Immune Related Adverse Events: Isolated ACTH Deficiency with Nivolumab/ Ipilimumab Combination Therapy

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INTRODUCTION

- Immunotherapies have become revolutionary treatment modalities for several malignancies including patients with advanced melanoma and non-small cell lung carcinoma.
- New immunotherapy treatments can result in unique adverse events due to increased inflammation in any organ in the body. Common immune-related adverse events include vitiligo, colitis, hepatitis, pneumonitis, and endocrinopathies, most commonly thyroiditis.

CASE PRESENTATION

- A 77-year-old male with metastatic choroidal melanoma treated with 2 cycles of Ipilimumab and Nivolumab presented to the hospital with complaints of generalized weakness, malaise, loss of appetite and 20 lb. weight loss over a two-week period.
- His concerns were initially attributed to progression of his known malignancy, however he developed further symptoms of intermittent fevers with eosinophilic leukocytosis, hypotension, disorientation, lethargy, tremors, incoherent speech, and urinary incontinence.
- Further work-up with MRI brain showed no new metastases or abnormalities and EEG was without epileptic foci. Infectious workup was unrevealing except for a questionable right lower lobe infiltrate on chest x-ray, which was subsequently treated with antibiotics. CT chest/abdomen/pelvis showed pulmonary metastases without further abnormalities.
- With symptoms concerning for possible adrenal insufficiency, a random cortisol was checked resulting at 1.7 ug/dL. Adrenocorticotropic hormone (ACTH) stimulation test confirmed the diagnosis of adrenal insufficiency with the highest resultant level of 9.3 ug/dL. A low ACTH level of <5 confirmed the diagnosis of secondary adrenal insufficiency.
- Treatment was initiated with methylprednisolone 60mg intravenously every 12 hours with concern for auto-immune hypophysitis related to immunotherapy. Symptoms began improving rapidly with steroid initiation.
- Further Endocrine evaluation revealed mild TSH elevation but otherwise normal FSH, LH, Prolactin, and insulin growth factor-1.

DISCUSSION

- This case uniquely exhibits immunotherapy induced isolated ACTH deficiency, rather than hypophysitis. Hypophysitis can occur with an adverse event rate up to 17% while on Ipilimumab, however isolated ACTH deficiency is rarer.
- Diagnosis is challenging with symptomatology mimicking common malignancy complaints. It is important for all physicians to be able to recognize symptoms of secondary adrenal insufficiency, especially as a side effect of immunotherapy, as this condition is life threatening and requires immediate diagnosis and treatment.

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