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THYROID CANCER

Low-risk thyroid cancer that spreads outside of the neck has mutations in cancer-related genes

BACKGROUND

Most thyroid cancers have an excellent prognosis even though spread of the cancer to lymph nodes in the neck are common, with a 10-year survival >90%. Spread of the cancer outside of the neck is rare (<10% of patients) and is associated with significantly worse prognosis. Older patients with spread of the cancer outside of the neck have a 5-year survival of 60% to 80%. Risk factors for spread of the cancer outside of the neck can be determined by examining the tissue after surgery and include extension of the cancer through the thyroid capsule, invasion into blood vessels and aggressive cancer subtypes, especially poorly differentiated cancer. In rare instances, thyroid cancer lacking any high-risk features present with spread of the cancer outside of the neck. Recent studies have identified mutations in cancer-related genes that are also associated with more aggressive cancers. Molecular marker analysis can identify these gene mutations, both on biopsy samples and after remove to the cancer by surgery. The current study examined the features and molecular markers of thyroid cancer that initially appeared low risk but developed spread of the cancer outside of the neck.

THE FULL ARTICLE TITLE

Xu B et al. Primary thyroid carcinoma with low-risk histology and distant metastases: clinicopathologic and molecular characteristics. Thyroid. February 1, 2017 [Epub ahead of print].

SUMMARY OF THE STUDY

This was an analysis of patients with thyroid cancer treated at Memorial Sloan-Kettering Cancer Center between 1983 and 2009. Patients with thyroid cancer were identified through a search of the institutional databases and included patients with spread of the cancer outside of the neck either at presentation or during follow-up. Patients were considered to have low-risk cancer if they did not have a poorly differentiated component, gross extension of the cancer through the thyroid capsule or extensive spread into blood vessels and had <5 lymph nodes involved with cancer. Next-generation sequencing for detection of mutations was performed on a subset of patients

Of 123 patients identified, 60% had spread of the cancer outside of the neck at the time of presentation while in 40% the spread developed during follow-up period. Only 15 patients (12%) had low-risk features and all had spread of the cancer outside of the neck at the time of initial presentation. Of these, 11 were female and the average age was 63 years. The average size of the primary cancer was only 1.8 cm, and the smallest cancer was 2 mm. Also 8 patients had encapsulated follicular variant papillary thyroid cancer with invasion, 2 had infiltrative follicular variant papillary thyroid cancer, 2 had encapsulated Hürthle-cell carcinoma and ther was 1 pateint each with papillary microcarcinoma infiltrative follicular variant, encapsulated papillary thyroid cancer classical variant and encapsulated follicular carcinoma (n = 1 for each). The majority of these cancers had extensive fibrosis and calcifications.

Molecular analysis with next-generation sequencing was performed in 8 cases; RAS mutations were identified in 5 of these cases and TERT promoter mutations in 6 while a combination of TERT plus BRAF V600E or RAS mutations occurred in 4 cases. Overall, 4 of the 15 patients had died within 32 months of diagnosis. Distant cancer spread was most frequently present in the bone.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that patients with thyroid cancer that lack high-risk features have a very low rate of spread of the cancer outside of the neck. Those low-risk patients that do have spread of their cancer most frequently have spread of the cancer to bone at presentation and often have RAS and TERT promoter mutations in their cancer. This study suggests that TERT mutations may help to predict aggressive cancer in the absence of other risk factors and suggests that molecular markers be done on all patients with thyroid cancer.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Papillary microcarcinoma: a papillary thyroid cancer smaller than 1 cm in diameter.

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

Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): a new term has been used to describe a type of papillary thyroid cancer which is non-invasive. These cancers behave less aggressively than typical papillary thyroid cancer and have been shown to have low risk for recurrence and low risk for spread outside of the thyroid.

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 AfirmaTM Gene Expression Classifier and ThyroseqTM

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.

Mutation: A permanent change in one of the genes.

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.