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CLINICAL VIGNETTE

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Complications of immunotherapy in the course of long-term response in a patient with non-small cell lung cancer

Keywords: pembrolizumab, lung adenocarcinoma, immunotherapy

Case description

A 57-year-old patient was diagnosed with a right lung tumor on 16/11/2018. Oligobiopsy examination of the right lung tumor diagnosed adenocarcinoma. Molecular biology methods ruled out the presence of mutations in the *EGFR* gene or rearrangement in the *ROS* and *ALK* genes. Immunohistochemistry showed programmed cell death ligand 1 (PD-L1) expression in 90% of cells. Due to stage IV clinical advancement and high PD-L1 expression in tumor cells, the patient was qualified for pembrolizumab therapy. Treatment began in June 2019. After the third dose of the drug, there was a decrease in free thyroxine (fT4) to 0.84 nm/dL with a thyroid stimulating hormone (TSH) of 8.1 mIU/mL.

At the first follow-up, stabilization of the disease according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria confirmed by a computed tomography (CT) scan was described. Due to worsening hypothyroidism, a diagnosis of autoimmune thyroiditis was made, and L-thyroxine supplementation at a dose of 75 mcg/d was recommended. After six months of therapy, follow-up CT scans showed a partial response (PR).

In December 2019, adrenal insufficiency was diagnosed due to low cortisol and adrenocorticotropic hormone (ACTH). Hydrocortisone supplementation at a total dose of 20 mg per day was started. After the 29th infusion, the patient reported low-grade wrist pain accompanied by numbness in the fingers. Since we suspected carpal tunnel syndrome, the patient started treatment with meloxicam, and a temporary pain reduction was achieved. After the 46th infusion of immunotherapy, the pain significantly increased and swelling of the wrist joints appeared, limiting the patient's functioning. In addition, the patient reported pain in the hip and knee joints. Immunotherapy was discontinued and, due to the presence of immune-mediated arthritis, methylprednisone at a dose of 4 mg daily was added to the already-used hydrocortisone.

After an 8-week break, during which joint pain significantly decreased (CTC1), steroid doses were reduced to a substitutive dose of hydrocortisone, and treatment with pembrolizumab was resumed. On 01/02/2024 the patient received the 72nd cycle of immunotherapy administered from the 66th cycle every 6 weeks at a dose of 400 mg. The last chest CT scan performed in February 2024 confirmed a sustained partial response to treatment (PR according to RECIST 1.1).

Discussion

Immune checkpoint inhibitors (ICIs) have made it possible to significantly prolong survival in cancer patients [1–2]. Findings indicate greater benefit from immunotherapy treatment in patients who develop immune-related adverse events (irAE) of low severity [3]. Autoimmune hypothyroidism is the most common immunotherapy-induced endocrinopathy appearing in 8% of those treated with checkpoint inhibitors, while adrenal

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insufficiency is a relatively rare complication, affecting 1% of patients [3]. A complication requiring temporary discontinuation of treatment was autoimmune arthritis, which affects 5–10% of patients treated with ICIs. The symptoms can include stiffness and swelling in one or more joints, often accompanied by tendinitis [3, 4]. The course of treatment in our patient provides evidence of the possibility of achieving a long-term response to immunotherapy and the need for multispecialty care for patients undergoing immunotherapy.

Article Information and Declarations

Ethics statement

The patient gave consent to to present a case report about the course of disease and treatment. The patient shared the necessary medical documentation, including CDs with imaging studies.

Author contributions

A.S.G.-M.: conceptualization, writing — original draft preparation, visualization; M.D.-H.: conceptualization, writing — review and editing, supervision; I.G.-G.: writing — review and editing, supervision.

All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

Authors declare no conflict of interest.

Supplementary material

Figure S1.

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Supplementary material

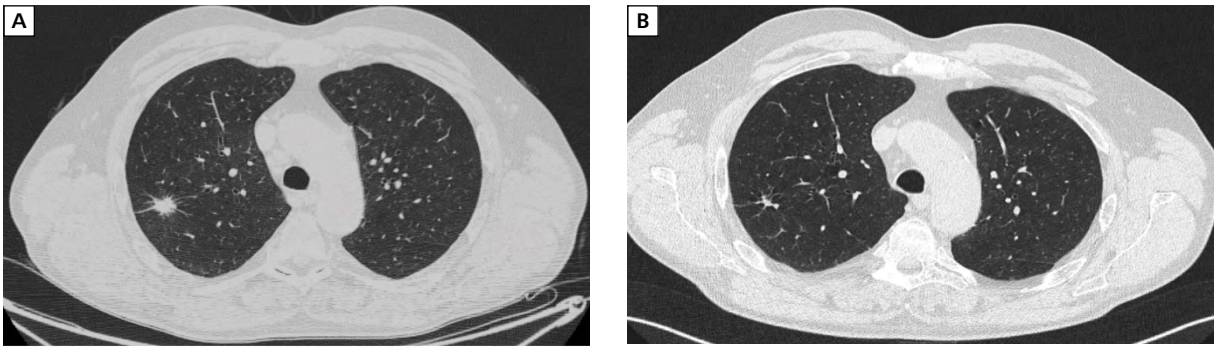

Figure S1. Chest computed tomography (CT) scans before (**A**) and after 6 months (**B**) of pembrolizumab treatment