Letter to the Editor

Elevated ^{131}I-MIBG activity in adrenocortical adenoma—what other imaging options do we have?

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Introduction

Metaiodobenzylguanidine (MIBG) functional imaging can detect neuroblastoma with high sensitivity and specificity (1). Its diagnostic accuracy for primary pheochromocytoma (PC), malignant PC, and multiple endocrine neoplasia is also very high (2). Therefore, ^{131}I/^{123}I-MIBG scintigraphy is recommended to screen for PC in patients with abnormal hypertension, especially in those with suspicious adrenal lesions (3). However, adrenocortical adenoma can cause false positive results, as illustrated by this case report.

Case presentation

A 54-year-old man presented with repeated headaches for 6 months and hypertension. Recorded blood pressure measurements were as high as 238/138 mmHg. Laboratory testing revealed a slightly elevated plasma cortisol concentration of 569.5 nmol/L (8 AM, normal range, 171–536 nmol/L). Plasma and urinary catecholamine concentrations were within normal limits and 24-h urinary total metanephrines were 1,616 nmol/d (normal range, 0–1,622 nmol/d). The serum renin/aldosterone levels was 21.84 (normal range, 0–32). The 8 AM adrenocor ticotropic (ACTH) levels were also within normal limits (35.47 pg/mL, normal range, 7–64 pg/mL). The patient was 172 cm in height and weighed 87.6 kg (body mass index, 29.6 kg/m^2). His physical examination was otherwise unremarkable (no signs of an excessive production of adrenocortical steroids such as in Cushing's syndrome). Both parents had a history of hypertension. Genetic testing was not performed. Unenhanced abdominal computed tomography (CT) performed at an outside hospital revealed a small homogeneous micronodule (<1 cm) in the left adrenal. He was then referred to our hospital for ^{131}I-MIBG scintigraphy. Scintigraphy showed elevated activity in the upper left abdomen at 24 h that was more prominent on the 72-h scan (*Figure 1A-1D*). Single-photon emission (SPECT)/CT imaging at 48 h confirmed uptake of ^{131}I-MIBG in the left adrenal (*Figure 1E-1M*). Although PC was suspected based on the imaging findings in the presence of severe hypertension, the laboratory findings were not consistent with PC. However, the patient's blood pressure remained poorly controlled despite medical therapy. He took perindopril (4 mg daily), indapamide sustained-release tablets (1.5 mg daily), spironolactone (40 mg daily) and bexinostat (60 mg daily) for blood control. Therefore, we elected to proceed with a left retroperitoneal laparoscopic adrenalectomy after obtaining informed consent. The final pathological diagnosis was adrenocortical adenoma (*Figure 1N-1O*). One

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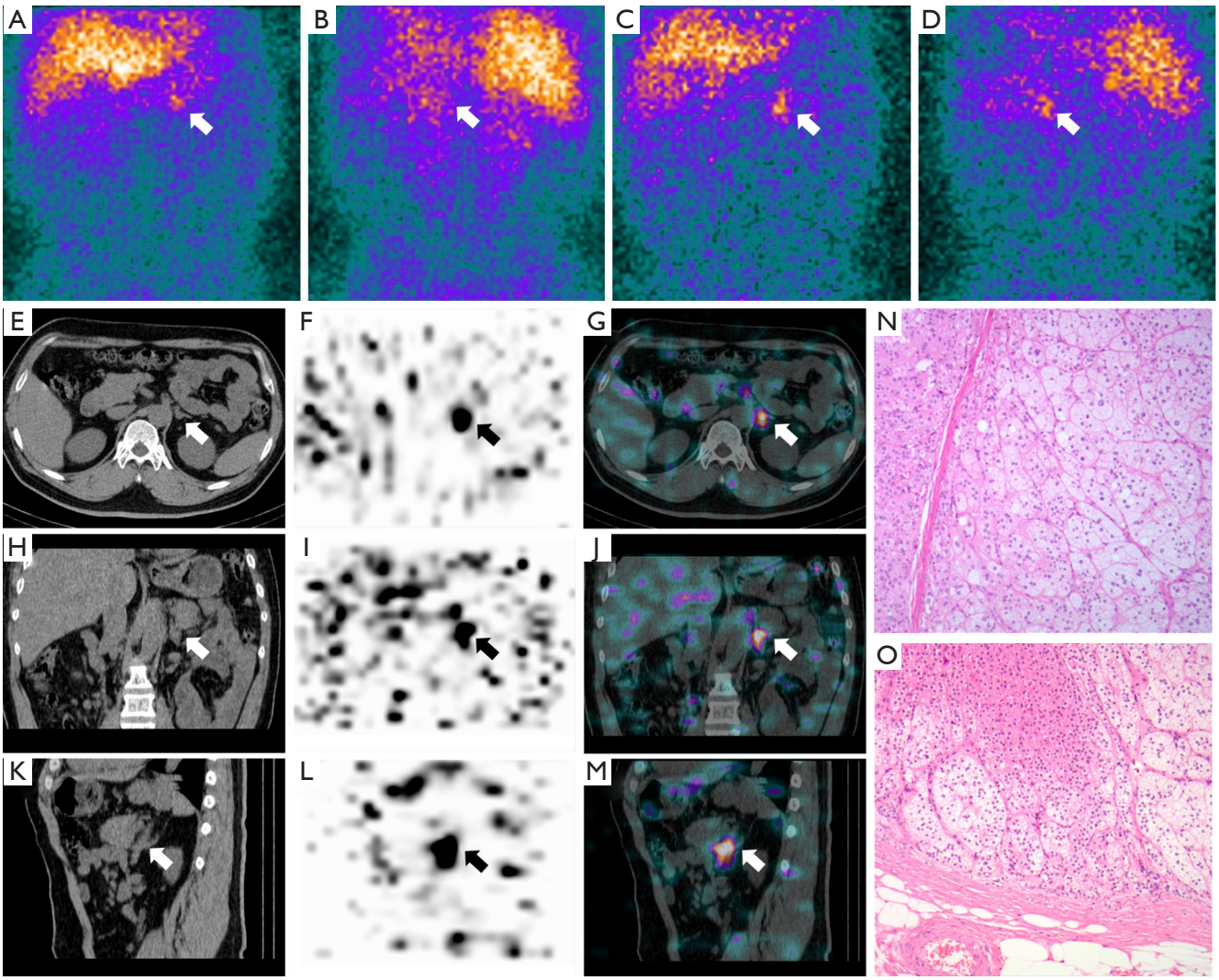

Figure 1 [131]I-Metaiodobenzylguanidine (MIBG) single-photon emission/computed tomography (SPECT/CT) and histological findings. A focus of elevated activity in the upper left abdomen was detected on imaging acquired 24 h after [131]I-MIBG administration (A, anterior view; B, posterior view); activity was more prominent on the 72-h imaging (C, anterior view; D, posterior view). SPECT/CT imaging (E-G, axial; H-J, coronal; K-M, sagittal) acquired 48 h after tracer administration confirmed that the abnormal activity corresponded to the small homogeneous nodule in the left adrenal (arrows). The largest dimension of the nodule was 0.9 cm. Adrenocortical adenoma was histologically proven following laparoscopic left adrenalectomy (hematoxylin and eosin stain; N, ×100; O, ×40).

month after operation, his blood pressure was controlled with bexinostat (30 mg daily) and terazosin hydrochloride (2 mg daily) and remained normal during one year of follow-up.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

A diagnosis of PC can be made when a patient has a history of hypertension, elevated serum and urinary metanephrine concentrations (catecholamine metabolites),

and positive findings on MIBG scintigraphy (1,4). However, approximately 6.2% of patients with negative results for urinary metanephrines, in these patients the MIBG results could be negative or positive (5). MIBG is the first-line functional imaging agent used in neuroblastoma imaging and has high sensitivity and specificity (1). Diagnostic accuracy of MIBG is also very high for primary and malignant PC and multiple endocrine neoplasia (5). The reported specificities and sensitivities of ^{123}/^{131}I-MIBG scintigraphy for PC range from 77% to 100% and 85% to100%, respectively (3,6,7). Other diagnoses that may cause positive MIBG scintigraphy include normal adrenal, adrenal metastasis of choriocarcinoma, adrenocortical adenoma (8-12), focal pyelonephritis, small ischemic kidney, hepatic hemangioma, dilated renal pelvis, and adenomatous polyp of the caecum (13-15). In our patient, elevated ^{131}I-MIBG activity was found in an adrenocortical adenoma. Previously reported adenomas causing false-positive MIBG scintigraphy were greater than 1.8 cm in diameter (10-12); however, the lesion in our patient was much smaller, measuring 0.9 cm in largest dimension. It is unusual for a lesion of this size to cause significant tracer uptake.

The mechanism responsible for abnormal MIBG uptake in adrenocortical adenoma remains unknown. Coexisting medullary hyperplasia, dense medullary granules within the nodule, and concurrent paraganglioma have been offered as possible explanations (10-12). Another possibility is disturbed cellular uptake of MIBG relative to that of noradrenaline (5,16).

Studies have shown that ^{18}F-fluorodihydroxyphenylalanine (^{18}F-FDOPA) positron emission tomography (PET)/CT can provide additional diagnostic and localization information regarding PCs, as ^{18}F-FDOPA uptake may be enhanced by overactivity of catecholamine exocytosis (17,18). Moreover, ^{18}F-FDOPA has shown better diagnostic performance than MIBG and ^{18}F-fluorodeoxyglucose (^{18}F-FDG), particularly for hypersecreting PCs, and has fewer drug interactions. We suggest that ^{18}F-FDOPA be used as the first-line tracer for PC diagnosis and staging.

Other imaging techniques can also be helpful to distinguish adrenocortical adenoma. Attenuation of these lesions is typically <10 Hounsfield units on unenhanced CT (19,20). On opposed-phase magnetic resonance imaging, adrenocortical adenoma demonstrates rapid washout and loss of signal (21). ^{18}F-FDG PET/CT can differentiate malignant lesions from adrenal adenomas using a maximum standard uptake value (SUVmax) cutoff of 3.1 (22,23). In addition, ^{11}C-metomidate has been suggested as a tracer to distinguish cortical and non-cortical adrenal lesions and is used to evaluate incidental adrenal masses (24,25). Furthermore, ^{131}I-6-betaiodomethyl-19-norcholesterol (NP-59) can accumulate in the adrenal cortex and has been reported to have high specificity and accuracy for identification of adrenocortical lesions, especially primary aldosteronism (PA) (26). NP-59 SPECT/CT is safe. It can provide accurate lateralization, and can improve clinical outcome in patients with PA-associated hypertension (27). In our case, based on the symptoms of the abnormal hypertension and laboratory results, PC and PA could not be excluded. However, NP-59 scan was not available in our hospital. The patient was referred a ^{131}I-MIBG scan to have further diagnosis.

According to the European Society of Endocrinology Clinical Practice guidelines, unilateral adrenalectomy is recommended for patients with a unilateral adrenal mass that secretes hormones or having imaging findings suspicious for malignancy (28). However, there is no clear consensus on the definition of abnormal cortisol secretion; therefore, indications for adrenalectomy remain controversial (29). Laparoscopic surgery is the standard approach for PC resection (6,7) and was utilized in our patient. Although his laboratory results were not consistent with PC, we elected to proceed with adrenalectomy because of poorly controlled hypertension. It was possible that the patient had a PC, PA, or functional adrenal mass that should have been surgically treated (6). After surgery, his blood pressure returned to normal.

Our case demonstrates that even a small adrenocortical adenoma can accumulate MIBG and cause a diagnostic dilemma when evaluating a patient for possible PC. Clinicians should be aware of other diagnostic options such as ^{18}F-FDOPA, ^{18}F-FDG, or ^{11}C-metomidate PET/CT and ^{131}I-NP-59 SPECT/CT.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was reviewed and approved by the Ethics Committee of Union Hospital, Tongji Medical College. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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