BRAF V600E GENETIC MUTATION ANALYSIS FOR UNKNOWN MALIGNANCY POTENTIAL THYROİD TUMORS AND PAPILLARY THYROID MICROCARCINOMAS

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Aim: The purpose of this study was to analyze the clinicopathologic parameters BRAF V600E mutational status in PTMCs and UMP TTs.
Material and Method: 72 PTMCs and 20 UMP TTs tissues were included in this study. Genomic DNA was extracted from parafin-embedded tumor tissue. The parafin-embedded thyroid tumor samples were cut into 5 µm sections. The tumor areas dewaxed and dissected. DNA was isolated using QIAamp® DNA FFPE tissue kit. We amplified exon 15 of the BRAF gene, which contains the BRAF V600E mutation with RFLP analysis by using the following primers. The PCR products were electrophoresed in polyacrilamide gel. Samples were stained with silver nitrate and imaged.
Results: BRAF V600E mutation frequency in PTMCs was % 41,6 (72/30), in UMP WDTs was % 80 (10/8). The BRAF V600E mutation was significantly associated with the classic variant of PTC % 73,3 (P= 0,047). Micro-PTCs BRAF positivitiy was significantly related to invasion of thyroid capsule % 66,67 (p=0,003) and absence of the tumor capsule % 80 (p=0,003). There was no significant correlation between the occurence of BRAF V600E mutation and advanced disease stages, extrathyroidal extension, cervical lymph node metastasis, age, gender, multifocality in PTMCs. The odd ratio for female sex in BRAF positive PTMCs was 2,46 for Hashimoto thyroiditis in BRAF positive PTMCs was 2,12.
Conclusion: BRAF mutation was significantly associated with the classic variant, absence of the tumor capsule and penetration of the thyroid capcule in PTMCs. UMP WDT lesions of the thyroid with BRAF mutation may represent PTC precursors or less aggressive type of PTCs. Tumor recurrence and poorer prognosis wasn't associated with BRAF V600E mutation after a median follow up of 22 months.

Demographic characteristic

Groups			n	%
Tumor Types	**UMPTT**	20		21,74
	PTMC	72		78,26
Sex	**Male**	22		23,91
	Female	70		76,09
Age at Diagnosis	**<45 Yaş**	38		41,30
	≥45 Yaş	54		58,70
Tumor Diameter (mm)	**≤5 mm**	25		27,17
	>	67		72,83
Radiation History	**No**	90		97,83
	Yes	2		2,17
Type of surgery	**Lobectomy**	2		2,17
	Total Thyroidectomy	90		97,83
Central Node Dissection	**No**	84		91,30
	Yes	8		8,70
Lateral Node Dissection	**No**	88		95,65
	Yes	4		4,35
BRAF Mutation	**Mutant (Yes)**	38		41,30
	Wild Type (No)	54		58,70
Hashimoto Thyroiditis	**No**	56		60,87
	Yes	36		39,13
Graves Disease	**No**	88		95,65
	Yes	4		4,35
Regional Metastasis	**No**	89		96,74
	Yes	3		3,26
Distant Organ Metastasis	**No**	91		98,91
	Yes	1		1,09
RAI Treatment	**No**	43		46,74
	Yes	49		53,26
Preoperative Diagnosis	**No**	39		42,39
	Yes	53		57,61
Family History	**No**	85		92,40
	Yes	7		7,60

Tumor Diameter UMPTT and PTMC Groups

	Groups	N	Min.	Max.	Mean	SS
Tumor Diameter (mm)	**UMPTT Group**	20	6	65	23,40	17,23
	PTMC Group	72	1	10	6,70	2,33

General Characteristics of UMPTT Group

		n	%
Sex	**Male**	10	50,00
	Female	10	50,00
Age	**<45**	12	60,00
	≥45	8	40,00
Histological subtype	**UMPFT**	10	50,00
	UMPWDT	10	50,00
Hashimoto Thyroiditis	**No**	17	85,00
	Yes	3	15,00
Graves Disease	**No**	17	85,00
	Yes	3	15,00
RAI Treatment	**No**	20	100,00
Total Tiroidektomi	**No**	1	5,00
	Yes	19	95,00
Lobectomy	**No**	19	95,00
	Yes	1	5,00
Central Lymph Node Dissection	**No**	19	95,00
	Yes	1	5,00
BRAF Mutation	**Wild Tip (No)**	12	60,00
	Mutant (Yes)	8	40,00
Radiation History	**No**	19	95,00
	Yes	1	5,00

Some characteristics for BRAF (+) and (-) UMPTT Groups

UMPTT Groups	BRAF (-)	BRAF (+)	p
Age	45,83±11,41	43,63±6,93	0,631
Follow Up (month)	18,91±11,29	22,5±11,76	0,510
Tumor Diameter (mm)	18,58±12,88	30,63±21,11	0,129
Pre op. TSH Level (mIU/L)	0,84±0,94	1,8±1,95	0,155

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