The Clatterbridge Cancer Centre
NHS Foundation Trust

Immune-Related Adverse Event: Endocrinopathies- Adrenal Crisis

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.

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

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

Asymptomatic
Identified on routine blood tests

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

Hypoadrenalism is likely if cortisol is <100nmol/L

Cortisol 100-200nmol/L

Investigations
- Repeat cortisol at 9am ≤ 48 hours - if <200 arrange short synacthen test
- If <100 see "Cortisol <100" green strand
- Complete endocrine function panel if outstanding

Actions
- Monitor regularly (before each cycle as a minimum) and act as per algorithm if serum levels fall
- Continue immunotherapy
- Refer to IO toxicity team

Cortisol <100nmol/L

Investigations
- Repeat cortisol at 9am ≤ 24 hours – if <100 arrange short synacthen test
- Complete endocrine panel if outstanding

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

Actions
- Consider referal to endocrinology for advice/ further investigation
- Give emergency steroid advice and alert card
- Refer to IO toxicity team
- 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
- If headache present consider MRI brain with pituitary cuts

Cortisol (9am) >400 nmol/L

Adrenal insufficiency unlikely

Actions
- Consider other causes of symptoms
- Continue immunotherapy

Cortisol (9am) 100-400 nmol/L

Adrenal insufficiency possible

Actions
- Arrange short synacthen test
- Consider endocrine referral
- Complete endocrine bloods including prolactin, testosterone and ACTH
- Refer to IO toxicity team
- Continue immunotherapy

Cortisol (9am) <100nmol/L

Adrenal insufficiency likely

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

Actions
- Arrange short synachten test
- Consider endocrine referral
- Complete endocrine bloods including prolactin, testosterone and ACTH
- Give emergency steroid advice and alert card
- Refer to IO toxicity team
- Continue immunotherapy

Symptomatic
Severe or Life-threatening

Suspect adrenal crisis-
Hypotension (SBP <90mm Hg)
Postural hypotension (>20mm Hg drop)
Dizziness/Collapse
Hypovolemic shock
Nausea/ Vomiting
Abdominal pain/tenderness/guarding
Fever,
Confusion/ delirium
Coma,
Hyponatraemia/hyperkalaemia/ hypoglycaemia
Pre-renal/renal failure

Admit patient

Immediate Intervention
- Send endocrine panel including and ACTH prior to giving steroids
- Immediate management with an ABCDE approach
- Commence IV hydrocortisone 100mg QDS immediately without awaiting blood tests
- Urgent Endocrinology referral
- Rule out superadded infections

Society for Endocrinology [SfE] guidelines for adrenal crisis: www.endocrineconnections.com/content/5/5/G1

Next Steps are dependant on blood results
- Introduce steroid replacement hydrocortisone PO 20mg, 10mg, 10mg
- Reduce hydrocortisone to 10mg, 5mg, 5mg after 2 weeks
- Once stable on hydrocortisone replacement for 5-7 days if thyroid deplete then commence levothyroxine
- Arrange short synacthen test.
- Recheck testosterone after 3 weeks and replace if remains suppressed
- Give emergency steroid advice and alert card
- Refer to IO toxicity team

All patients with hypoadrenalism should be assessed for postural hypotension and fludrocortisone (50mcg OD) considered if persistant

Emergency advice regarding hydrocortisone 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 (for which the grade 1 hypothyriodism guidelines should be instituted)

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.

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