THE ROLE OF MICROENVIRONMENT EXPRESSION OF PD-1 LIGANDS AND CHEMOKINES IN CLINICAL OUTCOME OF HODGKIN’S LYMPHOMA

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Aim: Classical Hodgkin’s lymphoma (cHL) is characterized by only few malignant cells and an abundance of inflammatory cells. cHL infiltrating cells produce cytokines and growth factors that provide essential stimulatory signals for survival and proliferation of Hodgkin and Reed–Sternberg (HRS) cells. Moreover, clinical behaviour of cHL may be directly regulated by the cross-talk between HRS cells and other cells in their microenvironment. The aim of our study was to estimate the role of microenvironment expression of PD-1 ligands and chemokines in clinical outcome of cHL.

Methods: The case group comprised 49 patients with cHL (stage IIA: 23, IIB: 3, III-IV: 23). The patients received chemotherapy regimens (ABVD or BEACOPP 14/esc) and radiotherapy by indications. cHL specimens were obtained from lymph node biopsies of patients at diagnosis. PD-L1, PD-L2, MIP-1α, RANTES mRNA expression levels were analyzed in fresh tissue specimens using real-time RT-PCR.

Results: We observed that 26.5% (13/49) of cHL cases were PD-L1 negative, 16.3% (8/49) - RANTES negative and 14.3% (7/49) - both PD-L1 and RANTES negative. MIP-1α and RANTES expression levels were slightly higher in mixed cellularity cHL (p = 0.15), whereas PD-L1 – in nodular sclerosis cHL and advanced stages of disease (p = 0.19). PD-L2 expression level was independent of histological cHL variant or disease stage. All cases with the absence of both PD-L1 and RANTES markers had a complete response to the therapy and long-term remission. For the patients with increasing of RANTES/MIP-1α rate, a trend for a higher risk of relapse was observed (P = 0.09). ROC analysis revealed that PD-L1 expression level in tumor is an important marker which is associated with clinical outcome of cHL patients (Se = 87.5%; Sp = 64.5%; AUC = 0.75; p = 0.002). High PD-L1 expression was associated with reduced progression-free survival (PFS) in cHL patients. The 2-year PFS rate for cHL patients with high PD-L1 expression was 47% compared to 95% for low or absent of PD-L1 expression (p = 0.04).

Conclusions: Our results suggest that tumor microenvironment play an important role in clinical behavior of cHL. PD-L1 expression level can be used as a marker of prognosis in patients with cHL and represent an attractive target for a cHL immunotherapy in patients with poor outcome.

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