Stage-related PD-L1 expression in Kaposi sarcoma tumor microenvironment

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Abstract: Background The immune checkpoint molecule PD-L1 represents an important target in oncological immune therapy. The aim of our study was to evaluate PD-L1 expression and the composition of the tumor microenvironment (TME) in Kaposi sarcoma. Methods Immunohistochemical stains were performed for PD-L1, CD3, CD33, CD68, and CD168 in 24 Kaposi sarcoma samples. In PD-L1-positive cases, the double stains for PD-L1, CD31, podoplanin, and HHV8 were added. Results PD-L1 was observed in 71% of the samples and was predominantly located in the TME. PD-L1 expression was significantly higher in nodular stage than in patch/plaque stage. The TME consisted of CD68+/CD163+ macrophages, CD33+ myloid-derived suppressor cells and monocytes and CD3+ T-cells. The TME showed a peritumoral distribution in nodular stage, in contrast to a diffuse distribution in patch/plaque stage. In 12 samples (50%), no plasma cells were found. Conclusion In nodular stage of KS, the TME is pushed back in the periphery of the tumor nodules. The PD-L1-positive TME between the tumor cells might protect them from the immune attack. An anti-PD-L1 treatment might be promising in KS patients.

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Abstract

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Methods: Immunohistochemical stains were performed for PD-L1, CD3, CD33, CD68, and CD168 in 24 Kaposi sarcoma samples. In PD-L1-positive cases, the double stains for PD-L1, CD31, podoplanin, and HHV8 were added.

Results: PD-L1 was observed in 71% of the samples and was predominantly located in the TME. PD-L1 expression was significantly higher in nodular stage than in patch/plaque stage. The TME consisted of CD68+/CD163+ macrophages, CD33+ myloid-derived suppressor cells and monocytes and CD3+ T-cells. The TME showed a peritumoral distribution in nodular stage, in contrast to a diffuse distribution in patch/plaque stage. In 12 samples (50%), no plasma cells were found.

Conclusion: In nodular stage of KS, the TME is pushed back in the periphery of the tumor nodules. The PD-L1-positive TME between the tumor cells might protect them from the immune attack. An anti-PD-L1 treatment might be promising in KS patients.

KEYWORDS

Kaposi sarcoma, macrophages, PD-L1, plasma cells, tumor microenvironment

1 | INTRODUCTION

Kaposi sarcoma (KS) is a HHV-8 (human herpes virus type 8)-associated vascular proliferation.[1-3] As mentioned in most dermatopathological textbooks[4-6] and by the current World Health Organization (WHO) classification for skin tumors,[3] the tumor seems to be accompanied by plasma cells, which has been considered as an important diagnostic indicator. Furthermore, T cells, activated B cells, dendritic cells, monocytes, and tumor-associated macrophages (TAMs) have been identified as components of the tumor microenvironment (TME) in Kaposi sarcoma.[1,7,8]

The interaction between the immune system and the tumor cells is essential for cancer defense and cancer survival. This interaction is determined by several complex pathways.[9] One of these pathways is the signaling between PD-1 (programmed cell death 1) and its ligands PD-L1 and PD-L2.[9] PD-L1 is an immunomodulatory cell-surface glycoprotein, belonging to the B7 family.[10,11] Its expression is reported in many tumor cells, tumor infiltrating lymphocytes, and TAMs in various solid tumors. PD-L1 expression has been extensively studied in various skin malignancies.[12-16] Beyond melanoma, PD-L1 expression

Beatrice Joest was involved in a part of doctoral thesis.