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SEVERE SKIN IMMUNE-RELATED ADVERSE EFFECT TO THE FIRST PEMBROLIZUMAB APPLICATION. A CASE REPORT.

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Objective:

Pembrolizumab, a monoclonal anti-PD-L1 antibody, has increased both overall and progression-free survival when used as a first-line monotherapy in non-small cell lung carcinoma with PD-L1 positive immunocytochemical finding if compared to platinum-based chemotherapy. Although pembrolizumab does have a significantly lower adverse effects incidence, a whole class of immunotherapy drugs is associated with immune-related adverse effects (IRAE). The most common ones include: colitis, hepatitits, pneumonitis, hypothyroidism and hypophysitis. Skin-related adverse effects are of low incidence, especially those of higher intensity grades. Median onset of moderate to severe toxicity is around nine weeks. We present a patient who developed a severe skin reaction after first pembrolizumab application.

A 41 year-old female patient presented in the emergency room with prolonged dry cough and progressive dyspnoea. In initial physical examination, muffled heart tones and breathing sounds over the lung bases were noted. Initial CXR displayed diffuse reticulonodular interstitial pattern and

enlarged heart shadow. CYPHRA 21-1 and NSE were elvated (8,53µg/l and 21.66µg/l, respectively). The patient's condition was gradually worsening with progressive respiratory insufficiency. CT scan showed multiple bilateral nodous lesions with bilateral pulmonary lymphangiosis, mediastinal lymphadenopathy and pericardial and pleural effusions. An echocardiographic examination displayed extensive pericardial effusion with swinging heart phenomenon, due to which a pericardial drain was placed. Metastatic adenocarcinoma with probable origin in the lungs was proven by cytological analysis of pleural effusion sample. Immunocytochemisty was negative for ALK, ROS and EGFR oncomarkers, but came out PD-L1-positive in 50% of the sample cells. Pembrolizumab monotherapy was promptly initiated with no immediate complications. However, 5 days after the first application, the patient developed an extensive maculopapular rash covering her chest, abdomen, back, upper arms and legs. Since it was a grade 3 adverse effect related to checkpoint-inhibitor, a dermatologist was consulted and oral corticosteroid therapy was initiated which resulted in a quick withdrawal of the rash. Corticosteroid doses were gradually lowered. After 4 weeks, the rash withdrew completely and pembrolizumab application was continued.

We have presented the patient with severe skin reaction to pembrolizumab which developed very early in the treatment course. It was successfully treated in consultation with dermatologists. The use of PD-L1 inhibitors is on the rise, as well as the need for IRAE treatment and prevention. This means that non-oncology specialists should also be informed about potential adverse effects related to their organ of interest. This would allow for adequate and prompt response to rare, but clinically important complications.