Concomitant Primary and Secondary Adrenal Insufficiency due to Immune Checkpoint Inhibitor Therapy

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Supplemental Video

Presenting Author: Eileen Montalvan, MD, Internal Medicine Resident PGY2, North Alabama Medical Center, Florence, Alabama

Coauthors: Mohammed Afraz Pasha, MD, Internal Medicine, PGY2, North Alabama Medical Center, Florence, Al; Bethany Jackson, MD, Diabetology/Endocrinology, The Florence Endocrine Clinic, PLLC, Florence, AL.

Introduction

Use of Immune checkpoint inhibitors (ICPIs) in management of malignancies is associated with immune related adverse events (iRAE), which occur due to inhibition of immune checkpoints responsible for reinforcement of barriers against autoimmune responses. While the incidence of iRAE related endocrinopathies such as hypophysitis and thyroiditis is less than 20%, occurrence of concomitant secondary and primary adrenal insufficiency related to iRAE is rare. Hypophysitis induced by ICPIs manifests in the form of secondary adrenal Insufficiency, which is irreversible.

Case presentation

A 68 year old Caucasian female presented to the endocrinology clinic for evaluation of orthostatic hypotension. Her history was significant for metastatic melanoma treated with Ipilimumab for 1 year. Subsequently, she developed orthostatic hypotension resulting in recurrent falls. Evaluation during hospitalization revealed hypo-osmolar normovolemic hyponatremia. MRI of head showed hypophysitis. She was initiated on prednisone 80 mg and subsequently transitioned to hydrocortisone for treatment of secondary adrenal insufficiency. She, however, continued to have persistent symptoms of salt craving, increased fatigue and lightheadedness warranting an endocrinology referral. On physical examination, blood pressure was 152/80 mmHg and heart rate was 62 bpm. No orthostatic hypotension seen upon examination. Laboratory data revealed sodium of 135 mEq/L, chloride of 98 mEq/L, potassium 4.7 mEq/L, bicarbonate 24 mEq/L, glucose 104 mg/dL, BUN 9 mg/dL and creatinine of 0.8 mg/dL. Normal level of TSH 1.73 mU/L, low ACTH 1.8 pg/mL, low AM Cortisol 5.9 µg/dL and positive 21-hydroxylase antibody on multiple occasions.

Working Diagnosis

Hyponatremia due to adrenal insufficiency. The underlying etiology seemed to be adrenal insufficiency secondary to hypophysitis caused by Ipilimumab. However, laboratory investigations were further indicative of concomitant autoimmune primary adrenal Insufficiency with positive 21-hydroxylase antibody.

Management/ Outcome/ Follow-up

Patient was originally treated with high dose prednisone for hypophysitis. This was gradually decreased to replacement dose for adrenal insufficiency. She is currently stable with prednisone 5 mg daily.

Learning Objectives

- Familiarizing ourselves with the spectrum of endocrinopathies associated with the use of Immune checkpoint inhibitor therapy.
- Recognizing signs and symptoms of adrenal insufficiency.

References and Resources

Immunotherapy-induced endocrinopathies: assessment, management and monitoring.Nogueira,E, Newsom-Davis,T. et al. Ther Adv Endocrinol Metab
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