A 66-year-old woman with osteoporosis and hyperparathyroidism

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This section is about the immediate management and investigation of an acute presentation in general practice. It is inspired by, but not based on, a real patient situation.

Maree is a 66-year-old woman who you have seen recently for fatigue and joint aches. You know her from occasional consultations over many years. She has felt more nonspecifically unwell in the past few months and is worried something is wrong with her health. On questioning, she reports no other specific symptoms. Her examination is normal apart from some asymptomatic osteoarthritis in her fingers. She is slightly overweight and not very fit. She takes no medications and is a lifelong nonsmoker and nondrinker. She has not had any blood tests carried out for several years.

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What investigations would you order for Maree's symptoms and why?

Answer: Investigations should be directed towards her symptoms. They should include: a full blood count; measurement of levels of electrolytes, urea and creatinine, blood glucose, thyroid-stimulating hormone, serum and corrected calcium, vitamin D, parathyroid hormone (PTH), serum vitamin B_{12} and C-reactive protein; liver function tests; iron studies; and rheumatoid factor and antinuclear antibody tests. These tests screen for anaemia, iron deficiency, vitamin B_{12} deficiency, thyroid disease, common autoimmune diseases, disorders of calcium metabolism, liver and kidney disease and diabetes. Results would direct further investigations if needed. Measurement of creatine kinase level may be ordered if Maree is taking a cholesterol-lowering medication. It would be reasonable to also measure fasting cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride levels.

Coeliac disease serology and immunoglobulin studies should be considered but, in the author's opinion, are not first line tests at this stage. You should remind Maree to have a Pap smear, breast exam and mammogram. A bone density scan can be postponed in case she has any medical indications on blood testing that would fulfil a Medicare rebate.

Test results are normal apart from a vitamin D level of 28 nmol/L (moderately severe deficiency, normal range over 50 nmol/L), calcium level 2.7 mmol/L (reference range: 2.10 to 2.55 mmol/L), corrected calcium level 2.85 mmol/L, and PTH level 7.55 pmol/L (reference range: 1.0 to 7.0 pmol/L. Similar findings are found on repeat biochemical testing.

What investigations and management would you arrange next?

Answer: The findings are consistent with primary hyperparathyroidism and secondary vitamin D deficiency. Measurement of 24-hour urinary calcium excretion is required to exclude familial hypocalciuric hypercalcaemia (FHH). A family history of any symptoms and conditions relevant to this diagnosis should be taken (it is characterised by mild–moderate hypercalcaemia, PTH in the upper reference range or mildly elevated, marked renal calcium conservation and a family history of hypercalcaemia). Some cases of primary hyperparathyroidism are familial and should be considered. Once FHH is excluded and primary hyperparathyroidism is confirmed, Maree should definitely have a bone density scan and she now fulfils criteria for a Medicare rebate. If her condition is not going to be managed conservatively, she should also have a dual phase sestamibi parathyroid scintigraphy scan of her neck to guide surgery. It is likely she has a single parathyroid adenoma, given the unsuppressed PTH level. Sporadic parathyroid adenomas are the most likely cause of primary hyperparathyroidism; parathyroid hyperplasia is uncommon, and cancer of the parathyroid gland is very rare. An ultrasound examination of her neck will not necessarily identify parathyroid abnormalities, particularly those present in the upper chest behind the sternum and ribcage, and therefore is not indicated. Maree should begin taking vitamin D supplements immediately, for example, cholecalciferol 1000 IU three times daily. Provided she can take these with a meal rich in calcium or dairy products she does not need to take calcium supplements.

Maree has a bone density scan and the findings (T-score of -2.62 in the hip and -2.45 in the spine) suggest a diagnosis of osteoporosis. Her sestamibi parathyroid scan shows changes consistent with a single parathyroid adenoma of 1.3 cm diameter to the right and under the sternal notch inferiorly.

What do you tell Maree about her condition?

Answer: Maree should be informed that parathyroid adenomas are common and are

responsible for her raised calcium and PTH levels and the significantly reduced vitamin D level (which is typical but not essential in this condition). The condition occurs in more than one in 1000 postmenopausal women. The raised calcium level may be contributing to her symptoms: joint aches, fatigue and feeling non-specifically unwell. It can also can cause constipation, kidney stones, poor sleep, irritability, poor concentration, memory problems and depressed mood. It is also important to tell Maree that the raised calcium level may not be the only reason for her feeling unwell recently, although at this stage you have uncovered no other cause.

You discuss with Maree the need for surgical removal of the abnormal gland and arrange a referral to an endocrine or head and neck surgeon experienced in parathyroid disease. Maree will also need to see an endocrinologist before the operation to confirm her diagnosis and to provide physician support for her perioperative care. Her blood calcium level will be monitored closely for a few weeks after surgery.

When is parathyroid surgery indicated for hyperparathyroidism?

Answer: This is indicated in any patient with hyperparathyroidism who is well enough to have surgery and has a life expectancy long enough for surgery to be an option. The criteria from international guidelines indicating surgery include: age less than 50 years; presence of osteoporosis; a history of renal calculi or elevated 24-hour urinary calcium excretion; or severe hypercalcaemia (with corrected calcium ≥3.2 mmol/L). Timing of the surgery becomes more urgent with higher calcium levels and with more symptoms and complications (e.g. osteoporosis, constipation, renal calculi, high 24-hour urine calcium or hypertension).

Maree wants to know how to minimise the risk of her osteoporosis worsening. What do you tell her?

Answer: You should explain what osteoporosis is and that the bone loss may be halted by reversing the cause (removal of the parathyroid adenoma) and by using specific medications, if required. It is likely she will gain a few percent annually in bone mass across consecutive years following parathyroidectomy and cure of her primary hyperparathyroidism. She should have bone density testing annually at first and then every two years. You could also discuss with her minimisation of falls risk, for example by modifying her home environment and footwear, and the potential effects of certain medications (e.g. psychotropic or antihypertensive agents).

What do you tell Maree about the causes of her osteoporosis?

Answer: It is wise not to assume that the hyperparathyroidism is the only cause of the osteoporosis or fatigue. Depending on her other test results and postoperative course, other causes should be excluded. Causes of osteoporosis include genetic factors, ageing, oestrogen deficiency (in women), testosterone deficiency (in men), exogenous or endogenous corticosteroid excess, premature menopause, serious eating disorders, hyperthyroidism, hyperparathyroidism, adrenal and pituitary disease, chromosomal abnormalities, malabsorptive conditions (especially coeliac disease), rheumatoid arthritis and multiple myeloma.

Other risk factors include being slim or underweight, smoking, drinking alcohol to excess, certain medications, lack of weight-bearing exercise, prolonged bed rest and sedentary behaviour.

Outcome: Maree consulted the endocrine surgeon and subsequently underwent an uncomplicated parathyroidectomy. She recovered well without symptomatic hypocalcaemia and continues on a dose of 2000 IU cholecalciferol. She is yet to discuss further treatment options for osteoporosis with the endocrinologist. However, after excluding other causes of low bone density, no specific further therapy may be required following parathyroidectomy except for the optimisation of her 25(OH) vitamin D level and elemental calcium intake. ET

Common fallacies: parathyroid disease, vitamin D and calcium metabolism

- **PTH level must be raised in cases of primary hyperparathyroidism in the presence of a raised corrected serum calcium level.** If the PTH level is not raised but still in the 'normal' reference range, it is inappropriately high for the raised corrected serum calcium level. Hence, primary hyperparathyroidism is still the most likely diagnosis if the corrected calcium level is raised.
- **25(OH) vitamin D level must be very low in cases of primary hyperparathyroidism.** It often is but may also be mildly low or in the normal range.
- **A raised serum calcium is always abnormal.** Total calcium may be modestly raised in the presence of high blood albumin levels (e.g. with dehydration). The corrected serum calcium is of more diagnostic significance as it takes serum albumin level into account.
- **Vitamin D intake should be supplemented in the presence of a high PTH level and both reviewed at a later date.** The vitamin D level takes 3 to 4 months to normalise in the absence of hyperparathyroidism.
- **Vitamin D supplementation is safe in patients who have vitamin D deficiency and primary hyperparathyroidism.** This is correct. This approach when undertaken preoperatively may also help to prevent the postoperative condition of 'hungry bones syndrome', in which transient symptomatic hypocalcaemia occurs likely because of a bony deficit in calcium.
- **A normal sestamibi parathyroid scan excludes hyperparathyroidism.** This scan is performed to guide surgical intervention. Sometimes it may appear falsely normal, especially if the adenoma is small or inactive. In such instances, a 4D CT scan may have greater sensitivity. Before parathyroidectomy, an experienced endocrine surgeon should be consulted.