CASE REPORT

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

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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

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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
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.

In addition to these findings, the fusion images of 123I-metiadobenzylguanidine (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 1. Daily Record of Home Blood Pressure and Heart Rate.

| Day | Morning BP | Morning HR | Night BP | Night HR | After Miction BP | After Miction HR |
|-----|------------|------------|----------|----------|-----------------|-----------------|
| 1   | 124/99     | 99         |          |          | 177/122         | 63              |
| 2   | 135/101    | 89         |          |          |                 |                 |
| 3   | 125/95     | 76         | 139/105  | 86       | 180/109         | 61              |
| 4   | 127/101    | 76         | 130/93   | 67       | 191/119         | 57              |
| 5   | 127/99     | 76         | 147/89   | 56       | 195/111         | 62              |
| 6   | 119/84     | 76         |          |          | 215/124         | 62              |
| 7   | 126/94     | 69         |          |          | 201/118         | 61              |

Bold-faced type indicates blood pressure after miction.

BP: blood pressure, mmHg; HR: heart rate, bpm.
**Table 2.** Laboratory and Endocrinological Findings.

| Laboratory findings | Endocrinological findings | Normal value |
|---------------------|---------------------------|--------------|
| WBC (/μL) 5,350     | Cortisol 6.5 μg/dL        | 4.5-21.1     |
| RBC (×10^6/μL) 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 (×10^3/μL) 20.9 | TSH 2.41 μIU/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 μg/day   | 1.1-22.5     |
| Amylase (IU/L) 64   | u-Noradrenaline 154 μg/day| 29.2-118    |
| BUN (mg/dL) 14.2    | u-Dopamine 680 μg/day     | 100-1,000    |
| Cr (mg/dL) 0.65     | u-Metanephrine 0.08 μg/day| 0.05-0.20   |
| Na (mEq/L) 140      | u-Normetanephrine 0.40 μg/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).
Promoting catecholamine secretion into the blood, paraganglioma, the contraction of the urinary bladder during miction stimulates the mechanoreceptor 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 hypotension 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 secretional 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 hypotension, hypertension with palpitation, sweating, headache, chest pain and hypertensive crises.

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