

Imaging of Medullary Thyroid Carcinoma and Hyperfunctioning Adrenal Medulla Using Iodine-131 Metaiodobenzylguanidine

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Scintigraphy with radiolabeled metaiodobenzylguanidine was performed in a patient with MEN Type IIa having a pheochromocytoma of the right adrenal gland, adrenomedullary hyperplasia of the left adrenal gland and a primary medullary thyroid carcinoma. The scintigraphic findings demonstrate visualization of all the above mentioned pathologies.

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Radioiodinated metaiodobenzylguanidine ($[^{131}\text{I}]$ MIBG) has proved useful in localizing catecholamine producing tumors such as pheochromocytoma, neuroblastoma, as well as adrenomedullary hyperplasia (1-4). We report a patient with MEN Type IIa in whom, using $[^{131}\text{I}]$ MIBG, we were able to diagnose and localize a pheochromocytoma in the right adrenal gland and visualize a medullary hyperplasia of the left adrenal gland. In addition, a primary medullary thyroid carcinoma (MTC) which contained elevated tissue catecholamines was detected by MIBG scintigraphy in this case.

CASE REPORT

The patient, a 26-yr-old white female, is a member of a family with MEN Type IIa syndrome. Her father had unilateral adrenal pheochromocytoma and a medullary thyroid carcinoma. Her paternal uncle had bilateral adrenal pheochromocytoma with MTC. Her paternal grandmother died of metastatic thyroid carcinoma. One daughter of a paternal uncle showed abnormal calcitonin stimulation to calcium infusion. The patient's sister and the paternal uncle's son and other daughter had normal biochemical screening tests. The patient denied a history of hypertension, headaches, excessive sweating, palpitation, or chest pain. The patient was asymptomatic with a blood pressure of 140/80 mmHg and had a 1-cm nodule in the left upper pole of the left lobe of the thyroid. Twenty-four-hour urine collection on two different occasions demonstrated free catecholamines levels of 297 $\mu\text{g}/24$ hr (normal 120 $\mu\text{g}/24$ hr) and metanephrines levels of 0.2 and 0.4 mg/24 hr (normal 0.9 mg/24 hr). The patient's plasma

0.4 mg/24 hr (normal 0.9 mg/24 hr). The patient's plasma catecholamines were as follows: norepinephrine 951 ng/l (normal 148 \pm 35), epinephrine 144 ng/l (normal 42 \pm 35), and normetanephrine 414 ng/l (normal 84 \pm 30). The serum calcium was normal on three occasions.

Computerized tomography (CT) showed a 2-cm right adrenal gland tumor and the left adrenal which was considered to be of normal size (Fig. 1A). Two weeks later, after informed consent was obtained, her thyroid was blocked with Lugol's solution and $[^{131}\text{I}]$ MIBG imaging was performed at 24, 48, and 72 hr following the i.v. injection of a standard dose of 0.5 mCi (18.7 MBq)/1.7m² body surface area, as previously described (4). The images showed bilateral abnormal adrenal uptake (Fig. 1B), as well as focal uptake in the thyroid gland (Fig. 1C). The uptake in the adrenal glands using a previously published scale (4) was grade 3+ on the left and 4+ on the right side.

The patient subsequently had a bilateral adrenalectomy with right and left adrenal glands weighing 20 g and 6 g, respectively. Gross and microscopic examination of the surgical specimen demonstrated a pheochromocytoma in the right adrenal gland and nodular hyperplasia of the left adrenal gland. Three weeks following bilateral adrenalectomy, the patient underwent total thyroidectomy and was found to have a 1.5-cm nodule in the left lobe and a 1-cm nodule in the upper pole of the right lobe of the thyroid. Microscopic examination revealed bilateral medullary carcinoma of thyroid with production of amyloid. Calcitonin level at the time of thyroidectomy was 4,007 pg/ml (normal 0-100), which fell postoperatively to 3,700 pg/ml. Both adrenal glands and the left lobe of the thyroid were assayed for norepinephrine (NE) and epinephrine (E) by standard methods as described by Crout (5). The right adrenal gland tissue NE and E levels were 4,506 $\mu\text{g}/\text{g}$ and 1,749 $\mu\text{g}/\text{g}$ and left adrenal gland tissue NE and E levels were 178 $\mu\text{g}/\text{g}$ and 771 $\mu\text{g}/\text{g}$. The NE and E levels of the thyroid tumor were 5.05 $\mu\text{g}/\text{g}$ and 0.83 $\mu\text{g}/\text{g}$, while that of nontumor tissue were 1.1 $\mu\text{g}/\text{g}$ and 0.04 $\mu\text{g}/\text{g}$, respectively.

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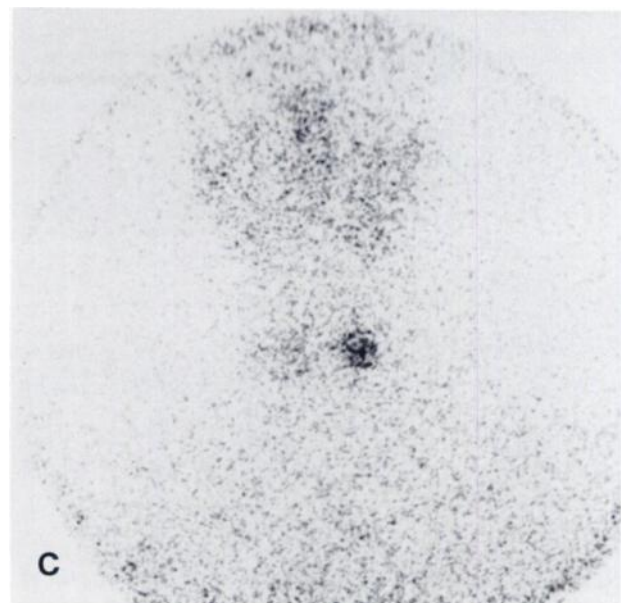
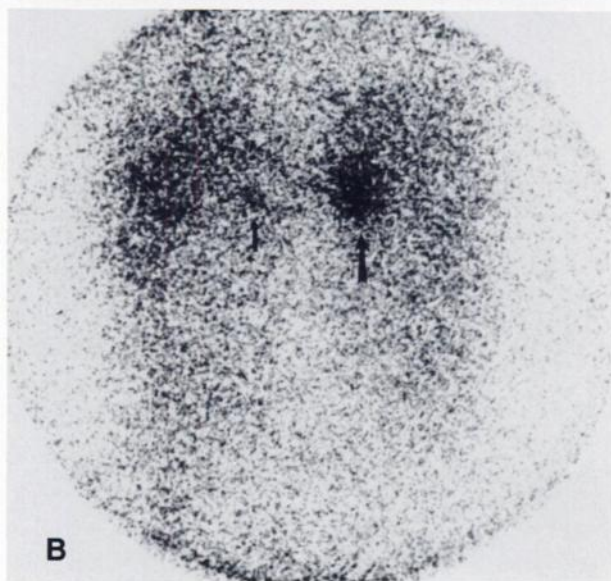
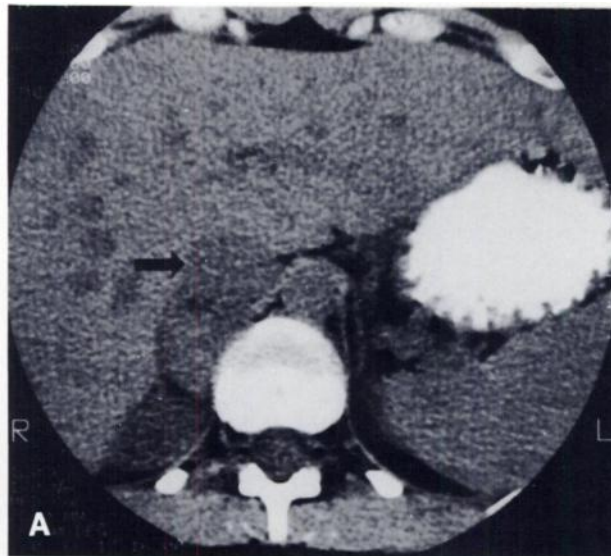


FIGURE 1

A: CT of abdomen showing 2-cm tumor of right adrenal gland (arrow). B: [¹³¹I]MIBG image of posterior mid abdomen showing grade 4+ uptake in right adrenal (large arrow) and grade 3+ in left adrenal (small arrow). C: Anterior [¹³¹I] MIBG image of head and neck. There is significant uptake of radiotracer in left lobe and faint uptake in right lobe

DISCUSSION

Adrenal-medullary hyperplasia is considered to be a precursor of pheochromocytoma in MEN Type IIa and medullary hypertrophy reduces the normal corticomedullary anatomic ratio (6). In our patient, the presence of pheochromocytoma of one adrenal gland and a nodular medullary hyperplasia of the other gland adds some support to the hypothesis that nodular medullary hyperplasia may be one of the stages of a fully developed pheochromocytoma.

MEN Type IIa syndrome has been attributed to a defect in a single stem cell system originating in the neural crest (7). It is, therefore, not surprising to hypothesize a medullary thyroid carcinoma producing catecholamines.

Voelkel et al. (8) in their study reported significant concentration of NE and E in liver metastasis from

medullary thyroid carcinoma, while none was detected in the normal liver. They found no detectable catecholamines in primary medullary thyroid carcinoma. In our patient, the tumor contained catecholamines levels that were five times that found in nontumor thyroid tissue. Whether catecholamines found in the thyroid were produced by thyroid gland or were stored in thyroid gland is not clear at the present time.

In addition, this case demonstrates the utility of functional imaging in that the anatomic abnormality may be minimal and difficult to detect, yet the functional difference may be great and allow for detection. In our case, the right adrenal pheochromocytoma weighed 20 g and was easily diagnosed by CT, while the abnormality of the left adrenal which weighed only 6 g was missed by CT, yet detected by MIBG imaging. Thus, although the spatial resolution of MIBG imaging may be less than that of CT, the functional abnormal-

ities allowed for detection of tumor, hyperplasia of adrenal medulla, and medullary thyroid carcinoma.

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