Immunotherapy has been causatively associated with a number of endocrinopathies, including hypophysitis, hypopituitarism, adrenal insufficiency, and hypothyroidism. Patients may present with nonspecific symptoms, which may resemble other causes such as brain metastasis or underlying disease, and a high index of suspicion should therefore be maintained. The most common clinical presentation includes headache and fatigue. Adrenal crisis is a medical emergency, and must be excluded.

**Management Plan:**

- **Assess:** TSH, T4, T3, ACTH, LH, FSH & cortisol, prolactin, and testosterone

  **Abnormal results:**
  - **Hyperthyroidism**
    - Beta blockers (propanolol) with prednisolone 0.5-1mg/kg/day if symptomatic
    - Taper steroids over 3-6 weeks
    - Defer immunotherapy until symptomatic improvement

  - **Hypothyroidism**
    - Thyroxine 50mcg - 100 daily (start with 25 mcg daily if any history of heart disease or arrhythmia) if TSH>10 or FT4 low
    - If any features of hypoadrenalism exclude adrenal insufficiency with short synacthen test before starting thyroxine

  - Repeat TFTs in 4-6 weeks and titrate dose according to TSH
  - If TSH 5-10 repeat TFTs in 4-6 weeks

**Management:**

- Ensure cortisol within normal parameters
- Monitor TFT's every cycle
- Refer to endocrinologist if any issues
- Continue immunotherapy

**Adrenal crisis**

Defined by severe dehydration, hypotension or shock

**Moderate (Grade 2)**

**Suspect endocrinopathy based on symptoms**

- Headache, visual field defects, fatigue, weakness, asthenia, anorexia, nausea and vomiting, lethargy

**Management Plan:**

- **Assess:** TSH, T4, T3, ACTH, LH, FSH & cortisol, prolactin, and testosterone

  **Abnormal results:**
  - If 9am cortisol <100nmol/l hypoadrenalism is likely
  - If 9am cortisol 100 - 400nmol/l then a short synacthen test is needed to exclude hypoadrenalism
  - Pituitary MR scan if visual field defects consistent with pituitary disease (usually temporal visual field defect) or headache
  - Refer to endocrinologist for advice and hormone replacement if required

  **Resume immunotherapy when patient clinically stable**

- Exclude other causes

- Repeat TFTs in 1-3 weeks time

**Hypothyroidism (Mild)**

Asymptomatic or isolated hyper/hypothyroidism

**Management Plan:**

- **Assess:** TSH, T4, T3, ACTH, LH, FSH & cortisol, prolactin, and testosterone

  **Abnormal results:**
  - Beta blockers (propanolol) with prednisolone 0.5-1mg/kg/day if symptomatic

  - Taper steroids over 3-6 weeks

  - Defer immunotherapy until symptomatic improvement

  - Close monitoring of TFTs as subsequent hypothyroidism is common.

  - If asymptomatic then repeat TFTs after 2 weeks then every 4 weeks for at least 3 months

  - Thyroxine 50mcg - 100 daily (start with 25 mcg daily if any history of heart disease or arrhythmia) if TSH>10 or FT4 low

  - If any features of hypoadrenalism exclude adrenal insufficiency with short synacthen test before starting thyroxine

  - Repeat TFTs in 4-6 weeks and titrate dose according to TSH

  - If TSH 5-10 repeat TFTs in 4-6 weeks

**Severe or Life-threatening (Grade 3 + 4)**

**Suspect adrenal crisis**

Severely unwell patient: severe dehydration, hypotension or shock

**Management Plan:**

- Admit patient- URGENT endocrinology advice

  - Immediate hydrocortisone 100 mg intravenously (IV) every 6 hours

  - Commence IV hydration if indicated

  - Exclude infection/sepsis

  - Asses:** TSH, T4, T3, ACTH, LH, FSH & cortisol, prolactin, testosterone prior to iv steroids

  - ECG

  - Withhold next cycle of treatment

  - MR imaging brain with pituitary cuts

**Adrenal crisis**

Defined by severe dehydration, hypotension or shock

**Ongoing Management:**

- Once symptoms or laboratory abnormalities are controlled and overall patient improvement is evident, treatment with immunotherapy may be resumed and initiation of corticosteroid taper should be based on endocrinology advice, however some patients may require chronic hydrocortisone replacement. Gonadotrophin and TSH may recover but ACTH deficiency rarely does.

- Beware of complete discontinuation of steroids due to prolonged adrenal suppression.

- Continue hormone replacement as required.

- Monitor endocrine function as appropriate.

- Repeat MRI brain as indicated.

Adapted from Clatterbridge Cancer Centre Guidance.

Developed by Dr Ruth Board and Dr Simon Howell March 2016.

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