EP-095 A case of hypophysitis with panhypopituitarism after the use of the immune check point inhibitor pembrolizumab

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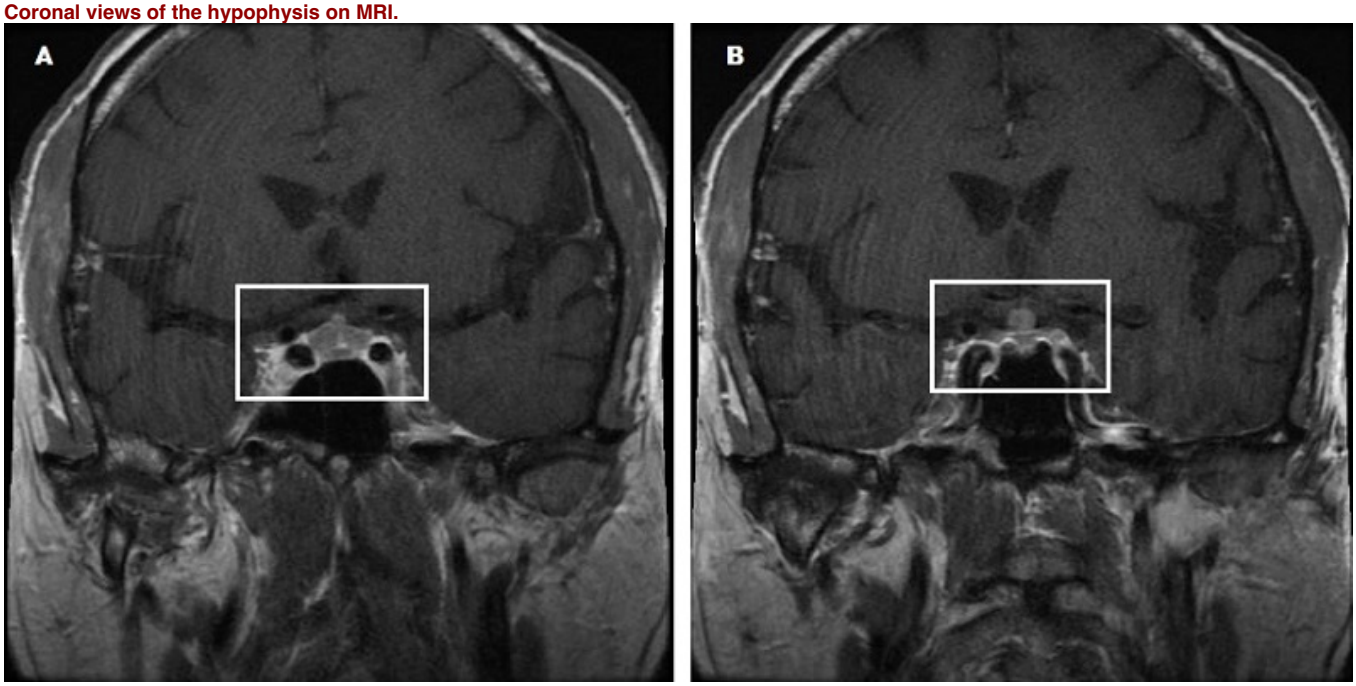
OBJECTIVES

Immune checkpoint inhibitors (ICIs) belong to a new group of anticancer drugs targeting T-cell proteins involved in the activation of immune response toward malignancies. As ICIs become more important in oncology, their use is also increasing. ICI-induced immune system activation could lead to the loss of self-tolerance, presenting as autoimmune inflammation and dysfunction of various tissues and organs. Among the endocrinological damages, thyroiditis and hypophysitis seem to be the most common. Type 1 diabetes mellitus and adrenalitis are rare immune-related adverse events. We aimed to present a case with panhypopituitarism and hypophysitis after pembrolizumab use.

CASE

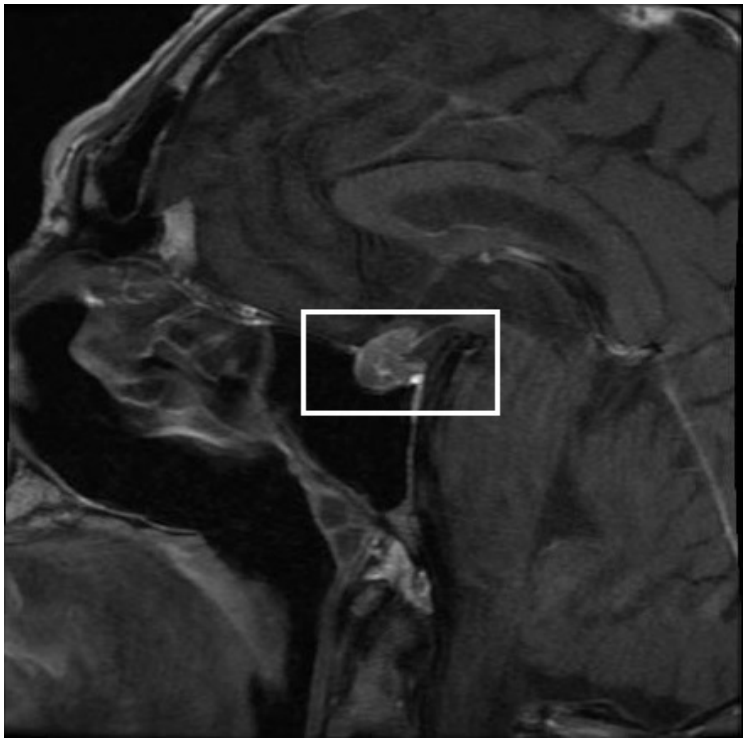
A 56-year-old male patient with metastatic lung cancer for 9 months. He was referred to our clinic after the detection of low thyroid-stimulating hormone (TSH), free thyroxine (fT4), adrenocorticotropic hormone (ACTH) and cortisol levels in the examinations performed due to weakness, headache, nausea-vomiting complaints. On physical examination of the patient, blood pressure was 105/65 mm/hg, heart rate was 77 per minute, other systemic examination was normal. Plasma glucose: 92 mg/dl (normal: 70-99 mg/dl), sodium: 138 mEq/L (normal: 132-146 mEq/L), potassium: 3.84 mEq/L (normal: 3.5-5.5 mEq/L) detected. In hormonal tests; TSH: 0.09 mU/L (normal: 0.55-4.78 mU/L), fT4: 0.81 ng/dl (normal: 0.89-1.76 ng/dl), free triiodothyronine: 2.54 ng/dl (normal: 2.3-4.2 ng/dl), follicle-stimulating hormone: 1.5 U/L (normal: 1.4-18.1 U/L), luteinizing hormone: 0.1 U/L (normal: 1.5-9.3 U/L), prolactin:16.6 mcg/L (normal: 2.1-17.7 mcg/L), free testosterone: <0.40 pg/ml (normal: 3.6-25.7 pg/ml), total testosterone: <0, 07 ug/L (normal: 0.86-7.83 ug/L), insulin like growth factor-1: 40 mcg/L (normal: 81-225 mcg/L), growth hormone: 0.2 mcg/L (normal: 0.05-3 mcg/L), cortisol: 1.1 mcg/L (normal: 5.2-22.4 mcg/L), ACTH: <5.0 pg/ml (normal: <46 pg/ml) were detected. In urinalysis, the density was 1.017. In pituitary magnetic resonance imaging (MRI); the height of the pituitary gland is 7.5 mm in the midline, and the upper contour of the gland is convex. After intravenous contrast agent injection, the gland parenchyma was contrasted in a heterogeneous structure, and the infundibulum was interpreted as being in the midline and thicker than normal. The patient had no visual complaints but visual field test revealed bilateral superior hemianopsia. The patient was diagnosed with hypophysitis and panhypopituitarism and was started on 1 mg/kg methylprednisolone treatment because he has severe acute symptoms like headache, nausea-vomiting. 3 days later, L-thyroxine 50 mcg/day was added to the treatment. After the treatments applied, the patient achieved rapid symptomatic improvement. High-dose steroid therapy was given for 2 weeks until symptoms resolved and then the dose was reduced. Treatment was continued with physiological dose replacement.

Coronal views of the hypophysis on MRI.



(A) diffuse enlargement of the pituitary gland (B) thickening of the pituitary stalk

Sagittal views of the hypophysis on MRI.



Diffuse enlargement of the pituitary gland and thickening of the pituitary stalk.

CONCLUSIONS

Hypophysitis is one of the most common endocrinopathies associated with checkpoint inhibitor therapy and commonly presents with headache, fatigue, weakness, and other nonspecific symptoms. Hypophysitis cases due to immune check point inhibitors may present with isolated anterior pituitary hormone deficiency or panhypopituitarism. In the literature, it was stated that thyroid hormone deficiency was reported less frequently than adrenocorticotropic or gonadotropic deficiencies. Panhypopituitarism, although rare, should not be ignored. MRI images are variable. Reversible pituitary enlargement may be seen on brain MRI, but importantly, brain MRI may be normal in patients with hypophysitis. Early diagnosis and appropriate treatment are crucial. Treatment is supportive and includes hormone replacement. The management of patients clearly requires long-term onco-endocrinological care.