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PAX8-PPARG REARRANGEMENT OCCURS IN ONLY 1.9% OF FOLLICULAR ADENOMAS AND IS LIKELY TO BE AN ONCOGENE MARKER FOR FOLLICULAR CARCINOMA

Klemke M, Drieschner N, Laabs A, Rippe V, Belge G, Bullerdiek J, Sendt W. **On the prevalence of the PAX8-PPARG fusion resulting from the chromosomal translocation t(2;3)(q13;p25) in adenomas of the thyroid.** Cancer Genet 2011;204:334-9.

SUMMARY

BACKGROUND

Distinguishing follicular adenomas from follicular carcinomas in thyroid fine-needle aspiration biopsies (FNAB) is a major diagnostic challenge. Molecular markers may help to achieve this distinction. The chromosomal rearrangement t(2;3)(q13;p25) is a recurrent cytogenetic aberration in follicular neoplasias of the thyroid leading to a fusion of the genes encoding the thyroid-specific transcription factor PAX8 and the peroxisome proliferator–activated receptor gamma (PPARγ). When first described the PAX8-PPARG rearrangement was considered to be a marker of follicular carcinoma (1). However, it was also found in follicular adenomas with a prevalence that ranged from 0 to 54.5% in different reports (summarized in the paper being reviewed here). The purpose of this study was to determine the prevalence of the PAX8-PPARG rearrangement in a large series of follicular adenomas using frozen tissue samples.

METHODS AND RESULTS

Tissue samples were snap frozen at surgery. The PAX8-PPARG rearrangement was detected by two methods: fluorescence in situ hybridization (FISH, a cytogenetic method) and by reverse-transcription polymerase chain reaction (RT-PCR).

Of 192 follicular adenomas, the authors identified only two tumors that were positive for the PAX8-PPARG rearrangement. In a review of 16 reports in which the rearrangement was detected by RT-PCR, it was found in 35.9% of 245 follicular carcinomas and in 8.2 % of 281 follicular adenomas. However, when the data in the literature using the cytogenetic FISH method for detection is combined with that of the authors, only 5 of 265 (1.9%) were positive for the PAX8-PPARG rearrangement.

CONCLUSIONS

The results indicate that the chromosomal t(2;3)(q13;p25) rearrangement and the resulting fusion of PAX8 and PPARG is rare in follicular adenomas. Its prevalence is overestimated in studies using RT-PCR.

COMMENTARY

Because molecular studies will be increasingly used in the evaluation of thyroid biopsy material, the results of this brief report are very important. In recent studies of FNAB material, the PAX8-PPARG rearrangement has been studied. It was found in 1 of 84 biopsies in one study with the pathology showing a follicular carcinoma (2), but it was not was found in any of 235 samples in another biopsy study (3). These studies were all done by RT-PCR, the method that could lead to false positives according to the current report. However, because of the rarity of the PAX8-PPARG rearrangement, only 8.2% when detected by RT-PCR, it is probably appropriate to send patients who have this molecular marker to surgery, although the data from this study suggest that false positives are lower than previously reported, even by RT-PCR. Some believe that large follicular adenomas are precursors to follicular carcinoma. The presence of the PAX8-PPARG rearrangement provides some evidence for this concept. Nevertheless, the RT-PCR may result in a fourfold increase of false positive diagnosis of follicular carcinoma when the pathologic diagnosis is follicular adenoma.

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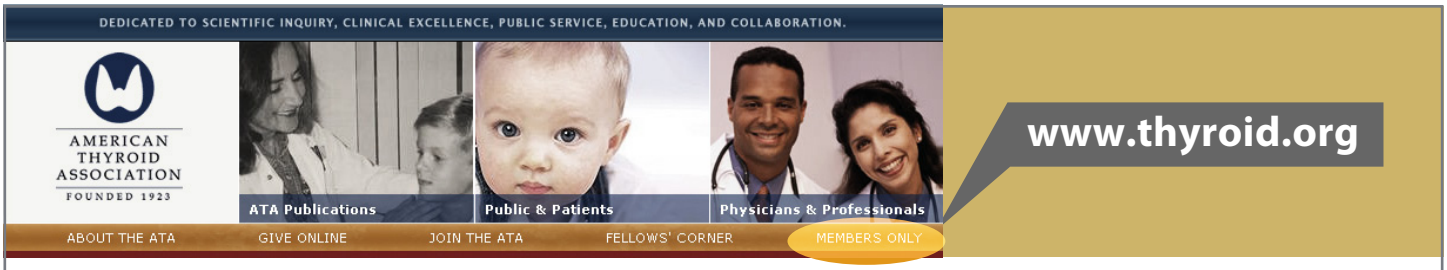

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