Immune-Related Adverse Event: Endocrinopathies – Hypophysitis

The Clatterbridge Cancer Centre NHS Foundation Trust

Immunotherapy has been causatively associated with a number of endocrinopathies that may present with nonspecific symptoms, which may resemble other causes such as brain metastasis or underlying disease. This includes inflammation of the pituitary gland. The pituitary gland is responsible for secreting hormones that govern the activity of the thyroid, adrenal and gonadal glands. Where pituitary inflammation occurs this often leads to deficiency in the hormones governing these glands and insufficiency of one, two or all end organs can occur.

CAUTION **If the patient is on steroids (prednisolone/dexamethasone) then serum cortisol will likely be suppressed – please discuss with endocrinology team before commencing replacement**

***Endocrine function panel:**
U&E, LFT, TSH, Free T4, free T3, ACTH, LH, FSH & cortisol (between 9-11am if possible), prolactin, blood glucose +/- testosterone/oestrogen

Asymptomatic
Identified on routine blood tests

Biochemical alteration in cortisol with serum level <200nmol/L

Cortisol insufficiency is likely if cortisol is <100nmol/L

Cortisol 100-200nmol/L

Investigations
- Repeat cortisol at 9am ≤ 48 hours – if <200 and no other endocrine function abnormality arrange short synacthen test.
- *Complete endocrine function panel.

Actions
- Monitor regularly (before each cycle minimum) and act as per algorithm if serum levels fall
- If cortisol replaced then evaluate TFTs 1 week later and replace as required
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine advice if unsure
- Continue immunotherapy

Cortisol <100nmol/L

Investigations
- Repeat cortisol at 9am ≤ 24 hours – if <100 replace as below
- *Complete endocrine panel

Treatment
- Replace with hydrocortisone 20mg/10mg/ 10mg
- Reduce to 10g/5mg/5mg after 2 weeks

Actions
- Consider referral to endocrinology for advice/ further investigation
- If cortisol replaced then evaluate TFTs 1 week later and replace as required
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine advice if unsure
- Give emergency steroid advice and alert card
- Refer to IO Toxicity Service
- Continue immunotherapy

Symptomatic
Mild/Non-life threatening

Suspect endocrinopathy based on symptoms

Tiredness/fatigue, headache, weight loss, susceptibility to infection, normal BP with no postural drop

Investigations:
- 9am Cortisol and ACTH
- MRI brain with pituitary cuts

Cortisol (9am) >400 nmol/L

Cortisol insufficiency unlikely

Actions
- Consider other causes of symptoms
- Continue immunotherapy

Cortisol (9am) 100-400 nmol/L

Cortisol insufficiency possible

Actions
- Consider endocrine referral
- *Complete endocrine panel
- If cortisol replaced then evaluate TFTs 1 week later and replace as required
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine advice if unsure
- Refer to IO Toxicity Service
- Continue immunotherapy

Cortisol (9am) <100nmol/L

Cortisol insufficiency likely

Treatment
- Commence hydrocortisone 20mg/10mg/10mg
- Reduce down to 10mg/5mg/5mg after 2 weeks

Actions
- Consider endocrine referral
- *Complete endocrine panel
- If cortisol replaced then evaluate TFTs 1 week later and replace as required
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine advice if unsure
- Give emergency steroid advice and alert card
- Refer to IO Toxicity Service
- Continue immunotherapy

Symptomatic
Severe headache, visual disturbance, evidence of focal neurology

Combination of mild/moderate symptoms and pituitary inflammation on MRI

If severe symptoms/signs of hormonal insufficiency with no headache/visual disturbance/pituitary inflammation then follow adrenal crisis algorithm

Investigations:
- Endocrine Panel inc ACTH
- MRI brain with pituitary cuts

Admit patient

Immediate Intervention
- Commence IV methylprednisolone 2mg/kg/day for a minimum of 3 days without awaiting blood tests
- If clinically improved with mild/resolved symptoms switch to prednisolone starting at 60mg OD and reducing every 3 days
- Once at 10mg prednisolone introduce steroid replacement hydrocortisone 20mg, 10mg, 10mg
- Reduce hydrocortisone to 10mg, 5mg, 5mg after 2 weeks
- Continue weaning prednisolone till stop but continue hydrocortisone replacement
- Once stable on hydrocortisone replacement for 5-7 days commence thyroxine
- Recheck testosterone/oestrogen after 3 weeks, if low consider replacement and seek endocrine advice if unsure.
- Consider urgent Endocrinology referral
- Give emergency steroid advice and card
- Refer to IO Toxicity Service

Further emergency advice regarding hypophysitis is outlined in the **SfE guidance**
If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced prior to commencement of thyroid replacement (see grade 1 hypothyroidism guidelines)

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Interrupt SACT immunotherapy until discussed with Acute Oncology Team. Please contact on-call oncology/haematology team for advice. Ensure that the patient has monitoring/follow up planned with their oncology/immuno-oncology team.