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Pituitary Pars Intermedia Dysfunction with Laminitis in a Horse

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Abstract : Pituitary pars intermedia dysfunction (PPID), often referred to as equine Cushing's disease, is a common endocrine disorder often diagnosed in older horses. A 13-year-old 460 kg Warmblood gelding showed clinical signs suggestive of PPID, including hypertrichosis, fat redistribution, polyuria and polydipsia (PU/PD), and weight loss. Physical examination, complete blood cell count, and serum chemistry results were normal. However, dexamethasone suppression and plasma adrenocorticotropic hormone (ACTH) level tests confirmed PPID. Three months after the confirmed diagnosis, the horse was referred again with symptoms of laminitis. Radiography and venography were performed to evaluate the laminitis severity level. However, the foot condition continued to worsen, and the horse was eventually euthanized. The purpose of this case report is to describe clinical signs and diagnosis of PPID with laminitis.

Key words **:** pituitary pars intermedia dysfunction, dexamethasone suppression test, laminitis, horse.

Introduction

Laminitis is associated with several systemic diseases that may result in changes in the hoof structure of horses. Although previous research has focused on the inflammatory forms of laminitis disease, recently, endocrinopathic laminitis associated with equine metabolic syndrome (EMS) and pituitary pars intermedia dysfunction (PPID), or a combination of these diseases, have been considered the most widespread basal diseases associated with laminitis in horses (15). The most common disease associated with endocrinopathic laminitis is EMS (40% of endocrinopathic laminitis cases), but PPID is similarly involved (37.5% of endocrinopathic laminitis cases) (3).

Moreover, PPID is the most frequent endocrine disorder diagnosed in aged horses (13). Clinical signs of PPID include hypertrichosis, polyuria and polydipsia (PU/PD), muscle wasting, weight loss, abnormal distribution of fat, and laminitis (10,12). Diagnostic aspects of PPID include clinical signs, histological indicators, and endogenous hormone levels, including adrenocorticotropic hormone (ACTH), insulin, and cortisol levels, which can be assessed through various tests such as the dexamethasone suppression test (DST), the thyrotropin-releasing hormone (TRH) stimulation test measuring cortisol or ACTH, the combined DST-TRH test, and the domperidone stimulation test (1,5,6,11,13). In support of clinical signs of PPID, determination of seasonally adjusted plasma ACTH levels is currently recommended to confirm a diagnosis of PPID (18).

The purpose of this case report is to describe a case of equine PPID focusing on PPID-induced laminitis and its diagnosis.

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Case

A 13-year-old 460 kg Warmblood gelding was referred to the J&C Equine Hospital, Icheon, Korea. The owner described the horse as being PU/PD with weight loss despite an increased appetite. On examination, the horse was assessed to be in poor condition with a pendulous abdomen and hypertrichosis (Fig 1). Temperature, pulse, and respiratory rates were within the normal range. In addition, testing revealed that the horse had a normal complete blood cell count and serum chemistry profile. A tentative diagnosis of PPID was made based on the animal's history and clinical signs.

Measurement of cortisol and endogenous plasma ACTH levels were performed to confirm the diagnosis. For the DST-based assessment of cortisol level, blood was collected at 5 p.m. in a plain Vacutainer® tube for basal cortisol level determination. On the next day at 5 p.m., 40 μg/kg of dexamethasone was intramuscularly administered to the horse and 15 h later, a second blood sample to determine the cortisol level was collected in a plain Vacutainer® tube. To perform the plasma ACTH level test, blood was collected in a plastic EDTA Vacutainer® tube. The sample was centrifuged, and the separated plasma was placed in a plain Vacutainer®. The plasma sample was frozen and sent on ice to the testing laboratory (IDEXX Laboratories, Korea).

The baseline plasma cortisol level was 2.2 μg/dL. The level of the plasma cortisol at 15 h after the administration of 40 μg/kg dexamethasone was 2.1 μg/dL. The plasma ACTH level was 104.7 pg/mL. The results showed a plasma cortisol level above 1 μg/dL at 15 h after dexamethasone injection, as well, the plasma ACTH level was elevated, indicating that

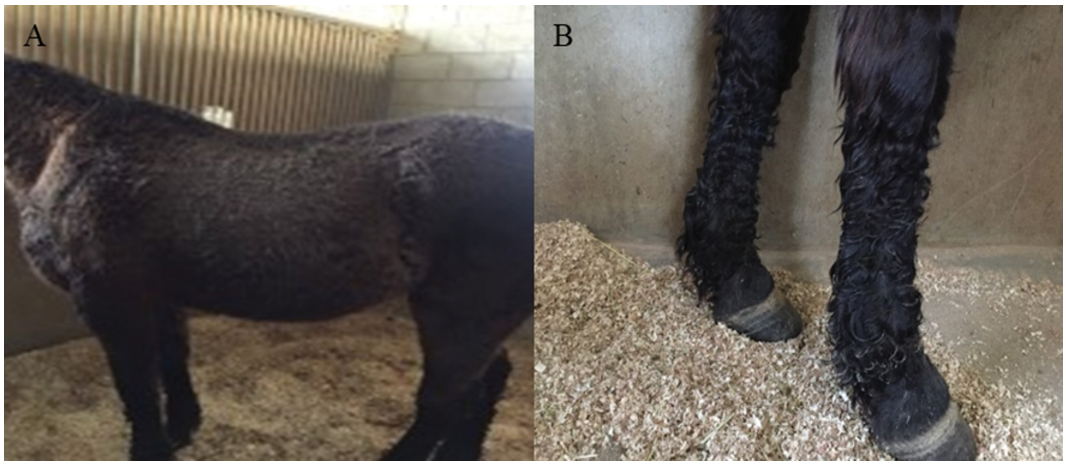

Fig 1. A. A patient diagnosed with pituitary pars intermedia dysfunction had been recognized by the hair coat that fails to shed (hypertrichosis). B. Note that the patient had been suffering from chronic laminitis and had excessive hair growth on limbs.

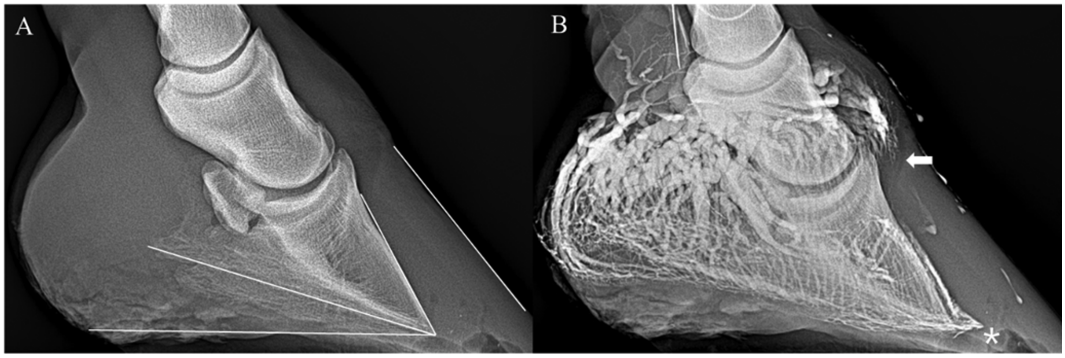

Fig 2. A. Lateromedial radiograph of the patient diagnosed with PPID. The dorsal surface of the hoof, dorsal surface of the distal phalanx, solar surface of the distal phalanx, and the ground surface are emphasized by white lines. There is evidence of dorsal capsular and phalangeal rotation of the distal phalanx, an increased angle between the solar surface of the distal phalanx and the ground surface, and decreased sole depth. B. Venogram of the laminitic foot of the patient diagnosed with PPID. The apex of the distal phalanx descends distally to the circumflex vessels (asterisk), and the coronary plexus is distorted with reduced contrast and evidence of reduced blood supply (arrow).

the horse was positive for PPID. Based on the results, the owners were informed of the need to provide the horse with optimal health management, including high-quality feed, dental care, deworming, and hoof care. In addition, to avoid the development of laminitis, a reduction in the provision of soluble carbohydrates was advised.

Three months after the PPID diagnosis, the horse was again referred to the J&C Equine Hospital exhibiting symptoms of laminitis. Radiography (56 kV, 0.08 s; lateromedial view) and venography with digital radiography (Galaxy R, Medien International Co., Gyeonggi-do, Korea) were performed to confirm laminitis presence. The horse was sedated with medetomidine hydrochloride (Equadin, Dongbang Inc., Suwonsi, Korea), and a site over the lateral palmar digital vein was clipped and scrubbed. An abaxial sesamoid nerve block (Lidocaine HCl 2% Injection Daihan, Daihan Pharm Co. Ltd., Seoul, Korea) was achieved. A tourniquet (2.5 cm wide, 50 cm long) was placed above an adhesive bandage (Elastikon, Johnson & Johnson, New Brunswick, NJ, USA) that had been applied to the fetlock. Iopromide contrast (25 mL; LG Life Sciences Ltd., Seoul, Korea) was injected into the palmar digital vessels through a 21 gauge, 1.9 cm butterfly catheter set (HMS scalp vein, Hankook Medical, Changwonsi, Gyeongnam, Korea). All radiographs were obtained within 45 s of contrast injection. Subsequently, the tourniquet and catheter were removed, but the bandage was left in place for 30 min.

The radiographic results showed evidence of dorsal capsular and phalangeal rotation, an increased angle between the solar surface of the distal phalanx and the ground surface, and a decreased sole depth (Fig 2A). The venogram showed that the apex of the distal phalanx had descended distally to the circumflex vessels, and the coronary plexus was distorted with reduced contrast and evidence of reduced blood supply (Fig 2B). After those assessments were completed, the physical and foot conditions of the horse continued to worsen, and the horse was eventually euthanized.

Discussion

In the current case, a tentative diagnosis of the PPID was made because the 13-year-old horse showed typical clinical signs of PPID, including PU/PD, weight loss, and hypertrichosis, which are considered frequent clinical signs of

PPID in horses (1,16,12). Aging is also a risk factor for PPID, with 21.2% of horses older than 15 years being diagnosed with PPID (12). Ponies and Morgan horses are more susceptible than other horse breeds, but there appears to be no sex-dependent susceptibility to PPID (14). Although uncommon, other clinical signs of PPID include narcolepsy, blindness, and abnormal estrus (14).

Anemia, neutrophilia, lymphopenia, eosinopenia, hyperglycemia, hyperlipemia, increased liver enzymes, and glucosuria have been reported in horses with PPID (8). However, the patient had normal complete blood cell count and serum chemistry results. Many horses with PPID and hyperglycemia have insulin dysregulation (7). Recent research has focused on the role of hyperinsulinemia in the pathophysiology of laminitis, but the exact mechanisms are currently unknown (2). The patient's insulin level was not assessed.

The patient underwent DST and endogenous plasma ACTH assessments to confirm the tentative PPID diagnosis. DST is a well-accepted and recommended test for diagnosing PPID in horses and provides test sensitivity and specificity levels of 100% (5). Determination of resting plasma ACTH level is considered a good alternative to DST in the diagnosis of PPID as it is reported to have a sensitivity of 90.9% and a specificity of 100% in horses (1). However, seasonal changes in plasma ACTH levels should be considered when interpreting endocrine test results (4). Although a definitive diagnosis of PPID relies on gross and histopathologic examination of the pituitary gland, in the present case, we performed DST and assessed resting ACTH concentration; the results confirmed the diagnosis of PPID in the patient.

Optimal PPID treatment approaches include a combination of health management and pharmaceutical interventions. In this case, we informed owners of the need to provide optimal health management and to prepare for the development of laminitis. In addition, we advised on the need to reduce the available amount of soluble carbohydrates and provide regular hoof care. As a pharmaceutical approach to PPID treatment, pergolide mesylate, a dopamine agonist, is considered the first-choice drug for stimulating dopamine receptors and resolving pituitary hormone levels and clinical signs (14). Cyproheptadine, a serotonin antagonist, and less commonly, trilostane, an inhibitor of adrenal steroidogenesis, have also been used to treat horses with PPID (17). A treatment limitation in the present case was the lack of pharmaceutical treatment due to the absence of approved drugs for use in horses with PPID in Korea.

Patients with PPID present with increased cortisol levels, which is a suspected cause of laminitis. Cortisol increases may decrease palmar digital blood flow, which can damage the lamellar attachment, and may increase protein catabolism within the dermis or epidermis of the hoof, weakening the lamellar interface (9). Laminitis occurs in approximately 30% of horses with PPID (10). Unfortunately, 73% of equine PPID cases are euthanized due to the development of PPID-related conditions (16). To minimize such losses in the horse industry, careful monitoring of horses with a previous diagnosis of endocrinopathic laminitis is recommended.

In conclusion, this case describes a clinical diagnosis of PPID in a horse in Korea, a rarely reported occurrence. It is hoped that this case will raise interest in endocrinopathic laminitis in horses in Korea. Regardless, clinicians should inform owners of horses with PPID of the need for health management, including diet control, and to prepare for the development of laminitis.

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