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THYROID CANCER

Cancer-associated gene mutation detection in fine needle aspiration biopsies increases the accuracy for diagnosing cancer

WHAT IS THE STUDY ABOUT?

Thyroid nodules are very common and can be found in up to 50% of the population. Most thyroid cancers are discovered by fine needle aspiration biopsy (FNAB) of thyroid nodules. While FNAB is a very accurate test, there are occasional cancers that are missed with the initial biopsy cytology reading. Further, FNAB cannot diagnose follicular or hurtle cell cancer; it can only state that the results are indeterminate. Up to 15-20% of FNABs are read as indeterminate. When these nodules are removed, only 15-20% are cancerous and the rest are noncancerous follicular or hurtle cell adenomas. This means that many patients are operated on for non-cancerous thyroid nodules. A lot of research has been done in trying to do a better job at identifying follicular or hurtle cell cancer with FNAB. In particular, examining FNAB specimens for the presence certain cancer-associated gene mutations that are related to thyroid cancer might be able to improve the diagnostic accuracy of FNAB. The study examined whether molecular analysis of cancer-associated gene mutations in addition to cytology improved the accuracy of FNAB in patients with thyroid nodules.

THE FULL ARTICLE TITLE:

Cantara s, et al. Impact of proto-oncogene mutation detection in cytological specimens from thyroid nodules improves the diagnostic accuracy of cytology. J Clin Endocrinol Metab 2010;95:1365-9.

WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to determine whether molecular analysis of cancer-associated gene mutations in addition to cytology improved the accuracy of FNAB in patients with thyroid nodules.

WHO WAS STUDIED?

This study examined 174 patients with thyroid nodules that were already scheduled to undergo surgery.

HOW WAS THE STUDY DONE?

The study group of 174 patients were already scheduled for thyroid surgery, either on the basis of an abnormal FNAB results or on the basis of the patient's clinical condition. Within the group 40.2% had a FNAB suspicious (22) or positive (48) for cancer, 28.7% (50) had a FNAB showing follicular or hurtle lesions and 31.1% (54) had a goiter or nodule that was causing choking or difficulty swallowing with noncancerous or inadequate results on FNAB. All patients had a repeat FNAB prior to surgery with molecular analysis looking for the cancer-associated gene mutation. At the time of surgery, all nodules were again sampled for molecular analysis.

WHAT WERE THE RESULTS OF THE STUDY?

Cancer-associated gene mutations were identified in 67 of 235 FNAB samples (28.5%). The two most common mutations were in the BRAF and RET/PTC genes. In all cases, the presence of either of these mutations was indicative of thyroid cancer. Another cancer-associated gene mutation (RAS) was associated with thyroid cancer 74% of the time and with noncancerous follicular adenoma 26% of the time. Looking specifically at indeterminate FNAB results, there were 7 mutations (17%) found. On final pathology 6 were thyroid cancer and 1 was a noncancerous follicular adenoma. Among the 34 indeterminate nodules without mutations, only 1 was thyroid cancer. Thus, adding the cancer-associated gene mutation analysis increased the accuracy of the FNAB diagnosis.

HOW DOES THIS COMPARE WITH OTHER STUDIES?

Numerous earlier studies have laid the groundwork for the present study. From previous studies it is known that the presence of BRAF mutations is highly specific for thyroid cancer – there has been only one false positive result in 2766 samples reported in the literature. The present study shows that screening FNAB for multiple cancer-associated gene mutations can be done.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The present study demonstrates that combining FNAB result with new techniques for molecular analysis

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significantly improves the accuracy of thyroid FNAB. Further studies will be needed to determine the most cost-effective use of molecular analysis in actual clinical practice.

— Frank Cranz, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

ABBREVIATIONS & DEFINITIONS

Thyroid nodule — an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Thyroid fine needle aspiration biopsy (FNAB) — a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

Indeterminate thyroid biopsy — this happens usually when the diagnosis is a follicular or hurtle cell lesion. Follicular and hurtle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurtle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

Cancer-associated genes — these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.