



## THYROID CANCER

# Distant metastases from low risk thyroid cancer are rare and associated with RAS and/or TERT Mutations

### BACKGROUND

The rate of thyroid cancer has been increasing over the last 20 years. Most of this increase has been in papillary thyroid cancer, which is the most common type of thyroid cancer. Fortunately, the vast majority of patients with papillary thyroid cancer do well and death from papillary thyroid cancer is rare. Because of this, the most recent guidelines from the American Thyroid Association emphasize an assessment of risk of the patient for cancer recurrence to help guide treatment and follow up after the initial thyroid surgery. Most patients with papillary thyroid cancer fall into the low risk category.

Spread of the cancer into the lymph nodes of the neck and outside of the neck increases the risk of recurrence. Spread of thyroid cancer outside the neck (metastases) is rare, occurring in between 1.2 and 13% of patients. However, when present in older patients, distant metastases are associated with a higher risk for death. Most patients who develop distant metastases from their thyroid cancer have evidence of aggressive features noted after surgery. Some unusual cases of distant metastases from low risk papillary thyroid cancer without these aggressive features can be a surprise to clinicians and have not been studied in detail.

The goal of the study is done to evaluate the features of low risk papillary thyroid cancer that develops distant metastases.

### THE FULL ARTICLE TITLE

Xu B et al. Primary thyroid carcinoma with low-risk histology and distant metastases: clinicopathologic and molecular characteristics. *Thyroid*. May 2017, 27(5): 632-640.

### SUMMARY OF THE STUDY

The 1983-2009 institutional database of Memorial Sloan-Kettering Cancer Center, New York, NY, identified 123 patients with distant metastases. A total of 11 cases of

low risk primary thyroid cancers who also had distant metastases were also retrieved from the pathology database at the same institution.

Of the initial group of 123 patients, 74 of the patients had distant metastases at presentation and 49 patients developed distant metastases and 97% (119 patients) were considered aggressive based the initial pathology. The remaining 4 were considered low risk based on pathology and these were added to the 11 additional patients low risk patients with distant metastases for further study.

The types of cancers were 1) encapsulated follicular variant of papillary thyroid cancer with invasion (8), 2) infiltrative follicular variant of papillary thyroid cancer (2), 3) papillary microcarcinoma infiltrative follicular variant (1), 4) encapsulated papillary thyroid cancer classical variant (1), 5) encapsulated follicular carcinoma (1), and 6) encapsulated Hurthle cell thyroid carcinoma (2). A total of 10 of the primary cancers were less than 2 cm in size, all 15 had negative surgical margins and 6 were multifocal. Of the 12 encapsulated tumors, 9 had focal capsular invasion and 3 had extensive capsular invasion

The metastatic sites included 12 bone metastases, 3 to the lung, 2 to the chest wall, and 2 to the liver, 1 to the brain, and 1 to the kidney, and 2 to the pelvic and buttock soft tissue. A total of 11 of the patients were symptomatic and the other 4 patients had incidental findings on imaging studies which demonstrated the metastases. Thyroglobulin levels post-operatively were noted in 6 patients and these levels varied from 1.2 to 7570 ng/mL.

The molecular testing was completed on 8 of the 15 cases. The results showed that 6 of these cancers had 2 or more mutations present. RAS mutations (4NRAS, 1HRAS) were present in 5 of the 8, 6 had TERT promoter mutations and in 4 of these 6 there were either BRAFV600E or RAS mutations present as well.





## THYROID CANCER, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Patients with low risk thyroid cancer are unlikely to develop distant metastases but when they do, there is a high rate of TERT promoter mutations. Although initial pathology is currently an excellent predictor of risk of cancer recurrence, further information from molecular testing may allow for more certainty. Future direction for

research will continue to focus on predicting risk earlier on in the disease process and may include testing for molecular mutations such as TERT promoter mutations.

— Julie Hallanger-Johnson, MD

### ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): <http://www.thyroid.org/thyroid-cancer/>

### ABBREVIATIONS & DEFINITIONS

**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.

**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, TERT and RAS.

**Mutation:** A permanent change in one of the 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. The two most common molecular marker tests are the Afirma™ Gene Expression Classifier and Thyroseq™

## Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of **October** is **Thyroid Nodule Awareness Month** and a bracelet is available through the **ATA Marketplace** to support thyroid cancer awareness and education related to thyroid disease.

