microscopic examination revealed well circumscribed lesion composed of thyroid follicular cells arranged predominantly in varying sized micro/macro follicular pattern filled with colloid and few solid sheets. The cells show mild anisonucleiosis with enlarged rounded nuclei and optically clear nuclei, occasional nuclear grooving, occasional micronucleoli and subtle irregular nuclear contour. Mitotic activity <2/10 HPF



Case 3

A 20 year old female presented with palpable swelling in the left thyroid lobe. The gross examination of hemi-thyroidectomy specimen revealed a well-circumscribed nodule with fibrous capsule confined to the thyroid gland without evidence of extra thyroidal extension. Microscopic examination revealed well circumscribed lesion composed of thyroid follicular cells arranged predominantly in varying sized micro/macro follicular pattern filled with colloid, few solid sheets and trabecular pattern. Cells show mild

anisonucleosis with enlarged rounded nuclei and optically clear nuclei with occasional nuclear grooving, occasional micronucleoli and subtle irregular nuclear contour seen.

The tumor was well circumscribed and entirely surrounded by thick fibrous capsule in all cases.

No evidence of capsular/ vascular invasion/ necrosis/ psammoma bodies/ intranuclear inclusions/ true papillae was seen in microscopic examination.

Diagnosis was made of Non Invasive Follicular Thyroid Neoplasm with Papillary like Nuclear Features (NIFTP) in all three cases.

DISCUSSION

All cases presented as well-circumscribed, encapsulated nodules without invasion. FNA cytology often yielded indeterminate results, leading to lobectomy for definitive diagnosis. No patients required total thyroidectomy or radioactive iodine, reinforcing the indolent nature of NIFTP. NIFTP presents a diagnostic challenge due to its nuclear features resembling those of papillary thyroid carcinoma (PTC), making it difficult to distinguish from the follicular variant of PTC (FVPTC) on initial assessment. The histopathological hallmark of NIFTP is the absence of invasive growth—capsular and vascular invasion and the tumor is well-circumscribed, distinguishing it from more aggressive neoplasms.[2]

The presented cases underscores the need for distinguishing NIFTP from more aggressive forms of thyroid cancer, as misclassification could lead to overtreatment, such as unnecessary use of radioactive iodine therapy or aggressive surgical interventions.

Challenges in Diagnosis

Molecular testing can help clarify the diagnosis, though it is not always available or necessary for every case. In clinical practice, pathologists must rely on a combination of histological findings, clinical presentation, and molecular results to make an accurate diagnosis.[5] Terminology surrounding NIFTP is still evolving, and there is ongoing debate about whether NIFTP should be classified as a carcinoma or as a benign tumor with malignant features. This lack of consensus has implications for treatment strategies, as some clinicians may still treat NIFTP as a carcinoma despite its favorable prognosis.[2]

CONCLUSIONS

Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP) is a newly recognized entity in thyroid pathology that offers a more nuanced understanding of thyroid neoplasms.

Its molecular and histopathological characteristics set it apart from more aggressive thyroid cancers, allowing for a more conservative management approach.

The prognosis of NIFTP is excellent, with an extremely low risk of recurrence or metastasis. Most patients with NIFTP require only surgical resection, and there is no indication for radioactive iodine therapy or aggressive postoperative monitoring.

As the understanding of NIFTP continues to evolve, it is important for clinicians and pathologists to remain vigilant in distinguishing it from more aggressive thyroid neoplasms.

Conflict Of Interests: No conflict of Interests.

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