Cognitive decline reversed by cinacalcet

H.J. WALLACE¹, I.R. WALLACE² and P. McCAFFREY¹

From the ¹Department of Elderly Care Medicine, Craigavon Area Hospital, Portadown, BT63 5QQ and ²Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast, BT12 6BA, UK.

Address correspondence to H. Wallace, Craigavon Area Hospital, 68 Lurgan Road, Portadown, Craigavon, Co. Armagh, BT63 5QQ, UK. email: hwallace02@qub.ac.uk

Introduction
An 85-year-old lady with decreased mood and low energy was found to have an elevated serum corrected calcium concentration of 2.8 mmol/L (reference range: 2.1–2.6 mmol/L). Plasma parathyroid hormone concentration was elevated at 390 pg/mL (reference range: 10–85 pg/mL). She had a past history of renal calculi. Renal function, full blood picture, erythrocyte sedimentation rate, 24-h urinary calcium excretion, serum immunoglobulins, chest X-ray and serum angiotensin converting enzyme concentrations were all normal. Myeloma screening was negative. Serum-corrected calcium concentrations fell following rehydration. A thiazide diuretic was discontinued. A sestamibi scan (Figure 1) was unhelpful in pre-operative localization. The patient declined parathyroidectomy.

One year later, she was admitted with dehydration with serum-corrected calcium concentration elevated at 2.93 mmol/L. This did not reduce in response to rehydration or diuretic therapy and had a minimal reduction with intravenous bisphosphonates. MMSE was 21/30 and serum-corrected calcium concentration was 2.85 mmol/L on discharge. Vitamin D concentration was low at 19 nmol/L (reference range: 50–100 nmol/L). She was not commenced on Vitamin D replacement.

The following day, she presented with marked confusion, abdominal pain and decreased responsiveness. CT scan of brain showed no acute changes. ECG was normal, and there were no signs of systemic infection. MMSE was 6/30, and serum-corrected calcium concentration was 2.92 mmol/L. Over the following 12 days, calcium did not reduce in response to repeated infusions of intravenous bisphosphonates. Her functional status had deteriorated and she was now fully dependent in all activities of daily living.

Nursing home placement was being advanced by the family and social services. A trial of the calcimimetic agent cinacalcet was commenced at a dose of 30 mg twice daily. Within 4 weeks, her serum-corrected calcium concentration was 2.15 mmol/L, MMSE was 26/30 and mood and functional status had improved (Figure 2). This lady has now returned to independent living and remains on a maintenance dose of cinacalcet 30 mg twice daily.

Discussion
Hypercalcaemia is common in the elderly and is most often due to primary hyperparathyroidism. We describe a case of intractable primary hyperparathyroidism with predominant symptoms of neurocognitive decline. Normalization of serum calcium with the calcimimetic agent cinacalcet resulted in a reversal of symptoms and a return to independent living.

Primary hyperparathyroidism (HPT) is characterized by chronic hypercalcaemia and an increased or inappropriately normal parathyroid concentration. The majority of patients are described as asymptomatic with a minority describing symptoms of hypercalcaemia. Neuropsychological symptoms are non-specific, and the relationship with

© The Author 2012. Published by Oxford University Press on behalf of the Association of Physicians. All rights reserved. For Permissions, please email: journals.permissions@oup.com
Hypercalcaemia is complex. A recent study demonstrated worse performance on tests of verbal memory and non-verbal abstraction in patients with primary hyperparathyroidism than normal controls. After surgical cure, improvements were seen in some but not all of these aspects of cognition.2

Parathyroidectomy is the treatment of choice in symptomatic individuals and in asymptomatic individuals who meet surgical criteria.3 Cinacalcet is a medical agent approved for the treatment of intractable hypercalcaemia in patients with primary hyperparathyroidism who decline or are unsuitable for parathyroidectomy. It is a calcimimetic agent, which is an allosteric modulator of the calcium sensing receptor, which is strongly expressed on the surface of parathyroid chief cells. It enhances the sensitivity of the calcium-sensing receptor to circulating extracellular calcium, resulting in an increase in intracellular calcium concentration and a reduction in parathyroid hormone secretion.4 It has been shown to be effective at reducing serum calcium concentrations in mild, moderate and intractable primary hyperparathyroidism,5 and 5-year follow-up shows this effect is persistent.6 A study of subjects with intractable primary hyperparathyroidism demonstrated a 17.6% reduction in serum calcium concentration and mild improvements on physical and mental well-being.7

Neuropsychological symptoms and hypercalcaemia are both common in the elderly and often occur together. In these patients, it is difficult to delineate the contributory effects of the hypercalcaemia and any underlying comorbidities. The Third International Workshop on Asymptomatic Primary Hyperparathyroidism suggest that cinacalcet may have a role in future as a therapeutic trial to determine pre-operatively the effects of lowering serum calcium concentration.8 Prior to commencing cinacalcet, the marked cognitive improvement seen in this case was not expected.

**Conclusion**

In this case, cinacalcet resulted in a rapid reduction in serum calcium concentration and a marked improvement in cognition and function. We are unaware of any cases describing such a marked improvement in cognition in response to normalization of serum calcium concentrations. We highlight the potential use of cinacalcet for treatment of intractable hypercalcaemia in patients with primary hyperparathyroidism who decline or are unsuitable for parathyroidectomy. We also highlight the difficulty in ascertaining the relative contribution to cognitive decline of hypercalcemia or a comorbidity.

**Conflict of interest:** None declared.

**References**


