Microfollicular Pattern & Absence of Pseudoinclusions are Common Cytologic Characteristics in Noninvasive Follicular Thyroid Neoplasms with Papillary-Like Nuclear Features

Background

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The noninvasive encapsulated follicular variant of papillary thyroid carcinoma was recently reclassified as noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) due to the indolent nature of this tumor.¹ The impact of this paradigm shift on the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is uncertain.² This study addresses the significance of this reclassification on TBSRTC, and evaluates whether there are cytologic features that can differentiate NIFTP from classical and infiltrative follicular variants of papillary thyroid carcinoma (PTC).

Design

A retrospective review of all thyroidectomies for PTC from 2011 -2015 was performed (see Figure 1). All cases with prior fine-needle aspirations (FNAs) were reviewed jointly by three pathologists to categorize PTCs into classical (cPTC), infiltrative/invasive follicular variant (IFVPTC), or NIFTP. The consensus diagnoses were correlated to the corresponding antecedent FNAs according to TBSRTC. All FNAs were blindly evaluated concurrently by cytologists and a cytology fellow for twenty four nuclear, cytoplasmic, architectural, and background features.

In total, 109 PTC thyroidectomies (72 cPTC, 20 IFVPTC, and 17 NIFTP) with 121 FNAs were identified. All surgical cases were re-evaluated and a consensus diagnosis was reached between the three pathologists. Where available, all FNAs were reviewed using two representative slides (one Papanicolaou and one Diff-Quik stain).

Suspicious for malignancy and malignant cytology were more frequently diagnosed in cPTC (81.9%) and IFVPTC (70.0%) when compared to NIFTP (29.4%).



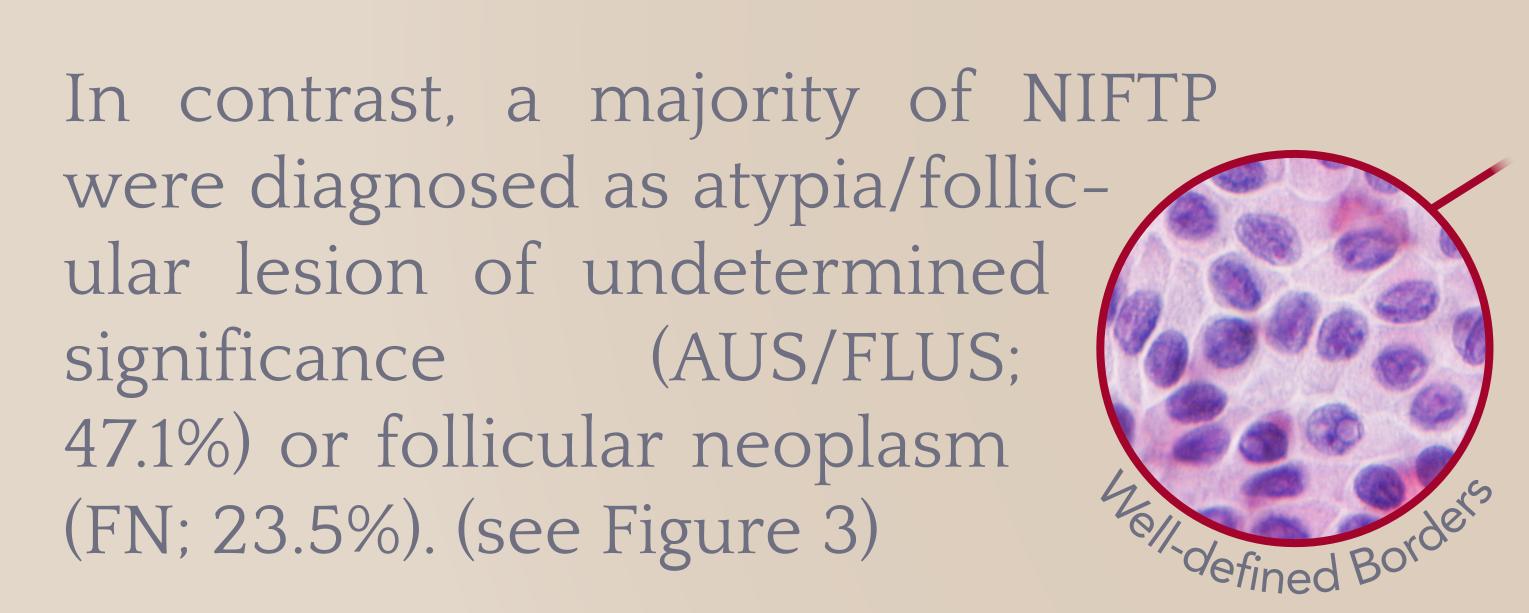
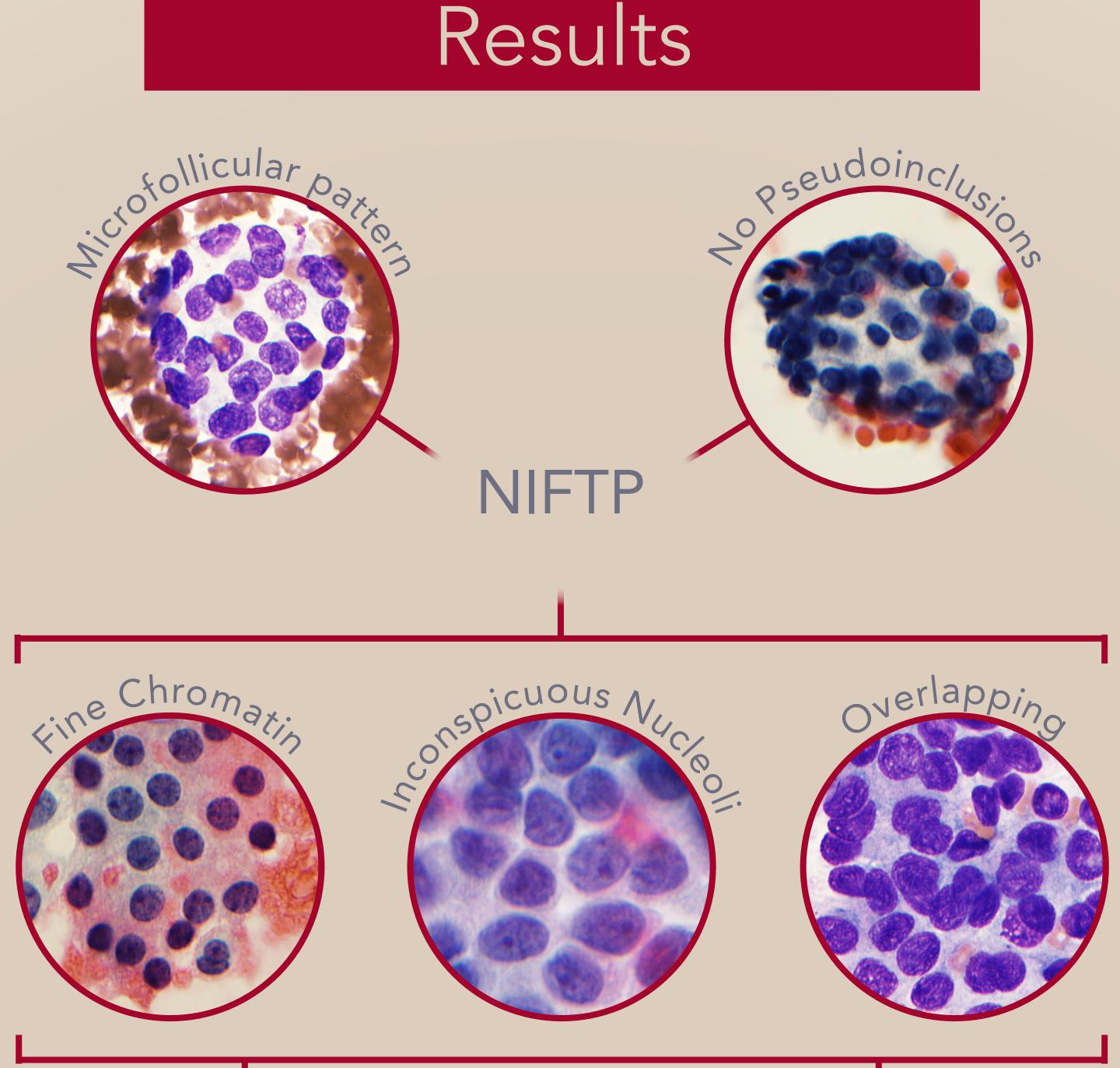


Figure 1: Of 419 thyroidectomy specimens initially evaluated, 109 were found to be suitable for this study. Matched antecedent FNAs were also reviewed, totaling 121.

idectomies - 2015 = 419	Final count n = 109
Exclude: Non-PTC, mets, microcarcinomas (210)	Exclude: Multiple nodules, FNA wrong lesion (11)
resections = 209	All PTCs & FNAs with slides n = 120
Exclude: No antecedent FNA (37)	Exclude: Slides not available (16)
Cs with dent FNA = 172	All PTCs with local FNAs n = 136
Exclude: FNA performed at outside institution, slides unavailable for review (36)	



cPTC

Figure 2: Some architectural, cytoplasmic, and nuclear features were shared among all three neoplasms on Pap and Diff-Quik stained smears.

The features most frequently observed in all entities were nuclear overlapping or crowding (greater than 94%), inconspicuous nucleoli (greater than 89%), and fine chromatin (greater than 77%). (see Figure 2)

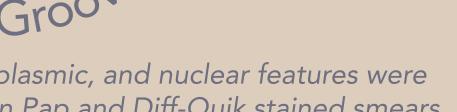
A predominantly microfollicular pattern was more commonly encountered in NIFTP (83.3%) than in cPTC (15.7%) or IFVPTC (50.0%).

NIFTP lesions more frequently had loosely-cohesive cellularity (27.8%) as compared to cPTC (13.2%) and IFVPTC (20.0%).

Pseudoinclusions were more likely to be absent in NIFTP (83.3%) than in cPTC (27.7%) or in IFVPTC (40.0%). Conversely, occasional (less than or equal to 2) or frequent (3 or more) pseudoinclusions were commonly seen in cPTC (72.3%) and in IFVPTC (60.0%).

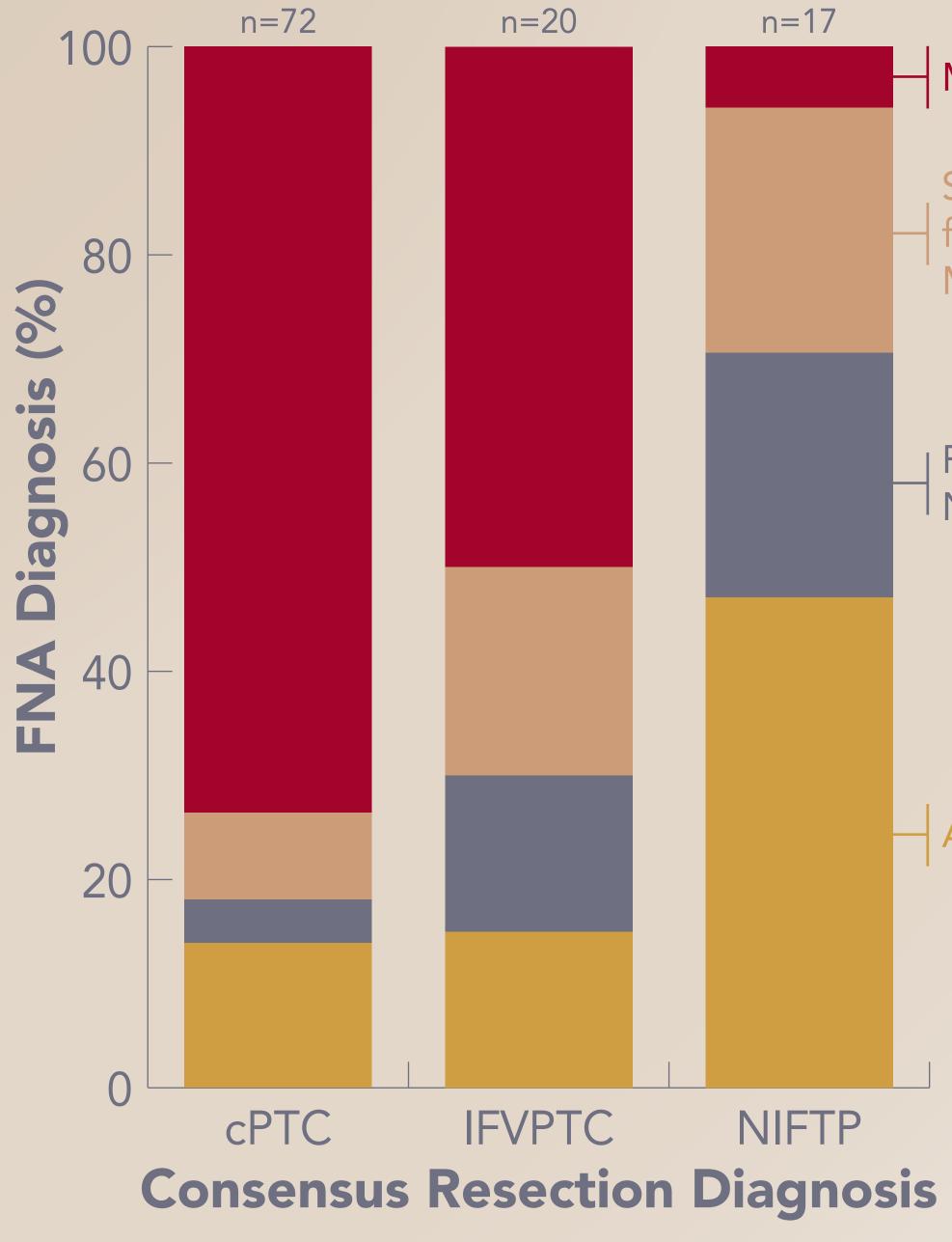
Well-defined cell borders were more likely to be present in cPTC (66.3%) than in IFVPTC (30%) or in NIFTP (22.2%).

Nuclear grooves were present in each FNA sample (for all cPTC, IFVPTC, and NIFTP lesions). However, frequent nuclear grooves (greater than 10 per high power field) were more common in cPTC (65.1%) and IFVPTC (80.0%) than in NIFTP (50.0%).



IFVPTC

Figure 3: NIFTP lesions were more likely to be called AUS/FLUS or SFN/FN on FNA than were cPTC or IFVPTC. All resection diagnoses reached consensus amongst three 100 — Malignant 80 | Follicular ⁷ Neoplasm - AUS/FLUS 20



Conclusions

While NIFTP is more often diagnosed as AUS/FLUS or FN, approximately one quarter of these lesions can have suspicious or malignant FNA diagnoses. However, the presence of microfollicles and absence of pseudoinclusions are frequently associated with NIFTP and may be helpful features suggesting caution when considering a suspicious or malignant FNA diagnosis. Similarly, well-defined cell borders, frequent and obvious grooves, and irregular nuclear contours may be helpful in identifying a suspicious or malignant lesion. We believe these observations merit further study.

Authors & References



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¹ Nikiforov YE, Seethala RR, Tallini G, et al. Nomenclature Revision for Encapsulated Follicular Variant of Papillary Thyroid Carcinoma. JAMA Oncology. 2016;2(8):1023. doi:10.1001/jamaoncol.2016.0386.

² Ali SZ, Cibas ES, eds. The Bethesda System for Reporting Thyroid Cytopathology. New York: Springer; 2010.

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