RADIATION INDUCED HYPOPITUITARISM

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Definition

- Pituitary is a tiny pea sized gland (master gland) which releases and stores different hormones.
- Hormones are chemicals that coordinate different functions in your body by carrying messages through your blood to your organs, muscles and other tissues.
- Hypopituitarism is a condition in which there’s a lack (deficiency) of one, multiple or all of the hormones made by the pituitary.
Causes of Hypopituitarism

- Tumors in or near the pituitary gland (which are usually benign, meaning not cancerous)
- **Radiation treatment, which can destroy pituitary gland tissue**
- Pituitary surgery
- Traumatic brain injury, such as with a head injury from an accident
- Certain infections such as tuberculosis or meningitis
- Hypophysitis (inflammation of the pituitary gland)
- Conditions that can infiltrate the pituitary gland (example, histiocytosis, lymphoma, hemochromatosis)
- Sometimes, the cause is unknown (called idiopathic).
Radiation induced Hypopituitarism

• Radiation-induced hypopituitarism is insidious, progressive and largely nonreversible.
  – Direct neuronal rather than vascular damage to the hypothalamus (more radiosensitive)
  – Altered neurotransmitter input from other brain centers

• Hypopituitarism

• ~30% of cases following SRT at 5-10 years
• ~30–50% following CRT at 5-10 years
Hypopituitarism: Sequence of hormonal decline

- GH
- FSH/LH
- TSH
- ACTH
Biochemical Work-up

• Morning blood test to check your cortisol

• Thyroid hormone levels

• Morning blood test for testosterone in men

• IGF-1; this reflects your GH levels - not a great screening test

• Pituitary hormone levels such as LH, FSH, prolactin
ACTH DEFICIENCY
Secondary Adrenal Insufficiency

- Fatigue malaise
- Postural dizziness and presyncope
- Gastrointestinal symptoms
  - Nausea
  - Vomiting
  - Diarrhea, abdominal pain
- Joint pain,
- Weight loss
- Loss of libido and irregular cycles
ACTH Stimulation Test

- 250 mcg ACTH[1–24]
  - Baseline, 30 mins, 60 mins
- Testing when AM cortisol levels between 5 and 15 mcg/dl (3-16 mcg/dl*)
- Testing any time of the day
- The cortisol response to ACTH stimulation tests
  - 14 to 15 µg/dL (assay)

* Munro V. The effect of time of day testing and utility of 30 and 60 minute cortisol values in the 250 mcg ACTH stimulation test. Clin Biochem. 2018
Management

- Hydrocortisone usually 15–20 mg total daily dose in single or divided doses (extra for travel)
- “Sick day rules”
- Stress-dose and emergency steroid administration
- Emergency card/bracelet/necklace regarding AI and an emergency kit containing injectable steroids
- Vaccinations

**Table 4.** Dose Equivalence for GCs

<table>
<thead>
<tr>
<th>Equivalent Dose</th>
<th>GCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg</td>
<td>HC</td>
</tr>
<tr>
<td>5 mg</td>
<td>Prednisone</td>
</tr>
<tr>
<td>0.75 mg</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>4 mg</td>
<td>Methylprednisolone</td>
</tr>
<tr>
<td>5 mg</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>25 mg</td>
<td>Cortisone</td>
</tr>
</tbody>
</table>

TSH DEFICIENCY
Secondary Hypothyroidism

- Tiredness
- Mental depression
- Sluggishness
- Feeling cold
- Weight gain (~5-10 pounds)
- Dry skin and hair
- Constipation
- Menstrual irregularities

Secondary hypothyroidism

• TSH may be low/ normal (inappropriately normal)
• FT4 needed for diagnosis
• Levothyroxine early morning fasting, daily medication - monitor FT4 not TSH
• Treat adrenal insufficiency before hypothyroidism - adrenal crisis
• Goal: FT4 in the mid-normal range
FSH/LH DEFICIENCY
Secondary hypogonadism

- Due to abnormal GnRH, FSH, LH
- Women: Amenorrhea, infertility, dyspareunia, hot flashes
- Men: Decreased libido, impotence infertility
- Diagnosis:
  - Estrogen levels in women
  - Testosterone levels in men
  - FSH low or inappropriately normal
Treatment of Hypogonadism

**Men**
- Gonadotropin therapy if fertility desired
- If not, different formulations of testosterone
- Target different with age, comorbidities, elderly, cardiovascular disease

**Women**
- Reproductive age: estrogen/progesterone birth control
- Post menopausal age: consider HRT

GH DEFICIENCY
Adult Growth Hormone Deficiency

- Impaired QOL
- Reduced exercise capacity
- Abnormal lipids, atherosclerosis
- Increased fat mass, decreased lean body mass
- Reduced bone density
Moreover, there is a paucity of data related to rare tumours involving the hypothalamic-pituitary area, such as chordoma, pituicytoma, optic gliomas, and germinomas.
CONCLUSION

• Radiation-induced anterior pituitary hormone deficiencies are irreversible and progressive.
• Regular testing is mandatory to ensure timely diagnosis and early hormone replacement therapy.
• Baseline pituitary hormone assessment, and dynamic testing for GH deficiency should begin one year after RT.
• ACTH deficiency though delayed may be life threatening.
• GH replacement is controversial.
Thank you for your attention!