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BORDERLINE THYROID TUMORS BETWEEN THE WESTERN AND ASIAN PHILOSOPHY

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INTRODUCTION

A histopathological classification of neoplasms reflects the biology and behavior of the tumors and serves as a guide for doctors and clinical management of patients, of the most significant changes in the 2017 WHO classification of thyroid tumors was: a new classification for encapsulated well-differentiated follicular tumors, in particular, introduction of tumors of borderline malignancy or uncertain malignant potential, identification of new variants of papillary thyroid carcinoma, subclassification of follicular thyroid carcinoma into minimally invasive, encapsulated angioinvasive and widely invasive types.[1]

The 2022 WHO classification has organized follicular cell–derived neoplasms into three categories: benign neoplasms, low-risk neoplasms, and malignant neoplasms. The low-risk neoplasms are borderline tumors that are morphologically and clinically intermediate between benign and malignant tumors. Although These neoplasms have the potential to develop metastasis, the incidence of metastasis is extremely low. Histologically, they are classified into three types including non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), thyroid tumors of uncertain malignant potential (UMP), and hyalinizing trabecular tumor (HTT). The term "tumor" was intended to reduce the risk of overtreatment for these low-risk neoplasms.[2]

Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is an encapsulated noninvasive neoplasm with a follicular growth pattern and nuclear features of papillary thyroid carcinoma (PTC).

The diagnosis of NIFTP is made after complete resection of the lesion and observing the following criteria:

1. Encapsulation or clear demarcation from adjacent thyroid parenchyma
2. Follicular growth pattern with no well-formed papillae
3. No psammoma bodies
4. <30% solid/trabecular/insular growth pattern
5. Nuclear features of PTC (nuclear score 2–3)
6. No vascular or capsular invasion
7. No tumor necrosis or high mitotic activity.[3]

Confirmation of NIFTP and exclusion of a potentially invasive thyroid neoplasm can only be made by an experienced pathologist based on strict criteria of inclusion and exclusion.[4] Although the main purpose of introducing NIFTP is to prevent overdiagnosis and overtreatment, Yasaman et al reported pelvic bone metastatic lesion in female patient diagnosed as NIFTP[5], also Hahn et al. identified central nodal metastasis in 1 of 34 cases of NIFTP in their series[6] which reminds us to be alert to the rare occurrence of distant metastasis in NIFTP.[5]

The main differential diagnosis for NIFTP is invasive encapsulated FVPTC as this lesion shares the well-circumscribed, often encapsulated structure, follicular architecture and papillary-like nuclear features with NIFTP and differs only with as much as a single focus of capsular or vascular invasion. Invasive encapsulated FVPTC harbors similar RAS-type mutations as NIFTP, follicular adenoma, and follicular carcinoma. In order to differentiate these diagnoses, the tumor capsule must be entirely submitted for microscopic examination to exclude invasion in the case of NIFTP.[6]

The terminology of thyroid tumors of uncertain malignant potential (UMP) was introduced in 2000 by Williams E D for capsulated follicular pattern tumors with diffuse equivocal or focal unequivocal papillary thyroid carcinoma type nuclear changes (PTC-Ns) and without definite invasion, i.e.; When PTC-Ns were observed equivocally, such as only nuclear clearing and nuclear grooves without nuclear pseudo inclusions,

thyroid lesions will be classified as WDT-UMP. When unequivocal PTC-Ns were seen in the entire part of the tumor it will be as encapsulated follicular variant papillary thyroid carcinoma. When unequivocal PTC-Ns were found in only part of the tumor, it will be classified as WDT-UMP.[7]

Hyalinizing trabecular tumor (HTT) is a benign, follicular-derived neoplasm composed of thick trabeculae with round or elongated cells having irregular and clear nuclei, and containing intra-trabecular hyaline material. Although rare, HTT is often misinterpreted due to its morphological overlapping characteristics with other thyroid neoplasms including papillary thyroid carcinoma (PTC), medullary thyroid carcinoma (MTC) and with all the rare trabecular patterned tumors encountered within the thyroid gland including trabecular fetal-type follicular adenoma, poorly differentiated carcinoma (PDC), intrathyroidal parathyroid tumors and metastases.[8]

The tumors show some mutual characteristics with papillary carcinomas (RET/PTC rearrangements) thus leading some experts to believe that they are merely a subtype of papillary carcinomas instead of a distinct category, to add up to the controversy, most authors considered HTTs to be always benign. In the following years though, cases were reported with malignant behavior, such as lymph nodes and pulmonary metastases, or detection of BRAF mutations, treatment is also an issue for debate. Since the majority of HTTs are benign, a lobectomy is the treatment of choice for these lesions. But taking in concern that even a few cases have a malignant potential and can lead to metastatic disease, a completion thyroidectomy and RAI treatment must be performed in these patients.[9]

It is essential to establish more accurate histological criteria to identify true cancers that may recur or metastasize and result in cancer death in significant proportion of the patients if left untreated. It is also essential to exclude benign follicular adenoma and indolent borderline/precursor tumors from lethal cancers because they can be treated with simple excision.

Western versus Asian philosophy in management of borderline thyroid tumors

Unfortunately, borderline/precursor tumors were often treated equally and as radically as lethal malignant thyroid tumors in western clinical practices, because only thorough examinations of the entire tumor capsule can establish the non-invasive nature of the tumor. under western logic and way of thinking that the first priority was given to avoiding missing malignancy rather than minimizing invasive tests.

In Asian society, a Chinese philosophy, Xiao Jing (the body, hair and skin, and all have been received from the parents, thus one does not dare damage them—this is the beginning of Xiao) has deep impacts on clinical practice. Diagnostic surgery is harmful and should be minimized to the patient, even if the surgery is restricted to a lobectomy. Significant numbers of patients later develop hypothyroidism, hypoparathyroidism and/or laryngeal nerve dysfunction and so surgery is acceptable in Asia only when the disease is intolerable or life threatening and the borderline/precursor tumors were neglected and were handled as if they were completely benign tumors.[10]

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