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A Case of Pituitary Dwarfism in a Dog: Improvement of Alopecia with Oral Melatonin

Seungkuk Oh, Dae-seung Baek, Yunhye Kim, Namsoo Kim, Jonghoon Kim, Namjung Kim*, Tae-ho Chung, Ju-min Kim***, Jinho Park and Chul Park[1]**

BK21 Plus and College of Veterinary Medicine, Chonbuk National University, Duckjin-dong Duckjin-gu, Jeonju 561-756, Republic of Korea
**Applied Entomology Division, National Academy of Agricultural Science, RDA, Suwon 441-100, Republic of Korea*
***Department of Animal Science, Joongbu Univeresity, Chungnam 312-702, Republic of Korea*
****DongA One Corporation, Seoul 150-763, Republic of Korea*

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Abstract : A 13-month old, intact female, miniature Schnauzer dog was presented with history of dermatitis, pruritus and pain of ear pinnae with delayed puberty. The basal serum growth hormone level was 0.01 ng/ml, which was much lower than the reference range (1.80-2.00 ng/ml). On the xylazine stimulation test, the dog was no responsive to administration of xylazine. The dog was diagnosed as isolated type pituitary dwarfism. Treatment was aimed to improve alopecia with oral melatonin. After initiation of treatment, alopecia of the ear pinnae has been improved.

Key words **:** Alopecia, Dog, Growth hormone, Melatonin, Pituitary dwarfism.

Introduction

Growth hormone (GH) is secreted by anterior lobe of pituitary gland in rhythmic pulses and its secretion is regulated by two hypothalamic hormones with opposing actions which are stimulatory hormone, GH-releasing hormone (GHRH) and the inhibitory hormone, somatostatin. Synthetic GH secretagogues such as ghrelin can also act as stimulator of GH release and it is an even more potent GH secretagogue than GHRH (3).

GH has two different effects: rapid catabolic effects and slow anabolic effects. Catabolic actions of GH are insulin antagonistic effect resulting in enhancement of lipolysis, gluconeogenesis, and restriction of glucose transport across the cell membrane. Slow anabolic actions are mediated via insulin-like growth factors (IGFs) which are mainly produced by the liver and have long-term growth promoting effects.

In dogs, congenital deficiency of GH or pituitary dwarfism has been reported in various breeds, however, this condition is encountered most often as a simple, autosomal, recessive inherited abnormality in the German shepherd dog (1).

There are two types of pituitary dwarfism depending on whether the concurrent hormone deficiency is present. In a dwarfism with an isolated GH deficiency, affected dog typically shows proportionate dwarfism. In a combined type pituitary dwarfism, deficiency of thyroid stimulating hormone (TSH) or prolactin (PRL) is accompanied with GH deficiency and may presents a disproportionate dwarfism.

Clinical feature of pituitary dwarfism includes growth retardation, endocrinal alopecia, soft and wooly hair, anestrus in female dogs, cryptorchidism in male dogs and mental dullness.

This case report describes the therapeutic effectiveness of oral melatonin on the alopecia caused by pituitary dwarfism.

Case

A 13-month old, intact female, miniature Schnauzer was presented to the Chonbuk National University Animal Medical Center with a history of delayed wound healing, pruritus and pain of ear pinnae and delayed puberty (Fig 1).

On the physical examination, bilateral alopecia on the ear pinnae and poor growth state were observed but the body

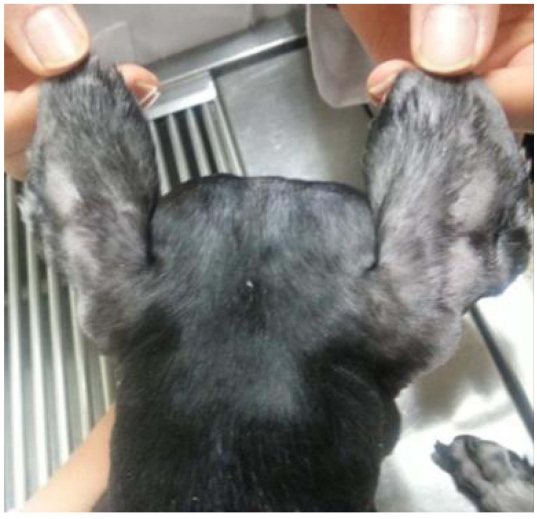

Fig 1. Bilateral alopecia of the outer ear pinnae of the patient dog was observed.

[1]Corresponding author.
E-mail : chulpark0409@jbnu.ac.kr

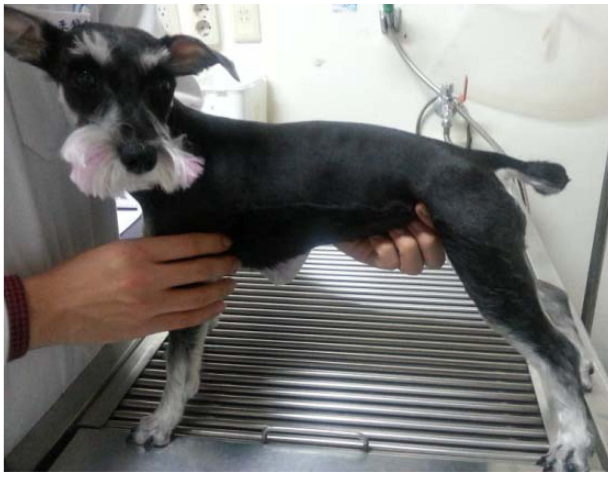

Fig 2. On the physical examination, the patient dog presented poor growth state with normal body proportion (proportionate dwarfism).

proportion seemed to be normal.

Results of complete blood count and serum chemistry were all within the reference range.

No specific abnormality was identified on the radiographs.

Dermatologic tests including trichogram, imprint smear and bacterial and fungal cultivation revealed no remarkable findings.

On the basis of poor growth state shown on the physical examination (Fig 2), GH deficiency was suspected. The serum level of GH was 0.01 ng/ml, which was much lower than the reference range (1.80-2.00 ng/ml). The serum level of thyroid hormones were within the reference ranges (fT4: 1.96 ng/dl, T4: 1.97 ng/dl, TSH: 0.11 ng/ml)

As the serum GH level was lower than reference range, we conducted a xylazine stimulation test for a dynamic function test of GH. Baseline GH level was 0.06 ng/ml and the results of each after 15, 30, 45, 60 minute were all less than 0.01 ng/ml which below the reference range (1.8-2.0 ng/ml). Measurement of GH, Thyroid hormones and PRL were conducted by a commercial laboratory (Neodin Vetlab, Seoul, Korea).

The dog was diagnosed as an isolated type pituitary dwarfism based on the history, physical examination and the result of xylazine stimulation test. Since the owner did not agree with GH or progestin therapy, treatment aimed to improve alopecia of the ear pinnae.

The therapy with oral melatonin was started on a dose of 3 mg/kg, q24h. After 1 month of the therapy, alopecia of the ear pinnae has shown improved and no adverse effect was observed.

Discussion

Although the results of the patient's signalment, history and physical examination make suspicion about pituitary dwarfism, the definitive diagnosis of GH deficiency is made by dynamic function test of circulating growth hormone. GHRH is used for the stimulation test due to its stimulatory effect on the GH. α-adrenergic drugs such as clonidine or xylazine are also used to test the GH secretory capability of anterior lobe of pituitary gland. However, the use of these drugs may cause some adverse reactions including sedation, bradycardia, hypotension, and collapse especially at high doses (5,9).

Ghrelin is a 28-amino-acid peptide which exists at fundus of the canine stomach (10), and has more potent GH stimulatory effect than GHRH. In 2006, there was a study about GH stimulation test using synthetic stretagogue ghrelin. In this study, plasma concentrations of GH, TSH, adrenocorticotropic hormone (ACTH), luteinizing hormone (LH), cortisol and PRL were measured 15 min before and 0, 5, 10, 20, 30, and 45 min after ghrelin injection in 6 German shepherd dogs with pituitary dwarfism and 8 healthy beagle dogs. Mean plasma GH response after ghrelin injection was significantly lower in the dwarf dogs compared with that in the healthy dogs. In none of the dogs with pituitary dwarfism, the ghrelin-induced plasma GH concentration exceeded 5 μg/l at any time after ghrelin injection. Administration of ghrelin did not affect the plasma concentrations of ACTH, cortisol, TSH, LH and PRL in either the dogs with pituitary dwarfism or in the healthy dogs (3).

Although the treatment of pituitary dwarfism should be aimed at restoring of GH deficit, there is no effective GH product available up to date. Canine GH is not available for therapeutic use and human GH has risk of antibody formation (11). Even though the porcine GH has identical amino acid sequence to that of the canine GH (2), porcine GH not commercially available and the results of the treatment of pituitary dwarfism with porcine GH are not satisfactory (5). Due to the unavailability of GH products, the only treatment option for restoring GH deficit is using medroxyprogesterone acetate (8) or proligestone (7). The progestin induces the expression of the GH gene in mammary gland and it has been shown that plasma GH and IGF-I levels can be elevated by administration of progestin (8). However, treatment with progestins may also have several potential side-effects, such as diabetes mellitus, cystic endometrial hyperplasia, recurrent pyoderma and associated pruritus (7,8), and this is the reason that the owner did not want to try a progestin therapy in this case. The increase in height depends on the status of the growth plates at the time of the treatment is initiated. Since a closure of the growth plate was identified with radiography which means no chance of further growth, we decided to focus on the improvement of the alopecia using oral melatonin ahead of other signs of GH deficiency. Melatonin is thought to play either a direct or an indirect role in the neuroendocrine control of moulting and hair growth in mammals (4). Melatonin increases growth initializing activity of secondary hair follicles in situ and hair shaft elongation in cultured hair follicles and was reported to induce the proanagen phase and to increase pelage development and cycle frequency (6). With these beneficial effects of melatonin, oral melatonin has been used for treatment of various forms of alopecia, such as recurrent flank alopecia, pattern baldness and alopecia-X with some successful outcomes. In this case, melatonin was used in alopecia caused by GH deficiency and showed satisfactory clinical improvement.

In conclusion, this case report describes the therapeutic effect of oral melatonin on alopecia caused by GH deficiency. Even the melatonin is not a mainstay of treatment in pituitary dwarfism, the administration of oral melatonin resulted in sat-

isfactory clinical improvement of alopecia without presenting specific adverse effect.

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개에서 뇌하수체 왜소증의 증례: 멜라토닌의 경구 투약에 의한 탈모의 개선

오승국 · 백대승 · 김윤혜 · 김남수 · 김종훈 · 김남정* · 정태호 · 김주민*** · 박진호 · 박철**[1]

전북대학교 수의과대학, *농촌진흥청 농업생물부, **중부대학교 관광보건대학, ***동아원(주)

요 약 : 13개월령의 중성화하지 않은 암컷 미니어처 슈나우저 개가 귓바퀴의 소양감, 통증 및 상처치유의 지연을 주증으로 내원하였다. 환자의 혈청 성장호르몬 농도가 참고범위 이하로 측정되었으며 자일라진 자극검사를 통해 뇌하수체 왜소증으로 진단되었다. 보호자가 원하지 않아 성장호르몬 및 프로게스틴 치료는 진행하지 않았으며, 탈모의 개선을 목적으로 멜라토닌 투여를 시작하였다. 멜라토닌 투여 이후, 귓바퀴의 탈모가 개선되는 것을 확인할 수 있었다.

주요어 : 개, 성장호르몬, 뇌하수체 왜소증, 탈모, 멜라토닌