Received: 21 July 2021 | Revised: 29 December 2021 | Accepted: 19 January 2022

DOI: 10.1002/vrc2.299

Vet Record CaseReports

CASE REPORT

Companion or pet animals

# The use of photobiomodulation therapy in the treatment of hair cycle arrest in a Pembroke Welsh corgi

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**Abstract**

Hair cycle arrest is a relatively common condition of double-coated breeds with a complex and poorly defined pathogenesis. Several therapeutic options have been described; however, the clinical response is often variable, and some treatment options can be invasive and may invoke adverse effects. Herein is described the first case of hair cycle arrest in a Pembroke Welsh corgi, which was successfully treated with photobiomodulation therapy. Photobiomodulation therapy (previously known as low-level laser therapy) proved to be a well-tolerated treatment, with no adverse effects appreciated. Videodermoscopy, a noninvasive technique, was utilised to objectively measure response to treatment and was a readily repeatable tool for in-hospital use. This case highlights a previously unrecognised breed to consider for the diagnosis of hair cycle arrest, as well a new indication for photobiomodulation therapy as a treatment option and videodermoscopy diagnostic analysis software as an aid in case management for practitioners moving forward.

**KEYWORDS**

alternative therapies, dermatology, imaging, internal medicine

## BACKGROUND

Hair cycle arrest, often referred to as alopecia X, is a relatively common condition of double-coated breeds such as pomeranians, chow chows, keeshonds, Alaskan malamutes, samoyeds and toy and miniature poodles. Clinical presentation includes noninflammatory, nonpruritic hypotrichosis to alopecia often accompanied by hyperpigmentation of the neck, truncal regions, caudal thighs and frictional regions, sparing the head and distal extremities.[1] Initial coat changes may be subtle, including the gradual development of a dull, dry hair coat. Lack of hair regrowth after clipping may precede frank alopecia.[2] Colloquially referred to as a cosmetic condition, the severe alopecia and hyperpigmentation can often be troublesome to owners and may represent underlying systemic disease, warranting pursuit of prompt diagnosis and establishment of effective treatment. Treatments such as growth hormone supplementation,[3] deslorelin,[4,5] o,p′-DDD (mitotane),[6] melatonin supplementation,[6] trilostane,[7] neutering,[8] medroxyprogesterone acetate[9] and microneedling[10] have reported variable efficacy, and as such, there is currently no gold standard treatment recommendation.

Photobiomodulation therapy (PBMT) is a nonthermal process involving endogenous chromophores eliciting photophysical and photochemical events at various biologic scales, including but not limited to the alleviation of pain or inflammation, immunomodulation and promotion of wound healing and tissue regeneration.[11] This noninvasive treatment modality is being used with increasing frequency in both human and veterinary medicine for alopecic disorders. In humans, a recent review evaluating the efficacy of PBMT on hair regrowth in patients diagnosed with male pattern hair loss, female pattern hair loss, alopecia areata and chemotherapy-induced alopecia concluded that photobiomodulation (PBM) devices are both safe and effective in patients with male and female pattern hair loss.[12] In a pilot study of canine patients diagnosed with noninflammatory alopecia (e.g., post-clipping alopecia, pattern alopecia, recurrent flank alopecia) treated with PBMT, coat regrowth was 'improved' to 'greatly improved' in all seven dogs after four weeks of treatment.[13]

Videodermoscopy is a noninvasive technique that employs a specialised video camera (dermoscope) to magnify and capture images of the skin surface in vivo and is often coupled with image analysis software.[14] This tool has become increasingly popular in human and veterinary medicine. It has been used mainly for the characterisation and diagnosis of pigmented and nonpigmented skin lesions,[15] but has also been used to assist in the noninvasive diagnosis and monitoring of hair disorders.[16,17] In a recent pilot study, videodermoscopy and the associated imaging software were utilised to describe several canine hair follicle parameters and appeared to be a well-tolerated, noninvasive diagnostic method for characterisation of hair follicle disorders in dogs.[16]

## CASE PRESENTATION

A 3-year-old, male, neutered Pembroke Welsh corgi presented to a veterinary hospital for evaluation of progressive hair loss of 2-year duration. Two years before presentation, the hair of the caudal thighs was clipped during a grooming appointment and failed to regrow. Approximately 6–8 months before presentation, abnormalities in the hair thickness were noted on the patient's dorsum; the hair was observed to be thinning in a bilaterally symmetric and progressive fashion. The hair loss on the caudal thighs and dorsum was stated to be nonseasonal and nonpruritic.

Before presentation, the patient was placed on a Royal Canin Hydrolyzed Protein diet in the event that the hair loss was allergic in aetiology. Throughout the elimination diet trial, the patient remained on monthly flavoured flea, tick and heartworm prevention. The patient was also receiving omega 3 fatty acid supplementation for general skin support. Total T4 and symmetric dimethylarginine (SDMA) performed 3 months before presentation were 2.4 $\mu$g/dl (normal = 1.0–4.0 $\mu$g/dl) and 7.0 $\mu$g/dl (normal = 0.0–14.0 $\mu$g/dl), respectively; no additional diagnostics or treatments had been pursued. The patient was then referred for further evaluation.

On presentation, the patient was bright, alert and responsive. Vitals were within normal limits, cardiothoracic auscultation was unremarkable, the patient was of appropriate body condition, and no musculoskeletal abnormalities were appreciated. The dermatologic exam revealed bilaterally symmetric noninflammatory hypotrichosis to alopecia of the caudal thighs and dorsal thoracolumbar regions (Figure 1a,e). Loss of both primary and secondary hairs was appreciated on the caudal thighs, whereas exclusively primary hairs were absent along the dorsal thoracolumbar regions. Marked hyperpigmentation was present on the hypotrichotic to alopecic areas on the caudal thighs; this finding was less severe along the dorsum. Few, multifocal comedones were present on the caudoventral abdomen. At the initial presentation, the owner reported that the dog was not pruritic along the hypotrichotic to alopecic regions. Clinical signs such as polyuria, polydipsia, polyphagia, panting, weight loss or gain and exercise intolerance were specifically inquired about; the owner reported that none of these was present.

**LEARNING POINTS/TAKE HOME MESSAGES**

- When presented with a patient with noninflammatory hypotrichosis to alopecia, performing the appropriate diagnostics to rule out underlying endocrine disease is critical for comprehensive case management.
- Laboratory results should be interpreted with consideration of the clinical state of the patient, and treatment protocols should be adjusted as such.
- Upon completion of blood work, urinalysis and the dermatologic database (cytologic evaluation, skin scrapes), biopsy for histopathology is often indicated for further workup of hypotrichotic to alopecic conditions.
- Videodermoscopy is a noninvasive tool that allows for both subjective and objective evaluation of the epidermis and hair shafts, thus aiding in diagnosis of disease(s) and evaluation of response to therapy.
- Photobiomodulation therapy is an effective, safe, alternative option for the stimulation of hair regrowth in patients with hair cycle arrest. This treatment option should be considered when the clinician and owner are aiming to decrease the risk associated with previously described therapies.

## INVESTIGATIONS

Given the nonpruritic, noninflammatory nature of the hair loss, the main categories of differential diagnoses considered were endocrinopathies, hereditary disorders and miscellaneous causes of alopecia.[1] Based on the differential diagnoses, the following diagnostics were performed: a complete blood count (CBC), chemistry profile, urinalysis, adrenal panel and

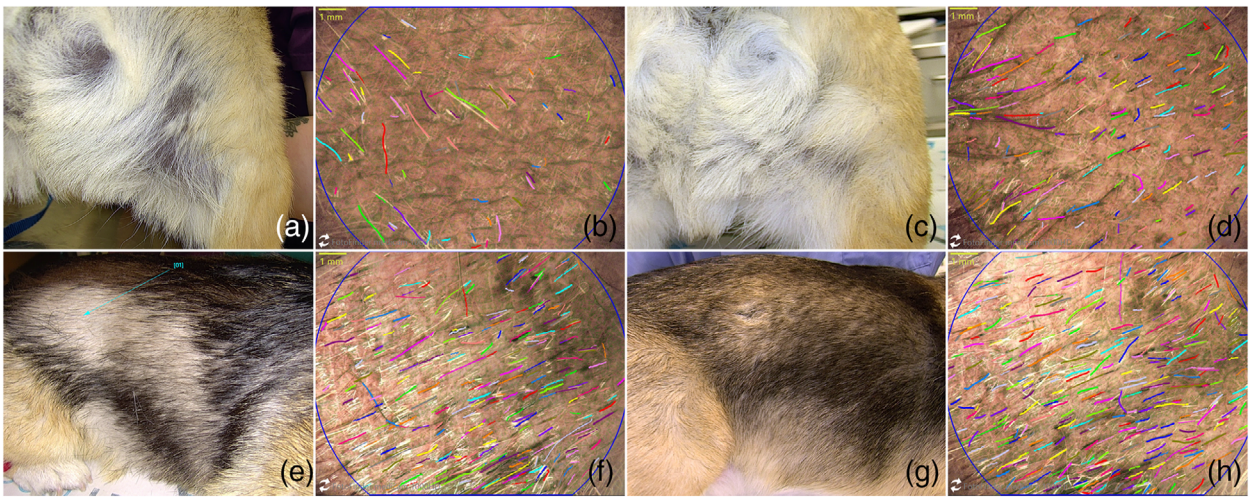


**FIGURE 1** Noninflammatory hypotrichosis to alopecia of the caudal thigh (a) and dorsal thoracolumbar region (e) before the start of therapy. Marked hair regrowth in both locations after 12 treatments of photobiomodulation therapy (PBMT) (c and g). TrichoScale Pro software analysis of hair shaft count pretreatment (b and f) and posttreatment (d and h) for each anatomical location

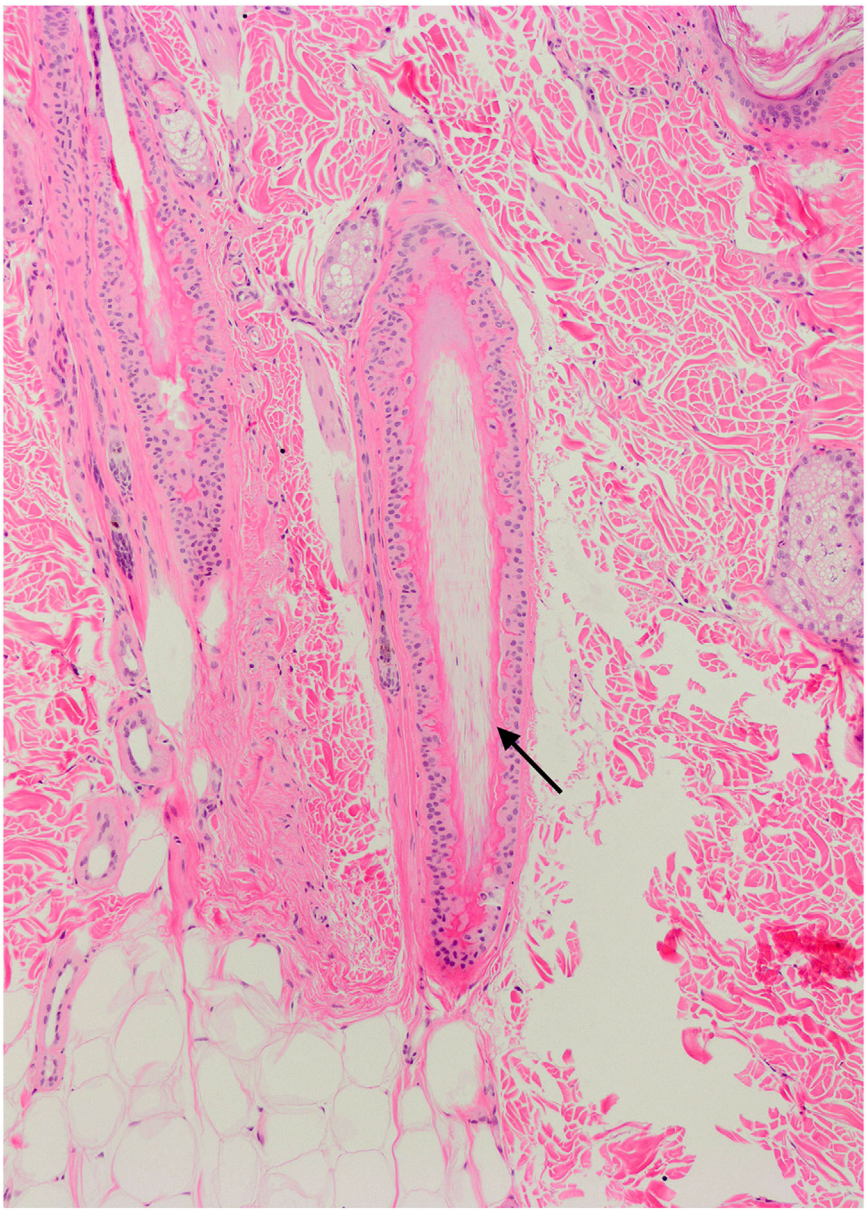

**FIGURE 2** Severe flame follicle formation characterised by excessive trichilemmal keratinisation (arrow)

skin punch biopsies for histopathology. Additionally, deep skin scrapes were performed on the caudoventral abdomen and a focal alopecic region on the caudal thigh to rule out demodicosis. CBC, biochemistry profile and urinalysis were unremarkable; deep skin scrapes were negative for demodectic mites and ova.

Hyperpigmented regions of hair loss along both the caudal thighs and dorsum (described above) were biopsied for histopathology and each site revealed consistent findings: marked widespread follicular cycle arrest with severe flame follicle formation (Figure 2) and few to no anagen bulbs present. Differential diagnoses based on these results included endocrinopathies, such as hypothyroidism and hyperadrenocorticism, as well as hair cycle arrest. The latter was assigned higher priority considering the lack of clinical signs consistent with endocrinopathy in addition to lack of histologic changes consistent with hypothyroidism and hyperadrenocorticism, respectively. Specifically, epidermal and follicular hyperplasia, follicular infundibular orthokeratotic hyperkeratosis and follicular tapering into a v-shaped ('toe-dancing hippo') configuration were not present on histopathology, making hypothyroidism an unlikely diagnosis. Likewise, epidermal and sebaceous gland atrophies were not present, thus decreasing the suspicion for hyperadrenocorticism.[2]

To evaluate adrenal hormone imbalances, an ACTH stimulation test was performed and serum was sent to the University of Tennessee College of Veterinary Medicine laboratory to measure the following hormones and their precursors: cortisol, androstenedione, estradiol, progesterone, 17 OH progesterone and testosterone. The adrenal panel revealed elevations of three of 12 steroid values evaluated. The pre-ACTH progesterone was 0.34 ng/ml (normal < 0.20 ng/ml), post-ACTH progesterone was 3.03 ng/ml (normal = 0.22–1.45 ng/ml) and pre-ACTH androstenedione was 0.74 ng/ml (normal = 0.05–0.36 ng/ml) indicating the presence of increased adrenal activity, potentially due to a partial deficiency of the enzyme 21-hydroxylase.

A total T4 was not repeated and a thyroid panel (including TSH) was not performed given the patient's normal T4 before presentation (during period of hair loss), the patient's repeatedly normal cholesterol on biochemical analyses and lack of systemic signs or histopathologic findings consistent with hypothyroidism.

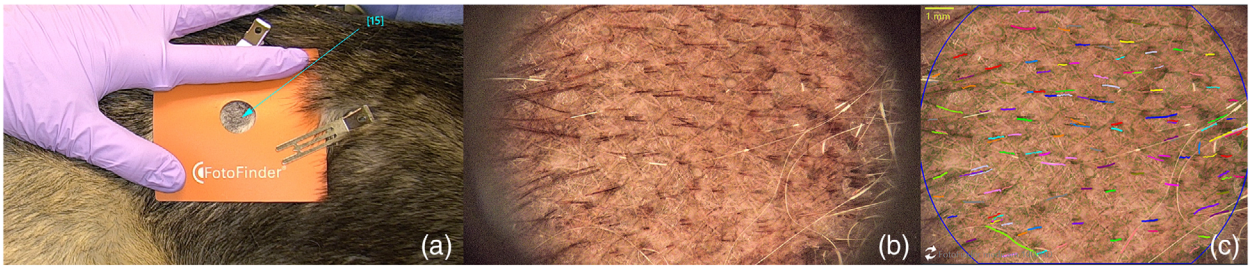


**FIGURE 3** Isolated area was clipped, and region of interest (blue arrow) was identified for dermoscopic analysis (a). Firm contact with the skin made before capturing images at 20× magnification (b) and performing TrichoScale Pro software analysis of hair shaft count (c)

Given the patient's history, dermatologic exam findings, histopathologic and laboratory findings, the patient was diagnosed with hair cycle arrest.

Macroscopic and microscopic images of the skin and hair of the caudal thigh and dorsal thoracolumbar regions were captured using a videodermoscope (Medicam 1000, FotoFinder Systems, Columbia, MD, USA), as seen in Figure 1b,d,f,h. To achieve this, the dog was gently restrained in a standing position and focally hyperpigmented, hypotrichotic areas on both the dorsal thoracolumbar region and caudal thigh were isolated and clipped per manufacturer's recommendations (Figure 3). Focal clipping is recommended to achieve greater visualisation and isolation of the individual hair shafts as they exit the skin. The FotoFinder stencil (Figure 3a) was secured onto the surrounding hair shafts once the region of interest was identified, providing a 1.75 × 1.75 cm delineated area for shaving. A thin layer of black hair dye (Tuxedo Black, Top Performance, Tops Pet Products, Beverly, MA, USA) was then applied to the shaved regions for enhanced detection of hair shafts. Per the product label, the dye was left on the skin for 15 minutes preceding thorough rinsing with room temperature water. Seventy percent isopropyl alcohol was applied with a soft gauze sponge to the region of interest and the head of the dermoscope to allow for optimal image clarity. After application of alcohol, the head of the videodermoscope was placed firmly onto the skin until hair shafts and the epidermis were well defined within the field of view. Images were obtained at 20× magnification. As seen in Figure 3b, initial dermoscopic evaluation revealed hyperpigmentation in a reticulated to honeycomb-like pattern, unremarkable follicular ostia and individual hair shafts of normal architecture. Individual dermal vessels were unable to be identified, given the severity of the hyperpigmentation present. All images were saved with the TrichoScale Pro software for future analysis (Figure 3).

## DIFFERENTIAL DIAGNOSIS

The diagnosis of hair cycle arrest is one of exclusion. Differential diagnoses include endocrine disorders (hypothyroidism, hyperadrenocorticism), parasitism (demodicosis) and hair follicle disorders.[1] Those particularly considered for this patient included the following: post-clipping alopecia, follicular dysplasia, alopecia areata, adrenal hormone imbalances, telogen effluvium, anagen effluvium, hypothyroidism and hyperadrenocorticism.

Histopathology may be helpful in identifying common characteristics of this condition, such as dermal atrophy, diffuse hair cycle arrest, prominent telogenisation of hair follicles and flame follicle formation.[2] Additional reported findings include alteration regarding the presence of kenogen follicles; specifically, decreased number of kenogen follicles as compared to other alopecic disorders yet increased numbers in comparison to unaffected dogs.[18] Histopathology should be utilised to rule out other hair follicle disorders.

## TREATMENT

Based on the diagnosis of hair cycle arrest, PBMT was initiated. This treatment was elected given its noninvasive nature and low potential for adverse effects. The MR4 ActiVet Pro, MultiRadiance Medical laser (Solon, OH, USA) was used at 250 Hz with probe emitting wavelengths of 905, 860, 660 and 465 nm. Similar wavelengths were used with the MR4 ActiVet Pro laser in a clinical trial assessing wound area reduction on chronic wounds in dogs with PBMT, revealing significant difference in the percentage of wound area reduction between the control and PBMT groups.[19] For optimum penetration depth and consistent dosing for the patient described herein, the direct contact technique was employed. Direct contact was made with each affected region (bilateral caudal thighs and bilateral dorsal thoracolumbar region) for 5 minutes, for a total of 20 minutes of laser therapy per session. The individual areas of irradiation were approximately 8 × 3 cm on each dorsal thoracolumbar region, and 6 × 4 cm on each caudal thigh. In the first week of therapy, treatments were administered on Monday, Wednesday and Friday. However, this proved unfeasible for the owner, so the frequency was decreased to twice weekly, with therapy administered on Monday and Thursday. Twelve total treatments (240 total minutes) were completed before dermatologic reassessment and repeat videodermoscopy. None of the treatments required patient sedation; all treatments were well tolerated with gentle restraint of the patient in a standing position. The protocol was adopted from a previous study evaluating the use of PBMT in dogs diagnosed with noninflammatory alopecia[12] in addition to the ActiVet Pro manufacturer recommendations.

## OUTCOME AND FOLLOW-UP

Upon completion of 12 PBM treatments, the dermatologic exam and videodermoscopy were repeated. Dermatologically, the previous few ventral abdominal comedones were

resolved, with no evidence of comedone formation elsewhere. As illustrated in Figure 1c,g, there was gross evidence of hair regrowth along both caudal thighs and along the dorsal thoracolumbar regions upon cessation of therapy. Both primary and secondary hair regrowths were apparent on clinical examination.

The same areas previously shaved along the caudal thigh and dorsal thoracolumbar region were prepared once more and dermoscopy was repeated as previously described. The total number of individual hair shafts was calculated using the same TrichoScale Pro software as used for baseline data. On the caudal thigh, the total numbers of hair shafts present within the field of view were 163 at the end of treatment, compared to 65 seen before initiating therapy. For the dorsal thoracolumbar region, 325 individual hair were identified at the end of therapy compared to the 246 identified at the baseline. A 32% increase in individual hair shafts was appreciated along the dorsum, whereas a 150% increase in individual hair shafts was seen on the caudal thigh. The previously noted hyperpigmentation was of lesser severity on both the caudal thigh and dorsal thoracolumbar region at cessation of therapy, appreciated both on dermatologic and dermoscopic exam; follicular ostia and individual hair shaft architecture remained unchanged, and dermal vessels were still unable to be visualised dermoscopically.

Up until the time of this writing this report, the patient had retained all hair regrowth achieved via PBMT. All hairs previously clipped for the posttreatment dermoscopic evaluation have regrown, and no evidence of previous clipping is appreciated on gross examination. Eight months after cessation of therapy, the patient remains free of clinical signs, and continues to show no evidence of an underlying endocrinopathy.

## DISCUSSION

To the authors' knowledge, this is the first reported case of hair cycle arrest in a Pembroke Welsh corgi. As such, it remains an important differential diagnosis for those that present with noninflammatory, nonpruritic alopecia. Furthermore, we show successful use of PBMT in treating hair cycle arrest, making it a suitable treatment option to pursue when considering a noninvasive therapy with no clinically evident adverse effects.

Hair cycle arrest has historically had several names, including adult-onset growth hormone deficiency (hyposomatotropism), growth hormone-responsive alopecia, castration-responsive alopecia, biopsy-responsive alopecia, congenital adrenal hyperplasia-like syndrome, and most recently, alopecia X.[1] Debate exists regarding potential abnormalities in the adrenal enzyme 21-hydroxylase role in the synthesis of cortisol and its precursors within the adrenal cortex; the reader is referred to publications that both support[20] and refute[21] the enzyme's responsibility for sex hormone imbalances potentially associated with the development of hair cycle arrest. In the case described herein, elevations were present in progesterone and androstenedione, both of which could be attributed to a partial deficiency of the 21-hydroxylase enzyme. However, the patient's hair successfully regrew in the absence of hormonal therapy, making attribution of disease to a hormonal disorder less likely. In the authors' opinion, the hormonal abnormalities detected were likely either nonspecific or coincidental rather than causative. Repeat ACTH stimulation test and adrenal panel were not performed in this case, given the previously reported poor correlation between clinical improvement and sex hormone normalisation[22] and the dog's lack of endocrine-related clinical signs.

Since the discovery of PBMT in the 1960s, PBM devices have been used to induce various therapeutic effects associated with a range of wavelengths.[12] The reported biological effects of PBMT include anti-inflammatory, pain reduction, improved wound healing, antibiosis, immunity and increased blood circulation, which are collectively termed the biomodulation effect.[12]

The exact mechanism by which PBMT stimulates hair regrowth is unknown; however, the primary mechanism is hypothesised to be stimulation of epidermal stem cells in the hair follicle bulge and shifting of the follicles into anagen phase.[23] One proposed mechanism includes photodissociation of inhibitory nitric oxide from cytochrome c oxidase, increasing ATP release and leading to induction of transcription factors such as nuclear factor kappa B and hypoxia-inducible factor-1.[23] The activation of various transcription factors such as these triggers several downstream events, ultimately leading to cellular proliferation and migration,[23] which is proposed to induce hair follicle activation and subsequent hair regrowth. The case reported herein supports previous findings in which PBMT was employed for the successful hair regrowth of seven dogs diagnosed with noninflammatory alopecia.[13] For this study, the manufacturer's manual was referenced for determining the therapeutic protocol. PBMT has shown a very low incidence of adverse events in human clinical studies evaluating its effect on hair growth; pruritus, erythema and a burning sensation have been described in humans,[12] none of which was appreciated in our case.

In this case, dermoscopy provided an objective quantification of hair regrowth, eliminating bias in evaluating patient response to therapy, as well as avoiding the need for repeated skin punch biopsies, a more invasive procedure for the patient.

In conclusion, 12 total doses of PBMT were effective in treating hair cycle arrest in a Pembroke Welsh corgi. This treatment modality proved to be noninvasive and well tolerated by the patient, which is of utmost importance given adverse effects associated with other treatments. In this case, videodermoscopy was essential for the quantification of hair regrowth and proved to be useful for the objective monitoring of response to treatment of a hair follicle disorder. Further investigations are required to establish the frequency at which this therapy is efficacious, as well as permanency associated with hair regrowth post treatment.

### ACKNOWLEDGEMENT

The authors would like to thank Dr. Ryan Jennings for assistance with histopathology images.

### CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

### FUNDING INFORMATION

The authors received no specific funding for this work.

## ETHICS STATEMENT

With full consideration of ethical and humane treatment of the patient, the primary author elected for the noninvasive treatment of photobiomodulation therapy. Additionally, it was elected to forego repeat biopsies for all ethical purposes.

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**How to cite this article:** Bello K, Diaz S, Cole L, Lorch G. The use of photobiomodulation therapy in the treatment of hair cycle arrest in a Pembroke Welsh corgi. Vet Rec Case Rep. 2022; e299. https://doi.org/10.1002/vrc2.299