

Thyroid Papillary Carcinoma and Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP)

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Editorial

Papillary thyroid carcinomas (PTC) are well differentiated malignant epithelial tumors with characteristic nuclear features and they originate from epithelial cells of thyroid follicle. Papillary thyroid carcinoma is the most common type of thyroid cancers, which composes 85-90% of all thyroid carcinomas. Number of patients diagnosed with thyroid cancer has significantly increased during the last two decades due to increased awareness of nodular thyroid diseases, developments in diagnostic methods, wide applicability of thyroid fine needle aspiration, new descriptions of histopathology criteria and increased radiation exposure. It is more common in males than females with some ethnic variations. Although it is very rare during early childhood, it is the most common thyroid cancer of this age group. The mean age is 46 years at the time of diagnosis. Tumor has some histologic variants, the most common ones are being classical and follicular variants.

Although PTCs generally show good prognostic course with indolent features. Some PTCs may demonstrate bad prognostic course. Prognosis is closely related to disease stage; 10-year survival is 99,8% and 40,7% in stage I and stage IV disease, respectively. 7th edition of AJCC TNM Classification System of Malignant Tumors (2010) reported size of primary tumor (>2cm), extra thyroidal extension, distant metastasis, lymphnode metastasis and age at the time of diagnosis (above 45 years) as the most important criteria in evaluating biological features of these tumors. In addition, multi focality, vascular invasion, in complete surgery, some specific variants and male gender have been suggested as potential prognostic factors [1-6].

Some histologic variants of these tumors are known to show aggressive behavior. In recent years, the frequency of follicular variant papillary thyroid cancer (FVPTC) has been shown to increase in frequency among these tumors and since FVPTCs not always have nuclear features of classical variant papillary carcinoma and some of them may show quite aggressive clinical behavior, debates on their diagnostic and prognostic features take an important place

in recent studies. Moreover, some molecular features of FVPTCs are different than classical variant PTC; they mostly demonstrate mutations as seen in follicular adenoma or follicular carcinoma. These types of tumors mostly show RAS mutations, while they rarely have BRAF mutations. Although the term “well differentiated tumor with unknown malignant potential” acquired currency for these tumors after 2000s, this description has led to some uncertainty in clinical management and therefore has not been approved. Some studies on this topic suggested that rather than nuclear features, capsule and vascular invasion were more important determinants in clinical behavior [7]. However, some other studies reported aggressive behavior in tumors with macro follicular hyperplastic nodular pattern though they partly have nuclear features of classical variant papillary carcinoma [8]. As suggested in the study by Can et al. [6], FVPTCs are more common than classical variant tumors of PTCs and they pose problems in clinical management of these patients while choosing appropriate treatment modality (RAI or complementary surgery/lymphnode dissection), since these approaches have many negative effects on health spending and psychological states of patients.

Recent studies have shown that about 10-20% of all thyroid cancers is composed of non-invasive capsulated papillary follicular variant (NIFVPTC) [9,10]. However, since there is no consensus on papillary nuclear changes in the diagnosis of NIFVPTC, there is difference of opinion. In addition, a group of specialist has recently suggested the term “Noninvasive follicular thyroid neoplasm with papillary like nuclear features (NIFTP)” instead of NIFVPTC [11]. Although NIFPT is less aggressive, whether these patients are exposed to unnecessary treatment and follow-up procedures is a recent question of debate. Contribution of clinical and laboratory parameters used in the evaluation of thyroid nodules to the diagnosis of PTC in follicular variant and NIFTP is still unknown. Clinicopathological criteria NIFTP; tumors exhibiting dominant follicular architecture ($\leq 1\%$ true papillae) and nuclear features of papillary thyroid carcinoma (2-3/3 nuclear score according to the

alterations in nuclear size and shape; nuclear overlapping, nuclear enlargement, nuclear membrane irregularities; irregular nuclear contours, nuclear elongation, intra nuclear pseudo inclusions, nuclear grooves, chromatin characteristics; nuclear chromatin clearing, glassy nuclei, peripheral margination of the chromatin) but not associated with necrosis, solid/trabecular/cirriiform growth patterns, tall cell or columnar cell cyto morphology or more than 3 mitoses per 10 high power field (HPF) were classified as FVPTC [11].

In the literature, only 2 subjects (0.6%) have been shown to have recurrence among 352 well-documented noninvasive FVPTC. One of these subjects had undergone complete excision and non-invasive nature of tumor was questionable in other patient. In general, data suggest that the rate of negative result is very low in the absence of invasion of this lesion [12-18].

Conclusion

In conclusion, further studies are required to evaluate long term results of the patients with clinicopathologic criteria of NIFTP and NIFTP should be classified in the group of low risk papillary thyroid cancer despite low rate of negative results.

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