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

Results

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.

Background

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 impact 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 (IFVPTC), and NIFTP lesions. Howev-

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 94%). (see Figure 2)

A predominantly microfollicular pattern was more commonly encountered in NIFTP (83.3%) than in cPTC (27.9%) or 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%).

In contrast, a majority of NIFTP were diagnosed as atypia/follicular lesion of undetermined significance (AUS/FLUS; 47.1%) or follicular neoplasm (FN; 23.5%). (see Figure 3)

NIFTP lesions were more likely to be absent in NIFTP (83.3%) than in cPTC (27.9%) or IFVPTC (40.0%). 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%).

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

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).

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. The impact of this paradigm shift on the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is uncertain. 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).

Figure 1: Cytodiagnostic spectrum initially evaluated, 159 were found to be suitable for detailed analysis. Noninvasive follicular thyroid neoplasms were subsequently reviewed, yielding 121.

A predominantly microfollicular pattern was more commonly encountered in NIFTP (83.3%) than in cPTC (27.9%) or 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%).

NIFTP lesions were more likely to be absent in NIFTP (83.3%) than in cPTC (27.9%) or IFVPTC (40.0%). 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%).

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 94%). (see Figure 2)

A predominantly microfollicular pattern was more commonly encountered in NIFTP (83.3%) than in cPTC (27.9%) or 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%).

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

Andrew D. Jones, MD
Nicholas P. Lau, MD
Yanhong Zhang, MD
Alaa Afify, MD
Eric C. Huang, MD, PhD

Figure 1: Cytodiagnostic spectrum initially evaluated, 159 were found to be suitable for detailed analysis. Noninvasive follicular thyroid neoplasms were subsequently reviewed, yielding 121.

Figure 2: Some architectural, cytologic, and nuclear features were shared among these neoplasms. Papanicolaou and Diff-Quik stained slides.

Figure 3: NIFTP lesions were more likely to be assigned AUS/FLUS or FN on FNAs than in cPTC or IFVPTC. All resection specimens were reviewed and diagnoses reached consensus amongst three pathologists.

Figure 4: Distribution of FNAs among the three major 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.