

A RARE CASE OF NIVOLUMAB-INDUCED ISOLATED ACTH DEFICIENCY

Introduction

Nivolumab is a monoclonal antibody which inhibits the immune checkpoint programmed cell death 1 (PD-1), promoting T-cell mediated immunity against cancer cells. Hypophysitis is a known complication of this treatment and is commonly associated with deficiency of multiple anterior pituitary hormones. We describe an unusual case of isolated ACTH deficiency after treatment with nivolumab for undifferentiated ovarian carcinoma.

Case

- A 63-year-old woman presented to the hospital for evaluation of dyspnea with minimal exertion and fatigue over the previous four weeks. She denied nausea, vomiting, abdominal pain, weight loss, fever, polyuria, headache, or vision changes.
- Medical history was significant for long-standing primary hypothyroidism treated with levothyroxine and undifferentiated carcinoma of the left ovary, diagnosed eighteen months prior to presentation.
- Previous treatments included surgical resection and cytotoxic chemotherapy with three cycles of paclitaxel and carboplatin.
- She was subsequently enrolled in a clinical trial in which she received treatment with nivolumab and rucaparib, a poly-ADP ribose polymerase-1 (PARP-1) inhibitor over the preceding eight months.

Labs/ Imaging

Labs at the time of admission:

AM cortisol	<1 ug/dl (4.46-22.7 ug/dl)
ACTH	<5 pg/ml (0- 46 pg/ml)
IGF-1	80 ng/dl (35- 201 ng/dl)
TSH	4.356 uIU/ml (0.4- 400 uIU/ml)
FT ₄	1.06 ng/dl (0.71- 1.51 ng/dl)
Prolactin	43 ng/ml (5.2- 26.5 ng/ml)
FSH	60.4 mIU/ml(26.72- 133.41 mIU/ml)
Serum sodium	141 mmol/L (136- 145 mmol/L)
Serum potassium	3.6 mmol/L (3.5- 5.1 mmol/L)

MRI Pituitary:

- No masses or areas of abnormal enhancement involving the pituitary gland.

Discussion

- Immune related adverse events (IRAEs) are commonly seen after treatment with checkpoint inhibitors.
- Hypophysitis is more commonly associated with CTLA-4 inhibitors and is less commonly seen with PD-1 and programmed cell death ligand 1 (PD-L1) inhibitors. The reason could be that CTLA-4 receptor is expressed by the pituitary cells, but the expression of PD-1 or PD-L1 receptors by pituitary cells is yet to be shown.
- Studies have shown that few patients have recovery of the hypothalamic-pituitary-adrenal axis after discontinuation of immunotherapy.

Conclusions

Our case demonstrates a rare case of isolated ACTH deficiency after treatment with the PD-1 inhibitor, nivolumab. After confirming the diagnosis, she was started on physiologic dose of oral hydrocortisone. Her symptoms improved significantly with treatment.

Although hypophysitis due to PD-1 inhibitor is uncommon, IRAEs are commonly seen during therapy with checkpoint inhibitors. It is important to monitor symptoms and signs related to IRAEs while on treatment with checkpoint inhibitors.

References

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