RISK OF MALIGNANCY MAY BE HIGHER IN CYTOLOGICALLY SUSPICIOUS THYROID NODULES THAT ARE SMALLER OR MULTIPLE

Castro MR, Espiritu RP, Bahn RS, Nery MR, Gharib H, Caraballo, PJ, Morris JC. **Predictors of malignancy in patients with cytologically suspicious thyroid nodules.** Thyroid 2011;21:1191-8. Epub October 18, 2011.

BACKGROUND

Fine-needle aspiration biopsy (FNAB) has a high predictive value for benign and malignant thyroid nodules but has a lower predictive value for indeterminate or suspicious nodules. Clinical data was extracted from an electronic medical record from January 2004 through September 2008 of patients who had undergone FNAB and thyroid surgery for cytologically suspicious nodules.

METHODS AND RESULTS

This was a retrospective chart review study at a single referral center, the Mayo Clinic. Review of the electronic medical records revealed that 573 (8%) of 7039 FNAB samples had a suspicious cytologic diagnosis. Of these patients, 111 did not have surgery and did not return for reevaluation. The remaining 462 patients with a suspicious biopsy underwent thyroid surgery. The demographic and clinical characteristics of this group are as follows: 69% female; mean (±SD) age, 53.7±15.2 years; prior head and neck radiation, 5.4%; multiple nodules, 65%; mean nodule size, 2.8±1.7 cm; and thyroid hormone therapy, 19.5%. Of these patients, 326 had lesions suspicious for follicular neoplasm or Hürthle-cell neoplasm, 126 were suspicious for papillary thyroid carcinoma (PTC), and 10 were suspicious for other neoplasms The malignancy rate was 15% for cytology that was suspicious for follicular and Hürthle-cell lesions and 77% for those suspicious for PTC. Age, elevated levels of thyrotropin (TSH), and history of radiation exposure were not associated with increased malignancy risk. Although the authors state that smaller nodules measured by ultrasonography had a higher risk of malignancy (2.6±1.8 vs. 2.9±1.6 cm; P = 0.008), 34% of nodules >4 cm were malignant. Multiple nodules, as compared with a single nodule, had a higher risk of malignancy (41.1% vs. 26.4%; P = 0.014). In patients with cytology suspicious for follicular and Hürthlecell neoplasm, malignancy risk was higher in those who were undergoing thyroid hormone therapy than in those who were not (37.7% vs. 16.5%; P =0.0004; odds ratio, 3.0), but the TSH values did not differ significantly between the thyroxine users and nonusers.

(medullary thyroid carcinoma, lymphoma, atypia).

Clinical

THYROIDOLOGY

CONCLUSIONS

The risk of malignancy is higher in patients with nodules that are cytologically suspicious for Hürthlecell or follicular neoplasms or PTC when the index nodule is smaller or if the patient has multiple thyroid nodules. This study demonstrates an increased risk of malignancy in patients using thyroid hormone therapy but the reason for this is unknown.

COMMENTARY • • • • • • • • • • • • • • • • •

This study has a number of difficulties, including its retrospective design and the incomplete information for the subjects. These data should not alter the belief that head and neck radiation exposure is a significant risk for thyroid cancer. First, only 5.4% of the cohort had radiation exposure and 55.6% denied radiation exposure. This means that 39% of the cohort were

either not asked about radiation exposure or it was not documented in the medical record. I also question the clinical significance of the statement that smaller size (2.6 ± 1.8 vs. 2.9 ± 1.6 cm; P = 0.008) is a risk factor for thyroid cancer, since the means of the two groups are very similar and 34% of nodules >4 cm were malignant. Because of the large number of patients, there is a statistical difference, but it may *continued on next page*



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not be clinically important. The increased risk of thyroid cancer in patients taking thyroid hormones is interesting based on the number of studies suggesting that the risk of thyroid malignancy is associated with higher TSH values, even within the normal range (1).

The take-home message is that this type of study is difficult even at an elite institution with excellent electronic medical records. This paper strengthens my opinion that clinical characteristics will not identify all patients who have cancer with a suspicious biopsy. The selection of patient with suspicious biopsies who should have surgery may rest with other characteristics of the nodule, including ultrasound characteristics (2, 3), mutational analysis, including BRAF (4, 5), gene expression (6), elastography (7), and 18fluorodeoxyglucose-positron-emission tomographic hypermetabolic activity (8). It is not yet clear which of these tests is the most cost-effective method to prevent unnecessary surgery in patients with a suspicious FNAB.

- Stephanie L. Lee, MD, PhD

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