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Thy3A and Thy3B nodules: is surgery the best treatment?

Dear Editor,

Nowadays thyroid nodules are very common in clinical practice. Clinically palpable nodules can be found in 4-20% of the adult population. If we consider ultrasound-detectable nodules 30-50% of the adult population may present a thyroid nodule.¹ Thus it is very important to distinguish benign nodules from malignant forms. Fine needle aspiration (FNA) cytology is currently the gold standard in thyroid nodule assessment in addition to the echographic features. However, more than three in four patients with a pre-operative diagnosis of indeterminate nodule receive an unnecessary surgery.² This study was designed to investigate if reporting indeterminate nodules into two different categories at the fine needle cytology is useful, in order to identify patients that really needs a surgical treatment.

We performed a retrospective analysis of the medical records of the patients with an indeterminate nodule (Thy3) who underwent thyroid surgery. Patients with also nodules suspicious for malignancy (Thy4) or malignant (Thy5) were excluded from the research. We also reported indeterminate nodules into Thy3A and Thy3B categories. According to these evaluations, 179 cases with indeterminate nodules (Thy3) had been treated surgically but only 161 were included in this study because of the lack of an exhaustive cytological report in the clinical charts assessed. The patients with proper documentation had a cytological finding of Thy3A in 61 cases and Thy3B in 100 cases. Of these, 124 were female (77%) and 37 male (24%), with a mean age of 51.9±12.7 years, ranged from 20 to 76 years of age. Carcinomas were found in 60 patients but only 42 of these were detected by FNA as indeterminate. Instead 28 patients had a diagnosis of thyroid carcinoma as well but in a position different from the nodule reported as Thy3, that was found to be benign at the histological examination. The data was analyzed by percentage of frequencies. Association between cytology and histological examination was analyzed using chi-square test of significance.

The comparison between cytological features and histological results showed a malignancy rate of 26.1%

(95% CI: 19.3-32.9%) considering the nodules underwent fine needle aspiration. Furthermore 28 carcinomas were found in other sites increasing the malignancy rate to 43.5% (95% CI: 35.8-51.1%). Using the reporting system of the last Italian Consensus for the Classification and Reporting of Thyroid Cytology, 16.4% of the Thy3A nodules (95% CI: 7.1-25.7%) and 32% of the Thy3B nodules (95% CI: 22.9-41.1%) proved to be malignant upon histological examination.

A significant difference was found between Thy3A and Thy3B nodules at a P value of 0.0287 ($\chi^2=4.79$).

The most used classification systems for reporting thyroid cytology are the Bethesda System, a six-tier classification, and the SIAPEC-IAP a five-tiered classification, by Italian Society for Anatomic Pathology and Cytology with the Italian Division of the International Academy of Pathology.

Indeterminate nodules are reported as Thy3 in the SIAPEC-IAP classification. This group encompasses all histological follicular-patterned lesions: adenomatoid hyperplasia, adenoma, oxyphilic cells lesions, some cases of follicular variant of papillary carcinoma and microinvasive follicular carcinomas. Then in these cases only histology can provide a definitive diagnosis. About 80% of Thy3 diagnoses are benign lesions, whereas only 20% are malignant tumors after histological examination. Some cases characterized by cytological alterations which are too mild to be included in Thy4 but which, on the other hand cannot be included in the benign category (Thy2), can be classified as Tir3. The choice to include these samples in the "low risk" category must be supported by an appropriate description in the medical report. Surgical excision of the lesion and histological examination is the suggested option for patients with nodules reported as Thy3. The surgical option (lobectomy vs. thyroidectomy) should be evaluated in the clinical and imaging setting. For solitary indeterminate nodules, without other ultrasonographic signs of thyroid disease in the contralateral lobe, and being aware of the need of undergoing another surgery, if the histological examination shows malignancy, a limited surgical procedure may be proposed. Postoperative diagnosis of malignancy would lead to a complete thyroidectomy in some cases, but two stage thyroid surgery has higher morbidity and increase costs if compared with initial total thyroidectomy. The latest Italian Consensus for the Classification and Reporting of Thyroid Cytology reviewed the classification and proposed an Italian classification system for thyroid cytology.

It distinguishes FNA cytology reported as indeterminate (Thy3/Tir3) into two different subgroups: Thy3A (Tir3A), or low-risk indeterminate lesion (LRIL),

and Thy3B (Tir3B), or high-risk indeterminate lesion (HRIL). According to this system, Nardi *et al.* suggest follow-up as the preferential option in the majority of cases with Thy3A nodules and eventually to repeat FNA. Furthermore, surgery is strongly recommended for Thy3B nodules.³⁻⁵ Calò *et al.* recommend surgery for all patients with and indeterminate nodule due to the lack of accurate predictors of malignancy such as clinical and cytological features. In their experience total thyroidectomy is the most suitable procedure in case of multiple lesions, hyperplastic nodular goiter, or thyroiditis.¹ According to the current literature, results from our study suggest that nodules reported as Thy3A and nodules reported as Thy3B have different risks of malignancy. While a surgical approach is generally adopted for patients with Tir3B cytology, it is not clear if surgery is always needed for Thy3A nodules. In our opinion the best treatment for both categories is total thyroidectomy. Nowadays surgical treatment has a low risk of complications if performed by surgeons with good experience in endocrine surgery. This approach turns out to be useful due to the high rate of malignancy. In addition, considering the whole gland, another surgery is required for patients who underwent lobectomy and had a malignant confirmation at the histological examination. A total thyroidectomy allows an easier replacement therapy, an eventually radiometabolic treatment, a proper follow up with scintigraphy and thyroglobulin as a marker of recurrences. It occurs to us that for a better management of indeterminate nodules, other studies are required in order to identify patients with an acceptable risk of malignancy and avoid unnecessary surgical procedures.

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