Highly accurate diagnosis of cancer in thyroid nodules with follicular neoplasm/suspicious for a follicular neoplasm cytology by ThyroSeq v2 next-generation sequencing assay

Yuri E. Nikiforov MD, PhD[1,*], Sally E. Carty MD[2], Simon I. Chiosea MD[1], Christopher Coyne MD[3], Umamaheswar Duvvuri MD[4], Robert L. Ferris MD, PhD[4], William E. Gooding MS[5], Steven P. Hodak MD[3], Shane O. LeBeau MD[3], N. Paul Ohori MD[1], Raja R. Seethala MD[1], Mitchell E. Tublin MD[6], Linwah Yip MD[2] and Marina N. Nikiforova MD[1]

Article first published online: 10 SEP 2014 *Cancer* 2014.

BACKGROUND

Fine-needle aspiration (FNA) cytology is a common approach to evaluating thyroid nodules, although 20% to 30% of FNAs have indeterminate cytology, which hampers the appropriate management of these patients. Follicular (or oncocytic) neoplasm/suspicious for a follicular (or oncocytic) neoplasm (FN/SFN) is a common indeterminate diagnosis with a cancer risk of approximately 15% to 30%. In this study, the authors tested whether the most complete next-generation sequencing (NGS) panel of genetic markers could significantly improve cancer diagnosis in these nodules.

METHODS

The evaluation of 143 consecutive FNA samples with a cytologic diagnosis of FN/SFN from patients with known surgical outcomes included 91 retrospective samples and 52 prospective samples. Analyses were performed on a proprietary sequencer using the targeted ThyroSeq v2 NGS panel, which simultaneously tests for point mutations in 13 genes and for 42 types of gene fusions that occur in thyroid cancer. The expression of 8 genes was used to assess the cellular composition of FNA samples.

RESULTS

In the entire cohort, histologic analysis revealed 104 benign nodules and 39 malignant nodules. The most common point mutations involved the neuroblastoma RAS viral oncogene homolog (NRAS), followed by the Kirsten rat sarcoma viral oncogene homolog (*KRAS*), the telomerase reverse transcriptase (*TERT*) gene, and the thyroid-stimulating hormone receptor (*TSHR*) gene. The identified fusions involved the thyroid adenoma associated (*THADA*) gene; the peroxisome proliferator-activated receptor γ (*PPARG*) gene; and the neurotrophic tyrosine kinase, receptor, type 3 (*NTRK3*) gene. Performance characteristics were similar in the retrospective and prospective groups. Among all FN/SFN nodules, preoperative ThyroSeq v2 performed with 90% sensitivity (95% confidence interval [CI], 80%-99%), 93% specificity (95% CI, 88%-98%), a positive predictive value of 83% (95% CI, 72%-95%), a negative predictive value of 96% (95% CI, 92%-100%), and 92% accuracy (95% CI, 88%-97%).

CONCLUSIONS

The current results indicate that comprehensive genotyping of thyroid nodules using a broad NGS panel provides a highly accurate diagnosis for nodules with FN/SFN cytology and should facilitate the optimal management of these patients.