Case Report

Dementia of Hypothyroidism in Geriatric Patients

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Abstract

The elderly presenting with cognitive complaints are common and it has always been the standard practice to screen for reversible causes before labelling with a diagnosis of dementia. Thyroid dysfunction is common among the elderly and clinical presentation is often nonspecific. The reversibility of dementia in hypothyroidism is affected by multiple factors, including the duration, aetiology of hypothyroidism and the presence of concomitant dementia aetiologies. It remains important to screen for thyroid function in the evaluation of dementia, as there is evidence to suggest that repletion of thyroid hormone in deficient patients can lead to cognitive improvement.

Keywords: hypothyroidism, dementia, delirium, psychosis

Introduction

As the world population ages, there will be more elderly utilising healthcare resources. Across the hospital setting, the percentage of elderly occupying the acute hospital beds may be as high as 60% in certain disciplines. Among the elderly admitted to a hospital, delirium and dementia are both common comorbidities and are often under-diagnosed. Delirium is often missed, which carries with it high morbidity and mortality. Delirium is known to be associated with iatrogenic complications like in-hospital falls, incontinence, functional decline, prolonged length of stay, increased risk of dementia and nursing home placement. Delirium is considered a medical emergency and it is important to look for acute medical causes including medications [1].

In approaching elderly patients with dementia, it is common practice to screen for potentially reversible causes of dementia prior to making a clinical diagnosis. The laboratory workup for dementia includes testing for thyroid function, serum vitamin B12 and folic acid, and if appropriate, testing for HIV and neurological manifestations of syphilis with a Venereal Disease Research Laboratory test (VDRL) or a Treponema pallidum particle agglutination assay (TPPA). It has been noted that up to 15% of dementias are potentially reversible [2,3].

In this paper, we present 2 cases of hypothyroidism with dementia and discuss the difficulty of diagnosing dementia of hypothyroidism due to a multitude of confounding factors.

Case 1

A 75-year-old Malay woman admitted for worsening visual hallucinations over the past year. She was a retired secretary. Her previous medical history included hypertension, dyslipidaemia and total thyroidectomy for a multinodular goitre a decade ago.
The visual hallucinations have been progressively getting worse, particularly in the week prior to admission. Corroborative history from her family included instances where she described an old woman and a young girl standing in their garden when the garden was empty, and her family overheard her asking the old woman and the young girl to “get lost or she will call the police”. Another instance was when she said there was a woman sitting on the benches outside their house, opened her window and shouted at the empty benches. She would get agitated while hallucinating, occasionally getting violent and throwing objects around the house.

Family reported she had progressive memory loss over the past two years. She asked the same questions repeatedly. A year ago, she was able to retain information for at least half an hour, but in recent months, she was only able to retain information for a few minutes. She had forgotten the names of her relatives and friends. Long term memory was preserved, as she could recall her previous address and previous occupation. She had stopped showering one year ago and her family had difficulty convincing her to take a bath or shower. There were no word-finding difficulties and her family noted she had remained relatively eloquent. She still had a sense of humour and would usually turn questions people asked into jokes when she could not provide an answer. Further history elucidated that the patient has been feeling well and thought she did not need medications. Hence, she defaulted clinic appointments and all her medications for the past 5 years, including levothyroxine.

Physical examination was unremarkable. Her skin was dry, and there was no goitre. She had a hoarse voice which had persisted since her thyroidectomy. She was disoriented to time, place or person, and an Abbreviated Mental Test (AMT) score was 1/10. Laboratory values are shown on in Table 1. Non-contrasted computed tomography of the brain showed background chronic microvascular ischaemia.

The provisional diagnoses include delirium secondary to electrolyte imbalance, dementia secondary to prolonged hypothyroidism and possible Alzheimer’s disease with behavioural and psychological symptoms of dementia (BPSD).

During admission, she was anxious, constantly looking for her husband and became distressed when her husband was not around. She also expressed concern that her husband has not been faithful despite reassurance from her family to the contrary, and constantly requested to be “brought home to Singapore” because she believed she was overseas. She was started on levothyroxine 50mcg OM. She required antipsychotic (haloperidol followed by quetiapine) to manage her psychotic symptoms which resulted in physical and verbal aggression. Antipsychotics were subsequently stopped as her symptoms improved. She exhibited labile mood, ranging from happiness to anxiety to anger to tearfulness throughout the day. A trial of sodium valproate for mood lability was initiated. A repeat AMT performed prior to discharge showed an improvement to 4/10 with these interventions.

When she was reviewed in clinic 4 months after her admission, her TSH had improved (Table 1). She was still confused and had hallucinations but had been less frequent. She was less reactive to her hallucinations and family felt her behaviour was manageable at home.

Case 2

An 83-year-old Chinese man presented with rectal bleeding secondary to haemorrhoids, weight gain and pain over first metatarsal-phalangeal joint secondary to gout flare. He was an ex-carpenter and his medical history included chronic constipation, hypertension, dyslipidaemia and ischaemic heart disease.

He exhibited strange behaviours during his admission, undressing himself and playing with his faeces. Cognitive history from his family noted that he had short term memory loss for over 2 years with aphasia, apraxia and executive dysfunction. He had been found wandering around the house opening and closing doors at night and telling old stories repeatedly.
Physical examination was unremarkable, and he had no goitre. He had dry skin and reflexes were normal. His AMT score was 2/10. Laboratory values are shown in table 1. Thyroid antibody test showed anti-thyroglobulin antibody levels 115.1 IU/ml (normal 0-4) and anti-thyroid peroxidase antibody levels 1856 IU/ml (normal <5.5). Non-contrasted computed tomography of the brain showed background chronic microvascular ischaemia and chronic lacunar infarcts with generalized age-appropriate cerebral involution with no significant lobar predominance or disproportionate hippocampal atrophy.

Provisional diagnoses included Hashimoto’s thyroiditis with hypothyroidism, delirium secondary to acute kidney injury, Haemoglobin drop, gout flare and electrolyte abnormalities and Alzheimer’s disease with BPSD. His behavioural symptoms improved during his stay. He was started on levothyroxine replacement (25mcg OM).

He was reviewed in clinic one month after discharge, and TSH had improved (Table 1). His family informed that he has been more alert, less confused and less lethargic.

**Table 1:** Laboratory findings of both cases

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>On admission</th>
<th>On review</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case 1</td>
<td>Case 2</td>
<td>Case 1</td>
</tr>
<tr>
<td>TSH (mU/L)</td>
<td>0.4-4</td>
<td>109</td>
<td>47.7</td>
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<tr>
<td>Free T4 (pmol/L)</td>
<td>10-20</td>
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<td>Free T3 (pmol/L)</td>
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<td></td>
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<tr>
<td>Serum B12 (pmol/L)</td>
<td>132-835</td>
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<td>352</td>
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<tr>
<td>Serum folate (nmol/L)</td>
<td>&gt;5</td>
<td>15.34</td>
<td>18.42</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>2.8-7.7</td>
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<td>Creatinine (umol/L)</td>
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<tr>
<td>Sodium (mmol/L)</td>
<td>135-145</td>
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<td>139</td>
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<td>Potassium (mmol/L)</td>
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<td>3.3</td>
<td>3.5</td>
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<tr>
<td>Calcium corrected (mmol/L)</td>
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<td>2.06</td>
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<td>Magnesium (mmol/L)</td>
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<td>0.9</td>
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<tr>
<td>Phosphate (mmol/L)</td>
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<td>0.54</td>
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<tr>
<td>C reactive protein (mg/L)</td>
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<td>Haemoglobin (g/dL)</td>
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<td>10.6</td>
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<tr>
<td>Platelet count (× 10³/µL)</td>
<td>150-450</td>
<td>377</td>
<td>199</td>
</tr>
</tbody>
</table>

^TSH for Case 1 and 2 had improved from 109 to 12.2 and 47.7 to 27.6 respectively by outpatient review

**Discussion**

Both hyperthyroidism and hypothyroidism has been associated with cognitive abnormalities [4-6]. In hypothyroidism, both overt and subclinical hypothyroidism have been correlated with poorer cognition [5,6]. Hypothyroidism is a common medical condition and prevalent in the geriatric population. The prevalence of clinical hypothyroidism amongst elderly women ranges from 5-20%, while clinical hypothyroidism amongst elderly men ranges from 3-8%, with autoimmune thyroiditis as being the commonest cause [7,8]. Cognitive dysfunction is a common feature in overt hypothyroidism, occurring in 66-90% of patients with hypothyroidism [9].
While dementia of hypothyroidism is potentially reversible, there is no conclusive evidence to suggest that the cognitive impairment can be completely ameliorated with levothyroxine replacement therapy. The Quality Standards Subcommittee of the American Academy of Neurology recommends the screening for hypothyroidism with a serum TSH in patients with cognitive impairment or dementia in view of high prevalence of hypothyroidism in the geriatric population and the possibility of clinical benefit with replacement [10]. However, due to the ubiquity of Alzheimer’s disease and vascular aetiologies, it is still rare to attribute cognitive abnormalities to aberrant thyroid function, particularly among elderly patients with multiple comorbidities and cardiovascular risk factors.

These two patients with profound hypothyroidism presented with dementia. The first patient had iatrogenic hypothyroidism secondary to a total thyroidectomy, while the second patient had autoimmune thyroiditis. Other causes to consider include iodine deficiency, previous treatment with radioactive iodine, and injury to the anterior pituitary.

Hypothyroidism presents with systemic symptoms such as lethargy, cold intolerance, weight gain, hair loss, dry skin, constipation and hoarseness of voice. Most systemic symptoms of hypothyroidism are non-specific and are only clinically apparent as a syndrome when presenting with multiple symptoms. Neither of our cases had fulminant signs of hypothyroidism, and the only systemic symptoms they manifested were dry skin and chronic constipation, both of which are common symptoms in a geriatric population regardless of thyroid function.

Neurologic manifestations of hypothyroidism may predate, occur simultaneously with, or after the onset of systemic symptoms [9]. In the two patients presented, the systemic symptoms were non-specific, and indistinguishable from any geriatric patient presenting with dementia or cognitive impairment. Since the systemic symptoms were vague, it was difficult for family to relate the onset of cognitive symptoms to presence of symptoms of hypothyroidism. Once again highlighting the utility of screening for thyroid function in such a population.

Cognitive impairment in hypothyroidism is well-described to manifest most commonly as poor short-term memory and concentration, while cortical features such as aphasia and apraxia are absent. Hypothyroidism can also present with other neuropsychiatric symptoms commonly termed as “myxoedema madness”. “Myxoedema madness” is not a well characterized entity, as most descriptions are found in isolated case reports due to its rarity. It can present with varying severity as inattentiveness, lethargy, affective symptoms, and psychotic symptoms such as hallucinations and delusions [10,11]. It has often been mistaken for a primary psychiatric disorder such as schizophrenia, particularly when other systemic symptoms of myxedema are absent [11]. Case 1 exhibited an absence of aphasia consistent with this classic presentation, as well as psychotic symptoms consistent with “myxoedema madness”. Both patients exhibited confusion and disorientation with aberrant behaviours that can be difficult to distinguish from delirium due to other factors or dementia with BPSD.

The pathophysiology of cognitive impairment in hypothyroidism is not well understood, although there is inconsistent evidence from single-photon emission computed tomography (SPECT) and positron-emission tomography (PET) studies to suggest a decrease in cerebral blood flow with concomitant decreased cerebral glucose and oxygen metabolism [13,14]. It should be noted that the computed tomography findings in both case 1 and 2 showed chronic microvascular ischaemia, yet no significant lobar predominance or disproportionate hippocampal atrophy that were expected with other etiologies of dementia.

Previous studies have suggested that in patients with overt hypothyroidism, adequate replacement with levothyroxine improves cognition or even lead to a complete resolution of cognitive impairment [2,6,15]. It has been postulated that the degree of recovery may be incomplete in patients with longer duration of hypothyroidism.
In case 1, patient had defaulted thyroxine replacement in the preceding 5 years, reflected in the extremely high TSH levels on presentation. In case 2, the duration of hypothyroidism is uncertain. The cognitive decline of 2-year duration may or may not be directly caused by hypothyroidism. It has been hypothesized that cognitive impairment due to hypothyroidism of a duration less than 2 years will show significant improvement on replacement of the hormone [12,16]. It is interesting to note that despite the prolonged duration of hypothyroidism in both patients, there was initial improvement in cognition and symptoms after initiating levothyroxine replacement. In case 1, AMT improved from 1/10 to 4/10 while in case 2, AMT improved from 2/10 to 5/10 during their hospital stay. Neither patient showed complete resolution of cognitive dysfunction. This rapid improvement in cognition could also be explained by a resolution of delirium. Complete cognitive recovery may take as long as 1.5 years after the return to a euthyroid state [2]. Neither patient had achieved a euthyroid state even on outpatient review, so it is possible that with sufficient follow-up and given sufficient time, their cognitive deficits may show complete resolution in response to levothyroxine treatment.

Lastly, the natural history of dementia in hypothyroidism is hard to elicit, as it can be confounded by other aetiologies of dementia which are irreversible [2]. It is entirely plausible for a patient to have a mixed dementia with multiple aetiologies, especially among the elderly with multiple comorbidities, and contributed by hypothyroidism. In both cases discussed, it was difficult to rule out a concomitant Alzheimer’s or vascular aetiology, considering their high prevalence in the geriatric population. It is also unclear if hypothyroidism is an independent risk factor for Alzheimer’s disease, as previous studies have shown no conclusive relationship [17,18]. In addition, if cerebral blood flow is in fact mediated by thyroid levels, hypothyroidism may actually predispose patients to vascular aetiologies as well. It can also be difficult to distinguish manifestations of Hashimoto’s encephalopathy from dementia of hypothyroidism, particularly in the context of autoimmune thyroiditis. Furthermore, mood disorders such as depression and anxiety are often associated with hypothyroidism, and mood disorders are also well known to have negative effects on cognition [19].

**Conclusion**

The reversibility of dementia in hypothyroidism is likely dependent on protean factors, including and not limited to the duration of hypothyroidism, the aetiology of hypothyroidism, and the presence of other concomitant aetiologies of dementia. It remains important to screen for thyroid function in the evaluation of dementia in a geriatric population, as there is evidence to suggest that repletion of thyroid levels in deficient patients can lead to partial if not complete resolution of cognitive decline.

**References**