A Case Study of Violent Psychosis Secondary to Previously Undiagnosed Chemo-Radiation Induced Hypothyroidism

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INTRODUCTION
Hypothyroidism is the most common thyroid disorder, affecting over 5% of the general population worldwide. Defined by high serum thyroid-stimulating hormone (TSH) and low thyroxine (T4) concentrations, hypothyroidism presents with a variety of physical and cognitive symptoms related to thyroidous’s extensive involvement in nuclear and cytoplasmic signaling pathways (See Figure 1). Less commonly appreciated is hypothyroidism’s relationship with psychosis. An often-overlooked differential diagnosis for patients suffering from new-onset hallucinations and delusions, hypothyroidism is a highly treatable cause of secondary psychosis. Coined myxedema psychosis (MP), hallucinations and delusions occur in <2% of patients with hypothyroidism. Meanwhile, 26-37% of MP cases present without any classic signs or symptoms of hypothyroidism, essentially serving as the first manifestation of thyroid pathology. This case describes the emergence of a paranoid, homicidal psychosis in the setting of previously undiagnosed chemoradiation-induced hypothyroidism which promptly responded to levothyroxine therapy.

CASE PRESENTATION
Background
- 68-year-old Caucasian male escorted to ED by police after discharging firearm at home
- Patient was experiencing threatening audiovisual hallucinations of late wife and her “new boyfriend,” prompting him to defend himself from perceived physical harm
- Past medical history: cT3N2c hypopharyngeal SCC 1.5 months s/p 5-week cisplatin chemotherapy and 70 Gy neck radiotherapy
- Psychiatric history: Major Depressive Disorder established 5 months prior to presentation, managed with venlafaxine 37.5 mg BID
- Perceptual disturbances first noted by daughter one month prior, with accounts of paranoia starting weeks before admission
- Somatic complaints: hoarse voice and difficulty ambulating

Examination
- Vitals: hypertensive
- Physical exam: unremarkable
- Psychiatric interview:
  - Appearance: disheveled
  - Attention: impaired
  - Orientation: person, situation
  - Behavior: pleasant, cooperative
  - Mood: depressed, anxious, frightened
  - Affect: congruent
  - Motor activity: grossly normal
  - Speech: soft, latent, intermittently muddled
  - Thought process: disorganized and circumstantial
  - STh: denied by patient
  - Delusions: paranoid, reference
  - Hallucinations: auditory and visual
  - Memory: poor recent and remote
  - Insight/judgment: poor
  - Impulse control: grossly intact
  - Fund of knowledge: intact to conversation
  - Language/vocabulary: normal
  - Cognition: impaired

Work-up
- Blood work: mild anemia, thrombocytopenia, and hyponatremia
- UDS: negative
- Sexually transmitted illness serologies, urinalysis, and vitamin B and D studies normal
- TSH elevated to 115.05 μIU/mL and free T4 depressed to 0.34 ng/dL
- Head CT and brain MRI demonstrated changes consistent with chronic microvascular disease

Initial Management
- Chlorpromazine 2.5 mg nightly started
- Home prescription of venlafaxine changed to 75 mg in the morning for complaints of poor sleep
- Hospital day (HD) #2: oral levothyroxine 100 mcg daily initiated

Hospital Course
- HD#3: onset of abnormal involuntary movements of extremities and face concerning for seizure-like activity
  - EEG: continuous and symmetric background without focal or diffuse abnormalities
  - Neurology consult: manifestation of REM sleep behavior disorder; rasing concern for underlying alpha-synucleinopathy
- HD#4: repeat blood work revealed TSH of 118.672 μIU/mL and free T4 to 0.35 ng/dL
  - Transitioned to IV levothyroxine
- HD#5: significantly diminished hyperkinesia noted
  - Improvements to alertness and mentation continued in coming days while perceptual disturbances became infrequent and less bothersome
- HD#8: TSH and T4 improved to 112.672 μIU/mL and 0.67 ng/dL respectively
  - Transitioned back to oral levothyroxine
- HD#14: patient displayed no residual signs of cognitive dysfunction or psychosis. Discharged home with scheduled endocrinology follow-up and referrals for outpatient polysomnography and neuropsychiatric evaluation

DISCUSSION
- Research suggests psychosis in MP may be due to alterations in neurometabolic activity and monoaminergic messaging
- MP highly responsive to levothyroxine therapy, with time to resolution frequency <2 weeks
- Mean TSH and free T4: 93 μIU/mL [60–139 μIU/mL] and 0.2 ng/dL [0.13–0.39 ng/dL]
- Literature suggests IV levothyroxine may expedite recovery compared to oral therapy
- MP frequently exhibits complete return to neurocognitive baseline post-treatment
- Characterization of MP limited to sporadic case studies given low incidence and atypical presentation
- Validated scales and diagnostic criteria for MP are lacking

CONCLUSIONS
- This case highlights the importance of clinical curiosity more broadly as well as explicitly in cases of chemoradiation therapy.
- By identifying an organic, secondary cause of psychosis in this case, we were able to be more proactive in our management.
- Despite wide variability in presentation and uncomplicated reversibility with levothyroxine therapy, validated diagnostic tools for MP are currently lacking.
- Easily missed in patients without a previous diagnosis of hypothyroidism, further research into MP is needed to better elucidate its underpinnings and avoid future incidences of violence.

BIBLIOGRAPHY