CASE REPORT

'Myxoedema madness' with Capgras syndrome and catatonic features responsive to combination olanzapine and levothyroxine

Maksim A Shlykov,¹ Swapnil Rath,² Alison Badger,² Gerald Scott Winder²

¹University of Michigan Medical School, Ann Arbor, Michigan, USA

²Department of Psychiatry, University of Michigan, Ann Arbor, Michigan, USA

Correspondence to
Dr Gerald Scott Winder,
gwinder@med.umich.edu

Accepted 29 August 2016

SUMMARY

We present the case of an elderly woman with hypothyroidism and no psychiatric history who presented with new onset of psychosis, paranoia, catatonic features and Capgras syndrome (CS). This case illustrates the spectrum of neuropsychiatric symptoms that may accompany hypothyroidism and the importance of considering thyroid dysfunction as a primary contributor to severe psychiatric symptoms, especially in previously stable patients. We demonstrate the effectiveness of combination levothyroxine and olanzapine, with its favourable cardiac profile, in the treatment of myxoedema madness. Antipsychotics can be weaned once psychiatric symptoms resolve and hormone levels are stabilised.

BACKGROUND

Hypothyroidism may present with severe neuropsychiatric symptoms that obfuscate the endocrine aetiology. Psychosis secondary to hypothyroidism is historically termed 'myxoedema madness' (MM).^{1–3} Treatment with levothyroxine alone typically resolves symptoms of hypothyroidism over the period of weeks to months, but psychiatric symptoms are more resistant and tend to take longer to correct. Psychiatric symptoms may take even longer to resolve in the elderly, who tend to be more frail. Further, these symptoms pose a danger to all patients, but especially geriatric patients who may already have difficulties with their activities of daily living. The addition of a select few typical and atypical antipsychotics has been shown to accelerate recovery, but these medications are not benign and have various side effects. It is therefore imperative to identify and treat MM using combination therapy that minimises side effects in order to ensure a prompt return to baseline.

CASE PRESENTATION

A 65-year-old woman with hypothyroidism managed with homeopathic porcine desiccated thyroid extract and no psychiatric history presented to psychiatric emergency services (PES) with a 1–2-month history of depression, insomnia, poor concentration and decreased appetite. Her thyroid-stimulating hormone (TSH) was 100.34 mIU/L with an unremarkable physical examination and mental status examination showing intact cognition (table 1). She did not meet criteria for psychiatric admission and was discharged with recommendations for prompt endocrine and psychiatric follow-up.

A week later, she was evaluated by an endocrinologist who documented paranoia, which led to a 1-week voluntary psychiatric admission at an outside hospital for confusion, depressive symptoms, hallucinations and mutism. Scant records indicated that she was started on 50 µg levothyroxine. Her inpatient laboratories were relatively unchanged and physical examination was unremarkable. She filed a written intent to terminate inpatient treatment and was discharged.

After discharge, she reportedly returned to baseline, but elected to resume her homeopathic thyroid regimen. After a month she ran out of the porcine thyroid extract and roughly 6 weeks post-discharge, the patient disappeared from home and was found wandering in the woods barefoot, responding to commands from the 'devil in (her) stomach'. Again evaluated in PES, clinicians were concerned for her paranoia about being watched and recorded. She also exhibited features of catatonia: stupor, mutism, latency and psychomotor retardation. Her TSH was 61.4 mIU/L and free T4 was 0.43 ng/dL. On physical examination she had partial loss of eyebrows (table 1). She was admitted to general medicine.

INVESTIGATIONS

Workup consisted of thyroid and paraneoplastic antibody levels, brain MRI, EEG and neurology consultation. These laboratory tests and studies were unremarkable, except for antithyroid peroxidase antibodies (TPOAb) that were elevated (table 1).

DIFFERENTIAL DIAGNOSIS

Considering her presentation, lack of psychiatric history, negative workup and similarities of her case to previous case reports on MM, we suspected hypothyroidism as a primary aetiology of her symptoms versus a primary thought disorder.⁴ Considering the patient's normal EEG and normal antithyroglobulin (TgAb) levels, Hashimoto's encephalopathy, was not high on the differential.

TREATMENT

She was started on levothyroxine 50 µg daily (later increased to 100 µg) and simvastatin 20 mg for elevated cholesterol (cholesterol 322 (<200 mg/dL), low-density lipoprotein cholesterol 243 (<130 mg/dL), triglyceride 108 (<150 mg/dL)). The psychiatry consultation team recommended olanzapine 2.5–5 mg orally/intramuscularly three times daily as needed for ongoing paranoia interfering with

CrossMark

To cite: Shlykov MA, Rath S, Badger A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-215957

Table 1 Notable laboratory findings spanning initial PES evaluation to outpatient follow-up after discharge

Test	Date	Result	Treatment status	Psychiatric evaluation	Range
TSH	6/30/15	100.34	Porcine dessicated thyroid extract	Depression, insomnia, poor concentration, decreased appetite, intact cognition	0.3–5.5 mIU/L
	7/6/15	91.61	50 µg Levothyroxine	Depression, paranoia, confusion, hallucinations, mutism	
	7/7/15	99.29			
	8/30/15	61.40	On admission: none Inpatient: 100 µg levothyroxine +10 mg olanzapine daily after titration from lower doses	Admission: psychosis, catatonic features, paranoia Inpatient: Capgras syndrome, but overall gradual improvement of symptoms with only residual paranoia at discharge	
	10/1/15	5.52	100 µg levothyroxine	Unremarkable	
T4	7/6/15	0.7	NA—see corresponding TSH values	NA—see corresponding TSH values	0.76–1.7 ng/dL
	8/30/15	0.43			
Thyroid peroxidase IgG	9/1/15	63	NA—no treatment indicated for this laboratory value	NA—no findings related to this laboratory value	0–30 IU/mL
Thyroglobulin antibody	9/1/15	<63	NA—laboratory within normal limits	NA—no findings related to this laboratory value	Weak +:138–265 IU/L Moderate–strong: >265 IU/L
Autoimmune/paraneoplastic encephalopathy panel*	9/1/15	–	NA—laboratory within normal limits	NA—no findings related to this laboratory value	–/+

*NMDA-R Ab, neuronal (V-G) K+ channel Ab, GAD65 Ab, GABA-B-R Ab, AMPA-R Ab, ANNA-1, ANNA-2, ANNA-3, AGNA-1, PCA-1, PCA-2, PCA-Tr, amphiphysin Ab, N-type calcium channel Ab, P/Q-type calcium channel Ab, ACh receptor (muscle) binding Ab, AChR Ab, AChR ganglionic neuronal Ab, CRMP-5-IgG.
PES, psychiatric emergency services; TSH, thyroid-stimulating hormone.

medical care. ECG showed normal sinus rhythm and a corrected QT interval of 455 ms. After admission to inpatient psychiatry, levothyroxine was continued and olanzapine was scheduled and increased to 10 mg at bedtime.

OUTCOME AND FOLLOW-UP

Paranoia and catatonic symptoms responded modestly to a single dose of olanzapine 5 mg given after the patient eloped from the general medicine unit believing her family members were impostors plotting against her. On day 3 of her stay she was cleared medically, and involuntarily admitted to inpatient psychiatry.

On psychiatric admission evaluation, she was highly guarded to questioning, particularly surrounding the events that led to her admission, vaguely reporting that she was ‘afraid someone was after (her)’. After several days of combination therapy, her paranoia and catatonia improved, allowing her to participate in unit groups and activities. Her Capgras syndrome (CS) resolved, though her thought content continued to be markedly deviated from baseline (corroborated by family) characterised by perceived sensitivities to medications, chemicals and electromagnetic radiation; being monitored and recorded; severe anxiety surrounding all hospital and legal paperwork; and guilt about her hospitalisation negatively affecting her family.

Despite her desire to leave the hospital and discontinue medications, her admission was not changed to voluntary given the outcome of her previous non-adherence. She complied with oral medications at the urging of family and deferred to treatment. Postdischarge care plan included oral antipsychotic and thyroid medications with medical and psychiatric follow-up. She was discharged after 14 days on the psychiatric unit.

At 1-week follow-up, the patient reported having discontinued olanzapine and simvastatin on day 5 postdischarge. She refused all medications other than levothyroxine. She endorsed ongoing mild preoccupation with radiation and chemicals, but otherwise reported improved mood with no significant paranoia or psychosis. She began to attend cognitive-behavioural group therapy for anxiety. Her TSH 1 month postdischarge was 5.52 mIU/L. Her 6-week psychiatric follow-up visit was unremarkable as she remained stable in her improvement.

DISCUSSION

The slowing of metabolic processes and accumulation of matrix glycosaminoglycans in tissues characteristic of hypothyroidism leads to well-known systemic signs and symptoms, including depression, apathy and attention deficits and, less commonly, psychosis, delusions and disorientation. CS and catatonia are two particularly rare points on this symptom spectrum that co-occurred in this patient. No correlation has been demonstrated between the severity of neurological symptoms and the degree of thyroid dysfunction, but symptoms tend to be less appreciable if hypothyroidism develops gradually.⁵ This patient’s physical examination was only remarkable for partial loss of eyebrows despite significant thyroid hormone deficiency. While TPOAb and TgAb levels were obtained, there is no known published evidence for their usefulness in diagnosing MM.

CS is characterised by the belief that people, often close relatives, have been replaced by ‘doubles’ or ‘impostors’. Patients recognise faces, but lack requisite emotional valence for proper perception. CS is believed to arise due to disconnection between the frontal lobes and hippocampus, a site of elevated T3 receptor concentrations, as well as from right hemispheric lesions.^{6–7} While CS has been associated with numerous organic causes, there are few confirmed cases of hypothyroidism with associated CS.^{8–10}

Catatonia was first described as a syndrome characterised by abnormal motor activity, behaviour and speech.¹¹ It does not occur on its own, but rather as a feature of another neuropsychiatric, infectious, metabolic or rheumatological disorder. Hypothyroidism is one such disorder.¹²

The standard treatment for hypothyroidism, once daily levothyroxine, was used in this case as first-line treatment. Not having Food and Drug Administration (FDA) approval, the American Association of Clinical Endocrinologists does not recommend the use of porcine dessicated thyroid extract in hypothyroidism due to insufficient evidence for effectiveness and safety over levothyroxine.¹³ The variable amounts of T3 and T4 in different supplement brands add another unpredictable risk as fluctuating thyroid hormone levels can cause or exacerbate cardiac symptoms, particularly in the elderly. In general, hypothyroidism is associated with increased cardiovascular morbidity.¹⁴

Thyroid hormone replacement gradually resolves most symptoms of hypothyroidism over weeks to months, while psychiatric conditions may persist longer, especially in the elderly.⁴ Previously efforts to hasten the improvement of psychiatric symptoms of MM have included typical (haloperidol) and atypical (risperidone) antipsychotics in addition to levothyroxine.⁴ While this combination therapy has been demonstrated to be effective in young and elderly patients,⁴ elderly patients may benefit the most from this approach due to their vulnerability.⁴

The patient's improvement was most evident after olanzapine was initiated. The patient returned to baseline after nearly 3 weeks of combination treatment with olanzapine and levothyroxine, comparable to response times seen in patients of similar age.⁴ This case stands apart from previous cases, however, in demonstrating the utility of olanzapine as an adjunct treatment of MM. Notably, olanzapine has a favourable cardiac risk profile as compared with other antipsychotics that have been used to treat MM.¹⁵

Learning points

- Organic causes for psychiatric symptoms should be considered, particularly in previously psychiatrically stable patients.
- Olanzapine can be used in combination with levothyroxine to accelerate return to psychiatric baseline.
- Patients with myxoedema madness and known heart dysfunction, arrhythmias or the elderly may benefit from the use of olanzapine in place of another antipsychotic due to its favourable cardiac profile.
- Antipsychotics can be weaned once the patient is back to baseline.

Contributors GSW was the attending physician for the case and is the primary guarantor of the overall content of the article. MAS, SR and GSW provided substantial contributions to the literature review and writing of the report. AB contributed substantially to drafting and revising the report, producing the table, contacting the patient and their family and carrying out extensive chart review. All authors have edited and approved the final manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Asher R. Myxoedematous madness. *BMJ* 1949;2:555–62.
- 2 Osterweil D, Syndulko K, Cohen SN, *et al*. Cognitive function in non-demented older adults with hypothyroidism. *J Am Geriatr Soc* 1992;40:325–35.
- 3 Heinrich TW, Grahm G. Hypothyroidism presenting as psychosis: myxedema madness revisited. *Prim Care Companion J Clin Psychiatry* 2003;5:260–6.
- 4 Hynicka LM. Myxedema madness: a case for short-term antipsychotics? *Ann Pharmacother* 2015;49:607–8.
- 5 Jain VK. Affective disturbance in hypothyroidism. *Br J Psychiatry* 1971;119:279–80.
- 6 Madoz-Gurpide A, Hillers-Rodriguez R. [Capgras delusion: a review of aetiological theories]. *Rev Neurol* 2010;50:420–30.
- 7 Ruel J, Faure R, Dussault JH. Regional distribution of nuclear T3 receptors in rat brain and evidence for preferential localization in neurons. *J Endocrinol Invest* 1985;8:343–8.
- 8 Madakasira S, Hall TB III. Capgras syndrome in a patient with myxedema. *Am J Psychiatry* 1981;138:1506–8.
- 9 Santiago JM, Stoker DL, Beigel A, *et al*. Capgras' syndrome in a myxedema patient. *Hosp Community Psychiatry* 1987;38:199–201.
- 10 Hines A, Stewart JT, Catalano G. A case of Capgras syndrome related to hypothyroidism. *J Psychiatr Pract* 2015;21:445–8.
- 11 Dhossche DM, Stoppelbein L, Rout UK. Etiopathogenesis of catatonia: generalizations and working hypotheses. *J ECT* 2010;26:253–8.
- 12 Iskandar M, Stepanova E, Francis A. Two cases of catatonia with thyroid dysfunction. *Psychosomatics* 2014;55:703–7.
- 13 Baskin HJ, Cobin RH, Duick DS, *et al*. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocr Pract* 2002;8:457–69.
- 14 Klein I, Danzi S. Thyroid disease and the heart. *Circulation* 2007;116:1725–35.
- 15 Beach SR, Celano CM, Noseworthy PA, *et al*. QTc prolongation, torsades de pointes, and psychotropic medications. *Psychosomatics* 2013;54:1–13.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow