Warpe BM et al. GAIMS J Med Sci 2026;6(2) (Jul-Dec): 92-95
Online ISSN: 2583-1763

Case Report

Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP): A Diagnostic Conundrum

Bhushan M. Warpe, Shweta S. Joshi, Sai Kaushal Manchikalapudi*

Department of Pathology, Krishna Vishwa Vidyapeeth (KVV), Karad city, Maharashtra, India

*** Correspondence:** Dr. Sai Kaushal Manchikalapudi, (Email: kaushalsai99@gmail.com)

ABSTRACT

Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is a recently recognized thyroid tumor that mimics papillary thyroid carcinoma (PTC) but demonstrates an indolent course and excellent prognosis. Accurate diagnosis is critical to prevent overtreatment.

We report a 20-year-old female with a gradually enlarging, painless midline neck swelling. Fine needle aspiration cytology (FNAC) performed twice yielded results suspicious for malignancy (Bethesda category V). Ultrasonography revealed a well-defined encapsulated nodule in the left lobe of the thyroid, categorized as TIRADS grade 3. CT imaging confirmed a circumscribed lesion with cystic and calcific foci, exerting mild pressure on adjacent vessels but without infiltration or lymphadenopathy. Based on these findings, a total thyroidectomy was performed. Gross examination revealed a tan-colored, encapsulated lesion measuring 2 × 1.5 × 1.4 cm. Histopathology demonstrated nuclear features of PTC with occasional psammoma bodies but no capsular/vascular invasion, papillary structures, tumor necrosis, or mitotic activity. A final diagnosis of NIFTP was made.

NIFTP poses a diagnostic challenge due to its cytological and radiological overlap with thyroid carcinoma. Awareness of this entity is crucial to avoid unnecessary aggressive treatment. Lobectomy is usually sufficient, but total thyroidectomy may be performed due to preoperative diagnostic uncertainty.

Keywords: NIFTP, thyroid neoplasm, papillary thyroid carcinoma, FNAC, case report

INTRODUCTION

The follicular variant of papillary thyroid carcinoma (FV-PTC), described in the 1970s, accounts for 5–41% of all PTC cases and represents the second most common subtype.[1,2] It has been subdivided into infiltrative and encapsulated forms, with the latter demonstrating indolent behavior.[3] In 2017, the World Health Organization (WHO) re-classified the encapsulated, non-invasive subtype as Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP), removing the carcinoma designation to prevent overtreatment.[1]

NIFTP is characterized histologically by follicular growth pattern, papillary carcinoma–like nuclear changes, and absence of invasive features.[3,4] Preoperative identification remains challenging, as cytology and imaging often mimic malignancy.[5] Consequently, patients may undergo total thyroidectomy instead of the more conservative lobectomy.

We present a case of NIFTP in a young female, emphasizing the diagnostic pitfalls and therapeutic implications.

CASE HISTORY

A 20-year-old female presented with a gradually progressive midline neck swelling of six months' duration. The swelling was painless, mobile, and

moved with deglutition. There were no associated systemic symptoms such as weight loss, voice changes, tremors, or heat/cold intolerance.

Clinical findings: On examination, the swelling measured 4 × 3 × 2 cm, was non-tender, and had smooth margins.

Investigations: FNAC performed in March 2025 was reported as "highly suggestive of malignant cells" without Bethesda categorization. A repeat FNAC in April 2025 yielded "suspicious for malignancy – Bethesda category V." Thyroid function tests were normal. Ultrasonography demonstrated a well-defined, encapsulated nodule in the left lobe (TIRADS grade 3). CT imaging revealed a circumscribed, lobulated lesion with cystic and calcific areas, exerting mild pressure on adjacent vessels but without infiltration or lymphadenopathy.

Management: In view of the cytology and imaging findings, the patient underwent total thyroidectomy.

Gross examination (Fig.1A to 1B): The left lobe contained a well-circumscribed, encapsulated, tan-coloured mass measuring 2 × 1.5 × 1.4 cm. The cut surface was firm, and the capsule appeared intact. The right lobe was grossly unremarkable.

Fig. 1A **Fig. 1B**

Figure-1 (Gross photographs): 1A shows external surface of thyroid showing left lobe having a well circumscribed nodular mass. 1B image depicts cut surface of left thyroid lobe which is a tan coloured, solid mass with no capsular invasion and normal appearing adjacent parenchyma.

Histopathological findings (Fig.2A to Fig. 2C): The lesion showed a follicular architecture with nuclear features characteristic of papillary thyroid carcinoma, including nuclear enlargement, overlapping, chromatin clearing, and irregular nuclear contours. Occasional psammoma bodies were noted. There was no evidence of capsular/vascular invasion, true papillary structures, tumour necrosis, or increased mitotic activity. Adjacent thyroid parenchyma appeared preserved. Based on these features, a final diagnosis of Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP) was established.

Fig: 2A **Fig: 2B**

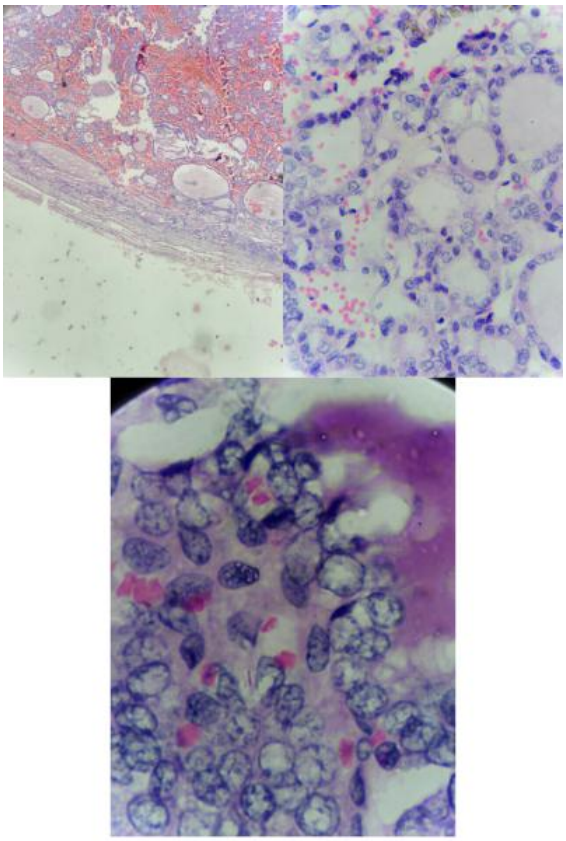

Fig: 2C

Figure-2 (Microphotographs): 2A shows intact capsule of the thyroid nodule. 2B and 2C show repetitive variably sized microfollicular pattern with nuclear features of papillary thyroid carcinoma including nuclear enlargement, overcrowding, chromatin clearing, nuclear contour irregularities (2A-H&E, x100, 2B-H&E, x400, 2C-H&E, x400)

DISCUSSION

Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) represents a

distinct pathological entity introduced by the WHO classification in 2017.[1] It was previously categorized under the encapsulated follicular variant of papillary thyroid carcinoma (EFV-PTC), but owing to its indolent clinical course and lack of invasive potential, the term "carcinoma" was deliberately removed.[2] This reclassification was intended to prevent unnecessary psychological stress and overtreatment associated with a malignant label.

Epidemiology and Clinical Presentation: NIFTP accounts for approximately 9–23% of thyroid tumours that were previously diagnosed as FV-PTC.[2,3] It is more common in women, with a mean age at diagnosis in the third to fourth decade of life.[4] Most patients present with a solitary, painless thyroid nodule discovered incidentally or during evaluation for cosmetic concerns. Compressive symptoms such as dysphagia or hoarseness are rare due to the typically small size and indolent growth of these tumours.[4,5] In our case, the patient was a 20-year-old female with an asymptomatic, progressively enlarging neck swelling, consistent with the usual demographic profile.

Diagnostic Challenges: Preoperative identification of NIFTP remains problematic. Fine needle aspiration cytology (FNAC) is limited because the diagnosis requires demonstration of capsular and vascular integrity, which cannot be assessed cytologically. Consequently, NIFTP aspirates are frequently reported as indeterminate, falling into Bethesda categories IV (follicular neoplasm/suspicious for follicular neoplasm) or V (suspicious for malignancy).[6,7] In our patient, FNAC findings from two centres were suspicious for malignancy, leading to a preoperative diagnosis of thyroid carcinoma.

Radiologically, NIFTP often presents as a well-circumscribed, encapsulated nodule, occasionally with cystic or calcific foci. On ultrasonography, these nodules usually correspond to TIRADS category 3 or 4 (low to intermediate suspicion).[8] CT or MRI may demonstrate mass effect without evidence of local infiltration or nodal spread, as in our case. However, these features significantly overlap with follicular adenoma and minimally invasive carcinoma, making preoperative differentiation unreliable.

Histopathological Features: Definitive diagnosis requires careful histological examination of the entire lesion and capsule. The diagnostic criteria proposed by Nikiforov et al.^2 and endorsed by the WHO include:
-Encapsulation or clear demarcation of the lesion
-Follicular growth pattern without true papillae (less than 1%).
-Nuclear features of papillary carcinoma, including nuclear enlargement, irregular contours, chromatin clearing, nuclear grooves, and overlapping.
-Absence of capsular or vascular invasion.
-Absence of psammoma bodies (rare foci may be permissible).
-No tumour necrosis or high mitotic activity.

Our case fulfilled all of these criteria: the lesion was encapsulated, composed predominantly of follicles, exhibited nuclear features of PTC, but lacked invasion, papillae, necrosis, or mitoses.

Molecular Pathogenesis: Molecular studies have provided further distinction between NIFTP and classical PTC. NIFTP is strongly associated with RAS mutations and shares similarities with follicular adenomas and carcinomas, while BRAF V600E and TERT promoter mutations, typically found in classical PTC, are usually absent.[2] This genetic profile correlates with the indolent clinical course and near-absence of metastatic potential.

Treatment Considerations: The reclassification of NIFTP has direct implications for clinical management. Since these lesions behave in a benign manner, lobectomy alone is considered adequate treatment.[1,2] Total thyroidectomy is unnecessary unless multifocal disease, bilateral nodules, or coexisting high-risk malignancy is present. Nevertheless, due to preoperative diagnostic uncertainty, many patients—such as ours—undergo total thyroidectomy, resulting in avoidable surgical morbidity and lifelong dependence on levothyroxine therapy.

Several studies have reported excellent outcomes in NIFTP patients treated with lobectomy alone, with no documented cases of recurrence or metastasis when strict diagnostic criteria are applied.[2,7] This underscores the importance of intraoperative caution and avoiding overtreatment.

Prognosis and Follow-up: -term follow-up data confirm the indolent nature of NIFTP. Large multi-institutional studies have shown no disease-specific

mortality and negligible recurrence risk in patients meeting the revised criteria.[7] Routine radioactive iodine ablation and intensive surveillance are unnecessary, further reducing patient burden. In our case, although total thyroidectomy was performed, the postoperative course was uneventful, and the patient remains disease-free.

Clinical Implications: This case illustrates the ongoing challenges in preoperative diagnosis of NIFTP. Cytological and imaging findings continue to mimic malignancy, often prompting aggressive surgical management. Greater awareness of NIFTP among clinicians and pathologists, coupled with strict application of histological criteria, is essential to prevent unnecessary total thyroidectomy and its long-term consequences.

CONCLUSIONS

NIFTP is a borderline thyroid neoplasm with indolent clinical behavior and excellent prognosis. Pre-operative differentiation from carcinoma remains difficult, leading to overtreatment in many cases. Histopathological examination of the entire lesion and capsule is mandatory for accurate diagnosis. Conservative surgery such as lobectomy is usually sufficient, minimizing unnecessary morbidity.

REFERENCES

1. Lloyd RV, Osamura RY, Klöppel G, Rosai J, editors. WHO Classification of Tumors of Endocrine Organs. 4th ed. Lyon: IARC; 2017.

2. Nikiforov YE, Seethala RR, Tallini G, Baloch ZW, Basolo F, Thompson LD, *et al*. Nomenclature revision for encapsulated follicular variant of papillary thyroid carcinoma: A paradigm shift to reduce overtreatment of indolent tumors. JAMA Oncol. 2016;2:1023–9

3. Goldblum JR, Lamps LW, McKenney JK, Myers JL. Rosai and Ackerman's Surgical Pathology. 11th ed. Philadelphia: Elsevier; 2018.

4. Thompson LD, Seethala RR, Asa SL, LiVolsi VA, Wenig BM, Franssila K, *et al*. Ninety-four cases of encapsulated follicular variant of papillary thyroid carcinoma: A name change to noninvasive follicular thyroid neoplasm with papillary-like nuclear features would help prevent overtreatment. Mod Pathol. 2016;29(7):698–707.

5. Gunasegaran JP. Textbook of Histology: Atlas and Practical Guide. 4th ed. Haryana: Elsevier; 2020.

6. Williams NS, O'Connell PR, McCaskie A, Garden OJ, Armitage J, Rowlands B, *et al*. Bailey and Love's Short Practice of Surgery. 27th ed. London: CRC Press; 2018.

7. Chereau N, Greilsamer T, Mirallie E, Pattou F, Mathonnet M, Gibelin H, *et al.* NIFTP: Are they indolent tumors? Results of a multi-institutional study. Surgery. 2019;165:12–6.

8. Pusztaszeri M, Bongiovanni M, Faquin WC, Mazzucchelli L, Auger M, Wang H, *et al*. The impact of non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) on the diagnosis of thyroid nodules. Gland Surg. 2019;8(Suppl 2):S86–97.

Source of support: Nil

Conflict of interest: None declared

How to cite: Warpe BM, Joshi SS, Manchikalapudi SK. Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP): A Diagnostic Conundrum. GAIIMS J Med Sci 2026;6(2): 92-95

https://doi.org/10.5281/zenodo.21467897