



THYROID CANCER

Mutations of the RAS oncogene are found in follicular variant papillary thyroid carcinoma

BACKGROUND

Cancer-associated gene mutations are present in over half of thyroid cancers. Molecular markers based on certain cancer-associated genes in thyroid biopsy specimens can be used to either diagnose cancer or to determine that the nodule is benign. The 2 most common gene mutations are BRAF and RAS. These mutations are associated with a high risk of cancer when detected on thyroid nodule biopsy specimens. The aim of this study was to examine the role of screening for RAS expression in thyroid biopsy specimens in patients with thyroid cancer.

THE FULL ARTICLE TITLE

Gupta N et al. RAS mutations in thyroid FNA specimens are highly predictive of predominantly low-risk follicular-pattern cancers. *J Clin Endocrinol Metab* 2013;98:E914-22. Epub March 28, 2013; doi: 10.1210/jc.2012-3396.

SUMMARY OF THE STUDY

The study included 921 patients who underwent a thyroid nodule biopsy between April 2007 and April 2009. All samples were evaluated with a panel of molecular markers. RAS mutations were found in 7.2% of the biopsies. The thyroid cytology results of these biopsies with positive RAS mutations were read as indeterminate in 93% , cancer in 4% and negative for cancer in 3%.

Of the 63 RAS-positive nodules resected, cancer was confirmed in 83%. These included 46 follicular variant

papillary cancers, 4 follicular cancers, one medullary thyroid cancer and one anaplastic thyroid cancer. Only 1/3 of the RAS-positive cancerous nodules had findings on ultrasound that were suspicious of cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study confirms that RAS mutations in thyroid biopsy specimens are strongly suggestive of thyroid cancer, with the vast majority being follicular variant papillary cancers. Further, initial cytology in thyroid biopsies from RAS-positive nodules is mostly indeterminate. Since an ultrasound is frequently not suggestive of cancer in RAS-positive nodules, screening for this mutation in nodules with indeterminate cytology can be helpful to determine whether surgery is indicated. Total thyroidectomy should be considered for initial surgical management of most patients with RAS-positive thyroid biopsy results.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

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.

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.

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.



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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.

Indeterminate thyroid biopsy: this happens usually 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.

Papillary thyroid cancer: the most common type of thyroid cancer.

Follicular thyroid cancer: the second most common type of thyroid cancer.

Medullary thyroid cancer: a relatively rare type of thyroid cancer that often runs in families. Medullary cancer arises from the C-cells in the thyroid.

Anaplastic thyroid cancer: a very rare but very aggressive type of thyroid cancer. In contrast to all other types of thyroid cancer, most patients with anaplastic thyroid cancer die of their cancer and do so within a few years.