□ CASE REPORT □

False-Positive ^{123}I -Metaiodobenzylguanidine (MIBG) Scan in a Patient with Angiomyolipoma; Positive MIBG Scan does not Necessarily Indicate the Presence of Pheochromocytoma

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Abstract

^{123}I -Metaiodobenzylguanidine (^{123}I -MIBG)-accumulation in angiomyolipoma (AML) is demonstrated. A 24-year-old Japanese woman presented with tumors in the right retroperitoneal space. The tumors, which accumulated ^{123}I -MIBG, had been thought to be adrenal pheochromocytoma before surgery. They were removed, and were found to be AML. ^{123}I -MIBG was accumulated in AML. ^{123}I -MIBG-accumulation in AML led to a false-positive diagnosis of adrenal pheochromocytoma. Catecholamine levels had been normal. No chromogranin cells were found in the histological examination of the tumors. MIBG accumulation does not necessarily indicate the presence of pheochromocytoma.

Key words: angiomyolipoma, ^{123}I -MIBG, pheochromocytoma

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Introduction

Iodine 123 -metaiodobenzylguanidine (^{123}I -MIBG) is widely used to localize pheochromocytoma (1, 2). As the molecular structure of MIBG is similar to that of noradrenaline, it is concentrated, released, and stored in the chromaffin granules (3). MIBG has also been used to localize neuroblastoma (4), medullary carcinoma of the thyroid (5), and carcinoid tumor (6, 7). Its diagnostic specificity for pheochromocytoma is reported to be high (2). False-positive findings in MIBG imaging have been reported to be rare (2, 3, 8). We describe a case of angiomyolipoma (AML). Accumulation of ^{123}I -MIBG by AML led to a false-positive diagnosis of adrenal pheochromocytoma.

Case Report

A 24-year-old Japanese woman presented with right upper abdominal pain over a few days. Otherwise, she had been well and had no history of hypertension, headache, palpitation, or epilepsy. Abdominal ultrasonography demonstrated a

5.0×4.0 cm tumor above the right kidney (upper tumor) and another 1.0×2.0 cm tumor beneath the right kidney (lower tumor). The upper tumor was thought to be an adrenal tumor. Abdominal computed tomography scan (CT scan) and magnetic resonance imaging (MRI) (Fig. 1) suggested that the upper tumor could be pheochromocytoma and the lower tumor might be angiomyolipoma (AML). She was admitted for further evaluation in mid-November, 2004. She was 151.1 cm tall, and weighed 55.8 kg. Her body mass index was 24.5 kg/m². Blood pressure was 106/70 mmHg. Her neurological examination was normal. She did not have any clinical features of Cushing's syndrome. Routine laboratory examinations were normal. Urinary adrenaline was 6.8 µg/day (normal range, 3.0-15.0), urinary noradrenaline 93.8 µg/day (26.0-121.0), urinary dopamine 1,059.6 µg/day (190.0-1,100.0), urinary VMA 3.3 mg/day (1.3-5.1), urinary metanephrine 0.25 mg/day (0.12-0.49), urinary free cortisol 46.8 µg/day (11.2-80.3), urinary 17-KS 7.4 mg/day (2.4-11.0), and urinary 17-OHCS 6.6 mg/day (2.2-7.3). Plasma adrenaline was 25 pg/ml (normal range <100), plasma noradrenaline 221 pg/ml (100-450), plasma dopamine <5 pg/ml (<20), plasma aldosterone 100 pg/ml (29.9-159), and

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Figure 1. Gadolinium-enhanced abdominal MRI reveals two tumors; a 5.0×4.0 cm tumor above the right kidney (upper tumor in the text) and another 1.0×2.0 cm tumor beneath the right kidney (lower tumor in the text). A; the arrow indicates the upper tumor, which was not enhanced by gadolinium. B; the arrow indicates the lower tumor, which was diffusely enhanced by gadolinium.

Figure 2. ^{123}I -MIBG scan tomography (single photon emission computed tomography: SPECT) demonstrates the upper and lower tumors (upper and lower tumors in the text). The upper and lower tumors accumulated ^{123}I -MIBG (24 h after injection). A; the arrow indicates ^{123}I -MIBG-accumulation in the upper tumor. B; the arrow indicates ^{123}I -MIBG-accumulation in the lower tumor.

plasma renin activity 0.9 ng/ml/hr (0.3-2.9). Plasma cortisol was 21.0 $\mu\text{g/ml}$ at 8:00 (10.0-25.0). Plasma ACTH was 34.2 pg/ml at 8:00 (7.4-55.7). These hormone levels, including urinary and plasma catecholamines, were normal. However, plasma chromogranin A (CgA)-level was 623 ng/ml, which was above the cut-off value of 175 ng/ml. ^{123}I -MIBG scan tomography (single photon emission computed tomography: SPECT) was done. Both upper and lower tumors accumulated ^{123}I -MIBG (Fig. 2). She was thought to have an asymptomatic pheochromocytoma on the basis of MIBG-accumulation and increased plasma CgA-levels. Surgical removal of these tumors was done in February 2005. The right kidney, adrenal gland, and the tumors were removed en mass (Fig. 3). The cut surface revealed the adrenal gland (adrenal), upper tumor (A), lower tumor (B), and kidney (kidney). This cut surface demonstrated the topographic relationships among the adrenal gland (adrenal), upper tumor (A), lower tumor (B), and kidney (kidney). Histological examinations of the adrenal and kidney revealed no pathological abnormalities, and showed normal histology of adrenal and kidney. Histological examinations revealed that both up-

Figure 3. The right kidney, adrenal gland, and the tumors were removed en mass. The cut surface revealed the adrenal gland, upper tumor (A), lower tumor (B), and kidney. Histological examinations of the adrenal gland and kidney revealed no pathological abnormalities, and showed normal histology of kidney and adrenal gland. Histological examinations revealed that both the upper and lower tumors (A, B), which accumulated ^{123}I -MIBG, were AML (Fig. 4).

Figure 4. Histology of the upper tumor. A and B [hematoxylin eosin staining (HE)] demonstrate that the upper tumor contained proliferated smooth muscles and abnormal vessels but less proliferated adipose tissues. C [HMB-45 staining] demonstrates positive HMB-45 staining. In C, the arrow indicates positive HMB-45 staining. HMB-45 has a high sensitivity for angiomyolipoma. Histology of the lower tumor. D and E [hematoxylin eosin staining (HE)] demonstrate that the lower tumor contained more proliferated adipose tissue than the upper tumor, and that it is a typical angiomyolipoma. F [HMB-45 staining] demonstrates positive HMB-45 staining. In F, the arrow indicates positive HMB-45 staining.

per and lower tumors, which accumulated ^{123}I -MIBG, were AML (Fig. 4). Proliferated smooth muscle and abnormal vessels but a few adipose tissues were noted in the upper tumor (Fig. 4A, B). The tissue from the lower tumor demonstrated typical features of AML (Fig. 4D, E, F). The tissues

from both tumors were positive for HMB-45 staining (Fig. 4C, F). Both tumors were AML. The tissues from both tumors were negative for synaptophysin- and CgA-immunostainings (data not shown). Her plasma CgA levels decreased to 150 ng/ml one month after the operation.

Plasma chromogranin A (CgA) was determined by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Dako, Denmark) that used antibodies to a 23-kDa C-terminal fragment of human CgA, as reported previously (9, 10). As the reference value, 175 ng/ml was chosen as the upper cut-off value to avoid overlapping values with normal subjects (9). Written informed consent was obtained from the patient.

Discussion

This is the first report to demonstrate ^{123}I -metaiodobenzylguanidine (MIBG)-accumulation in angiomyolipoma (AML). We have shown a patient with tumors in the right retroperitoneal space. Accumulation of ^{123}I -MIBG had been thought to be adrenal pheochromocytoma before surgery. The tumors were removed. They were AML. Accumulation of ^{123}I -MIBG by AML led to a false-positive diagnosis of adrenal pheochromocytoma. MIBG-accumulation does not necessarily indicate the presence of pheochromocytoma.

Angiomyolipoma (AML) is a benign neoplasm composed of fat, vascular, and smooth muscle elements. Two types of AML are described; isolated AML and AML associated with tuberous sclerosis (9). This patient may have isolated AML. It is also possible that she may have AML associated with tuberous sclerosis. She developed a large angiomyolipoma at the age of 24 years old. This raises the possibility that she may have tuberous sclerosis. With isolated AML, most patients are aged 27-72 years, with a mean age of 43 years. With AML associated with tuberous sclerosis, the mean age of patients is 17 years.

Chromogranin A (CgA) is a general marker for neuroendocrine tumors. Plasma CgA levels have been reported to be high in patients with tumors of neuroectodermal origin such as pheochromocytoma and paraganglioma (10, 11). Circulating CgA assay was reported to be positive in 12 out of 12 patients with pheochromocytoma and negative in 92 out of

92 patients with non-chromaffin adrenal nodules (12). The present patient had a high plasma CgA level. However, she did not have pheochromocytoma. Her plasma CgA levels were 623 ng/ml before the operation and decreased to 150 ng/ml one month after the tumor removal. AML might have produced CgA in our patient.

The level of the tumor marker for neuro-endocrine tumor was elevated. She was thought to have asymptomatic pheochromocytoma, although hormone levels, including plasma and urinary catecholamines, had been normal. She underwent surgery. Histological examination revealed that the tumors were AML. Accumulation of ^{123}I -MIBG by AML led to a false-positive diagnosis of adrenal pheochromocytoma. MIBG-accumulation depends on increased blood flow delivery and MIBG uptake (13). The rich formation of abnormal vessels in AML might have caused ^{123}I -MIBG accumulation. Increased blood flow delivery and MIBG uptake caused the false-positive ^{123}I -MIBG accumulation in our patient with AML. We have shown ^{123}I -MIBG accumulation in AML. ^{123}I -MIBG scan has a high sensitivity and specificity for the diagnosis of pheochromocytoma (2, 3). However, false-positive MIBG accumulations have been reported (13-22). This seems to be contradictory. This contradiction stems from the interpretation of the data in references 2, 3 and 8. A high specificity of MIBG imaging for the diagnosis of pheochromocytoma was demonstrated. Most patients without pheochromocytoma in the previous reports have no tumors in or around adrenal glands. Therefore, the specificity presented there is not relevant to the cases where pheochromocytoma is suspected in patients with tumors detected with MRI.

Accumulation of ^{123}I -MIBG by AML led to a false-positive diagnosis of adrenal pheochromocytoma. AML could accumulate ^{123}I -MIBG. ^{123}I -MIBG scan might not be as specific as previously thought for the differentiation of pheochromocytoma.

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