JPTM
Journal of Pathology and Translational Medicine 2020; 54: 263-264
https://doi.org/10.4132/jptm.2020.02.05

BRIEF CASE REPORT

Noninvasive encapsulated papillary RAS-like thyroid tumor (NEPRAS) or encapsulated papillary thyroid carcinoma (PTC)

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In a recent case study, Ohba et al. [1] suggested that presence of papillae in absence of other criteria of malignancy and exuberant nuclear alterations (nuclear score 3 [2]) may not be sufficient for diagnosis of papillary thyroid carcinoma (PTC) and proposed the name "noninvasive encapsulated papillary RAS-like thyroid tumor" (NEPRAS) to encompass the borderline nature of the diagnosis [1].

CASE REPORT

Based on the diagnostic proposal of Ohba et al. [1], we revised our cases of tumors > 1 cm previously diagnosed as PTC and that were encapsulated/well-delimited (thick, thin, or partial capsule or well-circumscribed with a clear demarcation from adjacent thyroid tissue) and noninvasive (absence of capsular or vascular invasion) (n = 185). A total of 129 cases met all criteria for noninvasive follicular thyroid neoplasm with papillary like nuclear features (NIFTP) [3], and 11 were excluded due to the presence of papillae [4]. These and an additional 35 cases were initially considered encapsulated PTC, and nine were diagnosed as poorly differentiated carcinoma or an aggressive PTC subtype. Among the 11 cases not considered NIFTP due to the presence of papillae, eight had exuberant nuclear alterations (nuclear score 3 [2]). The three reported here had a nuclear score of 2 and would be reclassified from encapsulated PTC to NEPRAS [1]. Ultimately, we analyzed 43 cases of noninvasive encapsulated PTC and three of NEPRAS. None of the tumors carried the *BRAF*^{V600E} mutation, which was the only mutation investigated. Thus, the three cases diagnosed as NEPRAS met all criteria presented in Table 1. The characteristics of the patients are shown in Table 2.

None of these cases exhibited metastasis at presentation, were treated with radioiodine, or were maintained under TSH suppression. Excellent response to initial therapy was achieved in all three cases. No recurrence was detected after 36, 48, and 60 months of follow-up. Because of the small number of NEPRAS cases (n = 3), we did not perform statistical comparison between NIFTP and noninvasive encapsulated PTC, analyzing only patients with lymph node metastases at presentation and/or recurrence.

Ethics statement

The study was approved by the research ethics committee of Santa Casa de Belo Horizonte (No. 21968013.8.0000.5138). Informed consent was obtained from all individual participants included in the study.

DISCUSSION

Well-delimited or encapsulated thyroid neoplasms without vascular or capsular invasion or necrosis, with low mitotic index

Table 1. Criteria for diagnosing "noninvasive encapsulated papillary RAS-like thyroid tumor"

Criteria
Presence of papillae
Encapsulation or clear demarcation
No vascular or capsular invasion
<30% solid/trabecular/insular growth pattern
No tumor necrosis or high mitotic activity [2]
Nuclear score 2 [2]
Lack of *BRAF*^{V600E} mutation

Received: January 22, 2020 **Revised:** February 4, 2020
Accepted: February 5, 2020

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pISSN 2383-7837
eISSN 2383-7845

Table 2. Characteristics of three patients with NEPRAS

Sex	Age (yr)	Presentation	Tumor size (cm)	Nuclear score [2]	Papillae (%)	Associated thyroid pathology	Initial therapy	TNM/AJCC
F	35	Atoxic uninodular disease, US: hypoechoic solid nodule 4.5 cm[a], FNA: Bethesda IV	4	2	<1	Normal extranodular hyroid parenchyma	Total thyroidectomy	T2NxM0/ stage I
F	43	Atoxic multinodular disease; US: hypoechoic solid nodule 2.5 cm[a], two nodules 0.6 and 0.5 cm; FNA: Bethesda III	2.2	2	1	Benign nodular disease	Lobectomy	T2N0M0/ stage I
M	48	Atoxic uninodular disease, US: hypoechoic solid nodule 4 cm[a], FNA: Bethesda IV	3.5	2	1	Normal extranodular thyroid parenchyma	Lobectomy	T2NxM0/ stage I

NEPRAS, noninvasive encapsulated papillary RAS-like thyroid tumor; AJCC, American Joint Committee on Cancer; F, female; US, ultrasonography; FNA, fine-needle aspiration; M, male.
[a]Without suspicious findings for malignancy (irregular margins, microcalcification, taller-than-wide shape).

and < 30% solid/trabecular/insular growth patterns, and with nuclear alterations characteristic of PTC (nuclear score 2 or 3 [2]) are diagnosed as NIFTP or encapsulated PTC depending on the presence (PTC) or absence (NIFTP) of papillae [2]. NIFTP is a borderline tumor that requires no additional surgical complementation, adjuvant therapy with radioiodine, TSH suppression, or monitoring with serum thyroglobulin and neck ultrasound after complete resection [5]. In contrast, encapsulated PTC is a malignant tumor that must be staged. Even when restricted to the thyroid, surgical complementation, radioiodine ablation, long-term follow-up, and TSH suppression may be necessary depending on tumor size and patient age.

Although the present study comprises only case reports, the patients supported the observations of Ohba et al. [1] that lesions that do not exhibit other malignancy criteria or exuberant nuclear alterations despite the presence of papillae may be reclassified from malignant (encapsulated PTC) to borderline (NEPRAS). This proposal would result in changes of patient management, with the same implications as those seen for the change from noninvasive encapsulated follicular variant of PTC to NIFTP [2].

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Conflicts of Interest

The authors declare that they have no potential conflicts of interest.

Funding

No funding to declare.

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