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Hyperthyroidism and dementia

M Dennis, S G Parker

An 84-year-old woman was found to be hyperthyroid in 1986 and was treated with carbimazole. Serum calcium was also raised at 2.71 mmol/l and parathyroid hormone was in the normal range. In 1992 she was admitted to an acute medical ward with a two-year history of increasing and fluctuating disorientation, forgetfulness, lethargy and constipation. Serum total calcium was found to be 3.3 mmol/l, parathyroid hormone was elevated at 30 pmol/l, but neck ultrasound was normal. As the serum calcium settled to 2.9 mmol/l, the mental symptoms were felt not to be resulting from the hypercalcaemia. The patient was discharged home with additional support.

In 1994, she was referred as an out-patient to a physician for the elderly, now with a four year history of forgetfulness with a marked deterioration over the preceding seven months. She had become disorientated in time and place, suspicious, was neglecting herself, and frequently failed to recognise familiar persons. This picture was characterised by considerable day-to-day variation. She was supported in her flat by her family, five days per week home care, and meals-on-wheels. Accompanying the cognitive decline were symptoms of worsening urinary incontinence, and increasing deafness. Admission was arranged for further investigation and treatment. The serum calcium fluctuated between 2.74 and 3.2 mmol/l. Thyroid function, and investigations to exclude malignancy and delirium were all normal. At this time she appeared alert, though disorientated in time, with poor recall and concentration.

Questions

- 1 What is the most probable diagnosis?
- 2 How can a causal link between the diagnosis and the presence of cognitive impairment be established?
- 3 What is the management?

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Answers

QUESTION 1

Dementia secondary to hyperparathyroidism. Both primary hyperparathyroidism and irreversible cortical dementias are common in older patients. Reversible or arrestable causes of global cognitive impairment, however, frequently present with a fluctuating history, indicative of a subacute delirium, rather than the gradual deterioration seen in Alzheimer's disease.¹ In this particular case the variability in mental functioning may well have been due to fluctuating serum calcium levels. It is important that patients with hyperparathyroidism and impaired cognitive function are not labelled inappropriately as having asymptomatic primary hyperparathyroidism and irreversible cortical dementia, as this may lead to unnecessary delays in diagnosis and treatment. Elderly people may be more susceptible to the neuropsychiatric effects of hypercalcaemia; in a small series of elderly patients surgically treated for primary hyperparathyroidism, Heath *et al* found no relation between the degree of hypercalcaemia and presence of dementia.² Joborn *et al* similarly describe 13 elderly patients (mean age 73 years) with mild or moderate hypercalcaemia (mean serum calcium 2.93 mmol/l) associated with severe cognitive impairment.³

QUESTION 2

Treatment for hyperparathyroidism will clearly not significantly improve cognition in patients with underlying irreversible cortical dementia such as Alzheimer's disease, or vascular dementia. It is therefore important to obtain clear evidence of improved cognitive function following treatment of hypercalcaemia. In this case serial cognitive assessment using two simple and sensitive measures, the Mini-Mental State Examination (MMSE)⁴ and clock drawing⁵ were able to provide strong supportive evidence for linking the hyperparathyroidism with the patient's cognitive impairment. On admission MMSE score was 21/30 (figure 1) and there were also minor abnormalities on clock drawing (figure 2A). She was initially treated with intravenous fluids and pamidronate, and one week later, when serum calcium had returned to within the normal range, MMSE was 22/30. She was discharged with increased support at home and oral disodium etidronate. At one month follow-up the patient appeared cognitively intact with an improved MMSE score of 28/30 and normal clock drawing (figure 2B). There was clearly a time lag of some weeks before mental function returned to normal following the reduction in serum calcium. It is therefore important to follow up the patient for sufficient time in order to establish a causal link.

QUESTION 3

Once hyperparathyroidism has been established as responsible for the cognitive impairment it is important to consider surgical parathyroidectomy. Improvement in mental function after surgical treatment for hypercal-

Figure 1 Serial measurements of serum calcium and cognitive function, illustrating the inverse relationship between the two

Figure 2 Examples of clock drawing during hypercalcaemia (A and C), and normocalcaemia (B and D)

caemia is well recognised.^{2,3} In this case, following the initial reduction of serum calcium with intravenous fluids and pamidronate, the patient was maintained on oral disodium etidronate. Unfortunately, she was poorly compliant with medication, and was re-admitted to hospital two months following discharge with a clinical picture of delirium, declining mobility, and worsening incontinence. She was mildly clouded in consciousness with poor attention and concentration, disorientation, marked memory impairment, dyspraxia with poor clock drawing (figure 2C), and a MMSE of 8/30. Serum calcium was 3.66 mmol/l, parathyroid hormone was raised at 54 pmol/l, but with normal neck scan and thyroid function. The patient was therefore referred for surgery and, at operation, three enlarged parathyroid glands were found, two of which were excised. Calcium returned to normal within a week. Her mental state

Learning points

- hyperparathyroidism is a potentially reversible cause of global cognitive decline in the elderly
- dementia may occur in hyperparathyroidism with only mildly elevated serum calcium
- serial assessment of mental state and serum calcium whilst pharmacologically treating hypercalcaemia is important in establishing a causal link
- cognitive improvement may 'lag' behind reduction in serum calcium by some weeks

gradually improved, with MMSE of 20/30 three weeks postoperatively, and 23/30 after five weeks. She was discharged six weeks post-

operatively to residential care, at which time she was independently mobile, dressing herself, and requiring minimal prompting with hygiene. Continence had also improved with only occasional wetting at night. Two months after the parathyroidectomy her mental state had improved further with a MMSE score of 25/30 and normal clock drawing (figures 1 and 2D). Review six months later confirmed the clinical improvement.

Final diagnosis

Reversible dementia secondary to primary hyperparathyroidism.

Keywords: dementia; hypercalcaemia; hyperparathyroidism

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Multiple ileal perforations

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A 28-year-old man presented with fever (one month), abdominal pain (two days) and constipation (two days). Physical examination was suggestive of perforation with peritonitis. Scout films confirmed gas under the diaphragm and his chest X-ray was normal. Widal test was positive (1/250 titres) and blood culture sterile. Exploration revealed a small perforation in an indurated terminal ileum with frank fecal peritonitis. The perforation was closed in two layers.

On the fourth postoperative day, the patient developed a fecal discharge from the drain site. Re-exploration revealed multiple perforations in the terminal ileum; the most distal at the ileocecal junction. The terminal ileum (with 15 cm of healthy gut) and ascending colon were excised and both ends were exteriorised. Biopsy from the wall of perforation, sent initially, was reported to be nonspecific. Three days later, the patient again had fecal discharge from the wound. Another re-exploration revealed a fresh crop of perforations in the ileum and colon (near the resected margins). The involved gut was resected and both ends were again brought to the surface. Adequate supportive care was given in form of blood, plasma, albumin and intravenous lipids. Despite all these enthusiastic measures, the patient again developed a fecal fistula and succumbed on the third postoperative day. The biopsy report of the specimen sent at second surgery was received on the day of his death and revealed caseating granulomas in the excised tissue.

Question

What is the most likely cause of the gut perforation?

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