

Spay-Related Urethral Sphincter Mechanism Incompetence Concurrent with Pituitary-Dependent Hyperadrenocorticism in a Bitch

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Abstract : An 8-year-old spayed female, Yorkshire terrier dog was presented with a urinary incontinence. Unaware urine dribbling during sleeping was observed eight months after spaying. Polyuria and polydipsia were also reported. Physical examination revealed obesity and hypertension. Characteristic laboratory findings in this dog were polycythemia, hyperlipidemia and elevated hepatic enzyme. Other causes of the urinary incontinence were ruled out through further diagnostic tests and spay-related urethral sphincter mechanism incompetence (USMI) was made as a presumptive diagnosis. In addition, the dog was also diagnosed with pituitary-dependent hyperadrenocorticism. Both conditions can cause urinary incontinence in dogs; therefore, definite diagnosis was made through a therapeutic approach. The synthetic estrogen, diethylstilbesterol, was initially administered and successfully managed the urinary incontinence in this dog. To the best of the author's knowledge, this is the first case report describing the clinical and laboratory features of spay-related USMI concurrent with hyperadrenocorticism and treatment outcomes in our country.

Key words : bitch, diethylstilbesterol, spay, urinary incontinence.

Introduction

Urinary incontinence is defined as the loss of the ability to control voluntary micturition (1). Various conditions can induce urinary incontinence; however urethral sphincter mechanism incompetence (USMI) is the most common cause of urinary incontinence in the neutered dogs (8). Spaying is one of the common causes of urinary incontinence in bitches, with up to 20% of the neutered animals developing urinary incontinence within three years of ovariohysterectomy (3,7,8). Reduction of the urethral closure function after spaying is the primary reason for this condition; however which is not solely affected by plasma estrogen concentration and the exact underlying mechanism remains unknown (4,8). Diseases such as hyperadrenocorticism in dogs with USMI can also lead to urinary incontinence. Therefore, disease with polyuria should be definitely ruled out before diagnosis (5). Based on reports described previously (3,6,7), using alpha-adrenergic agonists or estrogens is a common medical management to control USMI in bitches.

This case report describes the clinical and laboratory features of spay-related USMI concurrent with hyperadrenocorticism and treatment outcomes. This is the first case report of USMI in a bitch that was treated with estrogen treatment in our country.

Case

An 8-year-old spayed female, Yorkshire terrier dog was admitted for evaluation of dribbling urine. The owner reported that the dog's micturition pattern changed about eight months after neutering and that her sleeping place was frequently wet during night time. However, the dribbling of urine was obviously unaware and a normal micturition pattern was also observed. Excessive consumption of water was also noted. When presented, the dog was alert and responsive. No other abnormalities were noted upon physical examination except for obesity (body condition scores 5 through 5) and hypertension (systolic blood pressure: 152 mmHg, Cardell Model 9401, Sham Veterinary Inc., Tampa, FL, USA).

A complete blood count revealed a high packed cell volume (PCV 59%, reference range 37-55%) and hemoglobin (Hb) concentration (23.9 mg/dl, reference range, 12-18 mg/dl). Serum chemistry tests showed mild hyperglycemia (136 mg/dl; reference range, 70-118 mg/dl), elevated alkaline phosphatase (ALP) (192 U/L, reference range, 15-127 U/L), elevated total cholesterol (456 mg/dL, reference range, 135-345 mg/dL), and high triglyceride (1377 mg/dL, reference range, 19-133 mg/dL). Urinalysis revealed inadequate urine concentration (urine specific gravity 1.010, reference range, > 1.030) and bacterial culture of the urine was negative. The results of radiologic examination revealed hepatomegaly and mild intervertebral disc space narrowing in the upper lumbar region (T13-L2). Neurological examinations revealed a full bladder; however, non-urinary

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tract signs of upper motor neuron disease were not detected. Structural abnormalities of the urinary tract, such as the ectopic ureter, pelvic bladder, and urovaginal fistulas were excluded using retrograde vagino-urethrography. Magnetic resonance images of spinal cords taken using a 0.2 T scanner (E-scan®; ESAOTE, Genova, Italy) revealed no abnormal findings. Based on the history and laboratory examinations, USMI after spaying was highly suspected as the cause of the urinary incontinence.

Polydipsia can cause urinary incontinence due to polyuria. This dog had historical polydipsia and laboratory examinations showed polycythemia, hyperlipemia and increased serum ALP level. Hyposthenuria was also detected. Other causes of polydipsia, such as renal insufficiency, hepatic insufficiency and other metabolic abnormalities were excluded through laboratory examinations and abdominal ultrasound. Further diagnostic investigations included the adrenocorticotrophic hormone (ACTH) stimulation test with synthetic ACTH (0.125 mg administered intramuscularly; Synacthen, Dalim Biotech, Seoul, Korea) and the high-dosage dexamethason (0.1 mg/Kg, IV; Choong Wae Pharm, Seoul, Korea) suppression test (HDDST). The basal and post-ACTH serum cortisol concentrations were 4.95 ng/dl (reference range, 1-6 ng/dl) and 33 ng/dl (reference range, 5.5-20 ng/dl), respectively. During HDDST, adequate suppression of the cortisol level was detected, with the cortisol concentration at 0 hour being, 7.02 ng/dl (reference range, 1-6 ng/dl) and at 4 and 8 hours being 1 ng/dl (reference range, 0-1.4 ng/dl), respectively. These data were consistent with a diagnosis of pituitary-dependent hyperadrenocorticism (PDH).

Based on the history, clinical signs, physical examinations and laboratory findings, the present case was diagnosed as PDH with presumptive spay-related USMI. To differentiate the exact cause of urinary incontinence, a medical trial was attempted with the owner's consent.

To confirm that the USMI was related to spaying, the treatment with synthetic estrogen (diethylstilbestrol, 1 mg/dog, q 24h, PO for 7 days, Sigma-Aldrich, USA) was started prior to

PDH treatment. Marked improvement was observed after one week of treatment, and urinary incontinence was no longer observed inside the house. However, intermittent urinary incontinence was observed outside of the house. Therefore, the current drug dose was continued for another week, and complete resolution of the clinical signs was observed after two weeks of the estrogen treatment. Gradual reduction of the drug dosage by 1 mg every week for four weeks was conducted, after which the dose was reduced by 1 mg every other week.

Trilostane (3 mg/kg q 12h, PO, Dechra Ltd., UK) treatment for PDH was started after the urinary incontinence was resolved and the dog was re-evaluated seven days later. An ACTH stimulation test was conducted four hours after the drug administration to evaluate the maximum effect of the trilostane. Polydipsia and polyuria was persistent and the dog's post-ACTH cortisol concentration was 8 ng/dl (reference range, 1-5 ng/dl). Therefore, the dose of the trilostane was increased (4 mg/kg q 12hrs, PO) and the dog was re-evaluated one month later. Upon re-evaluation, the water consumption was found to have decreased and the post-ACTH cortisol concentration was 2 ng/dl. After the serum cortisol concentration was within the reference range, the PCV and Hb concentration decreased. The serum ALP level and cholesterol levels normalized, but the triglyceride level was still elevated (801 mg/dL, reference range, 19-133 mg/dL) (Table 1).

The dog remained completely absent of clinical symptoms and had no evidence of estrogen-related side effects five months after admission.

Discussion

USMI most often affects middle-aged neutered bitches, and is relatively rare in male, although a few cases have been described (1,4). Unaware urine dribbling during sleeping is a typical history of USMI (1). For definite diagnosis of USMI, it is important to rule out other causes of urinary incontinence

Table 1. Laboratory findings in a dog with a USMI and PDH

	Day 0	Day 7 ^a	Day 45 ^b	Reference
WBC ($\times 10^3/\mu\text{l}$)	11.48	ND	8.51	6-17
Hb (g/dl)	23.9	ND	19.8	12-18
PCV (%)	59	ND	54	37-55
PLT ($\times 10^3/\mu\text{l}$)	440	ND	309	200-500
ALT (U/L)	36	20	29	19-70
ALT (U/L)	192	185	102	15-127
Tchol (mg/dl)	456	484	321	135-345
TG (mg/dl)	1377	1358	801	19-133
Glu (mg/dl)	136	130	107	70-118

*ND : not detected

^a; 7 days after administering trilostane 0.3 mg/kg twice a day

^b; 45 days after administering trilostane 0.4 mg/kg twice a day

such as ectopic ureters, neurologic disorders, detrusor instability and anatomic abnormalities of the ureter and bladder (1,6). According to a report described earlier (5), some other diseases that cause excessive water consumption can also induce urinary incontinence. It is crucial that precise examinations for renal and/ or hepatic insufficiency, diabetes mellitus, or hyperadrenocorticism are made.

In this case, the dog showed urinary incontinence eight months after ovariohysterectomy. Ectopic ureter and other anatomical abnormalities were ruled out through a retrograde vagino-urethrography. Neurologic examination and spinal cords MRIs were taken to exclude neurologic disorders. Urinary tract infection was excluded through the negative results of the urine culture. Based on a detailed evaluation of the history and several medical examinations, USMI was strongly suspected. However, laboratory examinations also revealed a systemic disease, hyperadrenocorticism, in this dog. Thus, the dog was diagnosed with PDH based on the results of an ACTH stimulation test and HDDST. PDH can cause polydipsia and polyuria (PUPD). In addition, PUPD can lead to cause urinary incontinence as a result of simple overflow of the bladder. Therefore, it is essential to rule out or adequately control of the polydipsia to ensure a definite diagnosis of USMI (5). In this dog, the amount of the water consumption was unchanged; however, the urinary incontinence was occurred eight months after neutering. Therefore, we decided to control the USMI using the synthetic estrogen, diethylstilbestrol (DES) prior to treating the PDH.

Medical management of spay-related USMI using alpha-adrenergic agonists or estrogen is preferred method (3,5,6). Phenylpropanolamine is a nonselective adrenergic agonist that works by stimulating the receptors of the smooth muscle to increase tone (6). However, this drug can cause hypertension, tachycardia, irritability, and hepatic glycogenolysis (9). The dog described herein had systemic hypertension; thus, the synthetic estrogen, DES, was chosen for the treatment. DES indirectly increases the urethral closure pressure by sensitizing the alpha-receptors in the urethral smooth muscle (3). The recommended dose (1 mg/dog q 24h for 3-7 days) was initially administered and the clinical signs were monitored. Seven days after the administration of DES, the incontinence was greatly resolved. After the complete resolution of the symptoms, DES was reduced to the lowest effective doses, which were 1 mg/dog every two weeks. DES also has rare side effects including bone marrow suppression, vulvar swelling,

mammary gland development and attractiveness to male dogs (1,7); however, this dog showed no side effects during the follow up periods.

After controlling spay-related USMI with estrogen, PDH treatment was initiated with trilostane. It is a competitive inhibitor of beta-hydroxysteroid dehydrogenase, which finally synthesizes aldosterone and cortisol (2). Trilostane is relatively safe and effective drug that has recently been used as an alternative treatment for mitotane.

In conclusion, we described the first case of spay-related USMI concurrent with PDH in our country. In addition, it is important to rule out other causes of urinary incontinence and monitor treatment outcomes with estrogen due to myelotoxicity.

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Reference

1. Acierno MJ, Labato MA. Canine Incontinence. *Compend Contin Educ Prac Vet* 2006; 28: 591-602.
2. Alenza DP, Arenas C, Lopez ML, Melian C. Long-term efficacy of trilostane administered twice daily in dogs with pituitary-dependent hyperadrenocorticism. *J Am Anim Hosp Assoc* 2006; 42: 269-276.
3. Angioletti A, De Francesco I, Vergottini M, Battocchio ML. Urinary incontinence after spaying in the bitch: incidence and oestrogen-therapy. *Vet Res Commun* 2004; 28: 153-155.
4. Holt PE. Simultaneous urethral pressure profilometry: comparison between continent and incontinent bitches. *J Small Anim Pract* 1988; 29: 761-769.
5. Reichler I, Hubler M, Arnold S. Urethral sphincter mechanism incompetence in spayed bitches: new insights into the pathophysiology and options for treatment. *Eur J Comp Anim Pract* 2008; 18: 187-190.
6. Scott L, Leddy M, Bernay F, Davot JL. Evaluation of phenylpropanolamine in the treatment of urethral sphincter mechanism incompetence in the bitch. *J Small Anim Pract* 2002; 43: 493-496.
7. Shiel RE, Puggioni A, Keeley BJ. Canine urinary incontinence part 2: treatment. *Ir Vet J* 2008; 61: 835-840.
8. Thrusfield MV, Holt PE, Muirhead RH. Acquired urinary incontinence in bitches: its incidence and relationship to neutering practices. *J Small Anim Pract* 1998; 39: 559-566.
9. Webster CR. Control of micturition. In: *Clinical pharmacology*. WY: Teton New Media. 2001: 40-41.

암캐에서 부신피질기능 항진증 및 난소제거 이후 발생한 요도 괄약근 기능부전 증례

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요 약 : 8연령의 암컷 요크셔 테리어견이 요실금을 주증으로 내원하였다. 환축은 요실금 증상이 나타나기 이전부터 다 음다뇨 증상을 가지고 있었으며, 난소제거 8개월 이후 야뇨증이 나타났다. 신체검사 상에서 비만과 고혈압이 확인되었 다. 실험실 검사에서 적혈구증가증, 지질혈증 및 간수치 증가가 관찰되었다. 다양한 검사를 통하여 난소제거 이후 발 생한 요도 괄약근 기능부전증이 가장 의심되었다. 이와 더불어, 본 환축은 부신피질기능 항진증을 가진 것으로 진단 되었다. 합성 에스트로겐인 디에틸stil베스테롤을 통한 치료적 접근에서 요실금 증상의 개선이 확인 되었으며, 이를 통하여 요도 괄약근 기능부전증이 요실금의 원인으로 확진 되었다. 결론적으로 본 증례는 부신피질기능 항진증과 더 불어 암캐의 난소 제거 이후 발생한 요도 괄약근 기능부전의 임상증상과 실험실 검사 결과 그리고, 치료 반응에 대한 국내 첫 증례보고이다.

주요어 : 암캐, 디에틸stil베스테롤, 난소제거, 요실금