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Introduction

According to Cancer Research UK statistics (2018) malignant melanoma is the fifth most common cancer in the UK, and each year there are around 16,000 people who are diagnosed with this deadly type of skin cancer.

Cutaneous melanocytic lesions can be divided into benign, and atypical melanocytic naevi, and the most aggressive type of skin malignancy, malignant melanoma (MM). The study aims to evaluate the staining pattern of PRAME expression in melanocytic tumours and highlights PRAME expression in primary and metastatic melanomas as well as other melanocytic lesions.

This research looks at the potential to explore the PRAME expression in melanocytic nevi, which could prove an invaluable tool to distinguish the benign/atypical nevi from melanomas. PRAME is a melanoma-associated antigen that was first identified through analysis of the specificity of T cell clones in a patient with metastatic melanoma.

The employment of PRAME antibody in a diagnostic laboratory can prove invaluable addition in the clinical setting distinguishing benign and malignant melanocytic lesions.

Materials and Methods

A total of 398 melanocytic tumours were examined for immuno-histochemical expression of PRAME, including 157 malignant melanomas and 151 melanocytic naevi. All IHC staining was performed on a Roche BenchMark Ultra fully automated immunostaining platform using commercially available antibody to PRAME (ABCAM) with a optimum dilution factor of 1:2000.

Each case has also been stained with Haematoxylin and Eosin (H&E).

The negative control was also run along the slides to determine the specificity of an antibody. No staining was observed when the primary antibody was omitted.

The scoring involved: 0 - no staining at all(0/100), scoring of 1% to 50% of tumour cells score as 1, labelling of 51% or more of tumour cells score as 2.

The Chi-Square statistical analysis was performed using GraphPad Prism software. P-value was generated to determine the sensitivity (labelling tumour cells) and specificity (distinction of nevi from melanomas).

Results

The nuclear labelling for PRAME was recorded in 77.7% of primary melanomas. The primary melanoma PRAME IHC expression was found in 80% of all melanomas in situ. According to melanoma histological subtypes, PRAME was expressed in 83.9% of superficial spreading melanoma, 100% of Lentigo maligna melanoma, Acral lentiginous melanoma (ALM) and Nodular melanoma.

Invasive melanoma reported 82.6% PRAME expression levels; naevoid melanoma expressed PRAME in 57.1% of cases, other types of melanoma stained positive for PRAME in 50% of cases.

The PRAME IHC expression was found to be lower for Desmoplastic (including Spindle cell Melanoma) - 42.9% of cases (Chart 1)

The Chi-square test of anti-PRAME IHC expression in all malignant melanoma subtypes studied here, revealed the p-value of 0.0294, which is statistically significant.

Discussion

The total of 137 cases of malignant melanoma that were studied the results demonstrate the 122 of these (77.7%) prove that PRAME is frequently expressed in malignant melanoma.

This correlates with the study conducted by (Lexcano et al., 2018) whereby diffuse nuclear immuno-reactivity for PRAME was found in 87% of metastatic and 93% of primary melanomas. Lexcano and colleagues (2019) emphasised the need for an alternative treatment for patients with unresectable melanoma stage IV in which other treatments such as BRAF V600E inhibitors have failed and the clinical trials 1 and 2 patients with primary metastatic melanoma are currently underway (Clinicaltrials.gov, 2018).

The expression of anti-PRAME may demonstrate its valuable aspect in difficult cases of malignant melanoma as this research study outlined PRAME IHC expression in a variety of melanomas.

Out of 68.2% of all melanocytic naevi studied lacked any PRAME expression.

Majority of the PRAME positive (37.6%) cases in naevi encountered in this project, were, in fact, atypical Spitz nevi as they may possess a more prominent risk for malignant behaviour.

An investigation by Kim et al., 2015 described the difficulty in diagnosing Spitz (Spitzoid) melanoma and Spitz naevus. The presence of atypical Spitz naevus and its sharing histological hallmarks with melanoma, is associated with the higher risk of developing malignant melanoma.

During the evaluation and discussing of findings of PRAME expression in naevi, there has been a consensus that positive immunoreactivity of PRAME in such cases does not mean malignancy.

PRAME expression would be an auxiliary tool coupled with other clinical findings such as dermoscopy, histological features, clinical setting, genetic profiling data, abnormal FISH findings that are present in metastatic melanoma but not naevi, to reach the diagnosis of melanoma.

PRAME is a member of the family of cancer-testis antigens (CTA), and an attractive target for immunotherapy.

Conclusion

PRAME is preferentially expressed in cutaneous malignant melanomas, as well as other tumours such as breast carcinoma, renal cell carcinoma, therefore normal tissue are not known to express it apart from tests, endometrium and adrenals.

Thus, by recognising and distinguishing the malignant melanomas from atypical naevi and subsequent diagnostic problems, utilizing the anti-PRAME antibody adjacent to other markers, could establish the solution in diagnostically challenging cases.

Further studies are required to analyse the expression in different types of malignant tumours such as lung, breast and colon cancers.

References


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