Incidence of Mutations in BRAF Gene in Dysplastic Nevi and Melanoma *in situ*

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Introduction & Objectives

Malignant melanoma has become one of the most frequent cancers in the Western world, with one of the fastest growing incidence rates among all cancers. Additionally, melanoma is one of the most aggressive cancers and all scientific research leading to a better understanding of the genetic basis of onset and progression of melanoma, as well as development of new treatments is significant.

BRAF mutation analysis in samples of dysplastic nevi and melanomas *in situ* may help enlighten the unclear role of dysplastic nevi as precursor melanoma lesions.

Our objectives were to determine and compare the frequency of BRAF mutations in dysplastic nevi and melanomas *in situ*, as well as determine whether there is an association between the presence of BRAF mutations and various personal, clinical and histopathological variables.

Materials & Methods

This study included 175 patients - 106 had a dysplastic nevus and 69 had a melanoma in situ (28 of whom had a lentigo maligna). The pathological slides were reviewed by a pathologist, subsequently DNA was extracted from tissue samples embedded in paraffin and analyzed using the competitive allele-specific TaqMan chain reaction by polymerase in real time in order to determine the presence of BRAF V600E and V600K mutations. The obtained mutation data were compared with personal, clinical and histopathological data using appropriate statistical methods.

Results

BRAF mutation was found in 88 (50,3%) patients - 68 patients had a V600E, while 20 had a V600K mutation. There was no statistically significant difference in the presence of BRAF mutation in patients with a dysplastic nevus and those with melanoma in situ (when patients with lentigo maligna were excluded from the study). The V600E mutation was significantly more common in patients with dysplastic nevi (89% of patients with mutation), while the V600K mutation was more common in patients with melanoma in situ (52% of patients with mutation). The frequency of BRAF mutation was significantly higher in younger patients. Additionally, younger patients had a higher frequency of V600E mutations, while older patients had a higher frequency of V600K mutations. A statistically significant correlation was also found between frequency of BRAF mutation and lesion localization (Table 1).

Table 1. Correlation of BRAF mutation and lesion localization.

Localization	BRAF mutation number (percentage)		Total
	No	Yes	
Trunk	45 (38,5%)	72 (61,5%)	117
Head	22 (84,6%)	4 (15,3%)	26
Upper limbs	7 (50%)	7 (50%)	14
Lower limbs	13 (72,2%)	5 (27,8%)	18
Total	87 (49,7%)	88 (50,3%)	175

Lesions on head and neck had the lowest frequency (15,3%), while lesions on the trunk had the highest frequency (61,5%) of BRAF mutations. However, no statistically significant correlation was found between localization of tumor and type of BRAF mutation, although patients with melanoma on the trunk had a somewhat higher frequency of V600E mutations compared to patients with lesions on the head and neck. No statistically significant correlation between the presence of BRAF mutation and sex, lesion size or previous melanoma diagnosis was observed.

Conclusion

The results of this study, in which there was no statistically significant difference in the presence of BRAF mutation in patients with a dysplastic nevus and those with melanoma in situ (when excluding patients with lentigo maligna), suggest that BRAF mutation in dysplastic nevi is a necessary, however in itself insufficient oncogenic trigger in the onset of melanoma. Accordingly, this research contributes to a better understanding of the etiopathogenesis of melanoma and the role of dysplastic nevi as precursor melanoma lesions.

References

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