PITFALLS OF ¹³¹I-METAIDOBOZENYL GUANIDINE (MIBG) DIAGNOSTIC SCANNING IN PHAEOCHROMOCYTOMA: TWO CASE REPORTS AND A LITERATURE REVIEW

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The ¹³¹I-MIBG diagnostic scan has been regarded as a sensitive investigation for localising tumours of chromaffin tissue origin. Two cases are presented in which this investigative modality was insensitive and misleading, when used to localise concomitant phaeochromocytomas at more than one site.

CASE REPORT ONE

A 43-year-old male presented to the Accident and Emergency Department with six weeks of sweating attacks and two weeks of increasing breathlessness, productive cough and blood-tinged sputum. On examination, he was distressed and hypoxic with severe congestive cardiac failure and blood pressure 210/110 mmHg. A chest radiograph confirmed widespread pulmonary oedema. Urgent mechanical ventilatory support and intensive care were required. Central venous pressure was elevated and echocardiography demonstrated dilated right heart chambers. Underlying pulmonary thromboembolism and myocardial infarction were excluded. Respiratory function improved after treatment of cardiac failure by intravenous diuretics and ventilatory support was discontinued after four days. Investigation of the persistently elevated blood pressure showed urine normetadrenaline 57.5 mmol/24 hours (Ref. 0.4-3.4 mmol/24 hours), strongly suggesting an underlying phaeochromocytoma. He was treated with phenoxybenzamine 20 mg t.d.s., metoprolol 100 mg b.d. and frusemide 40 mg daily, with good control of blood pressure and cardiac failure.

Subsequent investigations were directed to localising histumour and abdominal ultrasound showed a bilobulated solid mass of the right adrenal, with no other abnormality elsewhere. Diagnostic scanning with 18.5 MBq ¹³¹I-MIBG gave intense uptake at the right adrenal and, on the basis of these investigations, the diagnosis was of a solitary phaeochromocytoma of the right adrenal gland. However, a pre-operative CT scan demonstrated abnormal masses in both adrenal glands and the patient was subject to bilateral adrenalectomy. Histopathology confirmed encapsulated phaeochromocytoma of both adrenal glands. Antihypertensive medications were withdrawn and urinary catecholamine secretion became undetectable. However, serum calcitonin was found to be elevated and subsequent thyroidectomy revealed foci of medullary thyroid carcinoma, consistent with multiple endocrine neoplasia IIa syndrome.

Blood pressure and urinary catecholamine secretion are currently normal, 14 years after his initial presentation.

CASE REPORT TWO

A 38-year-old caucasian man was referred to our ‘cardiovascular risk’ clinic in October 1995. Hypertension had been diagnosed 15 years previously and he was taking regular nifedipine. In 1990 he developed sudden onset of right facial and arm weakness, which resolved within one hour. CT of the head and carotid doppler scans were normal and he was commenced on aspirin therapy. His blood pressure was 160/90 mmHg. Urea, electrolytes, urinalysis and renal isotope scan had been normal, and his nifedipine dosage was increased prior to discharge.

He described occipital headaches since the age of 14. These only lasted for a few moments, usually occurred with micturition and had increased in severity over recent months, commonly associated with nausea, sweating and anxiety. There was no haematuria, dysuria nor loin pain. Erectile impotence was present since his nifedipine dosage was increased. His father had died from a stroke aged 46 years. His weight was 80 kg and seated blood pressure 153/99 mmHg in both arms; he was euthyroid and further examination, including fundoscopy, was normal. The electrocardiogram and chest radiograph were both normal. Average daytime blood pressure was 155/100 mmHg with a normal nocturnal reduction (146/91 mmHg) during 24-hour recording. His anti-hypertensive medication was increased.

Further blood pressure measurement showed 140/80 mmHg resting, 150/90 mmHg post-exercise and 240/135 mmHg post-micturition. Post-micturition recording was associated with tachycardia and adrenergic symptoms. Subsequent 24-hour urinary collection confirmed the diagnosis of phaeochromocytoma, with normetadrenaline excretion of 123.8 mmol/24 hours. Ultrasoundography revealed a 5.5 x 3.9 cm mass within the wall of the bladder and normal renal tracts and adrenals. Four grams per day of metyrosine (which inhibits tyrosine hydroxylase and catecholamine synthesis) were administered but phenoxybenzamine 60 mg q.d. and atenolol 100 mg q.d. had to be added for adequate blood pressure control. CT scanning of thorax, abdomen and pelvis confirmed the bladder lesion and normal adrenal glands and also demonstrated a 5 cm metastasis involving the upper sternum. 20 MBq of radioiodinated MIBG (¹³¹I-metaiodobenzylguanidine) was used for diagnostic scanning and this revealed high uptake by bladder and sternum (sites identified by CT scanning, see Figure 1). No other significant sites of uptake were noted.

The diagnosis was of a primary bladder phaeochromocytoma with a solitary sternal metastasis, which raised the possibility of resective cure. Simultaneous sternectomy and partial cystectomy was considered but rejected and, for logistic reasons, sternectomy was rejected and, for logistic reasons, sternectomy was considered but rejected and, for logistic reasons, sternectomy was...
undertaken first in February 1996. A phaeochromocytoma was confirmed microscopically. Before partial cystectomy could be performed he developed shoulder pains and fever. Examination and investigations did not reveal a source of sepsis. An isotope bone scan (see Figure 2) revealed multiple metastatic bone deposits which had not been detected by the radiolabelled MIBG scan or CT scan. The plan for cystectomy was abandoned and the patient was referred for cytotoxic chemotherapy.

In June 1996, he presented with breathlessness due to multiple pulmonary emboli, confirmed by ventilation/perfusion lung scanning. Despite commencement of warfarin therapy, he died several days later. Autopsy confirmed pulmonary infarction and embolisation. Survey of adrenal glands, sympathetic and parasympathetic ganglia, carotid arteries and organs of Zuckerkandl were normal. The bladder tumour and multiple metastatic bony deposits were confirmed as phaeochromocytoma.

DISCUSSION

Phaeochromocytoma is a rare chromaffin tissue neoplasm with an annual incidence of approximately 1.3 per million.1 The urinary bladder is the primary site in approximately 1%,2 and surgical resection can result in potential cure, normalisation of blood pressure and control of symptoms.3 A disproportionate number of bladder phaeochromocytomas are malignant, undoubtedly having been present for many years prior to detection, often having arisen in childhood. Phaeochromocytoma is often suspected on the basis of adrenergic symptoms, and ambulatory blood pressure monitoring often reveals absence of the normal nocturnal fall in blood pressure and reversal of the normal inverse relationship between heart rate and blood pressure, but this was not noted in Patient 2.4 Measurement of urinary metadrenaline and normetadrenaline gives almost 100% sensitivity and is an important diagnostic investigation.5 Potential curative resection depends on accurate localisation by CT scan, MRI, radiolabelled MIBG scan or venous sampling. The 131I-MIBG scan has been regarded as reliable for identifying chromaffin tissue but our first case illustrates how reliance on this alone could have led to non-curative unilateral adrenalectomy. Even when combined with CT scanning, the 131I-MIBG scan led to an underestimate of the extent of metastatic disease in our second patient and to surgery, which otherwise would have been avoided.

Radioiodine-labelled MIBG diagnostic scanning
MIBG is a noradrenaline analogue that moves into adrenergic neurones by a specific, energy-dependent mechanism, and is concentrated within secretory granules. Following injection of 18.5 MBq of 131I-MIBG, the adrenal medullae may be faintly visualised, while a phaeochromocytoma can demonstrate intense focal uptake.6 Uptake is not dependent on the catecholamine-secreting capacity of the tumour and the 131I-MIBG scan is regarded as a useful investigation with high sensitivity.7 However, CT scan is a more widely available, also highly-sensitive investigation and is generally accepted as the localising modality of choice.8 Small, incidental adrenal adenomas occur in 1-2% of the population and must be considered when evaluating a CT scan.9 A series 131I-MIBG scanning yields 87.5% sensitivity and 100% specificity in localisation of all phaeochromocytomas,10 with 92.4% sensitivity and 100% specificity for malignant disease.11 Clinical consequences of false negative 131I-MIBG scan results have previously been reported,12,14 and drugs which can interfere with MIBG uptake are recognised.15 The interval between isotope administration and scanning is important in detection of bony metastases,16 and test sensitivity improves after treatment.14 The latter observation probably arises due to loss of high-uptake tissue and, consequently, greater availability of isotope for remaining tissue. Several studies also report failure of 131I-MIBG to identify metastatic disease in up to 40% of patients undergoing staging.17,18 By comparison, bone scintigraphy identified 74% of bony metastases in a group of 38 patients, which is more frequently than CT scanning or 131I-MIBG scanning alone.19 This modality has not received due
attention in phaeochromocytoma staging. Bone scintigraphy is an accepted adjunct to $^{131}$I-MIBG for detection of bone involvement in neuroblastoma, a tumour also derived from chromaffin tissue.20

The $^{131}$I-MIBG scan can be a useful test for location of phaeochromocytoma after biochemical confirmation has been made. We recommend CT scanning as the localising investigation of choice, reserving $^{131}$I-MIBG scanning for those with a negative CT study. Our second patient, however, reminds us that the $^{131}$I-MIBG scan is poor at staging metastatic disease, even when combined with CT scanning. Our experience indicates that, when malignant disease is encountered or suspected, bone scintigraphy should be performed to complement $^{131}$I-MIBG, to characterise the extent of metastatic spread.

REFERENCES:


