



THYROID CANCER

Suspicious readings of the Afirma gene-expression classifier include some noninvasive encapsulated follicular variant of papillary thyroid carcinomas

BACKGROUND

Thyroid nodules are commonly found on ultrasound of the neck and the evaluation of a thyroid nodule may include thyroid biopsy. Thyroid nodule biopsies are used to identify if a nodule is cancerous or determine the risk that a thyroid nodule may be cancerous. Sometimes, thyroid biopsy specimens are indeterminate, meaning that thyroid cancer cannot be definitively ruled in or out. In such cases, testing of molecular markers related to thyroid cancer may help determine the risk of cancer. One such molecular marker test is the Afirma gene expression classifier (GEC) test. The results of the GEC are either read as suspicious for cancer or benign.

Papillary thyroid cancer is the most common type of thyroid cancer. A group of expert pathologists have recently identified a subgroup of papillary thyroid cancer called noninvasive follicular variant papillary thyroid cancer that has a very low risk of relapsing after surgical removal. Because of this rather benign course, some pathologists have even questioned whether this subgroup is a cancer after all.

The aim of this study was to find out how often indeterminate thyroid biopsy specimens which were read as “suspicious” by the GEC test were ultimately diagnosed as noninvasive follicular variant papillary thyroid cancer after surgery.

THE FULL ARTICLE TITLE

Wong KS et al. Noninvasive follicular variant of papillary thyroid carcinoma and the Afirma gene-expression classifier. *Thyroid* 2016;26:911-5.

SUMMARY OF THE STUDY

In this study from Boston, 63 thyroid surgical specimens were reviewed from patients whose thyroid biopsy

samples were read as indeterminate and in whom the GEC test was reported as suspicious. The authors reported the following rates of final diagnoses for these specimens: 65% of cases had no cancer (ie. benign), 25% of cases had follicular variant papillary thyroid cancer, 2% of cases had classical papillary thyroid cancer and 8% of cases had follicular thyroid cancer. Of the 16 cases of follicular variant papillary thyroid cancer, 14 of them were noninvasive follicular variant of papillary thyroid cancer (88%).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that a GEC suspicious test result may include noninvasive follicular variant papillary thyroid cancer as well as classical papillary thyroid cancer. An important limitation of this study is that the authors did not examine the rate of noninvasive follicular variant papillary thyroid cancer in specimens that were not reported as suspicious by the GEC test. This study suggests that more research is needed to determine if the noninvasive follicular variant thyroid cancer can be diagnosed by molecular markers without proceeding to surgery.

— Anna Sawka, MD

ATA THYROID BROCHURE LINKS

Thyroid Nodules:

<http://www.thyroid.org/thyroid-nodules/>

Thyroid Cancer:

<http://www.thyroid.org/thyroid-cancer/>

Thyroid Surgery:

<http://www.thyroid.org/thyroid-surgery/>

**THYROID CANCER**, 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.

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 a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15–20% of biopsies and often results in the need for surgery to remove the nodule.

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.

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.

Papillary Thyroid Cancer: the most common type of thyroid cancer. There are 3 variants of papillary thyroid cancer: classic, follicular and tall-cell.

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.