Neuroendocrinology and Pituitary

ODP342

Panhypopituitarism Induced by CTLA-4 and PD-1/PD-L1 Inhibitor Immunotherapy

Nicole Hernandez-Cordero, MD, Yadiel Rivera-Nieves, MD, Nydia Burgos-Ortega, MD, Alexandra Rosado-Burgos, MD, Monica Ortiz-Rivera, MD, Luis Madera-Marin, MD, Loida Gonzalez-Rodriguez, MD, Milliette Alvarado-Santiago, MD, and Margarita Ramirez-Vick, MD

Background: Breakthroughs in oncology have led to the incorporation of immunotherapy to improve the prognosis in patients with advanced malignancies. Checkpoint inhibitors are immunomodulatory antibodies that enhance the immune system using PD-1/PD-L1 and CTLA-4 as primary targets. Pharmacologic disruption in checkpoints can trigger autoimmune-like manifestations in various organs systems, known as immune-related adverse effects. Endocrinopathies of the pituitary, thyroid, or adrenal glands have been described; with the most common being hypothyroidism, hyperthyroidism and hypophysitis. We report a case of hypophysitis induced by immunotherapy in a patient treated with ipilimumab and nivolumab for renal cell carcinoma with bone metastases. Clinical case: Case of a 63-year-old male patient with left renal cell carcinoma treated with nivolumab and ipilimumab, who presented with general weakness, malaise, disorientation, slow
Immunotherapy and severe hyponatremia in weeks after immunotherapy initiation. Denied headache, loss of consciousness, dizziness, involuntary movements, nausea, vomiting, abdominal pain, changes in bowel movements, swelling of skin or changes in skin color, decreased libido or erectile dysfunction, hair loss, polyuria, polydipsia, mood changes or hypoglycemia. Laboratory results showed serum sodium levels of 117 mEq/L, inappropriately normal ACTH (18.8 pg/mL), low serum cortisol in early morning (1.97 µg/dL), low TSH (0.17 mIU/mL) and low total T4 (4.39 µg/dL). Serum sodium levels improved to 136 mEq/L after administration of 3% NaCl and glucocorticoids, that were given due to concerns for adrenal insufficiency. Patient was discharged home on oral hydrocortisone and immunotherapy was discontinued. Repeated hormonal workup revealed previously identified central hypothyroidism and secondary adrenal insufficiency. Additionally, had an inappropriate lownormal FSH (11.10 mIU/L) and LH (2.62 IU/L), in view of a low total testosterone (< 2.5 pg/mL), suggestive of hypogonadotropic hypogonadism. Since the patient was asymptomatic for sexual dysfunction, hormonal work up was repeated later on, and found with normal gonadotropins and normal total testosterone levels (444 ng/dL; 93-740 ng/dL), with no evidence of hypogonadism. There was no indication for growth hormone therapy in view of abnormal IGF-1 for age (236 ng/mL). He is currently clinically stable on replacement therapy with hydrocortisone and levothyroxine. Conclusion: Immunotherapy-induced endocrinopathies are important adverse effects that clinicians should be aware of and monitored routinely in patients treated with checkpoint inhibitors. Hypophysitis typically manifests with fatigue and headache in the presence of adrenal insufficiency, hypothyroidism and hypogonadism with preservation of growth hormone. It this condition has been described with different immune checkpoint inhibitors, although incidence is higher with ipilimumab, as reported in this case. Recovery of some pituitary function is common, but persistent deficiencies can occur, particularly adrenal insufficiency that rarely resolves. Complications associated with hormonal deficiencies can be life-threatening and prompt recognition is warranted. 

Presentation: No date and time listed