STR-loci Allele Imbalance at 9p24.1 in Primary Mediastinal B-Cell Lymphoma

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Abstract

Primary mediastinal B-cell lymphoma (PMBCL) is the only non-Hodgkin's lymphoma variant responding to immune checkpoint (ICP) therapy approximately in half of the cases. However, no molecular markers predicting response to ICP have been described so far. In this study, we assessed the incidence of the loss of heterozygosity (LOH), elevated microsatellite alteration at selected tetranucleotides (EMAST) in tumor genomes and PD-L1 expression level in tumor cells of PMBCL patients.

Background

Molecular factors to determine the prognosis of immunotherapy response for PMBCL are not described yet. Programmed cell death ligand-1/ligand-2 (PD-L1/L2) expression levels in tumor samples have proven clinical utility for many solid tumors. The level of PD-L1/L2 expression could be affected by 9p24.1 chromosomal lesions (losses or gains). STR analysis of appropriate markers is the simplest way to detect these lesions.

Objective

To analyze possible association between STR-loci allele imbalance (AI) I in 9p24.1 and PD-L1 expression level in tumor cells of PMBCL patients.

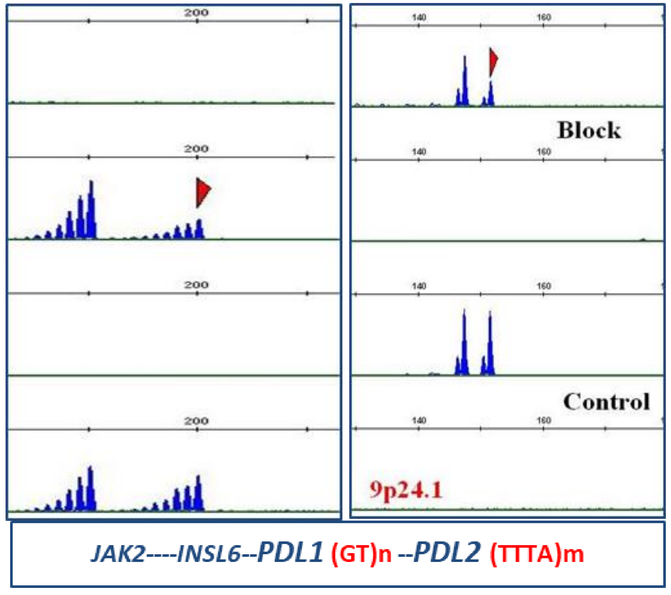


Figure 1. AI patterns in 9p24.1of PMBCL patients

Materials & Methods

DESIGN: Two STR-loci $(gt)_n$ and $(ttat)_m$ at 9p24.1 of the DNA of tumor cells were analyzed on a cohort of 36 PMBCL patients admitted to the National Medical Research Center for Hematology (Moscow, Russia) from 2013 to 2022. For six patients, STR data were compared with PD-L1 expression assessed by immunohistochemistry (antibodies Cell Marque, clone 28-8, ER2-pH 9 Leica, BOND-MAX)

SETTING: DNA was isolated from tumor biopsy samples taken at diagnosis. Control DNA samples were taken from the blood of patients in complete remission or from the buccal epithelium. STR-analysis for AI was done by PCR with original primers. The fragment analysis was performed on ABI3130 Genetic Analyzer.

PATIENTS: Inclusion criteria: de novo diagnosed PMBCL patients. Exclusion criteria: pretreatment.

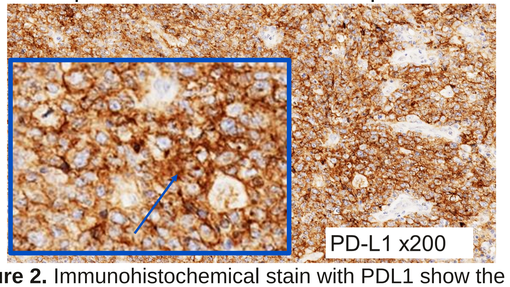


Figure 2. Immunohistochemical stain with PDL1 show the high overall PDL1 staining in tumor cells PMBKL(membranous brown color)

Summary

Heterozygosity level for $(gt)_n$ locus was 31 out of 36 patients (86%), AI was found in 16 out of 31 (51.6%). Heterozygosity level for $(ttat)_m$ locus was 20 out of 36 patients (56%), AI was found in 9 out of 20 (45%). One patient turned out to be homozygous for both loci. No patients were found with AI at one locus and a normal heterozygous variant at the second locus. PD-L1 expression in tumorc cells was evaluated for six patients. In two patients with aberrant STR loci, PD-L1 expression was found in 75%-100% of tumor cells. None of the four patients with normal 9p24.1 STR markers had PD-L1 positive cells.

The high incidence of AI in the 9p24.1 locus indicates its possible involvement in the pathogenesis of PMBCL. The association between AI and PD-L1 expression in tumor cells requires confirmation on an extended cohort of patients.

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