ECRONICON OPEN ACCESS

EC ENDOCRINOLOGY AND METABOLIC RESEARCH

Editorial

New Hypothesis: ANTI-PDL1 (Pembrolizumab) as an Immunotherapeutic Agent for Cushing Disease

Mehmet Celik[1]*, Serhat Ozcelik[2], Ece Celik[3] and Melike Ozcelik[4]

[1]*Department of Endocrinology and Metabolism, Faculty Medicine, Trakya University, Edirne, Turkey*

[2]*Department of Endocrinology and Metabolism, Kartal Lütfü Kırdar Training and Research Hospital, Istanbul, Turkey*

[3]*Division of Allergy and Clinical Immunology, Medical Faculty, Antalya University, Antalya, Turkey*

[4]*Department of Medical Oncology, Umraniye Training and Research Hospital, Istanbul, Turkey*

***Corresponding Author:** Mehmet Celik, Department of Internal Medicine, Division of Endocrinology and Metabolism, Medical Faculty, Trakya University, Edirne, Turkey.

Received: February 27, 2020; **Published:** March 14, 2020

The immune system is the main defense mechanism that perceives substances that are different from the body itself and acts to destroy them [1]. In particular, cancer cells are among the cells of the immune system's primary target, while they continue to proliferate and spread through escape mechanisms [2]. Recently, many studies focus on proteins called CTLA-4 and PD-1, which are located on the surface of T cells and prevent activation of the immune response when not necessary [3]. Programmed cell death 1 (PD-1) is a transmembrane inhibitory protein expressed on T cells, B cells and NK cells. The interaction of PD-1 with its ligand directly inhibits tumor cell apoptosis, promoting peripheral T effector cell depletion. The treatment modality that inhibits these transmembrane proteins is called "immune checkpoint therapy". In this therapy, antibodies that bind and block CTLA-4 and PD-1 proteins are used and these are called "immune checkpoint" inhibitors [4,5]. Antibodies that inhibit PD-1 (pembrolizumab, nivolumab) have been approved for a number of clinical indications and are searched for many other malignancy-related specific issues [6]. While 70 - 80% of ACTH-dependent Cushing Disease is caused by pituitary adenomas, 15 - 20% is seen as a result of ectopic ACTH/CRH production from non-pituitary tumors (neuroendocrine tumor). In vitro studies demonstrated PDL-1 expression in pituitary adenomas. We think that patients with higher levels of basic PDL-1 expression may achieve good responses after treatment with pembrolizumab, especially in case of lung cancer with ectopic ACTH production. In addition, we think that detection of hypocortisolemia after treatment with this agent should be evaluated as an effective response in the subjects with increased PDL-1 expression (Figure 1).

Consequently, further studies are required to evaluate the effectiveness of PD-1 inhibitors in the treatment of cushing disease.

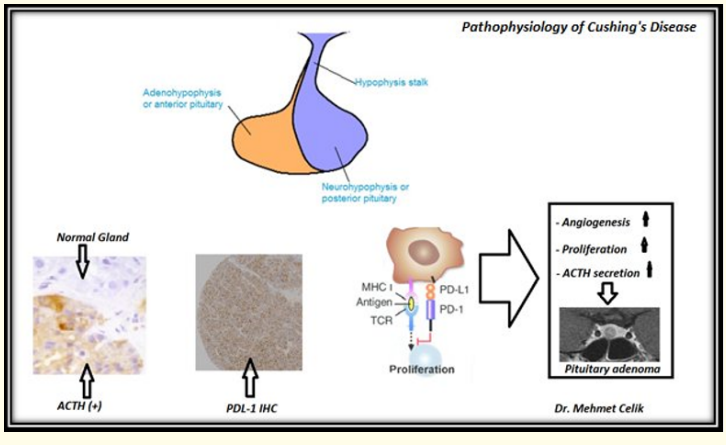

Figure 1: *PDL-1 and cushing disease.*

Bibliography

1. Travis J. "Origins. On the origin of the immune system". *Science* 324 (2009): 580.
2. Kim JM and Chen DS. "Immune escape to PD-L1/PD-1 blockade: seven steps to success (or failure)". *Annals of Oncology* 27 (2016): 1492-1504.
3. "The Nobel Prize in Physiology or Medicine 2018". NobelPrize.org. Nobel Media AB (2018).
4. Francisco LM., *et al*. "PD-L1 regulates the development, maintenance, and function of induced regulatory T cells". *Journal of Experimental Medicine* 206 (2009): 3015.
5. Amarnath S., *et al*. "The PDL1-PD1 axis converts human TH1 cells into regulatory T cells". *Science Translational Medicine* 3 (2011): 111ra120.
6. Fessas P., *et al*. "A molecular and preclinical comparison of the PD-1-targeted T-cell checkpoint inhibitors nivolumab and pembrolizumab". *Seminars in Oncology* 44.2 (2017): 136-140.

Volume 5 Issue 4 April 2020