

Presence of gene mutation helps guide thyroid cancer treatment

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A specific gene mutation may be useful in predicting the level of aggression of thyroid cancer and help guide treatment options and follow-up care, according to new study findings.

The mutation, called BRAF V600E, is a genetic alteration in the BRAF oncogene, a modified gene believed to cause cancer. The new research is reported in the September issue of the *Annals of Surgery*.

Past studies have shown that the mutation frequently occurs in the most common type of thyroid cancer, conventional papillary thyroid cancer or PTC, but this is the largest study to classify thyroid cancer by cell structure subtype and to show that the mutation is significantly associated with cancer recurrence after treatment, according to the research team.

The findings come at an important time as both the incidence of thyroid cancer and the number of patients who die from the disease is increasing in the United States. More than 33,000 new cases of thyroid cancer are expected to be diagnosed in 2007, according to the National Cancer Institute.

Most patients diagnosed with thyroid cancer have small, localized PTC but may receive aggressive treatment because their risk of recurrence and death cannot be reliably predicted prior to surgery, the study authors noted.



"There is a pressing need to identify a reliable preoperative approach for stratifying patients according to risk of thyroid cancer recurrence and death," said lead author Electron Kebebew, MD, who is an assistant professor of surgery and endocrine surgeon at the University of California, San Francisco and a research scientist with the UCSF Comprehensive Cancer Center.

"This study shows that a particular mutation is a reliable indicator, and testing for the mutation may be useful for selecting initial therapy, determining the need for and extent of surgery, as well as the need for ongoing monitoring and follow-up care," he emphasized.

In the study, the researchers examined tumor samples from 314 patients with thyroid cancer (245 with conventional PTC, 73 with follicular thyroid cancer and 29 with the follicular variant of PTC) to determine the presence of BRAF V600E and its association with factors such as tumor size, tumor stage, and patient outcome.

They found the mutation in 51 percent of patients with conventional PTC, in 1 percent of patients with follicular thyroid cancer, and in 24.1 percent of patients with follicular variant PTC.

In conventional PTC and follicular variant PTC, the mutation was significantly associated with older age, larger tumor size, and recurrent and persistent disease. These patients also showed a trend toward a higher rate of cancer formation in the lymph node due to metastasis (the transfer of tumor cells from one organ or part of the body to another organ or part) and higher stage cancer.

In patients with conventional PTC, the mutation was associated with older age, lymph node and other metastasis, and was an independent risk factor for recurrent and persistent disease. Median follow-up time of all patients in this study was six years.



Kebebew explained that identification of the mutation in patients with thyroid cancer could be very useful in a variety of ways. For example, patients with the mutation may be candidates for a more aggressive approach to surgery, such as removing the central lymph node along with the diseased thyroid, to avoid the possibility of metastasis following surgery. BRAF V600E testing could also be useful for deciding between low- or high-dose radioiodine ablation therapy.

"Advances in molecular biology techniques have improved our understanding of the genetic changes in cells that lead to the formation of cancer and have provided opportunities for identifying disease biomarkers like this mutation," added Kebebew. "It is critical to continue the drive to discover reliable biomarkers so we can better identify, treat and cure cancer."

Source: University of California - San Francisco

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