

## **LAPAROSCOPIC ENDOCRINE SURGERY**

### 1. Primary hyperparathyroidism

Primary hyperparathyroidism is a common endocrine disease. As a large proportion of patients remain asymptomatic, incidence varies depending on method of diagnosis and population studied. With increasing use of multi-channel biochemical analysers, elevation of serum calcium is being increasingly picked up and investigated. 25 in 100,000 population was the estimated incidence in the UK, though it may reach 1 in 500 women over the age of 45 years.

Primary hyperparathyroidism may present in numerous ways:

(i) Asymptomatic disease may be found in up to 50% of cases. It is unclear, as yet, if asymptomatic hyperparathyroidism progresses on to symptomatic disease. Current evidence suggests that up to 95% treated surgically claim improvement in well-being.

(ii) Renal manifestations. The main symptoms are: polyuria, back pain, colic and haematuria. There are two types of kidney lesions: anatomical (nephrolithiasis and nephrocalcinosis) and functional (a range of tubular and glomerular disorders).

(iii) Skeletal manifestations. Osteitis fibrosa cystica used to be a common feature and presentation, but has continued to decrease in incidence and is now rarely seen.

(iv) Articular manifestations. Chondrocalcinosis with attacks of pseudogout, traumatic synovitis and peri-arthritis are recognised complications of primary hyperparathyroidism.

(v) Neuromuscular and neuropsychiatric manifestations are difficult to evaluate because some of the symptoms may be non-specific or reflect degenerative or ageing features. Extreme weakness and fatigue improve after surgery. Depression, apathy, lethargy, confusion, personality changes, memory impairment and overt psychosis may also be seen.

(vi) Gastrointestinal manifestations.

Anorexia, nausea, dyspepsia, constipation and abdominal pain are frequent symptoms. Peptic ulcers seem to be a true manifestation and not just a coincidental finding. Pancreatitis may occur.

(vii) Hypertension and left ventricular hypertrophy are often present. This may be caused by a parathyroid hypertensive factor that has recently been identified.

Left ventricle hypertrophy regresses after parathyroidectomy, without a decrease in mean blood pressure, leading to speculation that PTH may have direct action on the myocardium.

(viii) Increased premature death. Studies suggest that there is an increased risk of premature death, with better survival for patients who had undergone parathyroidectomy.

Hyperparathyroidism is diagnosed by the finding of high serum calcium which is then confirmed by determination of the serum PTH concentration.

There is now general agreement that surgical exploration of the neck with the intention of removing all hyperfunctioning parathyroid tissue is the treatment of choice. Conventional teaching advocates a cervical approach with exploration of both sides of the neck, to identify all four parathyroid glands and removal of all enlarged glands. However, a solitary adenoma is the cause of the disease in 80-90% of patients and this has led to questioning of traditional teaching. With the development of thallium – technetium subtraction scanning for the localisation of parathyroid adenomas in 1983, unilateral exploration of the neck became feasible. It has, however, become clear that the ability of this technique to identify the site of the adenoma was size-dependent. Technetium-labelled sestamibi was then used and markedly improved localisation of the enlarged gland. Sestamibi accumulates in the mitochondria of parathyroid cells in a manner similar to that of thallium, but its emission spectrum enhances the sensitivity for both smaller and deeper lesions. The ability to accurately localise the adenoma has led to further questioning of ‘traditional’ teaching.

Currently, surgery focused on removing the identified abnormal gland is advocated. This can be performed by two methods :

(i) Focused unilateral cervical exploration: a 2-3 cm transverse skin incision is placed on the relevant side of the neck over the gland, the anterior border of the sternomastoid is retracted laterally and the adenoma exposed and removed.

(ii) Endoscopic or endoscopically-assisted parathyroidectomy. The localised adenoma is approached through a suprasternal incision. The gland is dissected as in open parathyroid surgery, with visualisation of the recurrent laryngeal nerve and ligation of the vascular pedicle. With experience, exclusion criteria are shrinking, as are mean operating times. Conversion rates are 8-14% with results and complications comparable to those of open surgery.

## Adrenals

Surgical adrenal dysfunction falls into two categories: (a) endocrinologically significant disease of the cortex and medulla or (b) non-functioning tumours, malignant or benign including those incidentally discovered on scanning. The adrenal gland consists of two embryologically separate parts. The outer cortex accounts for 85% of the gland, is yellow and is concerned with steroid synthesis and secretion. The inner medulla is responsible for the adrenal component of the sympatho-adreno-medullary system.

The cortex is composed of three layers; the outer zona glomerulosa, producing mineralocorticoids (aldosterone); zona fasciculata producing glucocorticoids (cortisol) and the inner zona reticularis producing sex hormones. The adrenal medulla synthesises adrenaline, dopamine and noradrenaline, which are released in response to direct neural stimuli of the adrenal medulla.

Adrenal abnormalities can be benign or malignant tumours or hyperplasia.

Aldosteronism (Conn's syndrome) is the excessive secretion of aldosterone. This may be: (i) Primary due to adrenal tumours, nodularity or hyperplasia or (ii) Secondary due to angiotensin stimulation in (a) cirrhosis, (b) nephrotic syndrome, (c) diuretic therapy and cardiac failure; or renin stimulation in renal artery stenosis or renin-secreting renal tumours.

In primary aldosteronism, there is inappropriate secretion of aldosterone independent of the influence of renin. In 64% this is caused by an aldosterone-producing adenoma; 32% idiopathic hyperaldosteronism and the rest is made up of carcinoma and hyperplasia. It is much more common in women (F:M = 2:1) and is rare in children; tends to present between 30-60 years and is usually discovered when hypertension is being investigated. The hypertension is moderate to severe, difficult to control and associated with hypokalaemia.

Symptoms, when they occur, are related to the effects of hypertension (headache) or hypokalaemia (polyuria, nocturia, muscle cramps, paraesthesia, muscle weakness or paralysis). However screening hypertensives using the plasma aldosterone concentration/plasma renin activity ratio (PAC/PRA) has shown that 60-84% of patients with 1° aldosteronism are normokalaemic. Screening hypertensives is now demonstrating that primary aldosteronism is much more prevalent than was previously thought.

Investigation is by measuring both the absolute plasma aldosterone concentration and the PAC/PRA ratio. With a PAC/PRA ratio >30, PAC >15mg/dl and PRA ≤ 1ng/ml/hr, the diagnosis is certain.

This can be confirmed using the (a) saline loading test; (b) oral salt loading test or (c) fludrocortisone suppression test.

Once the diagnosis of primary hyperaldosteronism has been established biochemically, aldosteroma and idiopathic hyperaldosteronism can be distinguished by (i) CT – high resolution, 3mm slices will pick up 80% of patients with a solitary adenoma. A solitary, hypodense mass > 1cm in diameter with a normal appearing contralateral gland supports the diagnosis. MRI will give similar information as a CT.

(ii) Selective adrenal sampling will distinguish between unilateral or bilateral aldosterone hypersecretion.

Treatment of aldosteroma is by unilateral adrenalectomy. As the tumours are usually small and well encapsulated, laparoscopic removal is now the gold standard. Surgery should be preceded by treatment with Spironolactone to allow potassium reserves to return to normal. Surgery will return the blood pressure to normal in 70% of patients.

Idiopathic hyperaldosteronism is treated with Spironolactone at a dose of 100mg/day increasing to 400mg/day until the potassium is normal and hypertension under control. The dose may then be gradually reduced. Spironolactone may not be sufficient to control the hypertension and other anti-hypertensive agent may need to be used.

Cushing's Syndrome – is caused by an excess circulating cortisol. The most common cause is iatrogenic administration of steroids. The other causes are:-

(a) Primary adrenal disease – (i) adenoma (ii) carcinoma and (iii) primary adrenal hyperplasia. (b) Secondary adrenal disease – (i) Cushing's disease, is adrenal hyperplasia caused by excess adrenocorticotrophic hormone secretion (ACTH) from a pituitary microadenoma and (ii) adrenocortical hyperplasia due to excess ACTH accretion from a non-pituitary source, 'ectopic ACTH syndrome'.

About 50% of Cushing's syndrome is due to a primary adrenal source. Primary hypercortisolism tends to present late, with symptoms and signs fully developed. These are: (i) Obesity – this may be gross with a 50% increase in body weight. The weight is typically truncal, with a protuberant abdomen, a 'buffalo hump' on the shoulders and wasting of the thigh and upper arm muscles.

(ii) Loss of connective tissue leading to a thinning of the skin with a purple, plethoric face and purple abdominal striae. The venules and capillary walls become very fragile; (iii) Hirsutism and virilism; (iv) Muscle weakness due to protein catabolism esp in proximal muscles; (v) Osteoporosis; (vi) Hypertension; (vii) Glucose intolerance and even frank diabetes; (viii) Psychological changes.

Diagnosis of Cushing's syndrome depends on demonstrating an inappropriate increase in serum glucocorticoid concentrations, with loss of the normal circadian rhythm. The ACTH concentration is also measured. If ACTH is low, a diagnosis of adrenal disease is made and the patient imaged to establish the site in the adrenal. If ACTH is high, a diagnosis of ACTH-dependent adrenal hyperplasia is made and the source of ACTH has to be found. Performance of the corticotrophin-releasing hormone (CRH) test and the high dose dexamethasone test will determine if the disorder is pituitary-based. Imaging of the pituitary fossa by CT or gadolinium enhanced MRI will demonstrate the lesion in up to 60% of cases.

Treatment of Cushing's syndrome due to a pituitary microadenoma is by microadenectomy trans-spheroidally. Success is about 60%. Failed treatment is best managed by bilateral adrenalectomy. These patients will require steroid replacement for life.

In patients with Cushing's syndrome due to a solitary adrenal adenoma or carcinoma, a well defined lesion of up to 10cms can be removed laparoscopically. Larger lesions or those with signs of malignancy will require open surgery.

It is important to remember that a unilateral cortisol-secreting tumour will suppress the opposite gland and all these patients will require steroid replacement until the pituitary-adrenal axis function has returned to normal. This can take up to 1 year.

Phaeochromocytoma is derived from the neural crest. They may occur wherever neuro-ectodermal tissue is found. 90% are solitary and occur in the adrenals, but 5% are bilateral or extra-adrenal. Symptoms are due to the secretion of adrenaline or nor-adrenaline, though they may be sporadic and paroxysmal. These consist of severe but transient hypertension, palpitation, tachycardia and sweating with pallor and anxiety. Occasionally patients may present with pulmonary oedema or severe arrhythmias which may be fatal.

It is associated with (a) Multiple endocrine neoplasia type 2 (MEN). In MEN-2 there is familial occurrence of phaeochromocytoma, medullary carcinoma of the thyroid and hyperthyroidism. (b) Neurofibromatosis and (c) Von Heppel-Lindau syndrome.

Investigation is (i) Biochemical with measurement of (a) Vanillylmandelic acid (VMA) concentration in 24 hours urine and (b) Urinary catecholamines and (c) Radiological for localisation. CT scanning will demonstrate up to 90% of the tumours. If the tumour is not found or there is a history of MEN-2, isotope screening with meta-iodobenzylguanidine (MIBG), which is specific for catecholanic producing tumours, will help localise the lesions.

Treatment is surgical excision after adequate blockade. Close liaison between the endocrinologist and surgeon is mandatory so that the patient has surgery in the optimal physiological condition. Close monitoring of the patient during surgery is mandatory if violent swings of blood pressure are to be prevented.

Incidentaloma. With increasing use of CT, 'non-functioning' adrenal lesions are being picked up. Some will be obvious simple cysts, haematomas or myelolipomas, for which nothing need be done. A proportion will be metastases from carcinomas, known and unknown. If one of the above does not exist the patient must be investigated to exclude endocrine disease. If there is no evidence of endocrine disease, the decision to remove the lesion is based on size. It is recommended that lesions 3cms or larger should be surgically removed. Smaller lesions can be followed by serial CT's and surgically removed if they enlarge.

### INSULINOMAS

Are the most common islet cell tumour with an incidence of 1-4/million. Median age at presentation is 45 yrs with a M:F ratio of 1:2. 90% of insulinomas are small (2cms or less), solitary and benign. 10% are associated with multiple endocrine neoplasia (MEN) type 1.

Patients present with symptoms of hypoglycaemia – light-headedness, altered mental status and abnormal behaviour, and tend to occur after a fast. The diagnosis is suggested by the presence of Whipple's triad – serum glucose <3mmol/litre when symptomatic, symptoms of hypoglycaemia with fasting and symptom relief with glucose. Fasting serum insulin levels of 6 $\mu$ U/litre or greater are diagnostic. In equivocal cases supervised 72 hour fast with measurement of glucose, insulin and L-peptide can be used.

Localisation of the tumour is by imaging with CT or MRI. This will usually pick up most lesions of 1cm or bigger. Somatostatin receptor scintigraphy may be used, though only 30% of insulinomas express somatostatin receptors. Endoscopic ultrasounds will localise between 70-90% of tumours and is the diagnostic modality of choice.

Arteriography, selective portal venous sampling and arterial calcium stimulation are now reserved for patients with persistent or recurrent disease.

Treatment is by surgical excision, with cure ratios ranging from 80-100%. As the tumours are small, the surgery is being increasingly undertaken laparoscopically. The pancreas is exposed through the gastrocolic omentum. An obvious tumour is enucleated and the gland examined with laparoscopic ultrasound to ensure there are no further tumours. (Tumours in the tail of the pancreas may require distal pancreatectomy). There is now no place for blind distal pancreatectomies in patients in whom the tumour is not found. These are best abandoned and further localising studies initiated. The complication rate for laparoscopic enucleation is similar to that with the open operation but recovery is considerably quicker.