Case report

SDHB gene positive metastatic paraganglioma associated with lesions which demonstrate both positive and negative uptake of 18FDG PET and 131MIBG

R. CASEY¹, D. SLATTERY¹, S. PRENDEVILLE², M. MOORE³, M. MAHER³ and D. O’HALLORAN¹

From the ¹Department of Endocrinology, ²Department of Pathology and ³Department of Radiology, Cork University Hospital, Cork, Ireland

Address correspondence to Dr R. Casey, Department of Endocrinology, Cork University Hospital, Cork, Ireland. email: ruthcasey232@gmail.com

Learning Points for Clinicians

Paragangliomas are rare catecholamine secreting neuroendocrine tumours. The diagnosis and management of these tumours is often difficult, particularly as a diagnosis of metastases is often made retrospectively when disease recurrence occurs. In recent years, the role of genotyping has allowed us to better predict which tumours are more likely to be metastatic. Mutations in the SDHB gene have been associated with higher rates of metastatic disease.¹

Unfortunately, mutations in this gene can also lower the sensitivity of radiolabeled metaiodobenzylguanidine (MIBG). MIBG scanning is considered the gold standard imaging modality for the diagnosis of recurrent disease but this case illustrates the potential diagnostic pitfalls associated with this imaging modality in cases of SDHB gene mutations. The case demonstrates the importance of genotyping as a diagnostic and predictive tool and the importance of clinical acumen in the face of negative test results.

Background

This gentleman underwent a MRI of pelvis in February 2011 for investigation of possible sacroiliitis on a background of known inflammatory bowel disease. This MRI demonstrated a 2.3 x 2.3 cm nodule posterior to the pubic symphysis in close proximity to the prostate. The patient underwent two ultrasound guided biopsies of the nodule but histology was inconclusive. The nodule was excised in July 2011 and intraoperatively the patient had a hypertensive crisis and urinary catecholamines and metanephrines were performed. Urinary metanephrines levels were elevated and patient was subsequently referred to the endocrine service. The patient denied any symptoms of anxiety, headaches, palpitations, weight loss or sweating. He had no history of hypertension and the only medical history of note was ulcerative colitis which was quiescent. The only symptom reported was left hip pain. He had no relevant family history. On examination the patient had no cutaneous or syndromic features but did have low grade hypertension.

Investigations

1. Serum chromogranin A 29 (<60 pmol/l);
   Serum chromogranin B 45 (<150 pmol/l).

Analysis performed on a radio-immunoassay at the Hammersmith laboratory in the UK.

© The Author 2013. Published by Oxford University Press on behalf of the Association of Physicians. All rights reserved. For Permissions, please email: journals.permissions@oup.com
2. Urine collection for metanephrines and catecholamines.

Analysis performed using high-performance liquid chromatography.

Urine volume measured 1500 ml;
Noradrenaline 1073 (50–900 mmol/24 h);
Adrenaline 38 (10–230 mmol/24 h);
Metanephrine 591 (25–1800 mmol/24 h);
Normetanephrine 9722 (50–2800 mmol/24 h);
Dopamine 1159 (50–3300 mmol/24 h).

3. Genetic analysis
Genetic analysis was performed in the West Midlands regional genetic laboratory, UK.
Heterozygous pathological deletion of exon 3 on the SDHB gene identified.

4. Radiology
18FDG positron emission topography (PET) CT scan revealed lytic lesions within the left petrous apex, left humeral head and mid right femoral diaphysis, which also showed increased uptake of 18FDG FDG and findings suggested skeletal metastases. There was avid uptake of radio pharmaceutical within these lesions on 131MIBG imaging. An area of lucency was noted in the left proximal femur on MRI Figure 1(a) and plain film. On MIBG scanning, there was no increased uptake Figure 1(b) of radio pharmaceutical within the lytic lesion.

5. Histology
(1) Histology of resected extra prostatic nodule showed a nested tumour which was strongly positive with the neuroendocrine markers chromogranin A and synaptophysin, in keeping with metastatic paraganglioma.
(2) Biopsy of the left femur showed multiple fragments of bone, fibro-connective tissue, haemorrhage and fibrosis which demonstrated both chromogranin and synaptophysin staining. The morphological and immunohistochemical findings were consistent with necrotic neuroendocrine tumour.

Discussion
Anatomical localization of phaeochromocytomas (PHEO) and paragangliomas (PGLs) is often confirmed by CT or MRI after a biochemical diagnosis. However, functional imaging remains the gold

![Figure 1. (a) Coronal Short TI Inversion Recovery (STIR) image shows a focal well-circumscribed focus of increased signal intensity (arrow) in the proximal diaphysis of the left femur. (b) 1131MIBG scan shows increased uptake of 1131MIBG in the left humeral head and mid right femoral diaphysis (arrows). There is also a focus of increased uptake in the right suprarenal area and left petrous apex at skull base (arrows). There is no abnormal uptake within the left femoral diaphysis.](image-url)
standard and practices have shifted in recent years with the discovery of specific genotype–phenotype correlations. MIBG remains the first line nuclear imaging modality and is essential in the diagnosis and work up for I 131MIBG therapy. I 131MIBG conveys function of the tumour. The sensitivity of I 131MIBG is reduced in patients with SDHB mutations and in dopamine secreting tumours. The sub-optimal sensitivity of I 131I MIBG for metastatic PHEO and PGL has been reported in studies and attributed to the de-differentiation of tissue that results in loss of norepinephrine transporters in the tumour. PET combined with radiolabeled somatostatin analogues has shown a high sensitivity for the detection of small tumours and particularly in the detection of metastatic disease involving lung and bone. In cases of metastatic PGLs or hereditary PGLs secondary to SDHB mutation, the superior nuclear imaging modality is 18F-FDG PET. In this case, we present the findings of a metastatic paraganglioma with metastatic deposits to the femur, in which there was no increased uptake of 18 FDG on PET or I 131MIBG. There are two possible hypotheses for the lowered sensitivity of functional imaging in this case. One explanation is that the areas of necrosis noted on histology interfered with the uptake of FDG and MIBG. The second possibility is that the genetic defect in SDHB caused a de-differentiation of the metastatic deposit. This case highlights the complex nature of this neuroendocrine tumour and the diagnostic dilemma faced due to the atypical behaviour of metastatic lesions on scintigraphy.

Conflict of interest: None declared.

References