Ultrasound is Cytopathologist's Best Friend in the Era of Noninvasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features

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The special issue for noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) in Journal of Basic and Clinical Medicine had an international collection of histopathologic and cytopathologic articles, but it contained no article on ultrasound features of NIFTP.

In the pre-NIFTP era, thyroid cells with papillary-like nuclear features are papillary thyroid carcinoma (PTC) by definition; therefore, ultrasound was irrelevant, except for needle localization during sampling. In the post-NIFTP era, cells with papillary-like nuclear features may come from an NIFTP; disregarding ultrasound may not be prudent for cytopathologists.

Ultrasound is equivalent to 1x histopathology (1), therefore, providing valuable information on the shape (oval/round, lobulated, or taller-than-wide) and marginal characteristics (sharp demarcated, spiculated or blurred). Also, since the nucleus of follicular cells blocks more sound waves than colloid, the echogenicity of the thyroid nodule correlates with the nuclear density of thyroid nodules on hematoxylin and eosin-stained tissue section (H&E). Microfollicular thyroid nodule, blue on H&E sections due to high nuclear density and sparse colloid, will appear darker than surrounding normal thyroid, i.e. "hypoechoic" on ultrasound. Thyroid nodules composed of normal sized follicles or macrofollicles, eosinophilic on H&E, will appear the same as surrounding thyroid, i.e. "isoechoic" on ultrasound.

If the follicles with papillary-like nuclear features but no papillae are aspirated from an oval to round nodule with sharp, regular margins, then the differential diagnosis is NIFTP versus encapsulated follicular variant of papillary carcinoma with microscopic invasion. In contrast, if the same aspirate were obtained from a lobulated or "taller-than-wide" thyroid nodule with blurred or spiculated margins, then "Papillary carcinoma, follicular variant (Bethesda VI/VI)" can be reported with confidence.

In general, the aspirates of NIFTP are in a microfollicular arrangement, less cellular and displayed subtle papillary-like nuclear changes (1, 2). Nuclear pseudoinclusions are infrequent (2, 3). In one institution's experience, frequent (≥3) pseudoinclusions virtually exclude NIFTP (3). Among 72 cases of NIFTP we reviewed (1), one case was an exception to the general findings. As shown in Figure 1, the aspirate was hypercellular, in macrofollicular arrangement of flat sheets, and had eight nuclear pseudoinclusions in one field.

In the post-NIFTP era, it would be wise to learn the basics of thyroid ultrasound (4) and become familiar with sonographic features of NIFTP (5-10), so that cytopathologists could interpret cytology in the context of ultrasound and provide the best care to the patients (1).

Conflict of Interest: None

References

Figure 1. A 65-year-old Caucasian woman presented with a 1.6 cm thyroid nodule for ultrasound-guided fine needle aspiration biopsy. A: The nodule was well-circumscribed, oval, isoechoic, and surrounded by a subtle hypoechoic halo. None of the suspicious ultrasound features such as marked hypoechoic, blurred, irregular, or lobulated margins, taller-than-wide shape, or microcalcifications were present. Gray-scale ultrasound. B: Focal 2+ intranodular vascularity on color Doppler ultrasound. C: The aspirate from the avascular area of the nodule was hypercellular and contained numerous sheets of monolayered epithelium (macrofollicular pattern) in a background of thin colloid seen only in Diff-Quik stained smear (left). Ultrafast Papanicolaou stain (right), 20x. D: At high power, the cells had focally enlarged nuclei, powdery chromatin and numerous pseudoinclusions (8 arrows) with a nuclear score of 3. Ultrafast Papanicolaou stain. 600x. However, the nodule appeared benign on ultrasound, therefore, “Suspicious for macrofollicular variant of papillary carcinoma, Bethesda V/VI” was reported in cytology. E: The lobectomy specimen showed a well-circumscribed tan nodule on gross inspection (inset), and was thinly encapsulated, eosinophilic colloid-rich nodule on histopathology, correlated to isoechoic nodule on gray-scale ultrasound. No invasion was found upon thorough sampling of the margins. Hematoxylin and eosin, stain, 1x (Image captured at 800 dpi by a UMAX Powerlook III flatbed scanner, Fremont, CA, USA). F: Macrofollicles filled with eosinophilic thin colloid. Inset: The nuclei had papillary-like features with elongated, grooved and clear nuclei (nuclear score 3). The final pathology was NIFTP. Hematoxylin and eosin stain, 100x; inset: 600x.
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