



CLINICOPATHOLOGICAL CHARACTERISTICS OF PAPILLARY THYROID CANCER IN CHILDREN WITH EMPHASIS ON THE PUBERTAL STATUS AND ASSOCIATION WITH BRAF^{V600E} MUTATION



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Background: Papillary thyroid cancer (PTC) composes more than 90 % of the thyroid cancer in children. PTC behaves differently in prepubertal children than in pubertal children and between children and adults. BRAF gene activating mutations may associated with aggressive character by creating aberrant activation. The most common mutation is BRAF^{V600E}.

Aims and Objectives: To evaluate clinicopathological characteristics of PTC patients with emphasis on the pubertal status and investigate association of BRAFV600E mutation with disease characteristics.

Methods: Medical records of 75 patients with PTC followed between 1983-2015 were reviewed retrospectively. BRAF^{V600E} mutation status was found in medical records of 56 patients.

Results:

- Mean age at diagnosis was 12.4±3.8 years (range: 1.3 to 17.8).
- There was no difference in sex, sign and tumor histopathology between prepubertal and pubertal children.
- Frequency of BRAF^{V600E} mutation was similar.
- Although prepubertal children had greater tumor size, there was no difference in pathological evidence of tumor aggressiveness.
- Lymph node and lung metastasis were more prevalent in prepubertal children.
- Prepubertal children needed at a greater frequency lateral neck dissection (p=0.02) and more frequently treated with second or more dose of radioactive iodine (p=0.04) but after excluding microcarcinoma patients, it was similar between two groups (p=0.07)
- Persistent disease or recurrence were more frequent in prepubertal children (p=0.02).
- BRAF^{V600E} mutation was found in 14(25%) patients and was high in classic variant PTC (p=0.024). It was similar in girls and boys, and in tumors larger or smaller than 1 cm.
- Multicentricity was high in BRAF^{V600E} mutation (p=0.01) but lymphovascular invasion, perineural invasion, thyroid capsular invasion, extrathyroidal invasion of the tumor were similar.
- There was no relation between BRAF^{V600E} mutation and lymph node and pulmonary metastasis at diagnosis.

Conclusions:

- PTC is more disseminated in prepubertal children
- BRAF^{V600E} mutation is not correlated with a more disseminated or aggressive disease.
- BRAF^{V600E} mutation is not the cause of the differences in the biological behavior of PTC in prepubertal and pubertal children.

Table 1: Comparison of some features of prepubertal and pubertal patients with PTC.

	Prepubertal n=18	Pubertal n=57	p
Age(year, mean±SD)	7.4±2.2	14.8±2.1	0.0001
Sex(n,%)			
Female	11(61.1%)	40(68.3%)	0.56
Male	7(38.9%)	17(31.7%)	
Initial signs (n,%)			
Nodule	13(75 %)	39(67.3%)	0.61
Goiter/Lymphadenopathy	5(25%)	15(32.7%)	
History of radiotherapy(n,%)	3(16.6%)	9(15.8%)	0.59
Status at diagnosis (n,%)			
Multicentricity	10(55.5%)	27(47.4%)	0.24
Vascular invasion	6(33.3%)	22(38.6 %)	0.61
Perineural invasion	5(27.8 %)	12(21.1 %)	0.30
Capsule invasion	9(50%)	21(36.8 %)	0.14
Ekstrathyroidal extension	6(33.3%)	17(29.8 %)	0.76
Lymph node metastasis	10(55.5%)	24(42.1%)	0.41
Lung metastasis	5(27.8%)	5(8.8 %)	0.05
Mean tumor diameter (cm,)	2.9±1.7	1.9±1.5	0.03
Microcarcinoma (n,%)	2(11.1%)	21(29%)	0.04
Tumor histopathology(n,%)			
Classical variant	8(44.4%)	32(56.1%)	0.42
Subtype	10(55.6%)	25(43.9%)	
Diffuse sclerosing	2	3	
Follicular	8	21	
Solid	-	1	
BRAF ^{V600E} (n,%)			
Positive	2(15.4%)	12(27.9%)	0.48
Negative	11(84.6%)	31(72.1%)	

Table 2: Comparison of treatment management and outcome between prepubertal and pubertal patients .

	Prepubertal	Pubertal	p
Radioactive Iodine Therapy			
One dose	8(50%)	36(80%)	0.04
Second or more dose	8(50%)	9(20%)	
Total thyroidectomy	16(88.9%)	53(93%)	0.62
Near- total thyroidectomy	2(11.1%)	4(7%)	
Neck dissection			
Central dissection	8(53.3%)	34(82.9%)	0.024
Lateral dissection	7(46.7%)	7(17.1%)	
Remission	9(50%)	48(84.2%)	0.020
Persistent disease	5(27.8%)	8(14%)	
Recurrence	4(22.2%)	1(1.8%)	
Hypoparathyroidism			
Transient	-	3(5.2%)	0.61
Permanent	2(11,1%)	4(7.0%)	