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Patient Information
Primary Hyperparathyroidism

The Parathyroid Glands

There are four parathyroid glands, and they lie at the base of the front of the neck, one behind the upper and lower poles of the lobes of the thyroid. The parathyroid glands are intimately involved with maintaining calcium balance in the body. When the blood calcium (serum calcium) falls the glands secrete parathyroid hormone (PTH), this quickly brings calcium from the skeleton and increases both calcium excretion and reabsorption in the kidney to raise the serum calcium and restore the balance. Should the calcium be elevated PTH secretion is suppressed allowing the serum calcium to fall. PTH also increases the conversion of inactive vitamin D to active vitamin D (calcitriol) within the kidney, the calcitriol helping increase calcium absorption from the gut.

Primary hyperparathyroidism

Primary hyperparathyroidism (PHPT) occurs when PTH production becomes autonomous.

Mostly of the time (80 – 85% of patients) this is a single parathyroid gland that forms a parathyroid adenoma. They are generally sporadic though very rare cases might run in families.

Familial disease, occurring in 10 – 20% of cases, usually involves all the parathyroid glands, which are hyperplastic, rather than one being an adenoma. The familial conditions are multiple endocrine neoplasia (MEN), hyperparathyroidism-jaw tumour syndrome and familial hyperparathyroidism. Any family history of PHPT should stimulate a consideration of familial disease.

Diagnosis

In the developed world PHPT is now usually diagnosed because the serum calcium has been checked within routine bloods, found to be elevated then investigated, this is the case in about 80% of patients. PHPT is the most common cause of hypercalcaemia in this situation.

In resource poor environments however patients still normally come to attention because of symptoms, this is the case in >80% of patients.

What symptoms and signs might the patient have?

The classical description, from when patients presented with symptoms, was 'bones, stones, groans and psychic moans', but as patients are diagnosed earlier these symptoms are less pronounced.

However even at quite modest elevations of the serum calcium the patients might feel subtly unwell, it can be difficult for them to put their finger on and because it can be difficult to describe to their doctor, or for the doctor to appreciate, symptoms might not receive due attention. These common symptoms are fatigue, poor sleep, lassitude and inner tension. The relationship between increasing calcium and increasing symptoms is not completely clear but by and large as the calcium increases even modestly one may expect to find bone pain, muscle pain and/ or cramps, memory loss, anxiety, constipation, nocturia (passing urine at night out of the ordinary for that patient), polyuria (passing excessive urine during the day) and thirst, parasthesiae (abnormal sensations, often in the peripheries), depression, to the rarer frank neuromuscular dysfunction, abdominal or loin pain and unsteady gait now being rarities with very elevated calcium.

There may be a history of osteopaenia or osteoporosis, including fragility fractures at the wrist, hip, pelvis and vertebrae – leading to loss of height and/or kyphosis (forward curvature of the spine), and patients may have had or be suffering with renal stones.

A family history of renal stones, premature osteoporosis, previous neck surgery and hyperparathyroidism may help draw attention to familial disease.

If there is a hard, dense neck mass one must immediately be suspicious of parathyroid cancer especially if the calcium and PTH are markedly raised. Palpable neck masses otherwise are more likely to be the thyroid.

Whom is PHPT most common in?

PHPT is more common in women (1:500) than men (1:2000) and is found between the ages of 50 – 60 years. Lithium treatment increases the risk. There is a weak link to previous head and neck irradiation.

Other diagnoses to consider

Generally the finding of hypercalcaemia with an elevated PTH diagnoses PHPT. However this picture can also be found with an uncommon genetic condition – familial hypocalciuric hypercalcaemia (FHH) – so the doctor will need to demonstrate an elevated urine calcium (often corrected for the patient's kidney function) to exclude this condition. FHH often runs in families, the patients appear healthy, do not get stones or bone disease and are not cured by parathyroidectomy. Genetic testing can confirm this diagnosis.

The other important diagnoses for the doctor to consider are cancer (humoral hypercalcaemia of malignancy), multiple myeloma, lymphoma and leukaemia, sarcoidosis, milk alkali syndrome, excessive vitamin D intake, thyrotoxicosis, hypercalcaemia secondary to thiazide diuretics, immobilisation

Diagnostic Tests

The diagnosis is confirmed by finding a high calcium with inappropriately detectable or elevated PTH; this will generally need to be repeated at least once; the patient should not be taking thiazides; lastly inappropriately elevated urine calcium excretion must be present. The higher the urine calcium the more the case for surgery is made. If appropriate dedicated imaging of the kidneys may be done to look for stones or renal calcification – again making the case for surgery more clearly.

Vitamin D is often measured, because vitamin D deficiency can raise the PTH – because the body not being able to get calcium from the gut has to use PTH to get it from the skeleton; the general bloods may show a low phosphate and alkaline phosphatase if elevated, can indicate the extent of bone disease.

Only if the patient would consider an operation, or wishes to have the information to make a more informed decision on the pros and cons of an operation, should parathyroid localisation studies be done. Generally this requires two separate imaging techniques to be used, sestaMIBI (a nuclear medicine scan) scanning and ultrasonography is the most common pairing. The MIBI scan can be improved with single-photon emission CT, very dedicated neck CT can help and in some patients and centres MRI is used.

The bone density will often be assessed using dual energy X-ray absorptiometry (DXA), and if it is low it can help make the case for

Treatment

Parathyroidectomy

If the patient is symptomatic or asymptomatic but has other indications for surgery the parathyroidectomy should be considered/ performed. The most important thing is finding a surgeon who is experienced in parathyroid surgery, that surgeon should have good outcomes and will work closely with the endocrinologist and diagnostic imaging; the surgeon should be able to consider minimal access surgery in appropriate cases.

For patients with a single parathyroid – presumed parathyroid adenoma – the better option now is to consider minimal access surgery, where only the involved gland is operated on, though a small scar, sometimes under local anaesthetic. Perioperative nerve stimulation can be used to protect the nerves to the voice box and increasingly intraoperative measurement of PTH can determine when the offending gland has been properly removed. Some centres will do microscopy on the sample as it comes out to be certain it is parathyroid tissue.

A good surgeon should expect 95% cure rates and very experienced surgeons up to 99% cure.

If generalised parathyroid hyperplasia – four-gland disease – is present, often in familial disease then the decisions for surgery are more difficult. The best chance of cure is at the very first operation, when every scrap of parathyroid tissue must be removed. The endocrinologist, surgeon and diagnostic imaging must know multi-gland disease is what is suspected.

Preparation for and Follow up post surgery

Ideally patients having surgery will be vitamin D replete with an appropriate calcium intake – this provides the body with the calcium it needs from the gut, rather than the skeleton and protect from 'hungry bones' pulling the calcium from the bloodstream after the parathyroidectomy.

Post-operative care should ensure the wound heals and the voice is preserved. Between one to two days after surgery the calcium might fall to its lowest and might need to be treated. PTH level might quickly return to normal but completely normal secretion may take longer to recover – this entails monitoring the bloods in the weeks and months following surgery. Patients must be warned about symptoms of hypocalcaemia – parasthesiae, cramps or numbness around the mouth and/or in the peripheries, and told to take oral calcium therapy if they occur, with or without a blood test as appropriate. If wound swelling or breathing difficulties occur they must seek immediate attention.

A decision on whether the condition has been cured should be made six-months post surgery. The calcium should be checked yearly.

If the PHPT is not cured a thorough reassessment is needed.

Monitoring instead of surgery

Some patients may neither need nor want an operation and the clinical picture, calcium, PTH, renal function and DXA can be monitored. These patients should avoid lithium and thiazides. If the picture changes reconsideration of the options must be done. Monitoring the condition is often done with lower serum calcium, no bone or renal disease and only modest urine calcium excretion.

A yearly calcium, renal function and PTH, with a DXA every one to two years will support the clinical assessment. Three quarters of patients have stable disease for up to a decade. Over two thirds of younger patients tend to progress to meet the criteria for surgery.

Bisphosphonates

These drugs can protect the skeleton if osteoporosis is present by increasing the bone density in the lumbar spine. We do not have the evidence to say that they protect against fractures however.

Cinacalcet

Cinacalcet lowers serum calcium and PTH by mimicking the action of calcium on its receptor. It is most often used in severe parathyroid disease secondary to renal failure, parathyroid carcinoma but can be used in very symptomatic patients with PHPT who are not well enough or who decline surgery.