ENDOCRINE CASE OF THE MONTH

Pitfalls of Adrenal Cortex Sparing Adrenalectomy in MEN IIa Syndrome

Multiple endocrine neoplasia type IIa (MEN IIa) is characterised by occurrence of medullary thyroid carcinoma, adrenal medullary disease and parathyroid hyperplasia in a patient with a normal phenotype. Phaeochromocytomas are common in these patients occurring in approximately 50% but are usually diagnosed after the presentation of the medullary thyroid carcinoma. There is uniformally bilateral adrenal disease at the cellular level even if this is not clinically apparent at presentation. The conventional management of phaeochromocytomas has been bilateral adrenalectomy but adrenal cortex sparing surgery, either unilateral adrenalectomy or subtotal resection, to maintain adrenocortical function in patients with hereditary pheochromocytomas is becoming a popular alternative strategy[1,2,3].

Are there important clinical problems posed by adrenal cortex sparing adrenalectomy in MEN IIa syndrome?

Case Report

A 44-year old male was referred to his primary care physician for investigation and management of hypertension. He complained of intermittent attacks of sweating, headaches, and palpitations during the preceding year and volunteered the information that his father had also been hypertensive, had 'renal masses' and died from a cerebral vascular accident. The clinical findings were those of a mildly hypertensive male with minimal grade 1 hypertensive fundoscopic changes. Ultrasound scanning of the abdomen demonstrated bilateral masses in the adrenal glands. Urinary catecholamines were markedly elevated (normal values in parenthesis) – noradrenaline 1188 nmol/24hrs (100 to 820 nmol/24hrs), adrenaline 1598 nmol/24hrs (15 to 190 nmol/24hrs), dopamine 3732 nmol/24hrs (540 to 4440 nmol/24hrs), metadrenalines 90.9 umol/24hrs (less than 6.5 u/24hrs), HMMA 187 umol/24hrs (less than 35 umol/24hrs). Other investigations included serum calcitonin 0.36 ug/l (less than 0.08u/l), serum PTH 8.5 pmol/l (0.8 to 8.5 pmol/l) and serum calcium 2.6 mmol/l (2.1 to 2.6 mmol/l). Genetic mutational analysis for MEN IIa revealed a single base pair substitution in codon 634 (exon 11) consistent with a diagnosis of MEN IIa.

Magnetic resonance imaging demonstrated bilateral large adrenal masses consistent with a diagnosis of bilateral phaeochromocytoma. The right mass was noted to extend inferiorly and posterior to the upper pole of the right kidney. (Fig1)

Metaiodobenzyl guanadine (MIBG) scanning demonstrated intense abnormal uptake in bilateral adrenal masses consistent with phaeochromocytoma. (Fig 2a, 2b).

In summary at this stage the investigations indicated a patient with MEN IIa syndrome with bilateral adrenal medullary phaeochromocytomas. The elevated PTH with calcium at the upper limit of normal suggested a diagnosis of hyperparathyroidism and the elevated immunoreactive calcitonin level indicated C cell hyperplasia with or without associated medullary thyroid carcinoma. The clinical priority was surgical treatment of the bilateral phaeochromcytomas. After preoperative preparation with phenoxybenzamine an open surgical procedure rather than laparoscopic was performed in view of the size of the adrenal tumours. The patient had requested an adrenal cortex sparing procedure in the hope of avoiding long term cortical steroid medication. The right adrenal gland was large (12 cms in greatest diameter) dumbell shaped and extended posterior to the inferior vena cava. This gland was totally excised. The left adrenal gland contained a large tumour mass (6 cm) which was carefully dissected and the phaeochromocytoma excised leaving a well vascularised intact cortex and adrenal vein in situ.

The patient's post operative course was satisfactory but a short synacthen test indicated pre dose and post dose cortisol levels of only 204 and 172 mmol/L respectively. There was clearly inadequate residual cortical function and the patient was commenced on

hydrocortisone and fludrocortisone. Three months post surgery he began to complain of further episodes of sweating, headaches and palpitations and developed recurrent hypertension. Urinary catecholamine levels were again elevated with total metadrenalines of 7.7umol/24hrs (less than 6.5umol/24hrs), HMMA 56 umol/24hrs (less than 35umol/24hrs). Magnetic resonance imaging of the upper abdomen revealed a small oval 2.2x1cm low signal mass in the region of the left adrenal bed (Fig 3). The signal features were not typical of phaeochromocytoma and an MIBG scan showed normal trace distribution without any evidence of any increased uptake. It seemed probable the excess catecholamine secretion was arising from the left adrenal remnant and after further alpha adrenergic blockade the left adrenal remnant was excised via a left posterior loin incision excising the 11th rib. Histology of this adrenal remnant showed cortical tissue but also hyperplastic adrenal medullary tissue consistent with residual phaeochromocytoma. The patient's subsequent post operative recovery was uneventful with blood pressure and urinary catecholamines returning to normal.

Once the patient had fully recovered from the second adrenal surgery a total thyroidectomy was performed removing a 10mm diameter medullary thyroid carcinoma within the right thyroid lobe with background focal C cell hyperplasia. Cervical lymph nodes from the paratracheal and bilateral carotid regions were free of disease. One enlarged hyperplastic parathyroid gland was excised the remaining 3 normal glands being left in situ.

Post operative calcium and calcitonin levels normalised satisfactorily.

Discussion

The most common presentation of MEN IIa is medullary thyroid carcinoma. An initial presentation with bilateral phaeochromocytomas,as in the present patient,is unusual accounting for only 9.6% of MEN IIa patients. Traditionally the treatment of phaeochromocytomas occurring in the setting of MEN IIa syndrome has been a bilateral total adrenalectomy. This strategy commits the patient to life long steroid hormone replacement and the possible risk of Addisonian crisis[4]. If only one phaeochromocytoma has been demonstrated by cross sectional imaging the alternative approach is to perform an unilateral adrenalectomy and wait for clinical and biochemical evidence of catecholamine hypersecretion from the contra lateral adrenal. Approximately half of such patients will require a further operation because of development of a phaeochromotcytoma at a later date.

This procedure has the benefit that the patient will not be steroid dependent until total adrenalectomy has been performed, the time period often being many years. In the present case the alternative strategy of an open subtotal adrenalectomy was performed leaving unilateral well vascularised cortex and an intact adrenal vein on the left side. This approach has been widely described in the literature[5,6] and offers the potential of advantages of

1. The patient will not be left with the significant problems of steroid dependence.
2. It is potentially a one step curative procedure.

There are however pitfalls which the present case highlights. In spite of careful gland dissection the patient can still be left with insufficient adrenal cortical tissue rendering them steroid dependent. The second potential problem with subtotal adrenalectomy is recurrent phaeochromocytoma also illustrated in the present case.

Although care was taken at the initial surgery to perform a complete resection of all phaeochromocytoma histological examination of the completed adrenalectomy showed remnants of hyperplastic adrenal medullary tissue.

An open adrenalectomy had been performed because of the size of the tumours. For smaller adrenal lesions a bilateral laparoscopic adrenalectomy is the method of choice, the magnification permitting better visualisation of the adrenal vascular supply and may facilitate a more precise dissection.

Legends for Figures

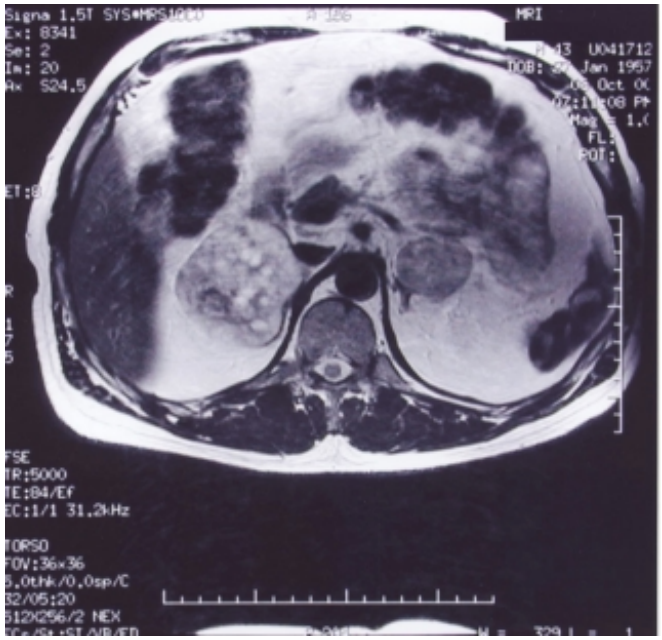

Figure 1
Magnetic resonance imaging showing bilateral adrenal masses consistent with phaeochromocytomas.

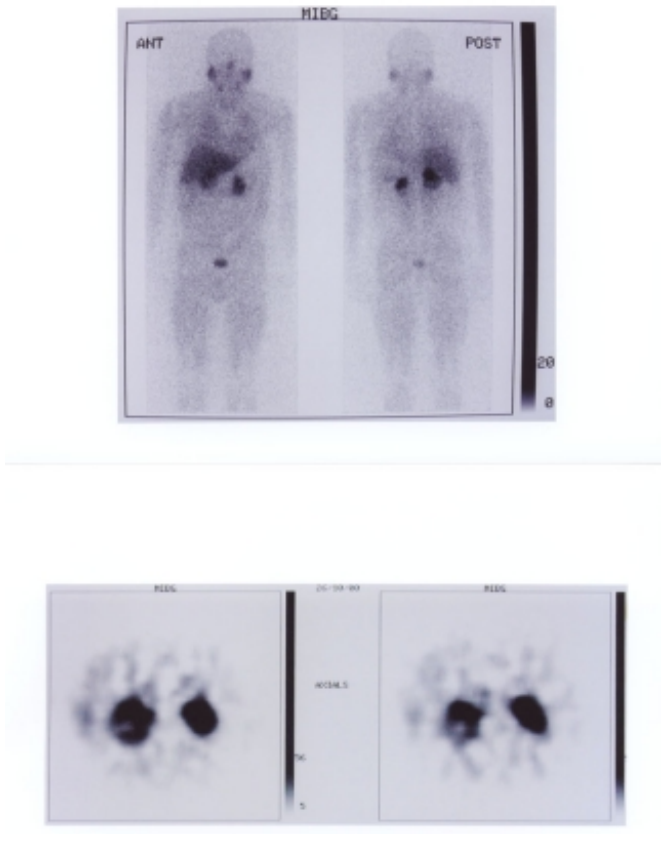

Figure 2a, 2b
Metaiodobenzylguanidine (MIBG) scanning showing intense bilateral adrenal gland uptake.

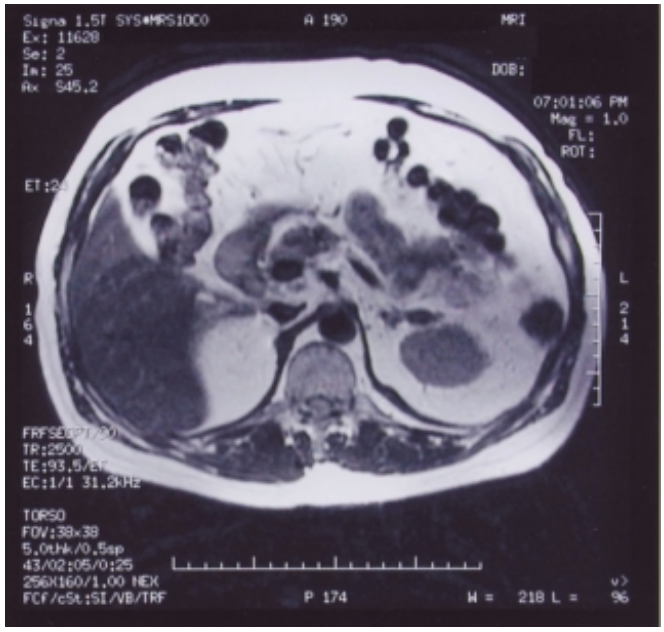

Figure 3
Magnetic resonance imaging demonstrating a small oval lesion in the left adrenal bed.

References

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