THE INCIDENCE OF BRAF MUTATION IN PAPILLARY THYROID CANCERS IS INCREASING

Mathur A, Moses W, Rahbari R, Khanafshar E, Duh QY, Clark O, Kebebew E. **Higher rate of BRAF mutation in papillary thyroid cancer over time: a single-institution study.** Cancer. March 15, 2011 [Epub ahead of print]. doi: 10.1002/cncr.26072.

SUMMARY

BACKGROUND

The incidence of papillary thyroid cancer (PTC) has increased greatly in the past decade. To investigate the reasons for this, the authors studied the molecular changes in the PTCs they have seen during the past 15 years.

METHODS

The authors studied 628 consecutive patients with PTC seen from 1991 through 2005. They had performed molecular testing on 228 tumor samples by analysis for the BRAF V600E point mutation, RET/PTC1, RET/PTC3, and NTRK1 rearrangements, and hotspot point mutations in KRAS and NRAS. They performed a time-trend analysis for the mutations over the three consecutive 5-year periods.

RESULTS

The authors found no differences between the three groups in the age at diagnosis, sex, ethnicity, primary tumor size, tumor–node–metastasis cancer stage, or rate of extrathyroidal invasion in the 628 patients. However, among the 228 tumor samples, the tumors in the most recent group, years 2001 to 2005, were smaller than those of the earlier groups. Somatic mutations were found in 92% of this group, but only 68% of tumors from 1991 to 1995 and 64% of tumors from 1996 to 2000 ($P<0.002$). The BRAF mutation was found in 88% of 2001–2005 tumors, 51% of 1991–1995 tumors, and 43% of 1996–2000 tumors. The higher rate of BRAF mutation in the most recent group did not correlate with any clinical variables. The incidence of the other mutations studied was not significantly different among the groups, although there were fewer RET/PTC3 mutations in the 2001–2005 group (4%) than in the other groups (16 and 15%, respectively).

CONCLUSION

The rate of the BRAF V600E mutation in papillary thyroid cancer increased significantly over a 15-year period at the authors' institution. This finding suggests that the higher rate of BRAF mutation may explain the increasing incidence of papillary thyroid cancer.

COMMENTARY

The very high rate of BRAF mutation in PTC in a San Franciscan population that was about 17% Asian is the first report I have seen that shows a rate of the BRAF mutation in the United States that is similar to that reported in Korea, where 90% of PTCs have the BRAF mutation (1). The BRAF mutation has not been associated with radiation exposure, but the RET/PTC3 mutation was associated with radiation exposure from Chernobyl (2). The data suggest that an environmental toxin may be playing a role in the epidemic of PTC that we now find. Fortunately, our sensitive methods for finding tumors at an early stage may prevent these tumors from spreading and recurring. Although retrospective analyses of PTC with BRAF mutations showed that they were more aggressive than PTC without this mutation (3), this was not apparent in the study under discussion. However, no data on recurrence were presented. Nevertheless, I speculate that finding the BRAF mutation in PTC tumors <2 cm is not likely to have an ominous prognosis because these tumors are generally associated with excellent survival after appropriate surgery.

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References

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