Hyperparathyroidism

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Abstract

Primary hyperparathyroidism is defined by the presence of hypercalcaemia (>2.6 mmol/litre) in the presence of inappropriate (i.e. not inhibited) or high PTH levels. The cause remains unknown and most patients (>85%) have a single adenoma. In modern medical practice most patients are deemed asymptomatic at the time of diagnosis. The traditional mnemonic of 'bones/groans/stones/moans' is rarely seen. A combination of neck ultrasound and Sestamibi scanning demonstrates the position of adenomas in some two thirds of patients and they can benefit from a *minimally invasive parathyroidectomy* done under general anaesthesia or under sedation/local anaesthesia. Patients with negative scans need bilateral neck exploration. Medical treatment is reserved for patients with failed surgical treatment or those with limited life expectancy considered too unwell for surgical intervention.

Secondary hyperparathyroidism is a physiological response to a metabolic drive (e.g. chronic renal failure) that leads to four-gland hyperplasia. Medical treatment of patients on dialysis aims to reduce the biochemical abnormalities that promote parathyroid glands hyperplasia. Despite such measures some patients develop hypercalcaemia and PTH levels several times higher than normal range and develop symptoms, hence surgical treatment becomes indicated. Four-gland excision is currently preferred in many centres though alternative treatments include total parathyroidectomy plus autotransplantation or subtotal parathyroidectomy.

Keywords Calcium; hyperparathyroidism; parathyroid; parathyroidectomy; thyroid

Introduction

The parathyroid glands were the last mammalian organs to be discovered. They were identified originally in 1849 by Sir Richard Owen in an Indian rhinoceros at the London Zoo and defined as a separate histological entity by Uppsala medical student Ivar Sandstrom in 1880. Von Recklinghausen in 1891 described *osteitis fibrosa cystica* – the bone disease specifically associated with severe hyperparathyroidism and Askanazy established the connection between parathyroid tumours and skeletal disease in 1904. In 1925, Felix Mandl performed in Vienna the first successful parathyroidectomy. In 1940s Fuller Albright described the key features of calcium, phosphate and bone metabolism and several disorders associated with this including hyperparathyroidism.[1]

The anatomy of the parathyroid glands is described in detail in the article on pp 403–407 of this issue. It is important to reiterate however that supernumerary glands are found in up to 13% of patients and that the location of the parathyroid glands can be very variable. Identification of these glands can sometimes be challenging for experienced parathyroid surgeons.

Parathyroid hormone (PTH) plays an important role in calcium homeostasis. PTH is an 84 amino acid peptide hormone that has a half-life of 2–3 minutes. This fast disappearance from the blood stream is the basis of demonstrating removal of all overactive parathyroid tissue by measuring the decline of PTH within 5–30 minutes. after the removal of a parathyroid adenoma. The chief cells in the parathyroid gland release PTH in response to hypocalcaemia so that serum calcium is maintained within a narrow range (2.12–2.65 mmol/litre).

The parathyroid cells detect small changes in serum calcium via the ***calcium sensing receptor*** (CaSR). When CaSR is stimulated by high calcium the PTH secretion is blocked. In primary hyperparathyroidism this feedback mechanism is altered so that PTH release continues in the presence of hypercalcaemia. PTH acts on the kidneys to increase calcium re-absorption (normal kidneys can reabsorb 99% of calcium) and decrease phosphate absorption whilst increasing vitamin D activation (via hydroxylation to form 1,25-dihydroxycholecalciferol). The increase in activated vitamin D leads to an increase in serum calcium by increasing intestinal and renal absorption of calcium and phosphate (Figure 1). PTH also inhibits osteoblasts and activates osteoclasts to increase bone erosion and release of calcium, which also raises serum calcium.[2]

Definitions

***Primary hyperparathyroidism* (PHPT):** hypercalcaemia driven by the inappropriate/high PTH secretion by one or more overactive parathyroid gland(s).

***Secondary hyperparathyroidism* (SHPT):** excessive secretion of PTH as a result of a chronic biochemical stimulus, such as chronic renal failure. Usually all four glands become hyperplastic.

***Tertiary hyperparathyroidism* (THPT):** a result of prolonged SHPT that is observed in patients whose renal failure has been corrected by successful kidney transplantation, but whose parathyroid glands remains overactive and autonomous.[2]

***Persistent hyperparathyroidism*:** biochemical evidence of hyperparathyroidism demonstrated within 6 months after parathyroidectomy.

***Recurrent hyperparathyroidism*:** biochemical evidence of hyperparathyroidism demonstrated after 6–12 months after parathyroidectomy.

Primary hyperparathyroidism

PHPT is the third most common endocrine disorder, with a prevalence between 0.1–0.4% and increasing incidence with age which peaks between 50 and 60 years. PHPT is the most common cause of hypercalcaemia in the outpatient setting.[3]

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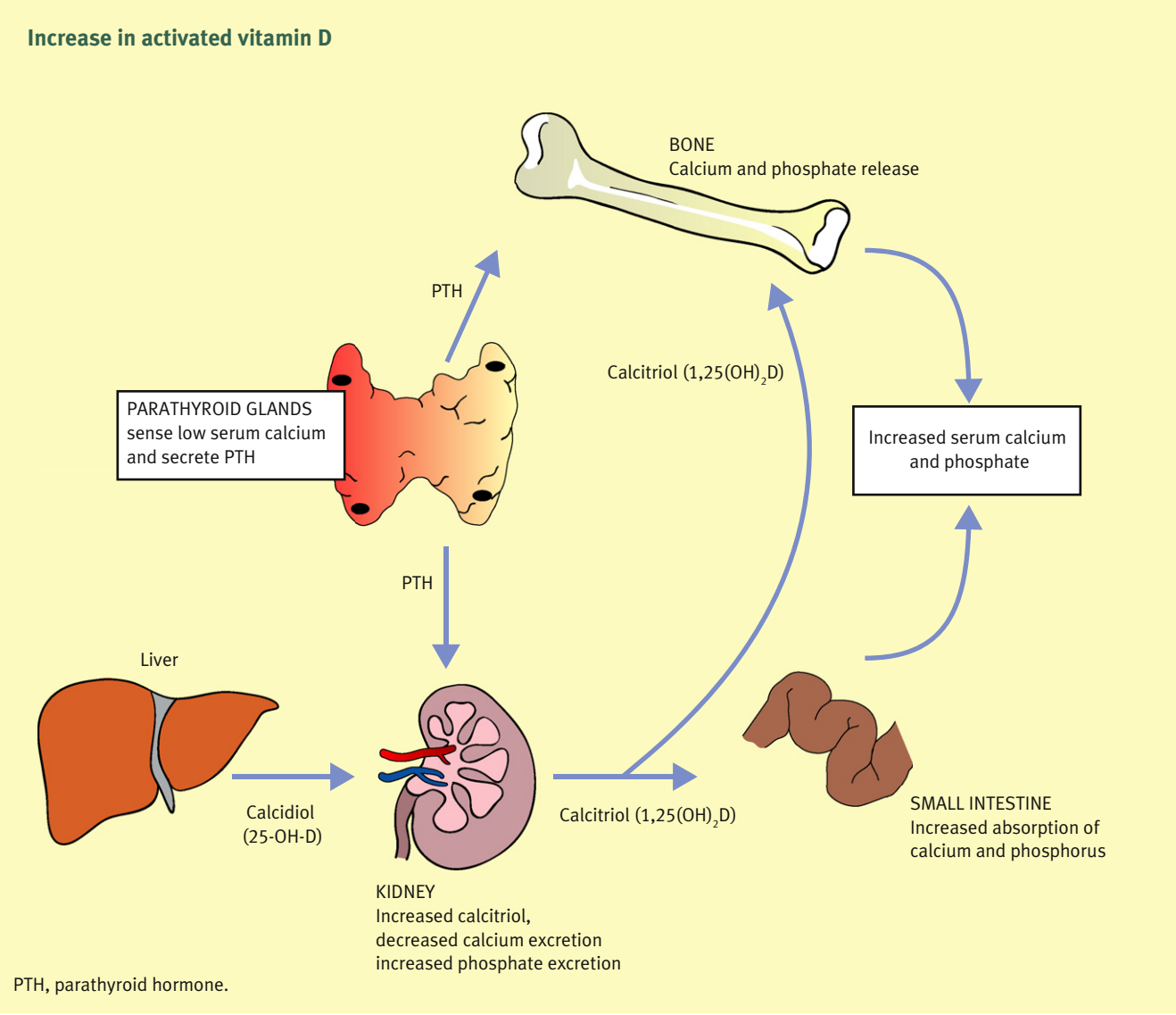

Figure 1

Aetiology

The vast majority of patients (>80%) have a single parathyroid adenoma. A minority of cases (<5%) can be caused by double adenomas and some 10% of cases have diffuse hyperplasia of all four glands. Parathyroid cancer is rare and accounts for less than 1% of cases. Approximately 5% of cases of PHPT are familial, predominantly as a part of the MEN-1 genetic syndrome.

The aetiology of sporadic parathyroid adenomas is essentially unknown. The incidence is dependent on gender (F>M) and increasing age (more common after 50 years). Previous neck irradiation and lithium therapy are risk factors.

The majority of parathyroid adenomas are sporadic and are essentially formed from cells with a genetic anomaly causing increased cell proliferation or loss of inhibition of cell growth. PRAD1 (cyclin D1) proto-oncogene rearrangement occurs in about 20% of adenomas where the *PRAD1* gene is inserted next to *PTH* gene enhancer elements and stimulates cell division when PTH secretion occurs. Some sporadic adenomas have mutations in the tumour suppressor gene for multiple endocrine neoplasia type I syndrome (MEN-1).

Parathyroid cancer is the least common endocrine malignancy (0.005% of all cancers). The natural history of parathyroid cancer is slow but progressive with a tendency for lymphatic spread and metastases to lung, liver and bone. Parathyroid cancer can occur in conjunction with hyperparathyroidism-jaw tumour (HPT-JT) syndrome, MEN-1 syndrome.[4]

Symptoms and signs of PHPT

The vast majority of cases in the western world are asymptomatic and found after routine blood tests. Although such patients might have vague symptoms and altered quality of life this remains controversial.[5] Non-specific symptoms reported in apparently asymptomatic PHPT include fatigue, depression, memory loss, decreased concentration and sleep problems. Although patients may not state these symptoms prior to surgery

they notice significant changes after surgery, with subsequent improvement in quality of life.[6–8]

The classic mnemonic associated with symptomatic PHPT is '*bones, groans, stones and psychic moans*':

- *bone* pain results from osteopenia or osteoporosis (due to excessive calcium resorption). Osteitis fibrosa cystica, the bone disease specific to PHPT, is rarely seen in modern clinical practice hence one rarely looks for the 'classical signs' of subperiosteal resorption in the distal phalanges and small punched out lesions in the skull. Osteoporosis is a more common bone disease related to PHPT. The bone integrity is altered by high bone turnover and loss of cortical bone. This bone loss is halted or reduced postoperatively.
- abdominal *groans* are due to nausea, constipation and peptic ulcers.
- *stones* refer to renal calculi (due to excessive renal calcium excretion).
- psychic *moans* correspond to the neuropsychiatric manifestations such as depression, dementia and confusion.

In addition, several cardiovascular conditions have been associated with PHPT including hypertension, valvular calcifications and left ventricular hypertrophy. These lead to an increased risk of cardiovascular mortality in cohort of hypercalcaemic patients when compared with normocalcaemic patients.[9]

Diagnosis

Diagnosis of PHPT is based on biochemical assessment and NOT on radiological criteria.

High calcium levels in the presence of inappropriate (i.e. non-inhibited) PTH levels demonstrate PHPT. PTH levels can be elevated or within normal range (though not decreased as it should normally be, in response to hypercalcaemia). The PTH levels are low/unmeasurable in other conditions associated with hypercalcaemia (e.g. bone metastases, vitamin D intoxication, thyrotoxicosis, sarcoidosis, Paget's disease of bone and Addison's disease).[10]

Other common biochemical abnormalities associated with PHPT are:

- Low phosphate levels.
- Low vitamin D levels. Preoperative correction of vitamin D levels is debatable and not part of routine clinical practice.
- Hypercalciuria. A normal or high urinary calcium-to-creatinine clearance ratio can be used to exclude FHH (see Familial syndromes associated with PHPT on p 456).

Differential diagnosis of different types of hyperparathyroidism are outlined in Table 1 and a decision-tree in patients with hypercalcaemia is described in Figure 2.

Imaging modalities

High-resolution neck ultrasound (US)

Normal parathyroid glands are not usually visualized on US, but for enlarged parathyroid adenomas US has a sensitivity of 72–85%. The technique fails to locate glands in the mediastinum or retro-oesophageal space and is less sensitive in the presence of multinodular goitre.

^{99m}Tc-sestamibi radionuclide scanning

^{99m}Tc-sestamibi is sequestered into mitochondria because of electrical transmembrane gradients. Its increased uptake in parathyroid adenomas is probably due to increased vascularity and number of mitochondria-rich cells. After intravenous injection of the radiotracer isotope one set of images is taken at 15 minutes and a further set of images is taken after 2–4 hours (Figure 3). The technique allows the detection of ectopic glands (particularly in the mediastinum).

Combination of ^{99m}Tc-sestamibi with US increases the sensitivity of preoperative localization up to 95% by demonstrating an area of increased tracer uptake ('hot spot') overlapping with the anatomical location on US scanning.

Computed tomography (CT) and magnetic resonance imaging (MRI)

CT is useful in patients with persistent PHPT. Characterization of parathyroid adenomas on CT is dependent on differential densities when compared to lymph nodes and thyroid tissue and typical adenomas enhance faster after contrast injection.

Single-photon emission CT (SPECT) can be used in conjunction with ^{99m}Tc-sestamibi scanning to help differentiate parathyroid from thyroid tissue and increases its sensitivity to 87% for solitary adenomas.

MRI can also detect abnormal parathyroid tissue in patients with recurrent disease. Adenomas usually have a high signal on T2 weighted images and have significantly increased signal intensity after gadolinium injection compared to surrounding structures.[11]

Assessment of other organs affected by PHPT

Bone loss in PHPT is predominantly cortical rather than trabecular and is seen most in the distal forearm and femur but are often indistinguishable to age-related or postmenopausal osteoporosis. Dual energy X-ray absorptiometry (DEXA) detects generalized osteoporotic changes, which may be related to PHPT.

Though very rarely indicated in modern surgical practice, simple X-rays of the skull and hands can demonstrate small punched-out skull lesions and bone resorption in distal

Comparison of biochemical features of primary, secondary and tertiary hyperparathyroidism (HPT)

	Serum calcium	Parathyroid hormone	Serum phosphate	Urinary calcium
Primary HPT	Raised/normal with vitamin D deficiency	Raised/normal	Low	High >100 mg/24 hours (excludes familial hypocalciuric hypercalcaemia)
Secondary HPT	Low/normal	Raised	High (renal), low (other cause of calcitriol deficiency	
Tertiary HPT	Raised	Raised	High (renal)	

Table 1

Decision-making in patients with hypercalcaemia

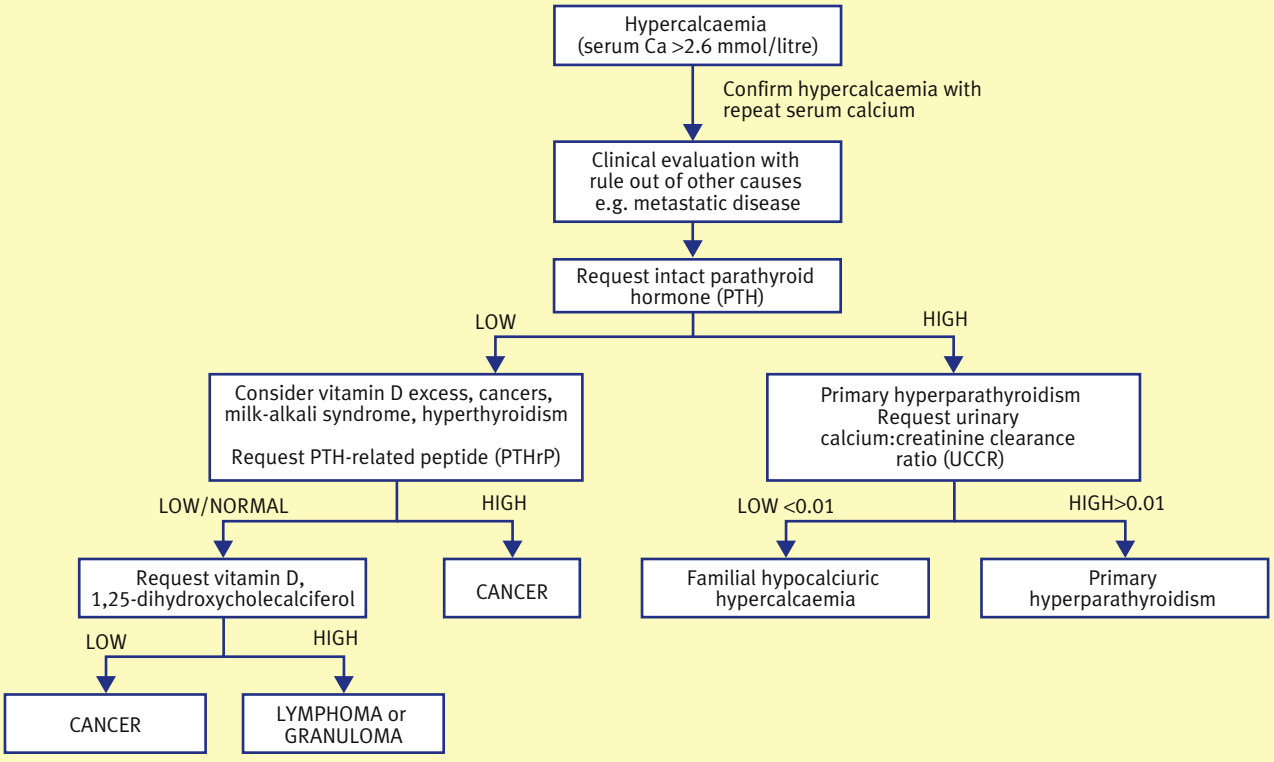

Figure 2

phalanges particularly in patients with severe osteitis fibrosa cystica.

Ultrasound or CT scans can be used to image the renal tract and detect renal calculi.

Management option for PHPT

Surveillance

Some consider that patients with mild asymptomatic disease may be managed by medical observation provided the calcium

Sestamibi scans

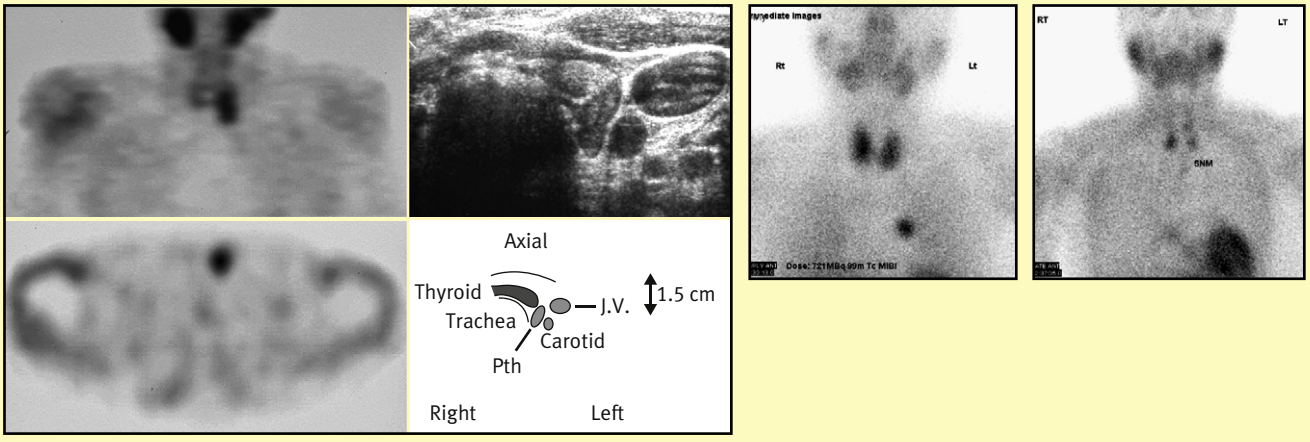

Figure 3

levels are mildly elevated and have normal bone and renal function. These patients can be monitored with regular DEXA scans, renal function and calcium levels and are advised to avoid factors aggravating hypercalcemia such as thiazide diuretics, dehydration, immobilization and high dietary calcium. However true asymptomatic PHPT is difficult to define as many supposedly asymptomatic patients notice an improvement in their well being after parathyroidectomy.

Medical treatment

The treatment aims are improving bone mineral density and balancing calcium homeostasis. There are currently no drugs specifically approved as first-line treatment for PHPT, but certain drugs can be used to treat certain aspects of the disease.

- Oestrogen replacement (hormone replacement therapy, HRT) can lower calcium concentration and have beneficial effects on bone mineral density by acting on the skeleton rather than the parathyroid glands. However due to the associated risks of HRT, it should not be used solely for treating PHPT.
- Selective oestrogen receptor modulators (SERMs) such as raloxifene significantly decrease calcium concentrations with presumably the same mechanism of action seen with oestrogen replacement, but the evidence is limited.
- Bisphosphonates improve bone mineral density, can suppress PTH-mediated bone resorption, but do not improve the serum calcium or PTH levels in the long term. Furthermore, when compared to surgery bisphosphonates do not show an improved fracture rate. Their use is limited to patients who are unfit for surgery or for temporary reduction of calcium levels in patients awaiting surgery.
- Calcimimetics (such as Cinalcet) are agonists of the CaSR that act as allosteric modulators to increase the sensitivity of CaSR to calcium stimulation, hence they can suppress PTH secretion and normalize serum calcium. However this drug does not alter bone mineral density and its effects on fracture risk and quality of life are unknown.[12]

The role of medical treatment is limited to patients with failed surgical treatment and those with limited life expectancy who are deemed unfit for surgical treatment.

Parathyroidectomy for PHPT

The excision of the enlarged parathyroid gland(s) is the only definitive cure for PHPT. It is offered to all symptomatic patients and those asymptomatic patients with significant hypercalcaemia (>2.80 mmol/litre) who are fit for surgery.

Specific guidelines for surgical treatment in asymptomatic disease were agreed at the National Institute of Health International Workshop on Asymptomatic Hyperparathyroidism in 2008 and include[9]:

- age younger than 50 years
- serum albumin-adjusted calcium more than 0.25 mmol/litre above the upper limit
- creatinine clearance reduced by 30% or more
- 24-hour total urinary calcium excretion greater than 10 mmol (400 mg)
- bone mineral density T score − 2.5 or less at the lumbar spine, hip or distal one third radius
- patient request.

Surgical options for PHPT: the traditional surgical approach to PHPT has been the bilateral cervical exploration (BCE) with identification of all four glands and excision of the single adenoma. This was shown to be curative in over 95% of patients. In the rare patients with 4-glands hyperplasia, subtotal parathyroidectomy can be performed leaving half of one gland behind or transplanting it into muscle away from the neck (such as the arm) to avoid further neck surgery for recurrence.

A unilateral approach was proposed first in the 1980s and has become established for more than a decade. It relies on positive preoperative localization using the combination of ^{99m}Tc-sestamibi and ultrasound parathyroid scanning. It can be done under general or local anaesthesia and the incision usually does not exceed 2.5 cm (minimally invasive parathyroidectomy, MIP). It allows for shorter operative time compared to BCE, equivalent success rates (in excess of 90–95%), improved cosmesis (smaller incision) and decreased pain. Some centres are performing MIP with radioguidance (i.e. with the help of a gamma probe, similar to the sentinel node biopsy method used in breast cancer).

As scans are positive in only two-thirds of patients, there is significant proportion of patients who still need BCE (i.e. those where the parathyroid adenoma cannot be localized radiologically).

More innovative but far less used approaches include endoscopic parathyroidectomy with video assistance or gas insufflation as first performed by Michel Gagner in 1996 at the Cleveland Clinic. Massive subcutaneous emphysema and hypercarbia were seen postoperatively and subsequent attempts reduced the size of the port incisions and CO_2 insufflation periods.[13]

Use of intraoperative PTH assay (IoPTH): IoPTH can be used to assess the adequacy of resection of overactive parathyroid tissue and reduce risk of operative failure; especially in patients with multi gland disease. In principle, PTH levels are measured at several time points: pre-skin incision, pre-excision (to avoid missing a further increase in PTH secondary to gland manipulation) and around 10–15 minutes post-excision. Results of the assay are available within 15 minutes and interpretation guides further intraoperative decisions. Several ways of interpreting such data have been proposed but the most well known is the Miami criteria based on a 50% or greater drop from the highest PTH level drawn to the PTH level drawn 10 minutes after gland excision indicates adequate resection. When the IoPTH levels remain elevated after MIP, a BCE may be necessary to locate the remaining abnormal tissue.

Several surgical series (including our own experience) have shown that in patients with a clear biochemical diagnosis of primary hyperparathyroidism and convincing and concordant sestamibi and ultrasound localization there is no need to include IoPTH in the decision algorithm.

Complications of parathyroidectomy: complications specific to neck exploration include recurrent laryngeal nerve injury and haematoma formation leading to airway obstruction and hypocalcaemia.

Postoperative hypocalcaemia is due to 'hungry bone syndrome', hypoparathyroidism (due to damage to remnant glands, or poor function of the implanted parathyroid after a total resection and auto-transplant) or hypomagnesaemia. Calcium and vitamin D

supplements may be required if the hypoparathyroidism persists and serum calcium should be monitored closely after surgery. As MIP patients often go home the same day, they are given routine postoperative calcium supplementation mainly if they had severe preoperative hypercalcaemia, had large gland(s) or had evidence of severe bone disease (raised alkaline phosphatase).

Persistent hyperparathyroidism (with normocalcaemia) after surgery is not uncommon and is secondary to a combination of factors including vitamin D deficiency, bone turnover and peripheral PTH resistance. Persistent/recurrent hyperparathyroidism with hypercalcaemia can occur due to incomplete excision of abnormal tissue. These complications can be minimized by using accurate preoperative localization studies and frozen section (to differentiate parathyroid from non-parathyroid tissue). IoPTH of the tissue aspirate can also be done to accurately identify parathyroids. However this is not used routinely.[13]

Familial syndromes associated with PHPT

Multiple endocrine neoplasia/MEN-1 (Wermer syndrome)

It is caused by an inactivating mutation of the menin gene on chromosome 11q13. It is an autosomal dominant condition with a high penetrance for PHPT, which is the initial presentation in 90–95% of MEN1 patients. The pathology is often hyperplasia and is treated with a subtotal parathyroidectomy (3½ gland excision) or total parathyroidectomy with auto-transplantation.

Multiple endocrine neoplasia/MEN-2A (Sipple syndrome)

It is an autosomal dominant condition caused by an activating mutation of the RET proto-oncogene leading to development of medullary thyroid cancer and phaeochromocytomas. PHPT associated with MEN2A tends to be milder and occurs in 20–30% of patients with either single or multiple gland abnormalities. Surgical options are less aggressive compared to MEN1 and involves assessment of parathyroid function/size at the time of thyroidectomy for medullary thyroid carcinoma.

Hyperparathyroidism-jaw tumour syndrome (HPT-JT)

It is an autosomal dominant disorder caused by *HRPT2* inactivating mutation. Patients commonly have PHPT at a younger age with single or multiple gland involvement and with an increased risk of parathyroid carcinoma. Surgical approach should be bilateral neck exploration rather than MIP to adequately identify all four parathyroids and assess for abnormal appearances. If parathyroid cancer is suspected, an en bloc resection would be performed. HPT-JT patients also develop mandibular or maxillary fibro-osseous tumours with renal pathology.

Familial hypocalciuric hypercalcaemia (FHH)

It is an autosomal dominant disorder linked to chromosomes 3q, 13p and 19q and is caused by inactivating mutations of the parathyroid cell calcium-sensing receptor on 3q (CaSR). It can often mimic the biochemical appearance of PHPT. This results in mild hypercalcaemia with high or mildly increased PTH levels with a low 24-hour urinary calcium excretion. The best study to distinguish FHH from PHPT is 24-hour urinary calcium to creatinine clearance ratio. FHH patients have a ratio of less than 0.01 and PHPT patients a ratio of more than 0.01.

Neonatal severe HPT (NSHPT) is caused by homozygous inactivating mutations of the CaSR and needs an immediate total parathyroidectomy to avoid death.[14]

Secondary hyperparathyroidism

Causes – pathophysiological mechanisms

Secondary hyperparathyroidism (SHPT) is commonly associated with chronic renal failure, but other causes should also be recognized:

- decreased calcium intake or absorption
- vitamin D deficiency
- renal hypercalciuria.

SHPT in chronic renal failure: Due to a decrease in glomerular filtration rate (GFR<40 ml/minute) there is a reduction in the filtered phosphate load and subsequent hyperphosphataemia. Raised phosphate levels act directly on parathyroid glands to stimulate PTH secretion. This is further stimulated indirectly by reduced 1α-hydroxylase enzyme activity in the proximal tubule (hence low levels of active vitamin D) and by lowering serum calcium levels via calcium-phosphate binding. The elevated PTH response initially maintains osteoblast activity and a stable bone turnover state. As the PTH elevation become more marked, complications of SHPT occur such as high bone turnover, osteitis fibrosa cystica and vascular calcification. There is also a change in the PTH set point and bone becomes resistant to the actions of calcitriol (reduced calcium mobilization).

Signs and symptoms of SHPT

In early renal failure, there are minimal clinical features of SHPT. Vascular calcification (widespread arterial medial and atherosclerotic neointimal calcification) leads to decreased vessel compliance and a subsequent increase in systolic blood pressure, widened pulse pressure and increased incidence of myocardial infarction.

Heterotopic (soft tissue) calcification occurs in the eye (red eye syndrome, band keratopathy), lung (restrictive lung disease with calcific nodules), heart (valve and annular calcification) and joints (periarticular – tumoral calcinosis with severe restriction and pain on movement) or skin calcification (calciphylaxis).

Bone disease occurs in several different forms.

- Osteoporosis: reduced bone density due to excess bone resorption, leading to increased fracture rates (which is also a feature of patients on haemodialysis).
- Osteomalacia: poor quality bone remodelling.
- Adynamic bone disease: a state of low-turnover bone disease, typically a result of resistance to PTH action or bisphosphonate action.
- Osteitis fibrosa cystic (rare in current clinical practice).

Biochemical abnormalities in SHPT

SHPT is characterized by high PTH levels (many times over upper limit of normal), hypocalcaemia, hyperphosphataemia and low vitamin D levels (Table 1).

Medical treatment for SHPT

Medical management of SHPT focuses on reducing the stimulation of the parathyroids by treating the two main mechanisms that mediate the process: hyperphosphataemia and low calcitriol levels.

- Hyperphosphataemia can be treated with reducing phosphate intake, phosphate-binding agents and dialysis. Controlling dietary intake and restricting protein intake can control hyperphosphataemia up to a GFR of 25–40 ml/minute after which dialysis may be needed in combination with phosphate binders as dialysis alone is not effective in removing phosphate. Traditional phosphate binders are calcium based and can cause hypercalcaemia and vascular calcification, but newer binders such as lanthanum carbonate and sevelamer are non-calcium based.[15]
- Treating calcitriol deficiency is indicated if PTH levels are elevated in chronic kidney disease stage 3 and 4. Calcitriol and alfacalcidol (active vitamin D analogues) are used routinely in dialysis patients but may be indicated pre-dialysis if phosphate binders and cholecalciferol do not suppress PTH. These vitamin D analogues can cause hypercalcaemia and increase intestinal calcium and phosphate absorption so should be started at a low dosage.[16]
- Calcimimetic agents (Cinacalcet) are effective at reducing PTH, calcium and phosphate levels, but its effects on altering the natural history of SHPT are still under investigation.[17] This new class of drugs is used extensively in patients with SHPT as a mechanism to avoid the need for parathyroidectomy in patients expecting a renal transplantation.

Parathyroidectomy for SHPT

The majority of renal patients with SHPT on haemodialysis do not need surgical intervention so medical management is always started first. Isolated PTH elevation is not an indication for surgery, however surgery is indicated when in combination with persistent hypercalcaemia (>2.6 mmol/litre absolute indication), uncontrolled hyperphosphataemia, elevated alkaline phosphatase levels (>300u/litre) and evidence of significant bone erosion (subperiosteal bone resorption on hand X-ray). Additional findings which may bear significance when considering surgery include poorly controlled hypertension, refractory pruritis, peripheral neuropathies, erythropoietin resistant anaemia. Significant calciphylaxis (calcium deposition in skin) is an absolute indication for surgery.[18]

The benefits of preoperative imaging in SHPT are controversial. Some use sestamibi scanning to assess for the existence of possible ectopic or aberrant glands.

Patients should be treated with calcitriol several days prior to surgery to reduce the risk of postoperative hypocalcaemia. Renal function is controlled by a dialysis session the day before parathyroidectomy. Platelet dysfunction is seen in renal failure patients on dialysis, which occurs under general anaesthesia and can be counteracted by desmopressin infusion at induction.

Operation for SHPT should include cervical thymectomy as supernumerary glands (up to 25% incidence) commonly found in thymic tissue can be responsible for recurrent SHPT.[18]

Surgical management involves a bilateral cervical exploration plus thymectomy. Total parathyroidectomy is currently preferred by many clinicians. Alternatively, subtotal parathyroidectomy (3½ gland excision) is done by inspecting all parathyroid glands and choosing to leave a remnant of the most normal-looking one either in-situ or as a transplant into the forearm muscles. The benefit of forearm transplantation is that, in case of recurrent SHPT, the autotransplanted tissue can be found easily under local anaesthetic rather than having to proceed to repeat neck exploration.

Tertiary hyperparathyroidism

Tertiary hyperparathyroidism (THPT) occurs when the parathyroids become autonomous and oversecrete PTH in the absence of an abnormal biochemical stimulus (e.g. once renal function has become normal after successful kidney transplantation). This may be explained by selection of autonomous cell clones, the progressive reduction of CaSR on parathyroid cells in chronic renal failure, which reduces the negative feedback response resulting in frank hypercalcaemia. Biochemically, the picture is similar to PHPT. THPT usually resolves within a year after renal transplant on its own, hence patients are observed for at least a year before considering parathyroidectomy. If the patient has frank hypercalcaemia in the immediate post-transplantation period, nephrocalcinosis or renal stones with persistently raised serum calcium, surgery is indicated.[19,20] ◆

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