A Case of Adrenal Crisis Secondary to Ipilimumab Induced Autoimmune Hypophysitis

Todd A[1], Thiraviaraj A[1]

[1] Department of Endocrinology and Diabetes, Altnagelvin Area Hospital, Londonderry, BT47 6SB

Case Description

A 42 year old man with history of stage IV malignant melanoma, previous craniotomy and frontal lobectomy and pulmonary lobectomy for lung metastasis, presented after his 3rd dose of Ipilimumab, with vomiting, abdominal pain, hypotension and pyrexia. He was treated as a presumed line sepsis.

Four days prior to admission, thyroid function test showed T4 of 7.9pmol/L and TSH 0.02mU/L. Following this he was started on levothyroxine. On admission, random cortisol was low at 24 nmol/L. He was treated with intravenous (IV) hydrocortisone initially for acute adrenal crisis with good effect.

A pituitary profile was carried out given possibility of pituitary involvement. This revealed pan-hypopituitarism. The results are in Table 1.

Test	May 2014	June 2014	admission
Normal values	At 2nd Chemo cycle	At 3rd chemo cycle	Three days after chemo
fT4 (12-22)	17.5 pmol/L	7.9 pmol/L	7.2 pmol/L
TSH (0.3-4.3)	2.24 mU/L	0.02 mU/L	0.07 mU/L
Cortisol	-	-	24 nmol/L
LH (1.7-8.6)	-	-	1.5 U/L
FSH (1.5-12.4)	-	-	5.1 U/L
Testosterone (11.4-27.9)	-	-	<0.2 nmol/L
IGF1 (9.8-28.3)	-	-	22 nmol/L
Prolactin(86-324)	-	-	135 mU/L

Table 1: Results of admission bloods.

Imaging

- On CT head, the pituitary was unremarkable.
- MRI pituitary showed an atrophic pituitary with homogenous enhancement, normal stalk and a preserved posterior pituitary bright spot.

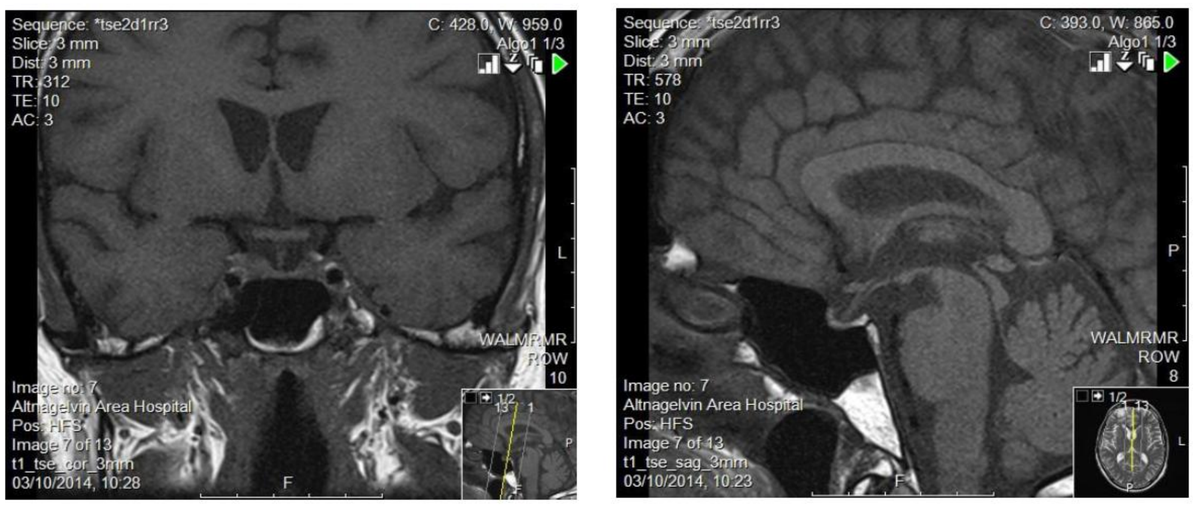

Figure 1:
MRI pituitary at time of presentation showing an atrophic pituitary.

Diagnosis

Given the finding of new pan-hypopituitarism, he was treated as an adrenal crisis secondary to Ipilimumab related autoimmune hypophysitis, despite lack of pituitary or stalk enlargement on imaging.

Management

There are no guidelines or consensus in the literature on how to manage Ipilimumab related hypophysitis. Some centres advocate use of high dose steroids [1], others believe high dose steroids do not affect the outcome [2].

Our patient received IV methylprednisolone at a dose of 1mg/kg for 3 days, followed by prednisolone starting at a dose of 1mg/kg tapered down over 4 weeks. He symptomatically felt improvement from this dose, but at 3 months post treatment continues to demonstrate panhypopituitism. He currently requires levothyroxine, testosterone replacement and hydrocortisone. It was decided due to his active malignancy that he should not receive growth hormone replacement. His most recent pituitary profile is below in table 2.

Test	July 2014	September2014
Normal values	1 week on therapy	3 months post therapy
fT4 (12-22)	pmol/L	7.9 pmol/L
TSH (0.3-4.3)	2.24 mU/L	0.02 mU/L
Cortisol	424 nmol/L	Synacthen Test (24 hrs off hydrocortisone) 0 min Sr Cortisol <10 nmol/L 30 min sr cortisol 38 nmol/L
LH (1.7-8.6)	4.2 U/L	-
FSH (1.5-12.4)	7.6 U/L	-
Testosterone (11.4-27.9)	18.7 nmol/L	-
IGF1 (9.8-28.3)	-	-
Prolactin(86-324)	216 mU/L	-

Table 2: Bloods at last review

Discussion

- This case describes adrenal crisis secondary to immune related hypophysitis caused by Ipilimumab and management of it with IV methylprednisolone.
- Frequency of immunotherapy as treatment for solid organ tumours is increasing and clinicians need to be aware of these life threatening side effects and their treatment. We think that the adrenal crisis was precipitated by the commencement of levothyroxine prior to admission. Thyroid function is monitored as part of Ipilimumab therapy. Recognition of secondary hypothyroidism and evaluation of hypothalamo-pituitary-adrenal axes prior to thyroid supplementation is important and needs to be highlighted to clinicians who frequently use this therapy.
- Current evidence on management of immune hypophysitis is sparse and consensus on treatment is absent. In this setting discussion with patient and individualised care planning remains the optimal approach. Further study is needed to clarify the most appropriate treatment.

References

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2. Min L. et al Systemic high-dose corticosteroid treatment does not improve the outcome of ipilimumab-related hypophysitis: a retrospective cohort study. *Clinical Cancer Research.* 2015 Feb 15;21(4):749-55

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Anna Todd
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