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Journal of Molecular Genetics and Medicine

2017
Vol.1 No.1:3

Thyroid Papillary Carcinoma and BRAF Mutation

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Received: September 15, 2017; **Accepted:** September 29, 2017; **Published:** October 06, 2017

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Citation: Celik M (2017) Thyroid Papillary Carcinoma and BRAF Mutation.
J Mol Genet Med Vol.1 No.1:3

The number of patients diagnosed with thyroid cancer has significantly increased during the last two decades related to increased awareness of nodular thyroid diseases, development in diagnostic methods, widespread application of thyroid fine needle aspiration and new descriptions of histopathologic criteria. Papillary thyroid cancer (PTC) is the most common thyroid cancer, which constitutes 85-90% of all thyroid carcinomas. PTCs are tumors with indolent course and have good prognosis. However, some PTCs may show bad prognosis. Ancak bazı PTK'lar kötü prognoz gösterirler. In 7th edition of TNM classification system of malign tumors of American Joint Committee on Cancer (AJCC) (2010), size of primary tumor, extrathyroidal extension, distant metastasis, lymph node metastasis and age of patient at the time of diagnosis (>45 years) were reported to be the most important criteria in determining biological features of tumor and treatment modality. In the management of these patients, histological variant of tumor, lymph node metastasis, extrathyroidal extension and tumor size (>1 cm) are also important for radioactive iodine treatment indication following suitable surgical intervention. In addition, multifocality, vascular invasion, incomplete surgery, some specific variants and male gender have been reported to be potential prognostic factors [1-4]. Some recent studies evaluating the effects of B type Raf kinase (BRAF) mutation on PTC progression and and prognosis demonstrated BRAFV600E mutation to be related to aggressive course [5-7], while some other studies reported no negative effect on the course [8-10].

BRAF (29-83%), RET/PTC (10-50%) and RAS (1-10%) mutations playing role in MAPK (Mitogen Activated Protein Kinases) pathway have been suggested to cause PTC by aberrant activation. Studies have demonstrated BRAF mutation to be the most common molecular damage in the genetics of thyroid cancer. Serin-threonin kinase RAF has 3 isoforms: ARAF, BRAF and CRAF. BRAF, which is the most common isoform found on thyroid follicular epithelium, is located on 7th chromosome and strongly stimulates MAPK pathway. The most common form of BRAF mutation is valine-glutamate substitution in residue 600 occurring as a result of thymine→adenosine change in 1799 position of exon 15. Stimulation developing as a result of this mutation in MAPK pathway causes proliferation and apoptosis of cells [5,11].

It has been suggested that PTC shows a more aggressive course and has tendency for invasion in subjects with BRAF mutation. BRAF mutation makes PTC more aggressive by inhibiting many tumor suppressor genes, decreasing tumoral differentiation, increasing pro-angiogenetic molecules and decreasing radioactive iodine uptake of tumor [5,11-13]. BRAFV600E mutation has been demonstrated to be related to high grade tumors (grade III and IV), lymphovascular invasion and metastasis. Studies emphasize BRAFV600E mutation positivity both in aggressive sub-types and classical type PTC [14,15].

BRAF mutation makes PTC having a more aggressive course by inhibiting many tumor suppressor genes, decreasing tumoral differentiation, increasing pro-angiogenetic molecules and decreasing radioactive iodine uptake of tumor. Therefore, it has been suggested that in subjects with BRAF mutation, clinical course is more aggressive and tumor tends to show invasion more commonly.

Conflict of Interest

None.

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