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THORACIC MALIGNANCIES, OTHER

1808P Role of evaluating tumor infiltrating lymphocytes, programmed death-ligand 1 and mismatch-repair proteins expression in malignant mesothelioma

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Background: Malignant mesothelioma (MM) is an aggressive and fatal tumor, mainly related to prolonged exposure to asbestos. MM can induce infiltration of immune cells and immunity-mediated death. Tumor microenvironment plays a major role in neoplastic progression, favoring tumor cell evasion from adaptive immunity and T-cell checkpoint pathways. Expression of programmed death-ligand 1 (PD-L1) on tumor cells and tumor-infiltrating lymphocytes (TILs) has been described in literature. Cancer cells expressing PD-L1 increase apoptosis of antigen-specific human T-cell clones and inhibit CD4+ and CD8+ T-cell activation, thus decreasing the immune action on the tumor cells. Some mismatch repair–deficient tumors make them sensitive to immune checkpoint blockade, because of the increased number of neoantigens encoded by cancers, which enhances anti-tumor response.

Methods: The aim of this study is to analyze the expression of PD-L1 on both tumor cells and TILs and to characterize TILs. Furthermore, MisMatchRepair (MMR) protein expression was evaluated. Immunohistochemistry was applied using the automated system BenchMark XT (VENTANA) for PD-L1 (DAKO, clone 22C3), CD4, CD8 and MLH1, MSH2, MSH6, PMS2.

Results: 55 malignant mesotheliomas, 10 from women and 45 from men, were studied. The range of age was 43-88 years old. Tumors consisted of 44 epithelioid, 3 sarcomatoid, 7 biphasic and 1 desmoplastic. 51 were localized to pleura and 4 to peritoneum. 18 tumors were in stage I, 13 in stage II, 15 in stage III and 5 in stage IV. For 4 cases the stage was not evaluable. Our results showed expression of PD-L1 $\geq$50% in tumor cells in 9 cases (5 epithelioid, 2 sarcomatoid, 1 biphasic and 1 desmoplastic). In two of these the positivity was observed both in tumor cells and in TILs. 15 tumors were negative and 31 showed a positive staining $\geq$1. A presence of TILs was observed in 53 cases. A prevalence of CD4+ expression was highlighted in 45 cases. 6 of them showed elevated expression of PD-L1 ($\geq$50%). Alteration in MMR staining was not found.

Conclusions: Our data underline the role of tumor immune microenvironment and its characterization in MM and open the possibility to use combined therapies according to different PD-L1 expression.

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