Papillary Thyroid Microcarcinoma: Clinico-pathological Correlation with BRAF V600E Mutation

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ABSTRACT

Background: Papillary thyroid microcarcinoma (PTMC) papillary carcinoma (n=1) are increasingly being detected due to the frequent use of ultrasonography. Their biology and management remain controversial despite the excellent prognosis. In recent years BRAF V600E mutation has emerged as a marker of aggressive behavior in papillary thyroid carcinoma (PTC) but its significance in PTMC is not clear.

Design: Clinical and histopathological features were reviewed in 129 PTMCs. The latter included histologic variant, tumor interface with non-neoplastic thyroid, nuclear features of PTC (well-developed or subtle), presence of cystic change, tall or polygonal eosinophilic (plump pink) cells, extrathyroidal extension (ETE), tumor-associated fibroblast/sclerosis/desmoplasia, stromal calcification, psammoma bodies and oncocytoma-like multinucleated giant cells. These features were correlated with BRAF V600E mutational analysis performed in all cases by single strand conformational polymorphism.

Results: Tables summarize significant clinico-pathological differences in BRAF V600E mutation positive and negative PTMCs. No significant difference was found between the two groups of PTMCs in age, sex, tumor size, multifocality, mean number of foci, tumor interface with non-neoplastic thyroid, stromal fibrosis/sclerosis/desmoplasia, extrathyroidal extension, intratumoral multinucleated giant cells, psammoma bodies and perithyroidal eosi

METHODS

RESULTS

In the last few decades, there has been a steady rise in the incidence of PTC, mainly attributed to increased diagnostic scrutiny including widespread use of thyroid ultrasonography coupled with fine needle aspiration. PTC has excellent prognosis with survival rates almost similar to the general population. Only a subset of PTCs shows biological recurrence/persistence with significant morbidity. This poses a challenge for the identification of the aggressive subset and their optimal management. BRAF V600E mutation has emerged as a marker of aggressive behavior in PTC. However, its exact significance in PTMC is not entirely clear. The purpose of this study is to review the prevalence of BRAF V600E mutation in PTMC, perform a histopathological correlation with mutation and to explore its possible association with aggressive features.

CONCLUSIONS

- The prevalence of BRAF V600E mutation in papillary thyroid microcarcinoma is similar to larger (>1 cm) papillary thyroid carcinoma at our institution.
- The morphology of mutated microcarcinomas is distinctive and characteristic histological features include infiltrative interface with non-neoplastic thyroid, stromal fibroblast/sclerosis/desmoplasia, and well-developed characteristic nuclear features of PTC.
- BRAF V600E mutation was significantly more prevalent in subcapsular sclerosing, tall cell and classic variant when compared with follicular variant of PTMC.
- Similar to PTC, presence of BRAF V600E mutation in PTMC is associated with aggressive features such as extrathyroidal extension and nodal metastasis, including lateral cervical lymph node metastasis.