Acta Medica Okayama

Volume 43, *Issue* 5 1989 *Article* 8

OCTOBER 1989

A case of unilateral adrenal medullary hyperplasia.

Yoshio Maki* Shin Irie†

Teruhisa Ohashi‡ Hiroyuki Ohmori**

*Okayama University,

†Okayama University,

‡Okayama University,

**Okayama University,

A case of unilateral adrenal medullary hyperplasia.*

Yoshio Maki, Shin Irie, Teruhisa Ohashi, and Hiroyuki Ohmori

Abstract

We report a case of unilateral hyperplasia of the adrenal medulla. The patient showed clinical features suggestive of pheochromocytoma. Removal of the hyperplastic adrenal gland resulted in complete disappearance of all prior symptoms, decrease of the plasma and urinary catecolamine levels and no high uptake in [133I] metaiodobenzylguanidine scintigraphy. A histological study revealed diffuse hyperplasia of the adrenal medulla. Up to now, there are relatively few reports of adrenal medullary hyperplasia in English literatures.

KEYWORDS: adrenal medullary hyperplasia, pheochromocytoma, ?^{131} I ?metaiodobenzylguanidine scintigraphy

---

*PMID: 2610007 [PubMed - indexed for MEDLINE]

Acta Med Okayama 43 (5) 311-315 (1989)

—Brief Note—

A Case of Unilateral Adrenal Medullary Hyperplasia

Yoshio Maki[a,*], Shin Irie, Teruhisa Ohashi and Hiroyuki Ohmori

Department of Urology, Okayama University Medical School, Okayama 700, Japan

We report a case of unilateral hyperplasia of the adrenal medulla. The patient showed clinical features suggestive of pheochromocytoma. Removal of the hyperplastic adrenal gland resulted in complete disappearance of all prior symptoms, decrease of the plasma and urinary catecolamine levels and no high uptake in [^{131}I] metaiodobenzylguanidine scintigraphy. A histological study revealed diffuse hyperplasia of the adrenal medulla. Up to now, there are relatively few reports of adrenal medullary hyperplasia in English literatures.

Key words : **adrenal medullary hyperplasia, pheochromocytoma, [^{131}I] metaiodobenzylguanidine scintigraphy**

The occurrence of hyperfunction of the adrenal medulla, causing permanent or paroxysmal hypertension, has long been known. In most cases a pheochromocytoma was thought to be the underlying cause, but a new entity, adrenal medullary hyperplasia, has recently been considered. This hyperplasia is not a common cause of hypertension, but an increasing number of cases are being reported by greater alertness and improved techniques.

A 66-year-old man was first advised of his hypertension (160/95 mmHg) and hypertensive retinopathy by a physician 7 years ago. In September 1986, he consulted an ophthalmologist of our hospital because of ocular pain and headache. His blood pressure was 212/108 mmHg, and he was referred to a physician, and then to our department for further examination.

Upon microscopic examination, the urine was found to be normal. Urinary levels of 17-hydroxycorticosteroid (17-OHCS) and 17-ketosteroid (17-KS), and the plasma level of cortisol gave no indication of increased activity of the adrenal cortex. Although plasma catecolamines showed normal levels, urinary catecolamine levels were high. Plasma levels of renin and aldosterone were normal (Table 1). Complete blood counts and biochemical data were all within normal limits. The blood sugar tolerance test revealed a diabetic pattern. The electrocardiogram revealed myocardial ischemia. Roentogenographic examination of the chest showed pleural thickening and adhesion due to old tuberculosis. Enlargement of the left adrenal gland was found by computalized tomography (CT) (Fig. 1), and scanning with [^{131}I] metaiodobenzylguanidine (^{131}I-MIBG) showed an accumulation of

a: Present address: Department of Urology, Kochi Central Hospital, 2-7-33, Sakuraicho, Kochi 780, Japan.
* To whom correspondence should be addressed.

Table 1 Hormone levels in blood plasma (p) and urine (u) of a patient with unilateral adrenal medullary hyperplasia

Hormone[a]	Before the operation		After the operation	
	Jul. 25	Sep. 26	Nov. 28	Dec. 4
Adrenaline (p) (<0.10 ng/ml)	0.08	0.09	0.02	0.03
Noradrenaline (p) (0.05-0.40 ng/ml)	0.13	0.23	0.25	0.33
Adrenaline (u) (<10 mcg/day)	45.6	27.1	15.1	5.3
Noradrenaline (p) (10-90 mcg/day)	609.7	212.2	220.3	137.1
Dopamine (u) (100-700 mcg/day)	3573.2	521.8	432.5	320.3
Renin (p) (0.3-4.0 ng/ml/h)		2.3	0.8	1.6
Aldosterone (p) (47-131 pg/ml)		136.9	34.9	61.7
Cortisol (p) (4.9-14.7 mcg/dl)		14.6	7.8	9.2
17-KS (u) (3-9 mcg/day)		3.62		
17-OHCS (u) (3-9 mcg/day)		3.82		

a: Normal values are shown in parentheses.
Abbreviations: 17-KS, 17-ketosteroid; 17-OHCS, 17-hydroxycorticosteroid.

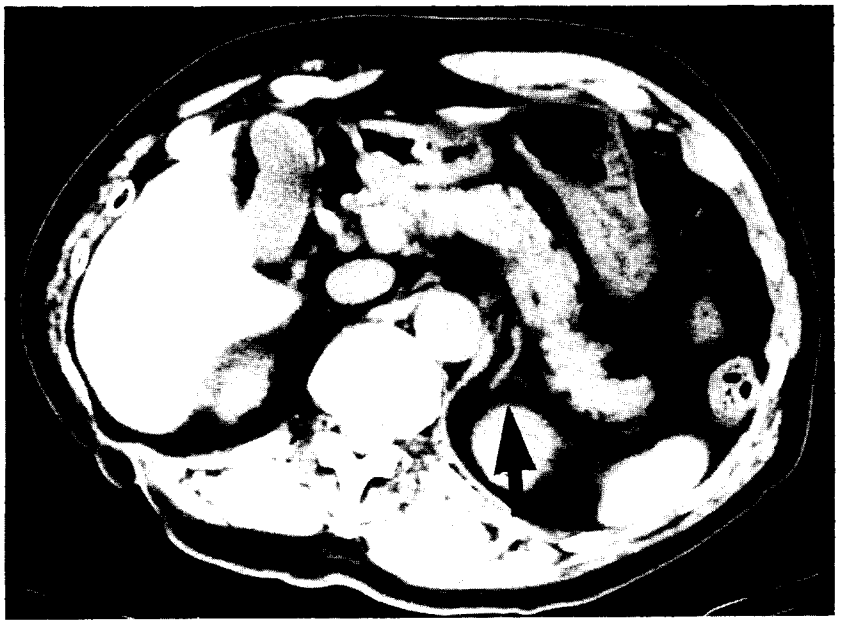

Fig. 1 CT scan of the abdomen of a patient with unilateral adrenal medullary hyperplasia. Arrow indicates the enlarged adrenal gland.

radiopharmaceutical in the left upper abdomen (Fig. 2A).

In November 1986, a left adrenalectomy was performed under general anesthesia. The left adrenal gland was diffusely enlarged, 50×32×8 mm in size. No abnormality was found in the right adrenal gland by visual inspection and palpation.

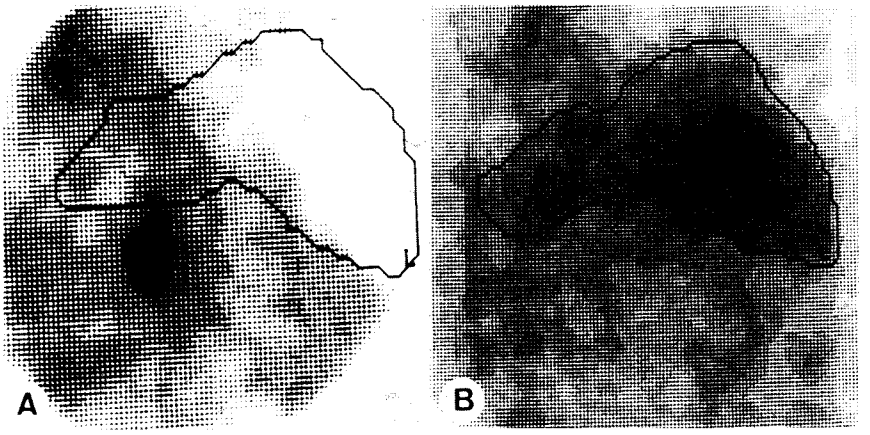

Fig. 2 [^{131}I] Metaiodobenzylguanidine scintigram of the abdomen of a patient with unilateral adrenal medullary hyperplasia. A: High uptake in the left hypochondric region before the operation. B: Disappearance of high uptake after the operation.

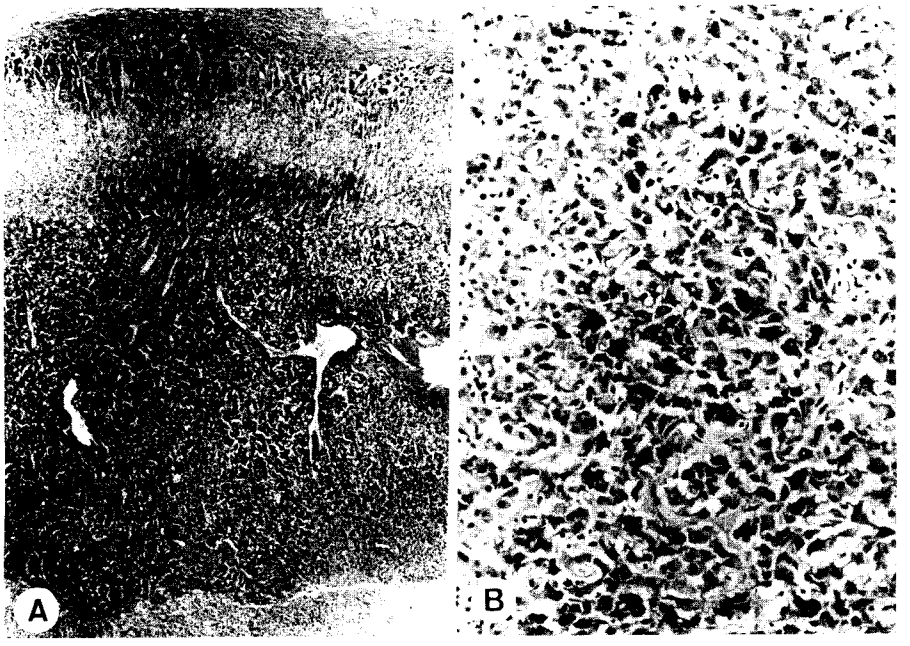

Fig. 3 Histological section of the left adrenal gland. A: Marked hyperplasia of the adrenal medulla. B: Cellular pleomorphism and vacuolation.

After the operation, the patient's blood pressure dropped to 116-140/70-80 mmHg. The high uptake of ^{131}I-MIBG disappeared in the scintigraphy (Fig. 2B). Urinary catecolamine showed much decreased levels compared with the data before the operation (Table 1), but these were still above normal values. This was supposed to be a compensatory hypersecretion of catecolamines from the remaining adrenal gland to maintain blood pressure.

In the cutting section, no tumor was found, and a histological study revealed diffuse hyperplasia of the adrenal medulla (Fig. 3A). The corticomedullary ratio was 1 : 1, which is much less than the normal ratio of 10 : 1. Microscopically, medullary cells showed pleomorphism and vacuolation, but no tumor was found (Fig. 3B). In the adrenal cortex, zona fasciculata and reticularis were no longer clearly distinguishable because of intense cell involution. Histological diagnosis was adrenal medullary hyperplasia.

There have been about ten reports on adrenal medullary hyperplasia producing the clinical features of pheochromocytoma, and most of them are reports of bilateral medullary hyperplasia. In 1957, Drukker and his associates reported a case of bilateral hyperplasia of the adrenal medulla, and this was the first report which regarded this condition as a clinical entity (1). Visser and Regina reported a case of bilateral adrenal medullary hyperplasia, which was found during necropsy of a patient with myocardial infarction (2), who had paroxysmal hypertension and increased urinary 3-methoxy-4-hydroxymandelic acid (VMA) during treatment for myocardial infarction. They did not find any tumor in other chromaffin tissues during necropsy. Montalbano and coworkers reported a case of unilateral adrenal medullary hyperplasia (3), in which removal of the hyperplastic adrenal gland resulted in amelioration of signs and symptoms. Our case was diagnosed as unilateral adrenal medullary hyperplasia by the findings of ^{131}I-MIBG scintigraphy and CT. But we can not neglect the possibility of the presence of medullary hyperplasia in the remaining adrenal gland in subclinical level because of the persistence of higher urinary catecolamine levels after the operation.

Adrenal medullary hyperplasia can occur unilaterally or bilaterally. Hypersecretion of adrenocorticotropic hormone (ACTH) causes diffuse and bilateral hyperplasia of the adrenal cortex. But the cause of the adrenal medullary hyperplasia is different. Embryologically, the adrenal medulla and the paraganglia differentiate from a common stem cell, and both of these respond to sympathetic nerve stimulation. In 1975, Carney and his group examined 19 patients with multiple endocrine neoplasia, type 2 (4). He proposed a hypothesis that diffuse adrenal medullary hyperplasia is a precursor of pheochromocytoma and that genetically defective pheochromocytes (or paraganglion cells) became hyperplastic due to unknown stimulus. According to their hypothesis, hyperplasia of chromaffin cells could occur in various chromaffin tissues. Adrenal biopsy or adrenalectomy was necessary to determine the site of hyperplasia in the previous cases. However, ^{131}I-MIBG scintigraphy made it possible to locate the site without an invasive procedure. In Drukker's case, hypertension and tachycardia persisted even after bilateral adrenalectomy. This might suggest the presence of hyperplasia of chromaffin cells in extra-adrenal tissue. ^{131}I-MIBG scintingraphy is also useful for extra-adrenal involvement. ^{131}I-MIBG scintigraphy, however, can not distinguish adrenal medullary hyperplasia from pheochromocytoma. More cases of adrenal medullary hyperplasia will be detected by the combined use of ^{131}I-MIBG scintigraphy and

CT.

References

1. Drukker W, Formijne P and Van Der Schoot JB: Hyperplasia of the adrenal medulla. Br Med J (1957) **1**, 186-189.
2. Visser JW and Axt R: Bilateral adrenal hyperplasia: A clinico pathological entity. J Clin Pathol (1975) **28**, 298-304.
3. Montalbano FP, Baronofsky ID and Ball H: Hyperplasia of the adrenal medulla. J Am Med Assoc (1962) **182**, 264-267.
4. Carney JA, Sizemore GW and Sheps SG: Adrenal medullary disease in multiple endocrine neoplasia, type 2. Am J Clin Pathol (1976) **66**, 279-290.

Received May 9, 1989; accepted August 1, 1989