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LETTER – ENDOCRINE TUMORS

The Importance of Diagnosing Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP) Based on the Defined Criteria

Pedro Weslley Rosario, MD[1]

Instituto de Ensino e Pesquisa da Santa Casa de Belo Horizonte, Belo Horizonte, Minas Gerais, Brazil

Dear Editor

We read with great interest the study by Eskander et al.[1] published in *Annals of Surgical Oncology*. The controversy addressed and the number of patients included make the importance of the study indisputable. However, in view of the unexpected results that differ from most previous series, and of the impact they may have on the actual concept of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) as an indolent neoplasm, we would like to express some concern about the methodology of the study and a certain divergence with its conclusions.

The criteria for the diagnosis of NIFTP are well established.[2] Making the retrospective diagnosis based only on the information provided in the original pathology report, without at least reviewing the slides in order to actively identify the findings that constitute the diagnostic criteria, does not seem to be possible. This analysis (retrospective and based only on the original report) becomes even more flawed when these reports were issued prior to the definition of NIFTP and the findings necessary to confirm or rule out the diagnosis. The pathologist may not have reported these findings of interest because, unlike now, they would not have changed the diagnosis of malignancy at that time. We are concerned with the inference that these findings were absent when reports did not expressly state certain results. This was assumed to be true in the study by Eskander et al.[1]

First, although the authors state that all tumors were encapsulated, this finding is incompatible with an infiltrative border which, according to the authors, was not reported in 89% of the cases. Second, it does not seem possible to confirm the diagnosis of NIFTP if the reports did not expressly state information about the absence of true papillae or psammoma bodies in 87% and 74% of cases, respectively. Third, although less frequent but important because of their contribution in cases of metastasis/recurrence, tumor necrosis, high mitotic rate, and morphologic features of an aggressive variant were unstated in 95, 90, and 90% of cases, respectively. Considering that these findings (infiltrative border, true papillae or psammoma bodies, tumor necrosis, high mitotic rate, and morphologic features of an aggressive subtype) exclude the diagnosis of NIFTP,[2] many of the tumors considered NIFTP in the study may in fact be carcinomas.

In addition to the main issue discussed above, adequate sampling of the capsule and of the whole tumor is necessary for the diagnosis of NIFTP.[2] We recognize that this analysis is indeed laborious, but the authors did not provide information about the sampling of the capsule and tumor.[1] This aspect also makes us question how many tumors considered by the authors to be NIFTP were in fact NIFTP. Finally, the authors did not provide any information about the histology of metastases in patients with NIFTP. Discrepancy between the primary tumor (NIFTP) and metastases has been reported, suggesting another origin (occult microcarcinomas) for the latter.[3]

We agree that the results of the study by Eskander et al.[1] reinforce that the retrospective diagnosis of NIFTP should not be made based only on the revision of the pathology report, especially when issued before appearance of this nomenclature, and assuming that the unreported findings were absent.[4,5] We also agree with the authors that the diagnostic criteria are strict and laborious. However, we

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P. W. Rosario, MD
e-mail: pedrowsrosario@gmail.com

believe that this effort is worthwhile, considering the benefits of changing the diagnosis of a patient who would be diagnosed as having 'cancer' to NIFTP.[2,4,5]

In our opinion, many of the tumors wrongly considered to be NIFTP that exhibited metastases/recurrence in the study by Eskander et al.[1] were not NIFTP. Thus, respectfully, what we do not agree upon is that, once adequate samples are obtained and the criteria defined are met,[2] as required for the diagnosis and as is done in many centers, the risk of metatases/recurrence in patients with NIFTP is as high as reported by Eskander et al.[1]. None of the 147 patients with NIFTP seen at our institution and not treated with radioiodine had persistent disease or recurrence during follow-up (median 72 months). The authors state that their results are the same as observed in three other studies.[6–8] In the study by Cho et al.[6], using the current diagnostic criteria,[2] only 2/95 patients had lymph node metastases (both with central micrometastases). Aburjania et al.[7] recognized that they "analyzed three out of six diagnostic criteria of NIFTP—tumor encapsulation, no vascular/capsular invasion, no tumor necrosis". In addition, the only supposed case of NIFTP that exhibited lymph node metastases had a multicentric tumor, and once again the authors highlighted that "notably all the primary tumor foci in thyroid were FVPTC, while all metastatic nodal tumors were PTC". Finally, these two studies[6,7] and the series of Parente et al.[8] reported no additional cases of persistent/recurrent disease after initial therapy among more than 200 patients without metastases detected at the time of surgery.

In conclusion, the diagnosis based only on the pathology report, without at least reviewing the slides, and using reports issued prior to the definition of NIFTP, is not only a limitation of the study, as acknowledged by the authors,[1] but also a formal impediment to the diagnosis of NIFTP. This is a concern highlighted by the American Association of Clinical Endocrinologists[4]—"the diagnosis cannot be based on the original pathology report"—and by the American Head and Neck Society[5]—"the diagnosis of NIFTP should not be based on retrospective interpretation of written pathologic reports created before May of 2016".

DISCLOSURE Pedro Weslley Rosario declares he has no conflicts of interest.

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