Immune Checkpoint Regulation in Molecular Subtypes of Endometrial Cancer: Expression of PD-L1 and PD-1

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Endometrial cancer is the 4th commonest cancer in women. The current treatment options show inconsistent results. There is a newer treatment option called targeted therapy. One example uses immune checkpoint inhibitors against Programmed cell death-1 protein (PD-1) present on T-cells and Programmed cell death ligand1 (PD-L1) on cancer cells to augment the body's immune anti-cancer response. A new molecular classification of endometrial cancers includes microsatellite mismatch repair deficient (MMR-D), abnormal p53 (p53abn), and wild-type p53 (p53WT) tumors. This study evaluated PD-L1 on cancer cells, and PD-1 on lymphocytes in the three molecular variants, and so determine therapeutic options. Sixty cases of endometrial cancer, 20 from each molecular group were studied using immunohistochemistry for PD-L1 and PD-1 antibodies. 98% of tumors expressed PD-L1 with no significant difference among the three groups. PD-1 tumor-associated lymphocytes showed a statistically significant increase in p53abn tumors vs both p53WT ($p=0.0197$) and MMR-D ($p=0.0038$). Poorly differentiated tumors showed increased PD-1 lymphocytes compared to well-differentiated ones ($p=0.0072$). P53abn are typically aggressive, poorly differentiated carcinomas. The statistically significant increased number of PD-1 positive lymphocytes in this tumor type with the high expression of PD-L1 suggests the PD-L1/PD-1 adaptive immune resistance may inhibit T-cell mediated anticancer responses, with resultant aggressive nature. Therapy using new immune checkpoint inhibitors that selectively block the PD-1 / PD-L1 interaction is possible. T-cell inhibition exerted by the tumor will be blocked, permitting the activation of T-cell-mediated destruction of tumor cells in this aggressive variant.

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