Lymph node involvement using One-Step Nucleic Acid Amplification (OSNA) according to BRAF gene mutation status in patients with papillary thyroid carcinoma submitted to lymph node dissection

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Introduction

The relationship between BRAF gene mutation and lymph-node metastases is controversial in papillary thyroid cancer (PTC). OSNA (One-Step Nucleic acid Amplification) is a molecular technique that measures the number of copies of mRNA of cytokeratin 19 (CK 19) and it is used as a marker of lymph node metastasis.

Aim

To analyze the influence of BRAF mutation status in the characteristics of lymph nodes in patients with PTC submitted to lymph node dissection.

Patients and methods

Patients and tumour characteristics	N = 20
Gender, n (%)	Female 12 (60) Male 8 (40)
Age (years), mean (SD)	50 (15)
Histologic variants, n (%)	Classical 16 (80) Follicular 2 (10) Cystic 2 (10)
Size (cm), mean (SD)	2.6 (1.8)

Lymph node characteristics	N = 277
sentinel, n (%)	36 (13)
Compartment, n (%)	Central 179 (64.6) Lateral 95 (34.3) Unknown 3 (0.1)
Weight (g), median (IQR)	0.09 (0.04-0.18)
Diameter (cm), median (IQR)	0.5 (0.3 – 0.8)

CK 19 copy number	result	definition
< 100	-	negative
100 – 250	-	Isolated tumor cells
250 – 5000	+	Micrometastases
> 5000	++	Macrometastases

OSNA interpretation

Results

Lymph node M1

Lymph node dissections	N = 21
Nodes per patient, median (IQR)	11 (8-16)
Global result, n (%)	OSNA-N0 3 (14.3) OSNA-N1 18 (85.7)
Positive nodes, median (IQR)	2.5 (1-7)
Percentage positive nodes, median (IQR)	25 (16.8 – 55.2)
Total tumour load (TTL), median (IQR)	26390 (2853 – 215598)
TTL/ total nodes, median (IQR)	2446 (327 – 10053)
TTL/ positive nodes, median (IQR)	4850 (1675 – 49963)

Lymph nodes	OSNA-N0	OSNA-N1	p-value
N, n (%)	189 (68.2)	88 (31.8)	
Weight (g), median (IQR)	0.08 (0.03 – 0.15)	0.11 (0.05 – 0.26)	0.008
Diameter (cm), median (IQR)	0.40 (0.30 – 0.70)	0.50 (0.4 – 1)	0.0005
Tumour load per node, median (IQR)		6700 (1900 – 18000)	
Type of M1, n (%) Isolated tumour cells MicroM1 MacroM1		 6 (6.8) 38 (43,2) 44 (50)	

BRAF status

Lymph node dissections	N = 21		
	BRAF-0	BRAF-1	p-value
OSNA-0	2	1	
OSNA-1	5	13	
			0.24

Positive Lymph node dissections	N = 18		
	BRAF-0 (n = 5)	BRAF-1 (n = 13)	p-value
Nodes per patient, median (IQR)	9 (4.7 – 11)	13 (8 – 17.5)	0.05
Positive nodes, median (IQR)	2 (1.7 – 3.2)	3 (1 – 7.2)	0.42
Percentage positive nodes, median (IQR)	25 (22.5 – 45.9)	25 (12.5 – 55.2)	0.92
Total nodes Weight (g), median (IQR)	0.75 (0.51 – 1.45)	1.11 (0.64 – 3.06)	0.38
Total tumour load (TTL), median (IQR)	3900 (2852 – 267727)	29860 (3875 – 142397)	0.92
TTL/ positive nodes, median (IQR)	3900 (1426 – 76202)	5100 (2900 – 23364)	1

Lymph nodes	N = 277			
	BRAF-0	BRAF-1	TOTAL	p-value
OSNA-0, n (%)	53 (79)	136 (65)	189	
OSNA-1, n (%)	14 (21)	74 (35)	88	
TOTAL, n (%)	67 (100)	210 (100)	277	
				0.028

Patients	N = 20		
	BRAF-0	BRAF-1	p-value
N, n (%)	7 (35)	13 (65)	
Age (years), mean (SD)	46.3 (13)	52.4 (17)	0.37
Tumour size (cm) mean (SD)	2.2 (1.8)	2.8 (1.9)	0.47
Tumour multifocality, n (%)	3 (42.8)	6 (46.1)	0.88
Tumour vascular invasion, n (%)	1 (14,3)	5 (38.5)	0.26
Tumour ETE, n (%)	2 (28.6)	6 (46.1)	0.44

OSNA-N1 Lymph nodes	BRAF-0	BRAF-1	p-value
N, n (%)	14 (16)	74 (84)	
Weight (g), median (IQR)	0.09 (0.04 – 0.17)	0.12 (0.05 – 0.33)	0.25
Diameter (cm), median (IQR)	0.45 (0.30 – 0.60)	0.60 (0.4 – 1)	0.08
Tumour load per node, median (IQR)	17950 (1300-8900)	6700 (2050 – 12000)	0.77
Type of M1, n (%) Isolated tumour cells MicroM1 MacroM1	 0 7 (50) 7 (50)	 6 (7.1) 31 (41.9) 37 (50)	> 0.05

Conclusions

There were no differences in morphological characteristics of dissected lymph nodes according to BRAF mutation. However, the probability of node metastasis is higher among those nodes with BRAF mutated tumours than in BRAF not mutated samples.

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