



Case report

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Pituitary-dependent hyperadrenocorticism in a terrier dog: A case report

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ABSTRACT

We report a case of pituitary-dependent hyperadrenocorticism in a 10-year-old, female, terrier dog. The animal was admitted due to polyphagia, weight gain, polyuria, polydipsia, hair loss, exercise intolerance and panting at rest. On physical examination, abdominal distention, truncal and bilaterally symmetric alopecia, thin hypotonic skin, comedones, bruising, hyperpigmentation and calcinosis cutis on the dorsal midline were observed. Hematologic investigations showed stress leukogram, high serum alkaline phosphatase activity, mild to moderate alanine aminotransferase activity, hypercholesterolemia, hypertriglyceridemia and hyperglycemia. Mild generalized interstitial lung patterns and hepatomegaly were detected in the radiographs. Bilaterally symmetric normal-sized adrenal glands were also diagnosed in ultrasonography. Diagnosis of pituitary-dependent hyperadrenocorticism was confirmed with low-dose dexamethasone suppression test. The dog was successfully treated with mitotane.

1. Introduction

Hyperadrenocorticism (HAC), or Cushing's syndrome, is an endocrinological disorder resulted from chronic exposure to excessive concentrations of glucocorticoids[1-3]. There are three types of Cushing's syndrome that can be iatrogenic or spontaneous[4]. Spontaneously occurring HAC may be associated with inappropriate secretion of adrenocorticotrophic hormone (ACTH) by the pituitary gland [pituitary-dependent HAC (PDH)] or a primary adrenal disorder (adrenal-dependent HAC)[3,5]. The most common cause of an increased ACTH concentration is PDH resulting from pituitary tumors that synthesize and secrete excessive amounts of ACTH. HAC occurs commonly in middle-aged dogs, but it's rare in cats[1,6]. Any breed of dogs can develop

HAC, but poodles, dachshunds and small terriers have the highest prevalence of PDH[3,4]. Some clinical manifestations of HAC in dogs are polyuria and polydipsia, increased appetite, abdominal obesity, weight gain, fatigue, muscle atrophy and skin problems. Laboratory findings include stress leukogram, low blood urea and an increase in serum activity of the enzymes such as alkaline phosphatase (ALP) and alanine aminotransferase (ALT) [3,4]. Common tests of HAC for screening dogs are the ACTH stimulation test, the low-dose dexamethasone suppression test (LDDST) and the urine cortisol: creatinine ratio[3,7]. No test has 100% diagnostic accuracy, nevertheless, LDDST is more reliable than others in diagnosis of HAC. Moreover, some tests were done to differentiate between types of HAC[6]. Diagnostic imaging is also advisable in all cases of suspected or proven HAC[2]. Treatment can be divided into two parts: surgical and medical therapy with drugs such as mitotane or trilostane[6,8]. Herein, we report PDH in a terrier dog, which describes historically.

2. Case report

A 10-year-old, female, terrier dog was referred to the Veterinary Animal Hospital of Shahid Bahonar University of

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All experimental procedures involving animals were conducted in accordance to the Guide for Care and use of Laboratory Animals published by the National Institutes of Health (NIH publication No. 85-23, revised 1985) and approved by the local ethics committee of veterinary collage of Shahid Bahonar University of Kerman.

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Kerman with a history of polyphagia, weight gain, polyuria, polydipsia and hair loss. Detailed history delineated that the case had exercise intolerance and panting at rest. On physical examination, abdominal distention causing pot-bellied appearance was seen. Dermatologic signs, including truncal and bilaterally symmetric alopecia, thin hypotonic skin, comedones, bruising, hyperpigmentation and calcinosis cutis on the dorsal midline were also observed (Figure 1). In accordance to the clinical signs, the Cushing's syndrome was suspected until to be confirmed. Therefore, blood sample was collected for clinicopathologic studies. Hematologic investigations showed stress leukogram that means neutrophilia without a left shift, lymphopenia, eosinopenia, monocytosis and mild erythrocytosis. High serum ALP activity, mild to moderate ALT activity, hypercholesterolemia, hypertriglyceridemia and hyperglycemia were also observed. No abnormality was found in the urinalysis except low urine specific gravity (< 1.020). Then, radiology and abdominal ultrasound were done. Mild generalized interstitial lung patterns and hepatomegaly were detected in the radiographs (Figure 2). Bilaterally symmetric normal-sized adrenal glands were also diagnosed in the ultrasonography. Unfortunately, owner refused other diagnostic tests, including CT scan and magnetic resonance imaging (MRI), because of financial problems. Then, endocrine testing was performed. Total serum thyroxine (T4) and free T4 were below the reference range. LDDST was done to evaluate hypothalamus-adenohypophysis-adrenal gland axis. So, concentrations of serum cortisol were determined before, 4 h and 8 h after dexamethasone sodium phosphate (0.01 mg/kg, I.V.) administration. The case exhibited serum cortisol suppression at 4 h ($< 1.4 \mu\text{g/dL}$), with a rise in cortisol concentration 8 h after administration. Accordingly, diagnosis of PDH was confirmed. The dog was recovered by therapeutic intervention with mitotane (initial induction 30 to 50 mg/kg/day, administered for 10 days followed by a maintenance dosage of approximately 50 mg/kg/week, divided into two equal doses). Recheck was done at 4 months later, and no other complications were identified at this time. All experimental procedures involving animals were conducted in accordance to the Guide for Care and use of Laboratory Animals published by the National Institutes of Health (NIH publication No. 85-23, revised 1985) and approved by the local ethics committee of veterinary collage of Shahid Bahonar University of Kerman.

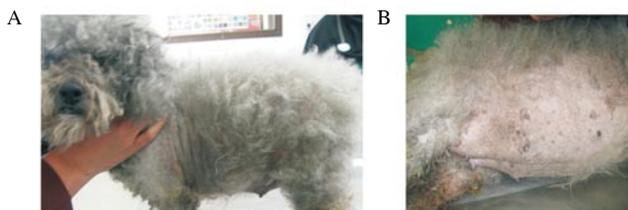


Figure 1. A 10-year-old, female, terrier dog with pituitary-dependent hyperadrenocorticism showing alopecia and abdominal distension. A: The bilaterally symmetrical alopecia and thin skin; B: Hyperpigmentation, and comedones.



Figure 2. Lateral radiographic view of the thorax and abdomen showing mild generalized interstitial lung patterns and hepatomegaly.

3. Discussion

One of the most common endocrinopathies of dogs is HAC. PDH is recognized as the commonest types of it[7]. Despite major importance, this endocrine disease is often unrecognized. In the present study, we report PDH in a 10-year-old, female, terrier dog.

In spite of rare human cases, HAC is a common endocrinological syndrome in dogs with an estimated incidence of 1 to 2 cases/1 000 dogs/year[1]. As we describe here, PDH occurs more in middle aged to older and smaller dogs. In contrary, corticotroph carcinoma of the pituitary was reported in an 11-month-old dog by Gestier *et al.*[9]. In comparison to our report in a female dog, no strong sex predilection was described regarding PDH[2,4]. This study was similar to other researches reporting polyphagia, polyuria and polydipsia as the most clinical symptoms (up to 90% of dogs), which were distinctly reported by this dog's owner[4]. Increased appetite is attributed to the glucocorticoid excess. Moreover, high glucocorticoids interferences with the antidiuretic hormone action, causes polyuria and following polydipsia. Exercise intolerance and panting of this dog may be attributed to decreased pulmonary compliance and muscle weakness[2]. As we report in this case, affected dogs may have abdominal distention causing pot-bellied appearance due to hepatomegaly and large bladder together with fat redistribution to the abdominal mesentery. Consistent with the results of other studies, we observed the dermatologic signs, including truncal and bilaterally symmetric alopecia, thin hypotonic skin, comedones, bruising and hyperpigmentation[7,10]. Calcinosis cutis as dystrophic calcium deposition in the dermis and subcutis were felt like firm, irregular plaques on the dorsal midline of this case. In comparison to our results, recurrent pyoderma with malassezia and HAC was reported in a Lhasa Apso dog in another study[11]. In contrary, endocrinologically-inactive ('silent') pituitary corticotroph (ACTH-containing) carcinoma was diagnosed with the absence of clinical signs in a 11-month-old neutered female Weimaraner by Gestier *et al.*[9]. Moreover, atypical cushing's syndrome was reported in dogs[12].

Similar to other studies, stress leukogram, high ALP and ALT

activities, hypercholesterolemia, hypertriglyceridemia and hyperglycemia were seen in hematologic investigations of the current case[11]. High blood cortisol concentration results in a stress leukogram but this abnormality is not specific and can observe by other diseases[10]. High serum ALP activity, as the most consistent finding, is present in 85% to 95% of HAC dogs[4,10]. Accordance with other studies, low urine specific gravity < 1.020 of the mentioned case is attributed to the polyuria[10]. In the present case, thorax and abdomen radiographic findings, including mild generalized interstitial lung patterns and hepatomegaly (the most consistent radiographic finding) were similar to other reports[4]. Although, ultrasonographic size of adrenal glands was in the normal range, absence of adrenomegaly did not rule out PDH in this case[7]. CT and MRI are the only reliable methods of evaluating the size of either the adrenals or the pituitary glands. Therefore, CT scanning and MRI are essential to evaluate these abnormalities[4]. Unfortunately, owner refused these diagnostic tests because of financial problems.

Incidence rates of endocrinopathies, especially HAC is underestimated due to careless examination and little attention to perform diagnostic endocrine tests. In the current case, total serum thyroxine (T4) and free T4 were below the reference range; so, HAC may be misdiagnosed as hypothyroidism[10]. We performed the LDDST because it is the test of choice for the diagnosis of HAC in dogs and differentiates the types[4,10]. The LDDST is more sensitive than ACTH stimulation test in confirming HAC, but it is not useful in the diagnosis of iatrogenic cases[4,13]. The LDDST is used to differentiate between PDH and functional adrenal tumor as well[4]. In the current case, suppression of serum cortisol at 4 h (at least 50% lower than the 0-hour value), with a rise in cortisol concentration 8 h after administration confirms PDH diagnosis[5]. Peterson stated that this escape from suppression is diagnostic for PDH, and further tests to determine the cause of HAC are not necessary[4]. Medical treatment, radiation therapy and hypophysectomy are the options. For medical management, both of mitotane and trilostane are documented as effective treatment for PDH[8]. Mitotane results in necrosis and atrophy of the adrenal cortex in which the zona reticularis is more sensitive than the zona glomerulosa[8]. Trilostane is more expensive than mitotane; thus, we chose mitotane as medical management. Compared with our finding, Sudhakara Reddy and Nalini Kumari determined ketoconazole as effective treatment for HAC[11]. Transsphenoidal hypophysectomy was performed to treat PDH in another study[1]. Selective pituitary or ectopic corticotroph tumor resection is also considered as the treatment of choice for PDH in human cases[13].

Conflict of interest statement

We declare that we have no conflict of interest.

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