

[CASE REPORT]

Miction-induced Hypertension Disclosed by Home Blood Pressure Measurement in a Patient with Small Paraganglioma

Masakazu Teragaki¹, Takayuki Yamamoto¹, Kota Hosomi¹, Youhei Tada¹, Keiko Maeda¹, Daisuke Nishiya¹, Chinami Miyazaki¹, Yasuhiro Takagi¹, Yuji Sakanoue¹, Yukio Nishida², Hiroshi Okuno³, Mika Tsuiki⁴ and Mitsuhide Naruse⁵

Abstract:

A 46-year-old woman complained of a 10-year history of headache, nausea, a precordial oppressive feeling and shortness of breath on miction. She had noted a marked elevation in her blood pressure after miction using home blood pressure measurement. Her catecholamine levels were less than twice the value of the normal upper limit. Several imaging modalities detected a urinary bladder tumor, and ¹²³I-metaiodobenzylguanidine scintigraphy showed positive accumulation. The diagnosis of urinary bladder paraganglioma was confirmed by partial cystectomy. We must keep in mind that paroxysms and hypertension associated with miction are important diagnostic clues of pheochromocytoma/paraganglioma. Home blood pressure measurement was very useful for detecting hypertension in this case.

Key words: urinary bladder tumor, hypertensive crisis, catecholamine, secondary hypertension, postmiction syndrome

(Intern Med 59: 793-797, 2020)

(DOI: 10.2169/internalmedicine.3255-19)

Introduction

We often encounter patients with reflex-mediated hypotension associated with coughing, defecation or miction in daily clinical practice. However, paroxysms with blood pressure elevation on miction are experienced in patients with paraganglioma of the urinary bladder as a rare disease (1-5).

We herein report a case of urinary bladder paraganglioma in which the marked elevation of blood pressure after miction recognized by home blood pressure measurement led to the precise diagnosis.

Case Report

A 46-year-old woman visited our clinic due to a 10-year

history of headache, nausea, a precordial oppressive feeling and shortness of breath on miction. She also sometimes felt transient sweating. She had already visited other clinics, such as those for cardiology, urology or psychosomatic medicine, but no diagnosis had been obtained. Starting two months before our visit, she had begun to measure her home blood pressure and had noticed a marked elevation in her blood pressure after miction. Early in the morning of our visit, she complained of the above-mentioned symptoms on miction.

There were no remarkable findings in her family or personal history aside from dyslipidemia. On a physical examination, her blood pressure was 156/112 mmHg, and her pulse rate was 76 beats per minute with regular rhythm. No heart murmur was audible, and no skin abnormality was found. On laboratory tests, there were no abnormalities in a

¹Department of Cardiology, Higashiumiyoshi Morimoto Hospital, Japan, ²High Care Unit, Higashiumiyoshi Morimoto Hospital, Japan, ³Department of Urology, National Hospital Organization Kyoto Medical Center, Japan, ⁴Department of Endocrinology and Metabolism, National Hospital Organization Kyoto Medical Center, Japan and ⁵Center of Endocrinology, Takeda General Hospital, Japan

Received: May 7, 2019; Accepted: October 11, 2019; Advance Publication by J-STAGE: December 6, 2019

Correspondence to Dr. Masakazu Teragaki, teragaki@med.osaka-cu.ac.jp

Table 1. Daily Record of Home Blood Pressure and Heart Rate.

	morning		night		after miction	
	BP	HR	BP	HR	BP	HR
Day 1	124/99	99			177/122	63
Day 3	135/101	89				
Day 4			125/87	65		
Day 5	125/95	76	139/105	86	180/109	61
Day 6	127/101	86	144/104	75		
Day 7	127/99	76	130/93	67	191/119	57
					208/120	54
Day 8			141/107	71	171/98	65
Day 9	119/84	76				
Day 10	123/94	73				
Day 11	126/94	69	147/89	56	195/111	62
Day 12					215/124	62
Day 13					201/118	61

Bold-faced type indicates blood pressure after miction.

BP: blood pressure, mmHg, HR: heart rate, bpm

urinalysis or urinary sediments. Hematuria was not found. The results of a complete blood count and biochemistry in the blood showed no abnormalities except for high low-density lipoprotein and triglyceride levels (206 and 135 mg/dL, respectively). There were no abnormal findings in her electrocardiogram and chest radiogram. She was strongly suggested to have hypertension based on her conventional office blood pressure.

She took home blood pressure measurements in the morning, at night and after miction with clinical symptoms, according to the Guideline for the management of hypertension 2019 (JSH 2019) (6). Her home blood pressure measurements are indicated in Table 1. She was also diagnosed with hypertension based on her home blood pressure. Her systolic blood pressure rose markedly after miction (from 119-147 mmHg to 171-215 mmHg), and the above-mentioned symptoms manifested as well. The results of basic laboratory and endocrinological tests are shown in Table 2. The measurement of catecholamine was outsourced to BML (Tokyo, Japan) and LSI Medience (Tokyo, Japan). A mild elevation was found in normetanephrine in spot urine (509 ng/mg-Cr) and in noradrenaline (154 µg/day) and normetanephrine in 1-day urine (0.40 µg/day). However, these levels remained less than twice the value of the normal upper limit, despite the repeated collection of one-day urine samples.

On abdominal ultrasonography, no stenosis was detected in either renal artery, but a solid mass 15×11 mm in diameter was seen in the wall of the urinary bladder, located slightly to the right of the midline on the ventral side of the wall (Fig. 1). The blood flow was rich inside the mass. Abdominal computed tomography (CT) and magnetic resonance imaging (Fig. 2) both showed the presence of a mass, the same mass that had been observed by abdominal echo. In addition to these findings, the fusion images of ¹²³I-

metaiodobenzylguanidine (MIBG) scintigraphy and CT revealed the accumulation of the tracer in the same region (Fig. 3).

The characteristics of miction-induced symptoms with marked hypertension and the urinary bladder tumor detected by several imaging studies were highly suggestive of paraganglioma, although the endocrinological findings did not meet the criteria described in the Guideline (7). While controlling the blood pressure using 8 mg of daily Doxazosin administration, the urinary bladder was partially resected with a laparoscopic procedure. An immunohistochemical analysis of the tumor revealed positive staining for synaptophysin and chromogranin A. The final histopathological examination confirmed the diagnosis of urinary bladder paraganglioma. After the operation, her home blood pressure was measured again under the same conditions as before the operation (within five minutes after miction). The blood pressure measured arbitrarily 5 times was 134/93, 125/85, 131/88, 124/84 and 135/95 mmHg-values that were all markedly decreased compared to before the operation (Table 1). Miction-induced hypertension and the associated symptoms disappeared with no medication, and the catecholamine levels in one-day urine returned to normal.

Discussion

Catecholamine-secreting tumors are called pheochromocytoma or paraganglioma and arise inside or outside of the adrenal gland, respectively. Sympathetic paragangliomas arise in the abdomen (75%), the urinary bladder and prostate (10%), the thorax (10%) and the base of the skull (5%) (8). In the genitourinary tract, the urinary bladder is the most common site for paragangliomas (79%) (1). The most common symptoms of urinary bladder paraganglioma are reportedly hypertension, headache, painless hematuria and syncope/palpitation (2). The triad of hypertension, macroscopic hematuria and hypertensive seizure at miction was reported variably in 55-100%, 47-63% and 33-53% of patients, respectively (1, 3, 4). However, Yamamoto et al. reported in their review of 235 Japanese patients that 33% of the patients had hypertension, 41% hematuria and 23% miction attack (5). These differences may be due to the number of non-functioning tumors included in each report. They also mentioned that only 1.4% of patients showed all 3 symptoms, and 10.6% had none of the symptoms.

In our case, the patient had been suffering from headache, nausea, precordial oppression and shortness of breath for roughly 10 years before she visited our facility but still remained undiagnosed. Home blood pressure measurement over the previous two months had revealed the marked elevation of her blood pressure after miction, which was an important clue suggesting the diagnosis of urinary bladder paraganglioma. Blood pressure is widely measured at home in Japan (9, 10) and is a useful diagnostic clue for detecting hypertension that cannot be detected in a clinical setting. It is important to unify the measuring methods (11), and con-

Table 2. Laboratory and Endocrinological Findings.

Laboratory findings		Endocrinological findings		Normal value
WBC (μL)	5,350	Cortisol	6.5 $\mu\text{g/dL}$	4.5-21.1
RBC ($\times 10^4/\mu\text{L}$)	497	PRA	0.6 ng/mL/hr	0.2-2.0
Hb (g/dL)	13.4	Aldosterone	118.8 pg/mL	29.9-159
Hct (%)	41.0	FT4	0.9 ng/dL	0.8-1.7
PLT ($\times 10^4/\mu\text{L}$)	20.9	TSH	2.41 $\mu\text{IU/mL}$	0.40-4.40
CRP (mg/dL)	0.0	Adrenaline	0.02 ng/mL	<0.10
T-Bil (mg/dL)	0.6	Noradrenaline	0.28 ng/mL	0.10-0.50
Alb (g/dL)	4.5	Dopamine	<0.01 ng/mL	<0.03
AST (IU/L)	22	u-Metanephrine	87 ng/mg-Cr	<200
ALT (IU/L)	24	u-Normetanephrine	509 ng/mg-Cr	<291
LDH (IU/L)	165	u-Adrenaline	8.7 $\mu\text{g/day}$	1.1-22.5
Amylase (IU/L)	64	u-Noradrenaline	154 $\mu\text{g/day}$	29.2-118
BUN (mg/dL)	14.2	u-Dopamine	680 $\mu\text{g/day}$	100-1,000
Cr (mg/dL)	0.65	u-Metanephrine	0.08 $\mu\text{g/day}$	0.05-0.20
Na (mEq/L)	140	u-Normetanephrine	0.40 $\mu\text{g/day}$	0.10-0.28
K (mEq/L)	4.2			
Cl (mEq/L)	104			
TC (mg/dL)	302			
HDL-C	69			
LDL-C	206			
TG (mg/dL)	135			
BS (mg/dL)	93			
Urine				
pH	7.0			
protein	-			
glucose	-			
sediment				
WBC	<1			
RBC	<1			

WBC: White blood cell, RBC: Red blood cell, Hb: Hemoglobin, Hct: Hematocrit, PLT: Platelet, CRP: C-reactive protein, T-Bil: Total bilirubin, Alb: Albumin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, BUN: Blood urea nitrogen, Cr: Creatinine, Na: Sodium, K: Potassium, Cl: Chloride, TC: Total cholesterol, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, TG: Triglyceride, BS: Blood sugar, PRA: Plasma renin activity, FT4: Free thyroxine, TSH: Thyroid stimulating hormone, u-urinary

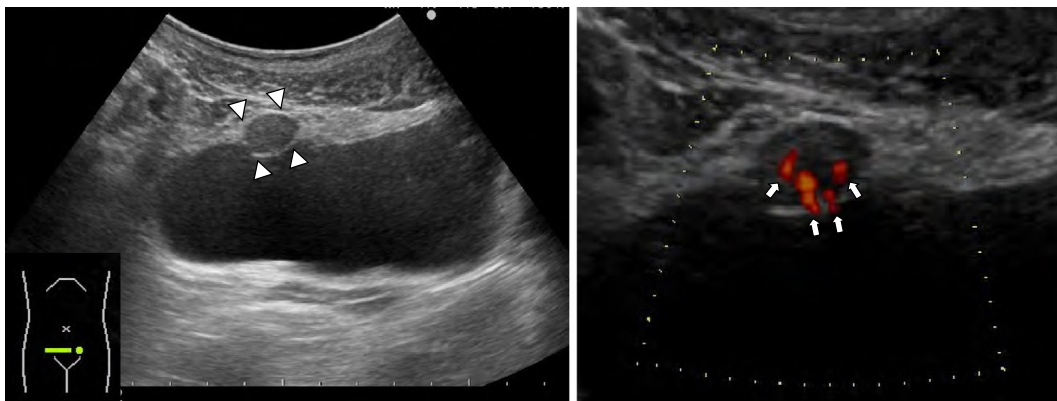


Figure 1. An abdominal ultrasonogram in the transverse section revealed a mass echo of 15×11 mm in diameter, located slightly to the right of the midline on the ventral side of the bladder wall (white arrowheads) (left panel). The signals of the blood flow in the mass could be seen in magnified image (white arrows) (right panel).

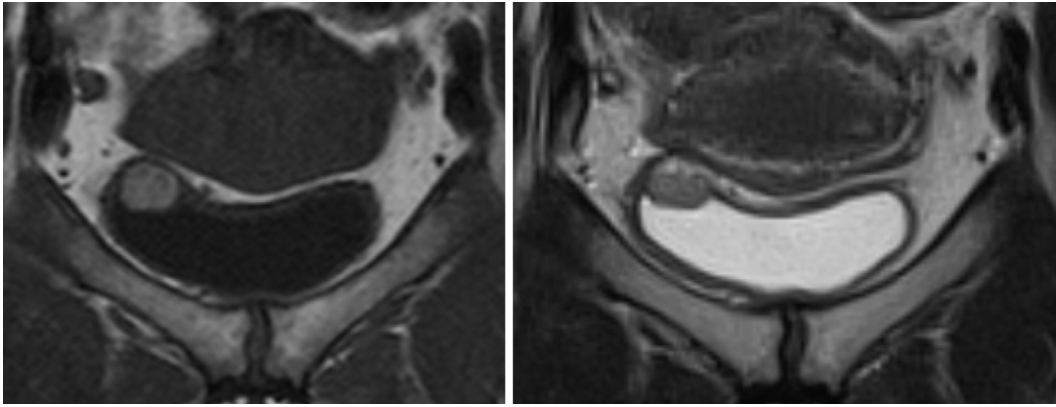


Figure 2. Magnetic resonance imaging in the coronal section revealed a mass in the urinary bladder, just as with abdominal echo and computed tomography (CT) (left panel: T1-weighted imaging, right panel: T2-weighted imaging).

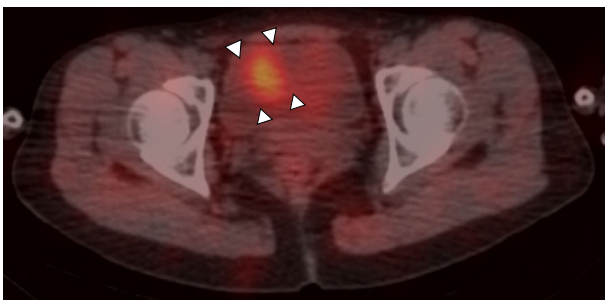


Figure 3. The fusion images of ^{123}I -MIBG scintigraphy and CT in the transverse section showed the accumulation in the bladder wall, which was located slightly to the right of the midline on the ventral side of the wall (white arrowhead). MIBG: metaiodobenzylguanidine

sulting the recent guideline is recommended when performing home blood pressure measurement (6). Fujishima et al. reported that 24-h ambulatory blood pressure monitoring may be useful for detecting transient hypertension induced by miction (12). However, it was also useful for recording spot measurements of blood pressure after miction with several symptoms, as in our case. Beilan et al. reported in their systematic review that, in 106 patients with urinary bladder paraganglioma, the mean tumor diameter was 3.9 cm (median 3.45 cm, range 1-9.1 cm) (1). The tumor in our case was quite small by comparison. When small-sized non-functioning paragangliomas are found incidentally, they must be given careful consideration if several characteristic symptoms on miction appear, even for small lesions, as in our case.

In everyday clinical practice, we often encounter patients with hypotension, presyncope or syncope on miction. This is well recognized as reflex-mediated syncope (13). Regarding the mechanism, miction stimulates the mechanoreceptor of the vagal nerve in the urinary bladder and causes vasodilatation of the peripheral arteries. However, in urinary bladder paraganglioma, the contraction of the urinary bladder during miction promotes catecholamine secretion into the blood,

which causes headache, tachycardia, palpitation, marked hypertension or syncope (14). It is necessary to be aware of the fact that syncope on miction may not only be caused by a decreased blood pressure, but that it also can be caused by an increased blood pressure.

Our case did not meet the endocrinological diagnostic criteria for pheochromocytoma/paraganglioma. According to the guidelines, the level of catecholamines usually exceeds three times the normal upper limit at the screening stage (7). It is recommended that sampling of the blood or urine be repeated or performed during a hypertensive attack. In our case, however, the catecholamine levels did not exceed twice the normal upper limit in spot and daily urine samples. One reason for this may be that sampling was performed during the interval between hypertensive attacks. Alternatively, the volume of catecholamine secretion may have been quite small due to the small tumor size. Jibiki et al. reported that the secretory capacity may be directly proportional to the size of the tumor (15). In our case, the specific symptoms of miction-induced hypertension and several prominent imaging studies in the urinary bladder strongly suggested urinary bladder paraganglioma, even though the catecholamine level did not meet the guideline criteria. Consequently, the patient underwent surgery and was diagnosed with paraganglioma histopathologically.

In conclusion, we encountered a case of urinary bladder paraganglioma in which the marked elevation of the blood pressure appeared after miction in association with specific symptoms. The records of home blood pressure measurement were a useful clue for the diagnosis. For the early diagnosis, it is important to consider pheochromocytoma or paraganglioma in patients with symptoms such as paroxysmal or persistent hypertension, hypertension with palpitation, sweating, headache, chest pain and hypertensive crises.

The authors state that they have no Conflict of Interest (COI).

References

1. Beilan JA, Lawton A, Hajdenberg J, Rosser CJ. Pheochromocytoma of the urinary bladder: a systematic review of the contemporary literature. *BMC Urol* **13**: 22-27, 2013.
2. Das S, Bulusu NV, Lowe P. Primary vesical pheochromocytoma. *Urology* **21**: 20-25, 1983.
3. Tsai CC, Wu WJ, Chueh KS, et al. Paraganglioma of the urinary bladder first presented by bladder bloody tamponade: two case reports and review of the literatures. *Kaohsiung J Med Sci* **27**: 108-113, 2011.
4. Deng JH, Li HZ, Zhang YS, Liu GH. Functional paragangliomas of the urinary bladder: a report of 9 cases. *Chin J Cancer* **29**: 729-734, 2010.
5. Yamamoto Y, Imamura R, Nakazawa S, et al. Paraganglioma of the urinary bladder managed by transurethral resection: a case report. *Jpn J Urol Surg* **26**: 231-234, 2013 (in Japanese, Abstract in English).
6. Guideline for the management of hypertension 2019 (JSH 2019). The Japanese Society of Hypertension, Ed. 2019(in Japanese).
7. Pheochromocytoma/paraganglioma Practice Guideline 2018. Japan Endocrine Society, Ed. 2018(in Japanese).
8. Lee JA, Duh QY. Sporadic paraganglioma. *World J Surg* **32**: 683-687, 2008.
9. Japan National Health and Nutrition 2010 [Internet]. [cited 2019 Sep 30]. Available from: <https://www.mhlw.go.jp/bunya/kenkou/eiyou/dl/h22-houkoku-01.pdf> (in Japanese).
10. Noda A, Obara T, Abe S, et al. The present situation of home blood pressure measurement among outpatients in Japan. *Clin Exp Hypertens* **13**: 1-8, 2019.
11. Kobayashi M, Obara T, Ohkubo T, et al. Practice and awareness of physicians regarding casual-clinic blood pressure measurement in Japan. *Hypertens Res* **33**: 960-964, 2010.
12. Fujishima S, Abe I, Kaseda S, et al. Ambulatory blood pressure monitoring in diagnosing a pheochromocytoma of the urinary bladder. A case report. *Angiology* **48**: 655-658, 1997.
13. Calkins H, Zipes DP. Reflex-mediated syncope, Chapter 43 Hypotension and Syncope. In: Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 11th ed. Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF, Eds. Elsevier Health Science, UK, 2018: 849-850.
14. Padevit C, John H, Ganz A, Wiesli P, Hauri D, Schmid C. Micturition syncope due to paraprostatic pheochromocytoma. *Urol Int* **74**: 276-277, 2005.
15. Jibiki K, Demura H, Naruse M, et al. Biochemical diagnosis of pheochromocytoma by determining normetanephrine and metanephrine concentrations in single voided urine. *Folia Endocrinol* **64**: 707-716, 1988 (in Japanese, Abstract in English).

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).