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BRAF V600E MUTATION IN WASHING LIQUID OF THYROID FINE NEEDLE ASPIRATION: A SURPRISING TOOL IN CYTOLOGICAL BENIGN NODULES

Monzani ML[1,2], Brigante G[1,2], Marino M[1,3], Bonacini L[1,2], Pignatti E[1,3], Cioni K[1,2], Madeo B[1,2], Rochira V[1,2], Santi D[1,2], Maiorana A[4], Carani C[1,2] and Simoni M[1,2,3]

[1]Unit of Endocrinology & Metabolism, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia; [2]Azienda USL of Modena, Italy; [3]Center of Genomic Research of the University of Modena and Reggio Emilia, Italy; [4]Department of Diagnostic and Clinical Medicine and Public Health, University of Modena and Reggio Emilia, Modena, Italy.

OBJECTIVE

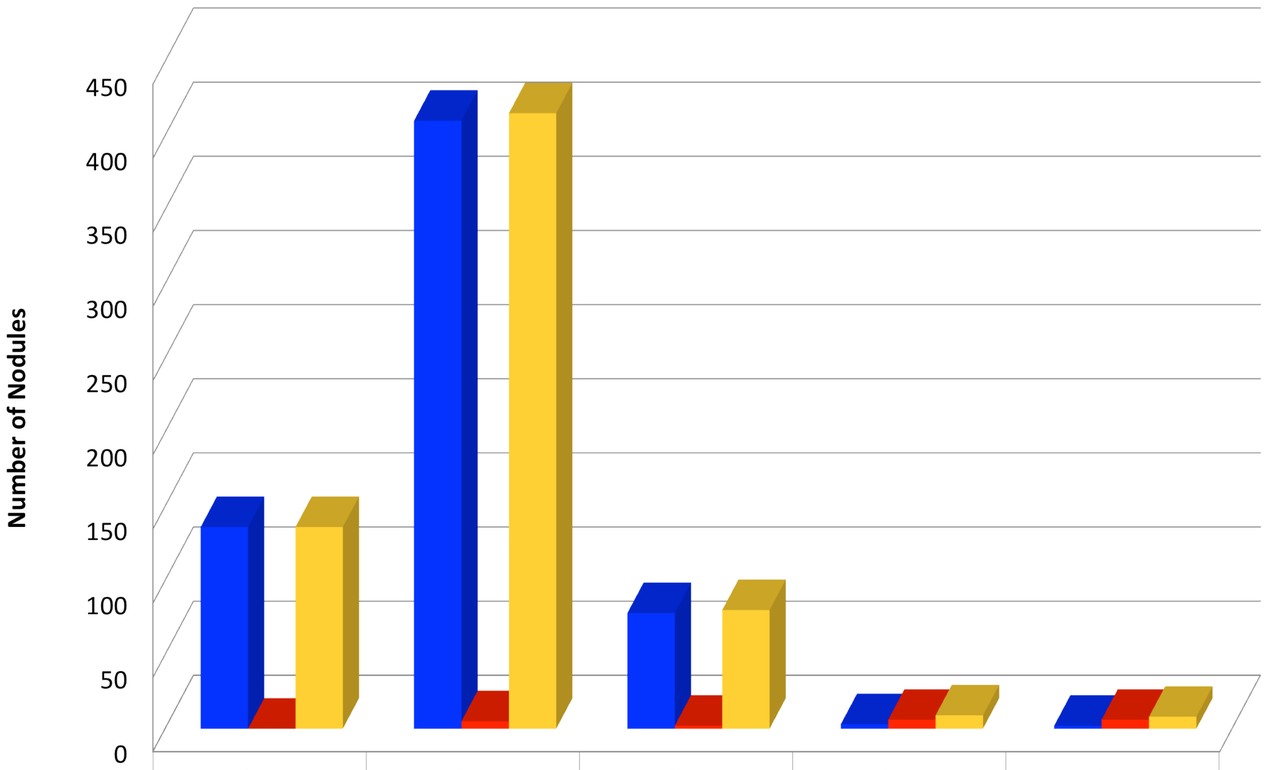
Thyroid fine needle aspiration (FNA) cytology is indeterminate in 15-25% of cases (1). Diagnostic accuracy of FNA can be improved by the combination of molecular and cytological analysis (2). In this study, washing liquid of FNA (wFNA) samples was tested for *BRAF* V600E mutation, using High Resolution Melting (HRM). The aim was to demonstrate whether *BRAF* analysis is accurate in wFNA and can be an additional tool when combined with cytology.

METHODS

Study design: cohort study involving 481 patients, corresponding to 648 FNA samples. All samples were subjected to both cytological (on cells smeared on a glass slide) and molecular analysis (on fluids obtained washing the FNA needle with 1 ml of saline) on the same aspiration. *BRAF* V600E analysis was performed by HRM after careful methodological validation for application to wFNA (sensitivity: 5.4%).

RESULTS

According to the American Thyroid Association guidelines (3), the 648 samples were classified in cytological categories ranging from Thy 1 (nondiagnostic) to Thy 5 (diagnostic for malignancy). The *BRAF* V600E mutation was found in 2 (2.5 %) Thy 3, 6 (66.6%) Thy 4 and 6 (75%) Thy 5. Surprisingly, 5 (1.2%) Thy 2 samples resulted *BRAF* mutated. *BRAF* V600E mutations were confirmed by pyrosequencing in scraped Thy 2 cytological samples. Patients underwent thyroidectomy and the diagnosis of papillary carcinoma was confirmed at histology.



	Thy1	Thy2	Thy3	Thy4	Thy5
WT	136	410	78	3	2
BRAF +	0	5	2	6	6
Totale	136	415	80	9	8

Fig 1: WT and *BRAF +* samples in each cytological category.

ID	Suspicious on US	Cyt	HRM on wFNA	Pyrosequencing on FNA	Histology	Stage
s1	Yes	Thy 2	*BRAF* V600E +	not assessed	Papillary thyroid microcarcinoma	pT1aNxMx
s2	Yes	Thy 2	*BRAF* V600E +	*BRAF* V600E +	Partially cystic papillary carcinoma	pT2NxMx
s3	No	Thy 2	*BRAF* V600E +	*BRAF* V600E +	Classical variant of papillary carcinoma	pT3mN1bMx
s4	No	Thy 2	*BRAF* V600E +	*BRAF* V600E -	No surgery	Not applicable
s5	Yes	Thy 2	*BRAF* V600E +	*BRAF* V600E -	Follicular variant of papillary carcinoma	pT1NxMx
s6	Yes	Thy 3	*BRAF* V600E +	not assessed	Classical variant of papillary carcinoma	pT3NxMx
s7	Yes	Thy 3	*BRAF* V600E +	not assessed	Classical and follicular variant of papillary carcinoma	pT1bNxMx

Table 1: Thy2 and Thy3 samples with *BRAF* mutation positivity at HRM.

CONCLUSIONS

BRAF assessment can be accurately performed on wFNA and improves the diagnostic performance, regardless of cytological results. In perspective, stand-by wFNA samples could be analyzed *a posteriori* in case of indeterminate cytology and/or suspicious findings on ultrasounds.

REFERENCES

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Contact information: marilu87@hotmail.it, manuela.simoni@unimore.it
www.endocrinologia.unimore.it