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Hypopituitarism as a rare complication of lung cancer immunotherapy

Key words: hypopituitarism, cancer immunotherapy, pembrolizumab, lung cancer

Although hypopituitarism is a rare complication of cancer immunotherapy (occurs in 0.1–2.4% of patients depending on publication and use of monoclonal antibodies), nowadays immunotherapeutic agents are the main notable cause of hypophysitis [1, 2]. We present a case of hypopituitarism in a patient with non-small cell lung cancer (NSCLC) treated with pembrolizumab.

A 62-year-old male patient was admitted to the Ward of Clinical Oncology to be qualified for systematic therapy. In the past, the patient underwent cardiological and cardiosurgical interventions, including coronary artery bypass, due to myocardial infarction (2 years before qualification for immunotherapy; under the supervision of a cardiac center). The histopathological result revealed squamous cell carcinoma (SCC) of the left lung (T3N0M0). The expression of programmed death ligand 1 (PD-1L) was estimated to be 70%. Until then the patient was treated by radiotherapy without therapeutic success because of developing metastases to the second lung, suprarenal gland and bones. The laboratory tests (Tab. 1) and CT scans were ordered. The features of prior myocardial infarction were the only findings on ECG. The Concilium qualified the patient for immunotherapy in a regime of 200 mg of pembrolizumab every 21 days.

Table 1. The results of patient's blood test before and after administration of prednisone

	Before treatment	After treatment	Reference range
Corticotropic axis			
ACTH [pg/mL]	< 1	54.28	7.20–63.60
Cortisole [μg/dL]	3.70	10.20	4.30–22.40
Thyrotropic axis			
TSH [mIU/L]	0.117	2.454	0.550–4.780
fT4 [ng/dL]	0.81		0.89–1.76
fT3 [pg/mL]	2.50		2.30–4.20
Inflammation markers			
CRP [mg/L]	179.127	162.459	< 5.00
WBC [K/μL]	21.47	13.75	[4.00–10.00]

ACTH — adrenocorticotropic hormone; CRP — C-reactive protein; fT3 — free triiodothyronine; fT4 — free thyronine; TSH — thyrotropic hormone; WBC — white blood cells.

According to RECIST 1.1 criteria, the patient's status after the first month was stable disease (SD). The change in the sum of measurable diameters of 2 included lesions was estimated to be 85%. When the patient was admitted to the ward to have the sixth cycle of therapy

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administered, he reported a group of symptoms suggesting hypopituitarism (weakness, drowsiness, low blood pressure). According to the clinical picture, hormonal tests were done (Tab. 1).The insufficiency in corticotropic and thyrotropic axes was reported, which led up to endocrinological consultation. The consulting physician suspected immunotherapy-related hypophysitis and recommended prednisone (1 mg/kg) per os, with further hospitalization in the Endocrinology Clinic [to do magnetic resonance imaging (MRI) of the hypothalamic-pituitary region and further diagnostics]. A decision on the substitution of thyroid hormones was temporarily delayed and later withdrawn due to improvement in the patient's condition and laboratory results.

On steroid therapy, the patient's condition improved, and normalization in corticotropic and thyrotropic axes followed. The patient opted for hospital discharge with prednisone; immunotherapy was temporarily stopped. The patient died at home from a suspected cardiovascular event 2 days later.

The effectiveness of prednisone in oncological patients with hypopituitarism as an immunotherapy complication remains inconclusive according to the available literature [1, 2]. On the other hand, prednisone is currently recommended by the European Society for Medical Oncology (ESMO) guidelines for immunotherapy-related hypophysitis treatment [3]. The long-term complications (iatrogenic Cushing syndrome) are indicated as a main high-risk disadvantage of intense steroid therapy, none of which correspond with the presented case.

Author contributions

J.K.G.: data collection, data analysis, manuscript writing; A.R.: data collection, data analysis, manuscript writing; G.R.: data collection, data analysis, protocol/project development, manuscript writing; K.Sz.: protocol/project development, data collection and management; S.M.: manuscript writing and editing.

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Conflict of interest

Authors declare no conflict of interest.

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