Association Serum Level Of PD-1 Receptor with Demographic, Clinical Pathological, Hormone Receptors, Molecular and Histological Subtypes in Breast Cancer Patients

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Abstract

Background: The critical role of immune checkpoints Programmed cell death receptor. Although (PD-1) has been extensively documented in a variety of malignant tumors, the basic regulatory mechanisms in breast cancer are still unclear. The objective of this study was to investigate the change in serum PD-1 concentration in pre-treatment and post-treatment groups, as well as the correlation with hormone receptors, molecular and histological subtypes. Method: The study included 82 female breast cancer patients diagnosed before beginning treatment (pre-treatment group), 60 female breast cancer patients diagnosed after undergoing treatment (post-treatment group), and 60 healthy individuals as controls. The sPD-1 levels are measured using ELISA technique. Data on tumors were retrieved from an electronic database at the oncology centre. Results: The highest levels of sPD-1 were detected in the pre-treatment groups, followed by post-treatment groups compared to the healthy group. The age group (40-69 years) had the highest level of PD-1 (6.51±1.68ng/ml) compared to other age groups. The serum level of PD-1 was significantly associated with age (p=0.01), family history (p=0.0001), and menopausal status (p=0.04) in the pre-treatment group. The level of PD-1 was significantly associated with the histological type of tumor (p=0.01), with a higher level seen in invasive tumor types. Furthermore, PD-1 levels were higher in the invasive lobular carcinoma subtype (p=0.03). In the post-treatment period, there was a significant association between PD-1 level and estrogen receptor status. PD-1 levels were higher in estrogen receptor-negative than in estrogen receptor-positive (1.354±0.121 vs. 0.896±0.0773 ng/ml, P =0.01). The higher level of sPD-1 (7.40±1.26ng/ml) was found to be associated with the Ki-67 value (>40%) in patients with breast cancer, and the lower level of sPD-1 (5.49±1.77ng/ml) was discovered in the Ki-67 value (<20%). Significantly, there is a positive correlation between sPD-1 level and Ki-67 expression (p=0.004). Conclusion: There was a significant association of serum PD-1 level with invasive carcinoma, particularly in invasive lobular carcinoma of patients with breast cancer, and a positive correlation with proliferation marker Ki-67 expression.

Keywords: Programmed cell death receptor (PD-1), Breast cancer, ER, PR, HER2, Histological type.

1. Introduction

The immune system in our bodies performs an essential function in protecting us from different diseases, including cancer cells 1. Immune suppression is known to be a trademark of cancer. Various receptors and their ligands, known as checkpoints, regulate this process 2,3. PD-1 was first described in the early 1990s as a type of immune checkpoint receptor constantly expressed on activated T cells and is inhibitory in nature by interaction with its ligands PD-L1 and PD-L2; it conserves healthy cells from excessive inflammatory or autoimmune reactions 4,5. Even though the importance of the immune checkpoints PD-1 and PD-L1 in a variety of malignant tumors has been well established, the fundamental regulatory mechanisms in breast cancer are obscure.6. In many countries, breast cancer is one of the most prevalent malignant tumors and the leading cause of cancer-related mortality among women 7,8. Multiple hereditary elements, environmental variations, and their complex interplay cause breast cancer 9,10. Concerning cancer cells' ability to evade the immune system, the discovery of the PD-1 (programmed death 1) and PD-L1 (programmed death-ligand 1) axis has been one of the most promising discoveries in cancer therapy in latest years 11,12. PD-1 is a highly vital component of the immune system. It is a type I transmembrane glycoprotein that belongs to the immunoglobulin CD28 superfamily 5,13. Breast cancer treatment with anti-PD-1 therapies was efficient, especially for patients with triple-negative breast cancer (TNBC) 14. Nivolumab is a PD-1 inhibitor that restores the anti-tumor activity of T cells by binding to PD-L1 on the surface of T cells. This blocks the immunosuppressive signaling pathway that is initiated by PDL-1/2 4,15. At the molecular level, breast cancer patients were classified into luminal A, luminal B, HER-2 positive, and triple negative groups according to the status of

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