



THYROID NODULES

Use of molecular markers on thyroid biopsy specimens to diagnose thyroid cancer

BACKGROUND

Thyroid nodules are very common, occurring in up to half of individuals who have any form of neck imaging study. Thyroid biopsy is performed on many thyroid nodules based on the size of the nodules or certain characteristics on thyroid ultrasound. Approximately 15-25% of thyroid nodules will have thyroid biopsy cytology read as “suspicious” or “indeterminate”, which generally leads to surgical thyroidectomy because of the difficulty in distinguishing between benign and cancerous nodules with this cytology. In order to improve the diagnosis of thyroid cancer, one approach that is increasingly used is to measure different molecular markers (genes and microRNAs) that are much more frequently present in thyroid cancer when compared to benign nodules. These molecular approaches are showing promise in helping to distinguish benign from cancerous nodules and avoiding unnecessary surgery. These two studies examine the use of molecular markers to help make a diagnosis in thyroid biopsies that are initially read as “suspicious” or “indeterminate”.

THE FULL ARTICLE TITLES

Prasad NB et al. Three-gene molecular diagnostic model for thyroid cancer. *Thyroid*. 2012;22:275-84.

Keutgen XM, et al. A panel of four microRNAs accurately differentiates malignant from benign indeterminate thyroid lesions on fine needle aspiration. *Clin Cancer Res*. February 20, 2012

SUMMARY OF THE STUDIES

In the Prasad study, the authors took biopsy samples from 95 thyroid nodules at the time of surgery. Of these biopsies, 27 had “indeterminate” or “suspicious” cytology. These samples were subjected to analysis of 10 genes previously shown to be promising candidates for

identifying cancer cells. The combination of 3 of these genes – MRC2 + HMGA2 + SFN – was shown to be very helpful in accurately predicting which nodules would be cancerous (96% test specificity, 91% test negative predictive value).

In the Keutgen study the authors evaluated a set of six microRNAs in 72 thyroid biopsy samples from patients with “indeterminate” thyroid nodules. All these patients had surgery. Of these 72 specimens, 50 were benign and 22 were cancerous on final pathology. The authors found that after using a sophisticated statistical model, four of the six miRNAs (miR-222, miR-328, miR-197 and miR21) when used in combination, were very helpful in accurately classifying 90% (65 of 72) of the samples. (100% test sensitivity and 86% test specificity for the diagnosis of cancer).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These 2 studies show that using a combination of thyroid biopsy cytology with molecular markers such as microRNA or gene analysis is feasible and may help in accurately distinguishing benign from cancerous nodules in those with “indeterminate” cytology, reducing the need for surgery for nodules that turn out to be benign. The selection of the best molecular markers is still a matter of debate.

— M. Regina Castro, MD

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <http://www.thyroid.org/what-are-thyroid-nodules>

Cancer of the Thyroid Gland: <http://www.thyroid.org/cancer-of-the-thyroid-gland>

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THYROID NODULES, continued

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.

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

Suspicious thyroid cytology: this happens when there are atypical cytological features suggestive of, but not diagnostic for malignancy. Surgical removal of the nodule is required for a definitive diagnosis.

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell.

Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

microRNA: a short RNA molecule that has specific actions within a cell to affect the expression of certain genes.

Molecular markers: genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign.

Test sensitivity: the proportion of patients with a certain disease in whom the test used to diagnose that disease is positive.

Test specificity: the proportion of patients without a certain disease in whom the test used to diagnose that disease is negative.

Negative predictive value: the likelihood that a patient does not have a disease when the test used to diagnose that disease is negative.