Preface

Indeterminate Thyroid Cytology

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Thyroid fine needle aspiration (FNA) cytology is, to date, the most widely used clinical test for diagnosis of thyroid nodules. In 2007, the National Cancer Institute at the National Institute of Health, USA, proposed a reporting system for thyroid FNA cytology, so-called the Bethesda system, and this system soon become the international standard of thyroid cytology (1). Following this recommendation, the United Kingdom Royal College of Pathologists (the British system) and the Italian Societies for Endocrinology and for Anatomic Pathology and Cytology (the Italian system) have updated their own diagnostic schemas as well (2, 3). In 2013, the Japan Thyroid Association published the guidelines for clinical practice for the management of thyroid nodules, including a diagnostic system for reporting thyroid FNA cytology (the Japanese system) (4). The Japanese system is adapted from the cytology practices of high-volume thyroid centers in Japan (5). Introduced in this special issue are the Bethesda system by Drs. Jing and Michael with beautiful illustrations (6), the updated 2014 version of the Italian system by Drs. Fadda and Rossi (7, 8), and the Japanese system by Dr. Kameyama et al. (9). Unfortunately, the British system is currently under revision process, and is not yet available for introduction, but may be added into this special issue at a later time once available.

All of these diagnostic systems are comparable to each other (8, 10), and the standardization of the diagnostic terminologies certainly allows for more efficient communication among pathologists, physicians, and patients. However, approximately 15%–40% of the FNA results fall into the indeterminate category (inadequate/non-diagnostic, atypia of undetermined significance, follicular lesion of undetermined significance, follicular neoplasm, suspicious for follicular neoplasm, Thy 3a, Thy 3b, TIR 3A, TIR 3B, or suspicious for malignancy), and there are some differences regarding how to handle the diseases in this category among the different reporting systems and clinical guidelines. A comparison of performance among the different diagnostic systems was analyzed and extensively reviewed by Bongiovanni et al. in this special issue (10). Many hospitals and institutes have also modified their diagnostic systems, so-called institutional systems, to their own practice in dealing with the patients with indeterminate thyroid nodules. A good example of institutional modification and the results for cytological and histological correlation were introduced by Zhu et al. from China (11). The Japanese system introduced by Kameyama et al. is another example, which is characterized by its own sub-classifications of the indeterminate category to identify high-risk patients with an indeterminate nodule for diagnostic surgery and treatment (9, 12). Sugino et al. and Zhu et al. reported a low resection rate of indeterminate thyroid nodules, and a high proportion of malignancy in surgically-treated patients with indeterminate nodules (11, 13). It is remarkable to note that this good performance in reducing unnecessary surgery in patients with benign nodules could be achieved without using any highly sophisticated molecular tests.

One of the areas making progress in thyroid cytology is molecular diagnosis using FNA samples. This technique has recently progressed rapidly, but has not yet been applied in many areas of the world. The molecular diagnosis was introduced in-depth by three world experts (Basolo, Takano and Ohori), along with their rich experience (14-16). We hope that the readers of this special issue are able to appreciate the potential of this approach in the future practice of thyroid FNA cytology, particularly for those in the indeterminate category. The molecular techniques may provide us an opportunity to identify the precursor lesions in thyroid tumorigenesis, while these lesions may be misclassified currently as benign follicular adenomas or low-grade malignant tumors.

One recent dramatic change in thyroid histopathology is the proposal of non-invasive encapsulated follicular variant of papillary thyroid carcinoma and well-differentiated tumor of uncertain malignant potential as biologically benign precursor lesions, rather than true malignant tumors, as presented by Nikiforov et al. at the 2015 Annual Meeting of Endocrine Pathology Society in Boston, MA (March 21, 2015) (17). A significant proportion of thyroid cancers in the indeterminate category was found to be the type of benign precursor tumors (48% of malignancy in suspicious for malignancy and 45% of malignancy in atypia of undetermined significance), as reported by Strickland et al. (18). Similarly, thyroid cancers in the indeterminate category have been classified as biologically indolent (low-stage and low-risk) by some other investigators (19-22). These findings may provide additional new insights into the indeterminate thyroid cytology. We hypothesize that the thyroid tumors at an early stage of thyroid carcinogenesis (borderline and precursor lesions) have a high probability of being classified into the indeterminate category due to their less well-developed morphological characteristics of malignant tumors (23, 24), which was also discussed in detail by Ohori in this special issue (16). A new reporting system for thyroid FNA cytology, which adapts these borderline lesions and recent progress of molecular tests, was proposed in this special issue by the editorial members (24). Furthermore, in this special issue, Sugino et al. analyzed the biological behavior of thyroid carcinomas in the cytological indeterminate category (13); Itô analyzed those in the ultrasound indeterminate category (25); and Liu et al. reviewed the behavior of non-invasive encapsulated follicular variant of papillary thyroid carcinoma (well-differentiated tumor of uncertain malignant

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potential) (26). Interestingly, these authors obtained different conclusions, indicating the requirement of further studies to reach a consensus.

This special issue collects the articles on the indeterminate category of thyroid FNA cytology from world experts, and introduces you to the experts’ views and opinions on how to approach the so-called “grey zone” in thyroid cytology (10, 27).

References:


18. Strickland KC, Howitt BE, Marquesee E, Alexander EK, Cibas ES, Krane JF, Barletta JA. The impact of non-invasive follicular variant of papillary thyroid carcinoma on rates of malignancy for fine-needle aspiration diagnostic categories. Thyroid 2015; [Epub ahead of print].


