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CASE REPORT

Therapeutic challenges in elderly patients with symptomatic hypercalcaemia caused by primary hyperparathyroidism

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ABSTRACT

Background: Hypercalcaemia resulting from primary hyperparathyroidism (PHPT) can cause a wide range of symptoms, including cognitive disorders, psychiatric symptoms and muscle weakness. Parathyroid surgery is the only definite cure for PHPT. When surgery is contraindicated or patients decide against it, several non-surgical treatment options are available.

Objective: To illustrate the treatment options of symptomatic hypercalcaemia caused by PHPT in the elderly and discuss these options in consideration of the available evidence.

Design: Consecutive case series.

Setting: University hospital.

Patients: Four older patients aged 79-87 years with symptomatic hypercalcaemia resulting from PHPT.

Results: Three patients had a parathyroid adenoma shown on a sestamibi scan. Normocalcaemia and resolution of symptoms was achieved by different treatment scenarios encompassing forced saline hydration, forced diuresis, intravenous pamidronate and cinacalcet, a calcimimetic drug. In one patient, no parathyroid abnormalities were revealed with imaging. Treatment with cinacalcet resulted in normocalcaemia and a strong improvement of symptoms.

Conclusion: In clinical practice, different treatment scenarios are chosen for the treatment of elderly patients with symptomatic hypercalcaemia caused by PHPT. The introduction of cinacalcet offers a new treatment paradigm. We propose to apply cinacalcet preceding elective surgery as an alternative option to standard therapy or as maintenance dose when surgery is not possible.

KEYWORDS

Calcimimetics, drug therapy, elderly, hypercalcaemia, hyperparathyroidism

INTRODUCTION

Hypercalcaemia resulting from primary hyperparathyroidism (PHPT) is one of the reversible causes of cognitive disorders in the elderly.[1] Apart from cognitive disorders, a wide range of other symptoms can occur, including psychiatric symptoms and muscle weakness.[2-4] Associated complications of PHPT include nephrolithiasis and osteoporosis.[3,4] Consequently, these symptoms and complications can cause a significant impairment in cognitive and functional status, and wellbeing. Efficient diagnosing and adequate treatment can prevent and resolve these problems. In most patients (99%), the cause of PHPT is benign, particularly a single adenoma (85%).[3,5] Different advanced imaging techniques are available, including CT imaging and sestamibi scanning, but in practice results are not always conclusive. A DEXA scan for diagnosing osteoporosis as an adverse effect of hyperparathyroidism is only necessary if certain other risk factors are present, such as a previous fracture, low body weight, etc., in accordance with the CBO guideline for osteoporosis and fracture prevention 2011.[6] Once PHPT is diagnosed, there are several treatment options, all with their specific advantages and disadvantages.[2,5] To illustrate these therapeutic challenges in clinical practice, we present four elderly patients with symptomatic hypercalcaemia caused by PHPT with their specific treatment scenarios.

Furthermore, we discuss the treatment options of symptomatic hypercalcaemia in elderly PHPT patients in consideration of the available evidence.

METHODS

Case series of four elderly patients with hypercalcaemia resulting from PHPT admitted to the University Medical Center Utrecht, between November 2008 and July 2009.

ILLUSTRATIVE CASE REPORTS

An 84-year-old woman was admitted because of low back pain, nausea, cognitive disorders including confusion, a failing short-term memory and hallucinations, muscle weakness and a depressed mood. She had a history of a hip fracture and osteoporosis. Investigations included a raised ionised calcium of 1.46 mmol/l (reference values 1.15 to 1.32 mmol/l), parathormone of 14 pmol/l (1-6 pmol/l) and 1,25-di-OH-vitamin D of 267 pmol/l (47.0 to 130.3 pmol/l). The calcium and vitamin D suppletion were stopped. Spinal MR imaging showed old wedge fractures (Th10-12, L5), while CT imaging and a sestamibi scan revealed a sub-aortic mediastinal parathyroid adenoma. Symptomatic treatment with the calcimimetic drug cinacalcet was started. After consultation with a surgeon, elective parathyroidectomy was planned and the patient was discharged in a relatively good condition. Within three weeks, acute readmission was necessary because of progressive nausea, probably a side effect of cinacalcet. After uncomplicated parathyroidectomy, calcium and parathormone levels normalised and symptoms largely attenuated.

A 79-year-old woman with a history of coeliac disease, secondary osteoporosis, hyperparathyroidism and a hip fracture was admitted because of a persisting ionised hypercalcaemia (1.48 mmol/l) and raised parathormone (19 pmol/l) with a normal 25-OH-vitamin D (31 nmol/l). Symptoms were progressive confusion, muscle weakness and under eating. Calcium and vitamin D suppletion had already been stopped six months before admission. CT imaging and a sestamibi scan revealed no parathyroid abnormalities. Treatment with cinacalcet resulted in normalisation of the ionised calcium (1.16 mmol/l) and a strong improvement of the cognitive and mobility problems. Surgical treatment was not performed.

An 80-year-old woman with known diabetes mellitus and hypertension was admitted because of symmetrical muscle weakness and fluctuating confusion. Laboratory investigations revealed a raised ionised calcium (1.65 mmol/l) and parathormone (19 pmol/l) with a normal 25-OH-vitamin D (53 nmol/l). Evidence for a parathyroid adenoma located caudodorsally to the thyroid gland was found on a sestamibi scan. Echography and a CT scan did not reveal parathyroid pathology. Treatment with forced saline hydration, forced diuresis and intravenous pamidronate resulted in normalised calcium with total resolution of symptoms. Two months later, uncomplicated parathyroidectomy was performed.

An 87-year-old woman was admitted because of confusion and repeated falls. She had an extended history with multiple bone fractures caused by falls since the age of 50, osteoarthritis, osteoporosis and a transient ischaemic attack. A sestamibi scan was performed because of an increased ionised calcium (1.56 mmol/l) and parathormone (9.6 pmol/l). This revealed a parathyroid adenoma located caudodorsally to the thyroid gland. Forced saline hydration did not result in sufficient reduction of the calcium level. Subsequent treatment with cinacalcet resulted in normalisation of the calcium with disappearance of symptoms. Two weeks later, successful parathyroidectomy was performed.

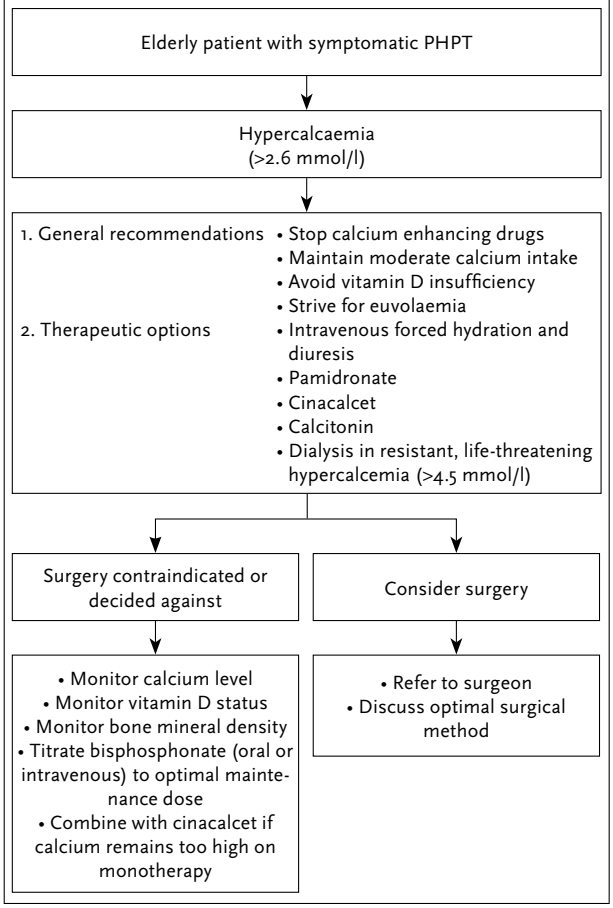
DISCUSSION

This case series illustrates different therapeutic scenarios in elderly patients with symptomatic hypercalcaemia caused by PHPT applied in clinical practice.
Recently, several reviews have focused on the current available treatment options in the management of patients with PHPT.[1,2,5] Sims *et al.*[1] report that the indications for parathyroid surgery, encompassing hypercalcaemia, renal disease, bone disease, abdominal or neuropsychiatric symptoms, are not changed by advancing age. Parathyroid surgery is the only definite cure for PHPT, but the risks and benefits of surgery need to be extensively considered in the elderly given their more fragile status and comorbidity. Preoperative imaging with echography, CT and sestamibi scans may help in the decision to offer surgery.[7] When surgery is contraindicated or patients decide against it, different non-surgical alternatives are available.[1,2] For acute treatment of severe hypercalcaemia, intravenous saline solution loop, diuresis and bisphosphonates are recommended.[2] Subcutaneous calcitonin is also an option, but its efficacy is limited to the first two days.[2] Cinacalcet, a calcimimetic drug, lowers PTH secretion by enhancing receptor sensitivity to extracellular calcium. Normocalcaemia can be achieved after one day of treatment, the response to cinacalcet can be persistent and cinacalcet is generally well tolerated.[4,8,9] The most common adverse events are nausea, vomiting and paresthesias.[10] Raloxifene and oestrogen therapy are

not recommended as first-choice treatment for elderly women because of the marginal effects on hypercalcaemia and the associated adverse events and risks.[1,4] General recommendations include avoidance of calcium-enhancing drugs (e.g. thiazide diuretics and lithium carbonate), of volume depletion by encouraging patients to drink sufficiently, and of vitamin D insufficiency.[5] Vitamin D deficiency stimulates PTH secretion and bone resorption. A low calcium diet may lead to further increases in PTH secretion and could aggravate bone disease. Moderate calcium restriction (<800 mg/day) is probably warranted when the serum vitamin D levels are high. In cases of resistant, life-threatening hypocalcaemia (>4.5 mmol/l or >18 mg/dl) haemodialysis against a low-calcium dialysate is necessary.

Given the available evidence and recommendations, our case series illustrates that different scenarios are chosen in clinical practice for the treatment of elderly patients with symptomatic hypercalcaemia caused by PHPT. However, little literature is available about medical treatment of symptomatic hypercalcaemia specifically in the elderly. No evidence-based recommendations have been made concerning the alternative treatment options besides surgery for this patient group. Conroy *et al.* (2003),[11] Boonen *et al.* (2004)[12] and Sims *et al.* (2004)[1] discussed the nonsurgical management of primary hyperparathyroidism in older patients, but the best treatment of symptomatic hypercalcaemia remained unclear and no algorithm was presented which encompasses current medical treatment options for elderly patients. The authors concluded more randomised controlled studies are necessary to provide recommendations concerning treatment of PHPT in the elderly, mainly for calcimimetics. Nowadays, cinacalcet seems a promising and relatively safe drug for the management of hypercalcaemia, as recent randomised double-blind placebo-controlled trials showed that cinacalcet normalises calcium and lowers serum PTH with similar rates of adverse events between treatment and placebo groups, but no effect on bone mineral density.[8-10] Recently, Aw[13] reviewed surgical and nonsurgical treatment options in the elderly and presented a short summary algorithm without focus on treatment options before elective surgery. However, a stepwise algorithm combining the treatment options of symptomatic hypercalcaemia in elderly patients before elective surgery as well as the treatment options when surgery is contraindicated is useful in clinical practice. Thus, we present a stepwise therapeutic algorithm for the management of elderly patients with symptomatic hypercalcaemia caused by PHPT (*figure 1*). In this algorithm, the introduction of calcimimetics offers a new treatment paradigm given the relatively fast mode of action and infrequent undesired effects. We propose to apply cinacalcet in symptomatic hypercalcaemia preceding elective surgery as an alternative option to the standard therapeutic strategies or as maintenance dose when surgery is contraindicated or decided against. Definite determination of the most appropriate treatment regimen for cinacalcet in elderly patients with symptomatic hypercalcaemia caused by PHPT, however, is not yet completed,[5,14-16] as more evidence is needed concerning both its short- and long-term efficacy and adverse events.

Figure 1. *Therapeutic algorithm for the management of elderly patients with symptomatic hypercalcaemia caused by primary hyperparathyroidism (PHPT)*



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