Severe hypothyroidism presenting as psychosis: a case of myxedema madness

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Objectives

• Describe the presentation, hospital course, and treatment of a patient with myxedema madness

• Describe the association between thyroid function and mental illness

• Discuss the clinical features associated the myxedema state
The Patient Case

• CC: “They forced me here”

• HPI
  – Patient is a 38 y/o African American female brought to the ED due to increased confusion and a change in mental status over the past two months
  – Reported symptoms included frequent staring, social withdrawal, & inappropriate laughter
  – The patient had religious preoccupations
  – She had jumped out of a moving car and refused to get back in resulting in EMS to be called
The Patient Case

- The initial Mental Status Exam
  - **Appearance**: Disheveled, paranoid and agitated with poor eye contact, responding to internal stimuli
  - **Speech**: Spontaneous, rapid, yelling at times
  - **Affect**: Labile, irritable, mood congruent
  - **Thought content**: Religious and persecutory delusions
  - **Thought process**: Tangential and illogical
  - **Judgment and insight**: Poor
  - Alert and oriented only to self
The Patient Case

- Past Psychiatric History: None
  - A similar but less severe episode occurred 10 years ago due to levothyroxine non-adherence

- Past Medical History: Hypothyroidism treated with levothyroxine 150 mcg PO daily

- Family History: None

- Social History:
  - Denied substance abuse/dependence
  - Reported to be high functioning prior to onset of symptoms
  - Employed at a local prison
  - Living with 21 year old daughter
The Patient Case

- Vital signs: BP 157/86; HR 95; RR 18; T 36.7
- Weight: 105 kg
- Laboratory findings:

  - CBC: WNL
  - UDS: negative
  - TSH: 220.52 uIU/mL (ref 0.5 – 5.0 uIU/mL)
  - Free T4: 0.4 ng/dL (ref 0.8 – 1.8 ng/dL)
January 10
• Uncooperative, irritable during interview
• Guarded, paranoid, appeared to be responding to internal stimuli
• Pressured, tangential speech
• Hyperreligious themes
• Denying any psychiatric or medical condition
• Levothyroxine 150 mcg PO daily was restarted; she initially refused
**January 12**
- Spent most of the day reading the bible
- Reported to be disoriented, confused, with rapid speech
- Did not remember any events from the prior day
- Continued to appear to be responding to internal stimuli
- Risperidone 1 mg PO at bedtime initiated → 2 mg on 1/13/2010
- Free T4 = 0.5 ng/dL (ref 0.8 - 1.8 ng/dL)
**Patient Course**

**January 14**

- First day of good eye contact although still somewhat guarded
- No longer appeared to be responding to internal stimuli
- Less spontaneous delusional content but voiced concerns around staff recording phone calls
- Risperidone 2 mg PO at bedtime and levothyroxine 150 mcg PO daily was continued and there was gradual resolution of all symptoms
January 20
• Able to voice an understanding that medication non-adherence most likely led to her psychiatric symptoms
• No paranoid, delusional, or hyperreligious content
• She was discharged the following day with no evidence of psychosis
• Risperidone 2 mg PO at bedtime continued until outpatient evaluation
• Free T4: 0.9 ng/dL (ref 0.8 - 1.8 ng/dL)
Myxedema Coma

- Impaired mental status, hypothermia and symptoms associated with general “slowing” of organ function
  - A medical emergency associated with a 30-40% mortality rate
- Presentation
  - Hypotension, bradycardia, hypoventilation
  - Hyponatremia, hypoglycemia
  - Non-pitting edema of extremities and face
  - Lipid abnormalities
- Causes
  - Undetected/untreated primary hypothyroidism
  - Acute illness (e.g. infection, myocardial infarction)
  - Iatrogenic (sedatives, opioids, amiodarone, lithium)
Neurologic Manifestations

• Generally not coma, despite the name
  – The most common presentation includes confusion, lethargy, and hearing loss

• Myxedema madness
  – Term first appeared in the literature in 1949
  – Psychiatric symptoms can range from subclinical to full psychotic or manic symptoms
  – No symptom cluster is indicative of myxedema madness
  – Most cases are a result of severe hypothyroidism
    • Few cases reported with subclinical hypothyroidism
  – Will generally appear after physical symptoms
    • Months, even years
Suggested Pathophysiology

- 5% - 15% of myxedema patients may experience some degree of psychosis

1) Thyroid hormone favors the brain in hypothyroid states – increasing exposure to T3 receptors found at high concentrations in the limbic system → psychosis in certain “vulnerable” patients

2) May increase in striatal dopamine receptor concentration and sensitivity

3) Increased tyrosine hydroxylase activity in the brain → increase dopamine production

References:

- Prim Care Companion J Clin Psychiatry. 2003; b5:260-66
- Pharmacol Biochem Behav. 1990; 37: 627-32
- Pharmacol Biochem Behav. 1987; 28:193-6
Thyroid Function and Mental Illness

• The relationship between thyroid dysfunction and mental illness dates back to at least 1888
  – Evaluation of thyroid stimulating hormone (TSH) is routine in a patient presenting with psychiatric illness

• *Hyperthyroidism* has been reported to cause both manic and psychotic symptoms

• *Hypothyroidism* has been reported to cause symptoms of depression
  – Described to a far less extent are symptoms of psychosis and/or mania related to hypothyroidism
• Multiple case reports of myxedema madness
  – May initially go unrecognized due to the insidious onset
    • Weeks to years
    • Some cases describe a sudden onset of symptoms
  – Patients’ ages ranged 12 to 73 years
  – Laboratory findings were variable
    • Subclinical hypothyroidism to overt/severe hypothyroidism
  – Clinical presentation is highly variable
    • Manic symptoms
    • Hallucinations, delusions, Capgras syndrome

Aust N Z J Psychiatry. 2010; 44: 292-4
Review of Literature

• Conflicting reports and no clear guidance for use

• Case reports describe four possible scenarios
  1. Improvement with an antipsychotic prior to thyroid replacement therapy
  2. Worsening with antipsychotics alone prior to thyroid replacement therapy
  3. Improvement with thyroid replacement therapy alone
  4. Improvement with thyroid replacement therapy AND concomitant antipsychotic treatment

• Does thyroid replacement therapy plus an antipsychotic improve/expedite outcomes?
Lessons Learned

• The importance of evaluating thyroid function in any patient presenting with a psychiatric illness

• Use of an antipsychotics may be used to treat target symptoms in severe cases

• The importance of medication adherence
  • Role of the pharmacist
Questions?