Relevance of Allele Imbalance in 9p24.1 and 16p13.13 STR Loci to PDL1 and HLA-DR Expression in Primary Mediastinal B-cell Lymphoma (PMBCL)

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INTRODUCTION

PMBCL is an NHL variant that responds to immune checkpoint inhibitors (ICIs) therapy in approximately half of the cases. Molecular factors predicting possible responses to immunotherapy for PMBCL are not yet described. Evaluation of programmed cell death ligand-1/ligand-2 (PD-L1/L2) expression level in tumor samples has proven clinical utility for ICI response prediction in various solid tumors. HLA-DR overexpression may be another marker associated with response to anti-PD-1/PD-L1 therapy. MHCII gene expression is associated with the transcription of the gene encoding the CIITA trans-activator, a crucial MHCII gene regulatory factor. The PD-L1 and CIITA gene expression level could be affected by copy number variations associated with 9p24.1 and 16p13.13 chromosomal lesions (losses or gains). Analysis of appropriate short tandem repeat (STR) markers is a straightforward way to detect these lesions.

AIM

To analyze the possible association of STR allele imbalance (AI) in 9p24.1 with PD-L1 expression level and STR AI in 16p13.13 with HLA-DR expression level in tumor cells of PMBCL patients.

METHOD

STR-loci at 9p24.1 and 16p13.13 of the paired tumor/control DNA samples were analyzed in a cohort of 27 PMBCL patients admitted to the National Medical Research Center for Hematology (2013-2020). STR data was compared with the expression of PD-L1 and HLA-DR, respectively. An immunohistochemical study of PD-L1, HLA-DR, and tumor DNA extraction was performed on mediastinal biopsy samples from archival paraffin blocks.

RESULTS

AI in the 9p24.1 was found in 14 of 27 patients (52%). PDL1 expression was found in 10 (6 with AI 9p24.1) of 27 patients (37%). AI in16p13.13 was found in 8 of 27 patients (30%). HLA-DR expression was observed in 20 (6 with AI 16p13.13) of 27(74%) patients with PMBCL. However, a significant correlation between STR aberrations and the expression of related genes has not been found (chi-square statistic, p>0.05).

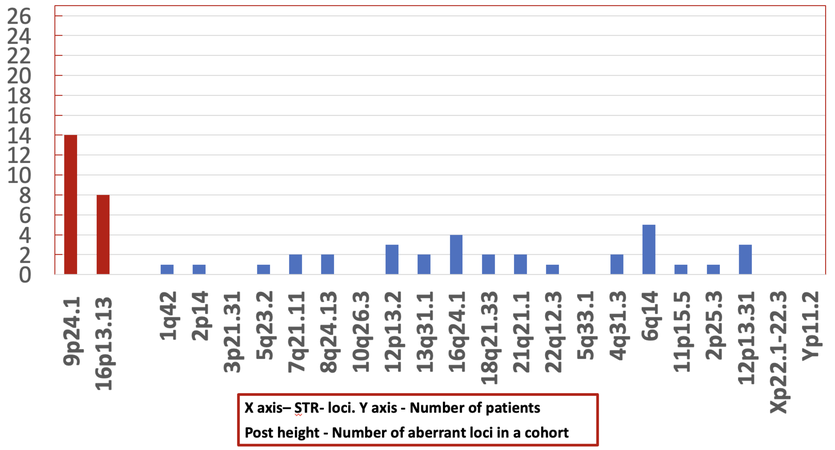


Figure 1. AI for PMBCL patients

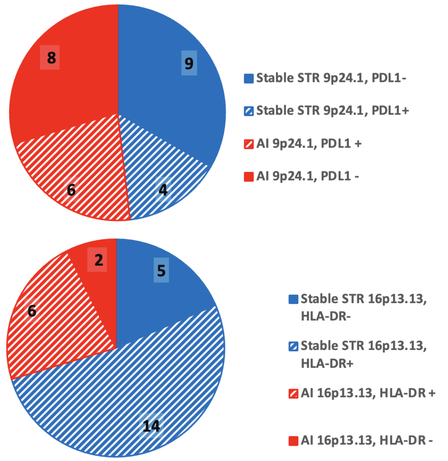


Figure 2. AI in 9p24.1 and 16p13.13 STR Loci to PDL1 and HLA-DR Expression in PMBCL

CONCLUSIONS

STR AI in 9p24.1 and 16p13.13 and PD-L1 and HLA-DR expression are highly frequent though probably independent events relevant to immunotherapy response in PMBCL.

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