

**PAPILLARY LESIONS IN THE THYROID GLAND; - INTERESTING FACTS.**Johanes Hadi Lunardhi<sup>1)</sup>**ABSTRACT**

*Papillary lesion in the thyroid gland is commonly a malignancy, and they are Papillary Thyroid Carcinoma (PTC)<sup>-2,3,4,9</sup>. Appropriate diagnosis and treatment of the disease almost demonstrates excellent survival<sup>4,10</sup>. On the contrary, there are some other papillary lesions in the thyroid which are not PTC.*

*Benign appearing encapsulated papillary lesion of the thyroid was formerly diagnosed as 'papillary adenoma', a benign neoplasm<sup>-5,8</sup>. If we look back several decades ago, we could find in textbooks the change of opinion that 'papillary adenoma' of the thyroid was considered malignant, and no more nomenclature of 'papillary adenoma' could be found in pathology textbooks after 1974<sup>1,7</sup>.*

*PTC has many variants in their morphologic presentation. The one interesting is the encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC). This disorder had been treated as cancer for many years. Another change has occurred a few years ago. This variant (EFVPTC) has now been proven a non-malignant disease; and a new name has been adopted for, as: non-invasive follicular thyroid neoplasm with papillary-like features (NIFTP); and has to be treated accordingly<sup>6</sup>.*

*The morphologic diagnostic features, classification of PTC and its variants, has been presented. Discussion is focused on the 'encapsulated' and the 'follicular' variants of PTC, to explain the connection on which site the NIFTP and the formerly named 'papillary adenoma', should be placed on or may arise from the new classification of thyroid neoplasm.*

*There are other thyroid cancers which produce papillary-like structures, which are not PTC. It is also important to notice some focal papillary fronds/buddings or hyperplasia, found in non-neoplastic thyroid diseases. These changes are delivered briefly on closing this presentation.*

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## INTRODUCTION

There was historical diagnostic changes of papillary lesions of the thyroid gland. In pathology textbooks. Before 1964, there was ‘papillary adenoma’ diagnosed from a microscopically benign encapsulated papillary thyroid tumor<sup>-5,8</sup>. After 1974 this nomenclature was omitted. All papillary lesions in the thyroid gland was then considered a malignancy<sup>-1,7</sup>. Interestingly, a few years ago Nikiforov et al, has published their multidisciplinary study of EFVPTC, and has concluded that this disorder should not be termed carcinoma. Consequently, management and treatment of EFVPTC evolved a change. This lesion could be treated without radio-iodine ablation; including to designate this disorder a new name of: non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)<sup>-6</sup>.

Diagnostic criteria of PTC including plenty of their variants, is important for the pathologist. It is also important for the clinician, especially the endocrinologists and the surgeons, to have similar point of view and understanding about PTC. The 2017-WHO classification of tumours has published a new section of ‘other encapsulated follicular pattern thyroid tumors’, and this part can explain where the formerly named ‘papillary adenoma’ and the NIFTP should belong<sup>-4</sup>.

There are other thyroid cancers which produce papillary-like structures, which are not PTC. It is also important to notice some focal papillary fronds/buddings or hyperplasia, found in non-neoplastic thyroid disorders.

This presentation will then be divided into:

- Historical evidence.
- Papillary Thyroid Carcinoma and its variants.
- The encapsulated PTC and Follicular pattern of thyroid papillary tumors.
- Mimicking PTC.

## HISTORICAL EVIDENCE

Up till 1964, diagnosis of “papillary adenoma” of the thyroid could be found in textbooks<sup>-5,8</sup>. Many clinical observations had proven that this microscopically benign appearing lesion could present nodal metastasis. Because of this reason ‘papillary adenoma’ was considered a malignancy, and the name ‘papillary adenoma’ was omitted, and could not be found in pathology textbooks after 1974<sup>-1,7</sup>. All papillary epithelial lesions in the thyroid gland was considered a malignancy. With the advancements of knowledge and observations on the behavior of various cases of PTC, abundant morphologic variants has emerged in the literatures. The one interesting is the EFVPCT. This disorder had been treated as cancer for many years<sup>-6</sup>. In 2016, Nikiforov et al, had

published their 26 year-research and multidisciplinary study on EFVPTC: and has resulted this as a non-metastazing tumor and could be treated without radio-iodine ablation. A new name was adopted for, as: non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)<sup>-6</sup>.

### **Papillary Thyroid Carcinoma and its variants<sup>-4,10</sup>.**

Morphologic features of PTC, can be described by the examination of the gross or macroscopic and the microscopic presentation. PTC can be so small of microscopic size or to a huge tumor; mostly solid, white, firm, clearly invasive; less than 10%, are completely encapsulated; another 10% show cystic changes; sometimes papillae are clearly seen. Microscopic features show up: numerous papillae, complex branching, with fibro-vascular core, and psammoma bodies are commonly present. The cell lining the papillae are single or stratified cuboidal, (some hobnail), with edematous stroma, infiltrated by lymphocytes and macrophages. They may form irregular follicles. Nuclear features are important sign for diagnoses; those are: ground glass, optical clear nuclei, nuclear pseudo-inclusions, nuclear grooves and nuclear micro-filaments (clearing).

PTC has a lot of microscopic variants; which includes:

- Papillary micro-carcinoma.
- **Encapsulated variant.**
- **Follicular variant.**
- Diffuse Sclerosing variant.
- Tall Cell variant.
- Columnar Cell variant.
- Cribriform Morular variant.
- Hobnail variant.
- Papillary Ca with fibromatosis/fasciitis-like stroma.
- Solid/trabecular variant.
- Oncocytic (oxyphilic) variant.
- Spindle Cell variant.
- Clear Cell variant.
- Warthin-like variant.
- Papillary Carcinoma with nodular exuberant fasciitis-like stroma; with squamous/muco-epidermoid component; or insular component;
- and some other more.

Among these variants, the ‘encapsulated’ and the ‘follicular’ will be paid attention, to explain the existence of the changes that happened along with papillary lesions of the thyroid gland.

### **The Encapulated PTC and Follicular pattern of thyroid papillary tumors<sup>-4</sup>.**

For these lesions, important features that must be paid attention are: the presence of follicles, availability of capsular and or

vascular invasion, and the PTC nuclear features. Examinations are focused to determine whether they have follicular pattern; are there clear or questionable capsular invasion. When encapsulated, Is that a thick capsule, a thin one, or just well demarcated. Are there true vascular invasion or equivocal; and do they have PTC nuclear features.

There are three thyroid tumors which attribute to explain the source of changes:

1) PTC encapsulated variant.

This variant occurs in 10% of PTC, having nuclear changes of PTC. with intact capsule or focally infiltrated; nodal metastasis may be present; blood-borne are rare; has a good prognoses (almost 100% survival rate). In the past it was diagnosed as: "Papillary Adenoma".

2) Tumors of Uncertain Malignant Potential (UMP).

This is a follicular pattern, encapsulated or well-circumscribed thyroid tumor, with questionable capsular or vascular invasion, irrespective of the availability PTC nuclear features. Two types are recognized:

- Follicular tumor of uncertain malignant potential (FT-UMP).

This follicular tumor has no PTC-nuclear features. It is

encapsulated or has well circumscribed margin; with questionable capsular / vascular Invasion. This tumor is considered indeterminate, between "follicular adenoma" and "follicular Carcinoma".

- Well differentiated tumors of uncertain malignant potential (WDT-UMP).

This is an encapsulated or well circumscribed tumor, composed of well differentiated follicular cells, with well developed or partially developed PTC-nuclear features, and questionable capsular / vascular invasion. When capsular/vascular invasion has been excluded by thorough examination, it is called NIFTP<sup>-6</sup>.

3) Non-invasive Follicular Thyroid neoplasm with Papillary-like nuclear features (NIFTP).

This tumor has certain important features as follows:

- An intact capsule, or clear demarcation (no invasion).
- Follicular pattern; < 1% papillae; no psammoma bodies; <30% solid, trabecular or insular pattern.
- Has ptc-nuclear features.

- No lympho-vascular or capsular invasion.
- No tumor necrosis.
- No high mitotic activity (<3/10hpf)
  - This tumor is considered to have extremely low malignant potential.
  - Nikiforov et al concluded: a non-malignant tumor; reduce overtreatment<sup>6</sup>.

After these findings, the 2017-WHO classification of tumors, has changed the classification of PTC and put the ‘encapsulated follicular type’ into a separate section, under the heading of “Other Encapsulated Follicular-Patterned Thyroid Tumors”<sup>4</sup>. Many studies have revealed that the non-invasive EFVPTC is associated with an excellent prognosis. It is then proposed to rename this entity as: “non-invasive follicular thyroid neoplasm with papillary-like nuclear features” (NFTNP); removing the word “carcinoma”, to reduce patient’s overtreatment<sup>6</sup>.

#### **Mimicking PTC**<sup>-3,4,9,10</sup>.

There are also other malignant thyroid tumors which may produce papillary structures, and resembles, but they are not really PTC. These structures can be found in Medullary Carcinoma, Hürthle Cell Neoplasm with papillary like structures, and Poorly Differentiated Carcinoma, insular type.

On the contrary, non-neoplastic thyroid disorders may also give rise to present focal papillary budding or fronds. They are not a PTC; and can be encountered in several benign thyroid lesions, like: Graves’ disease, multi-nodular goiter, Hyalinizing Trabecular Adenoma, Follicular Adenoma, and benign focal ‘clear’ nuclear changes, in Benign Multifocal Thyroiditis.

#### **SUMMARY**

The opinion of certain papillary lesion of the thyroid has changed from time to time. This includes the pathologic diagnoses, management and treatment of the disorder. It is due to the advancements of knowledge and understanding, and because of meticulous study and observations of multicenter and multi-disciplinary approach of the disease.

Currently, attention should be paid to two special variants of PTC, those are the encapsulated and the follicular variant. This has been discussed and explained to clear the understanding of what has been formerly named ‘papillary adenoma’ of the thyroid, a ‘follicular adenoma’ or ‘follicular carcinoma’ and the new concept of ‘NIFTP’.

Will there be another change of opinion on the problem of papillary thyroid lesion, only time will tell us later.

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