Association of Checkpoint Inhibitor-Induced Toxic Effects With Shared Cancer and Tissue Antigens in Non-Small Cell Lung Cancer


Importance
Immunotherapy with checkpoint inhibitors targeting the PD-1 (programmed cell death 1) axis has brought notable progress in patients with non-small cell lung cancer (NSCLC) and other cancers. However, autoimmune toxic effects are frequent and poorly understood, making it important to understand the pathophysiologic processes of autoimmune adverse effects induced by checkpoint inhibitor therapy.

Objective
To gain mechanistic insight into autoimmune skin toxic effects induced by anti-PD-1 treatment in patients with non-small cell lung cancer.

Design, Setting, and Participants
This prospective cohort study was conducted from July 1, 2016, to December 31, 2018. Patients (n = 73) with non-small cell lung cancer who received anti-PD-1 therapy (nivolumab or pembrolizumab) were recruited from 4 different centers in Switzerland (Kantonsspital St Gallen, Spital Grabs, Spital Wil, and Spital Flawil). Peripheral blood mononuclear cells, tumor biopsy specimens and biopsies from sites of autoimmune skin toxic effects were collected over a 2-year period, with patient follow-up after 1 year.

Main Outcomes and Measures
Response to treatment, overall survival, progression-free survival, and development of autoimmune toxic effects (based on standard laboratory values and clinical examinations).

Results
Of the cohort of 73 patients with NSCLC (mean [SD] age, 68.1 [8.9] years; 44 [60%] men), 25 (34.2% [95% CI, 24.4%-45.7%]) developed autoimmune skin toxic effects. Of the 73 patients with NSCLC, 25 (34.2% [95% CI, 24.4%-45.7%]) developed autoimmune skin toxic effects, which were more frequent in patients with complete remission or partial remission (68.2% [95% CI, 47.3%-83.6%]) than those with progressive or stable disease (19.6% [95% CI, 11.0%-32.5%]) (χ² = 14.02, P < .001). Nine T-cell antigens shared between tumor tissue and skin were identified. These antigens were able to stimulate CD8+ and CD4+ T cells in vitro. Several of the antigen-specific T cells found in blood samples were also present in autoimmune skin lesions and lung tumors of patients who responded to anti-PD-1 therapy.

Conclusions and Relevance
These findings highlight a potential mechanism of checkpoint inhibitor-mediated autoimmune toxic effects and describe the association between toxic effects and response to therapy; such an understanding will help in controlling adverse effects, deciphering new cancer antigens, and further improving immunotherapy.

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