Diagnostic criterion of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): absence of papillae

Dear Editor,

In contrast to most patients with differentiated thyroid "cancer" (DTC), individuals with noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) could be treated only with lobectomy. After surgery, these patients do not need to undergo adjuvant therapy with radioiodine and do not require thyroid-stimulating hormone (TSH) suppression nor the follow-up currently recommended for patients with DTC. However, criteria were established for the safe diagnosis of NIFTP [1], which is considered a "borderline" rather than a "malignant" tumor. The initial criteria included <1% papillae, which comprises the absence but also the presence of papillae in <1% of the tumor.

For any original diagnostic criterion, it is common that questions arise during its application in different centers around the world, which require clarifications and possibly adaptations or even changes. This evolution appears to be occurring regarding NIFTP. In an editorial published in this journal, Lloyd et al [2] proposed that "cases with any well-formed papillae should not be diagnosed as NIFTP." In fact, in a previous study, Cho et al [3] demonstrated the presence of *BRAF*^{V600E} mutation in NIFTP with <1% papillae but not in NIFTP without papillae. Bone metastasis was also detected in one patient and lymph node metastases in another in the first group [3].

To reiterate the importance of the change proposed by Lloyd et al [2], at our institution, the diagnosis of the follicular variant of papillary thyroid cancer (FVPTC) and now of NIFTP has only been made in the absence of any well-formed papillae, and we have found so far no case of persistent or recurrent structural disease in patients with noninvasive encapsulated FVPTC [4] or NIFTP [5,6], even in tumors ≥4 cm [7]. Specifically for this Letter to the Editor, we reviewed tumors >1 cm that met the remaining diagnostic criteria of NIFTP [1], but that contained papillae, and 11 patients had papillae in <1% of the tumor.

There were 9 women and 2 men, ranging in age from 23 to 78 years, whose tumors measured 1.2 to 5.4 cm. Lymph node metastasis was detected in one patient at presentation, and cervical lymph node disease was diagnosed in another patient after initial therapy. The first patient had undergone total thyroidectomy, and the second had initially been treated by lobectomy, but was submitted to thyroidectomy after the detection of cervical lymph node metastasis. Importantly, no other tumor focus was detected in the thyroid of either case, and the lymph node metastases showed histological findings identical to those of the primary tumor. In the first case, the tumor was positive for the *BRAF*^{V600E} mutation. In contrast, there were 122 patients with NIFTP without any well-formed papillae and without associated PTC. No case of metastasis was detected among these patients at presentation or during follow-up [5-7].

In agreement with the findings reported by Cho et al [3], our results reinforce adaptation of the NIFTP criterion considering the presence of any well-formed papillae to rule out this diagnosis [2], is indeed interesting. It should be noted that this stricter criterion [2] ruled out the diagnosis of NIFTP in <10% of patients at our institution who would have been diagnosed if the original criterion were applied [1]. As an advantage, we have found so far no case of metastases detected at presentation or after initial therapy among the more than 120 patients who continued with the diagnosis of NIFTP (without associated PTC), with a follow-up time of 18 to 150 months [5-7]. To ensure even greater safety that NIFTP is a neoplasm of excellent evolution, it seems worthwhile to exclude these few cases with <1% papillae [2].

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References

[1] Nikiforov YE, Seethala RR, Tallini G, et al. Nomenclature revision for encapsulated follicular variant of papillary thyroid carcinoma: a paradigm shift to reduce overtreatment of indolent tumors. JAMA Oncol 2016;2:1023-9.

[2] Lloyd RV, Asa SL, LiVolsi VA, et al. The evolving diagnosis of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Hum Pathol 2018;74:1-4.

[3] Cho U, Mete O, Kim MH, Bae JS, Jung CK. Molecular correlates and rate of lymph node metastasis of non-invasive follicular thyroid neoplasm with papillary-like nuclear features and invasive follicular variant papillary thyroid carcinoma: the impact of rigid criteria to distinguish non-invasive follicular thyroid neoplasm with papillary-like nuclear features. Mod Pathol 2017;30:810-25.

[4] Rosario PW, Penna GC, Calsolari MR. Noninvasive encapsulated follicular variant of papillary thyroid carcinoma: is lobectomy sufficient for tumours ≥ 1 cm? Clin Endocrinol (Oxf) 2014;81:630-2.

[5] Rosario PW, Mourão GF, Nunes MB, Nunes MS, Calsolari MR. Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Endocr Relat Cancer 2016;23:893-7.

[6] Rosario PW, Mourão GF, Oliveira LFF, Calsolari MR. Long-term follow-up in patients with noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) without a suspicion of persistent disease in postoperative assessment. Horm Metab Res 2018;50:223-6.

[7] Rosario PW. Long-term outcomes of patients with noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) ≥4 cm treated without radioactive iodine. Endocr Pathol 2017;28:367-8.