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# Use of fluorescent light energy for the management of bacterial skin infection associated with canine calcinosis cutis lesions

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**SUMMARY**

A 15-year-old male golden retriever who had been receiving prednisolone for orthopaedic problems for the past 2 years was presented for multifocal symmetrical alopecia, skin nodules and plaques on the dorsal aspect of the body. Cytology was compatible with calcinosis cutis due to suspected iatrogenic hypercortisolism, with secondary pyoderma. The Phovia system, a device that emits fluorescent light energy (FLE), was used as an adjunct to systemic antimicrobial and topical (spray and shampoo) therapies. Part of the lesions were covered with a towel and not exposed to Phovia, to evaluate efficacy. Cytology confirmed accelerated improvement of the Phovia-illuminated lesions compared with unexposed lesions. To the authors' knowledge, this is the first report of FLE being used to manage bacterial skin infection associated with canine calcinosis cutis. It highlights the importance of this type of topical management against bacterial skin infections.

**BACKGROUND**

Calcinosis cutis is a skin condition where mineral salts are deposited in the skin and one major cause is iatrogenic hypercortisolism.<sup>1–3</sup> Secondary (superficial or deep) bacterial skin infection can occur.<sup>3</sup> Therefore, in addition to the management of the underlying diseases, appropriate antimicrobial treatment is indicated, especially nowadays, in the era of multidrug-resistant bacteria. Topical therapy can reduce exposure to systemic antibiotics, by shortening the treatment course.<sup>4–5</sup> Fluorescent light energy (FLE; also referred to as biomodulation) has shown to be beneficial in the management of superficial and deep pyoderma in dogs.<sup>6–8</sup> This type of technology has never been reported as a therapy against bacterial skin infection of calcinosis cutis plaques. Herein, we report the adjunctive use of FLE in the management of secondarily infected calcinosis cutis plaques.

**CASE PRESENTATION**

A 15-year-old male golden retriever was referred in May of 2019 with a 2-year history of non-pruritic skin nodules on the dorsal aspect of the trunk (figure 1). The nodules initially appeared dorsally at the base of the ears and over time became widespread, affecting the dorsal neck, back and rump. With chronicity, affected areas also became alopecic. In addition, the dog's hair was clipped in the summer of 2017, and since then the hair has regrown very

slowly. The patient had contact with another dog who had no skin problems. No humans in the household had skin lesions. The patient was regularly vaccinated, dewormed with milbemycin and praziquantel (Milbemax; Novartis Pharma GmbH) and received monthly lotilaner (Credelio; Elanco) as flea and tick prophylaxis. The owner noticed that over the last year, the dog had developed very mild polydipsia (exact amount in millilitres unknown) and polyuria (only during the day). In June of 2017, the dog was diagnosed with hip dysplasia and arthritis. He was therefore receiving metamizole (18 mg/kg twice daily, Novalgine; Sanofi-Aventis Deutschland GmbH) and prednisolone (0.5 mg/kg once daily; company unknown) at the time of presentation. Furthermore, due to acute conjunctivitis, the dog was receiving the last 3 weeks a once-daily eye ointment containing dexamethasone, neomycin sulfate, polymyxin-B sulfate (Isopto-Max; Novartis Pharma GmbH) and a twice-daily moisturising eye drop (Pantevit; WDT). Four weeks before referral, the nodules were treated topically using eardrops once daily that contained miconazole, polymyxin B and prednisolone (Surolan; Elanco) and a twice-weekly shampoo containing miconazole and chlorhexidine (Malaseb; Dechra veterinary products Deutschland GmbH).

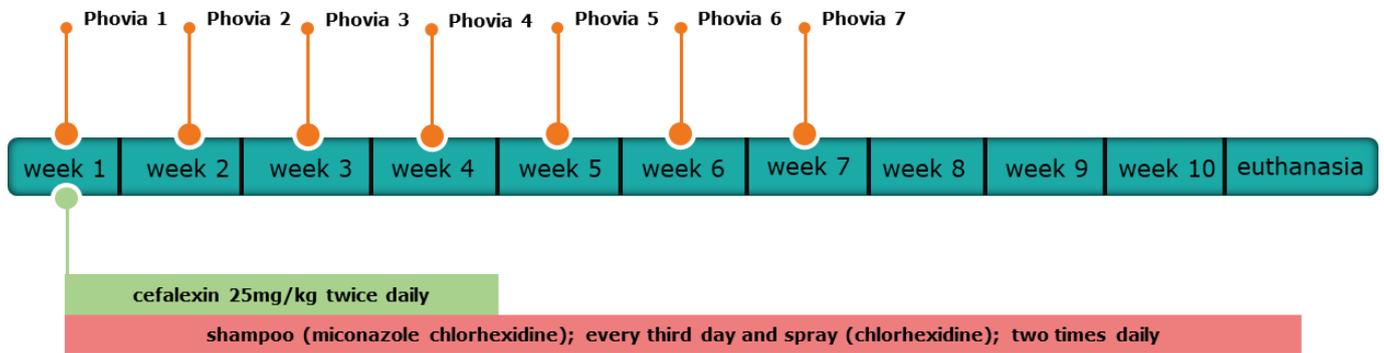
Physical examination revealed a grade 3/6 heart murmur, a pot-bellied abdomen and skin lesions. No other abnormalities were noted on general examination. The dermatological examination showed symmetrical, moderate alopecia and hypotrichosis on the dorsal and lateral aspects of the neck, thorax and back, and the dorsal rump. The hair coat was short due to slow regrowth since the last grooming and appeared as if it had been recently clipped. Multiple (more than 100 in total) but grouped, bilaterally symmetrical, firm whitish nodular dermal papules (0.3–1.0 cm) and plaques of different sizes (5 cm up to 30 cm) were observed on the dorsal aspect of both ear bases, the dorsal neck, the dorsal and lateral sides of the back, and the dorsal rump (figure 2). Brown adherent sebaceous scales were noted between these nodules and plaques as well as moderate to severe comedone formation.

Cytological examination (Romanowsky stain) of direct impression smears obtained from the nodules after squeezing them, 'scraping' the surface with a glass slide and then pressing it on the lesion, revealed moderate pyogranulomatous inflammation with intracellular and extracellular cocci



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**Figure 1** Timeline overview of the presentation and management of the patient.

(3+; [figure 3](#)) and focal multinucleated giant cells surrounding transparent crystals compatible with calcium salts. Multiple skin scrapings were negative for demodex mites. Serum chemistry panel showed an elevated alkaline phosphatase (1067 U/L; reference interval (RI): <141 U/L), gamma-glutamyl transferase (14 U/L; RI: <11 UL), glutamate dehydrogenase (19.4 U/L; RI: <9.6 U/L), alpha-amylase (1109 U/L; RI: 316–1047 U/L), lipase (418 UL; RI: <71 U/L), cholesterol (10.15 mmol/L; RI: 4.39–6.99 mmol/L) and triglycerides (8.6.36 mmol/L; RI: 0.26–2.12 mmol/L). Complete blood count showed elevated platelets (549 G/L; RI: 120–500) but otherwise no clinically relevant abnormalities. Total thyroxine (T4) was decreased (7.73 nmol/L). Urinalysis revealed a low specific gravity (1.018) and proteinuria (3+; dipstick). Based on the history, physical examination, and laboratory and cytological examination, our diagnosis was secondary superficial pyoderma and suspected calcinosis cutis due to suspected iatrogenic hypercortisolism. To confirm the diagnosis, skin biopsies, abdominal ultrasound and an adrenocorticotropic hormone (ACTH) stimulation test (measuring cortisol) were recommended.<sup>3</sup> Furthermore, a urine bacterial culture was recommended to exclude a subclinical bacterial cystitis. Due to financial constraints, the owner refused further diagnostic procedures. Because of the characteristic history and clinical picture, iatrogenic hypercortisolism with calcinosis cutis formation was highly suspected. Regarding the low T4, a euthyroid sick syndrome was suspected, and measurement of T4 and

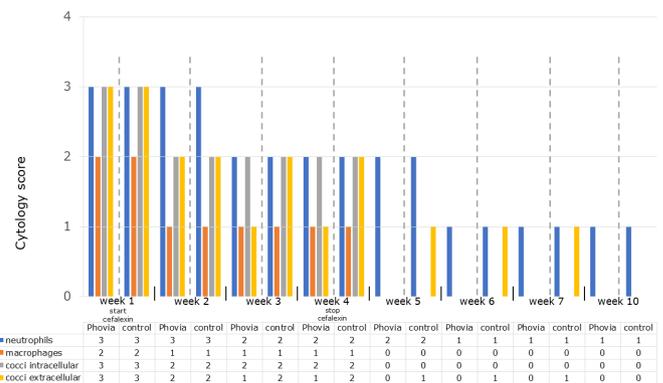
thyroid-stimulating hormone (TSH) was scheduled after the improvement of the suspected hypercortisolism.

**TREATMENT**

Verbal informed consent was obtained from the owner before all procedures. The calcinosis cutis was managed by gradually reducing the prednisolone dose (0.4 mg/kg orally every other day for 6 days, then 0.16 mg/kg every other day orally for 10 days, then 0.08 mg/kg every other day orally for 10 days and then withdrawal). The metamizole was also withdrawn and was replaced with meloxicam (0.1 mg/kg once daily, Metacam; Boehringer Ingelheim Pharma GmbH & Co. KG) as a treatment for arthritis. The eye ointment containing dexamethasone was also withdrawn, but the moisturising eye drops were continued as previously prescribed. Topical treatment of the calcinosis cutis lesions with dimethyl sulfoxide (DMSO) 99.7 per cent (Pro Vitas; Supplements ProVitas International S.L.) once daily was prescribed to hasten resolution due to its anti-inflammatory effects and ability to capture free radicals, as well as the promotion of translocation of substances via biological membranes.<sup>3,9</sup> Since the bacterial skin infection was generalised and because of the nature of the lesions, a deeper skin infection could not be excluded and the dog was treated systemically with empirical cefalexin (25 mg/kg twice daily, Cefalexin; CP-Pharma Handelgesellschaft mbH).<sup>5</sup> He was also treated topically (all the lesions) with chlorhexidine spray (Chlorexyderm; I.C.F.) twice daily and Malaseb shampoo (Malaseb Dechra veterinary products Deutschland GmbH) every third day to accelerate clinical improvement and to reduce the duration of systemic antimicrobial treatment ([figure 1](#)).<sup>4,5</sup> An FLE generating system (Phovia; KLOX Technologies Limited) consisting of a blue light-emitting diode (LED) device and a topical photoconverter gel was applied



**Figure 2** Presentation of the dog at the time of the first examination. Evidence of alopecia, comedones, brown adherent seborrheic scales and calcinosis cutis at (A) the thorax, back, dorsal rump and (B) dorsal neck.



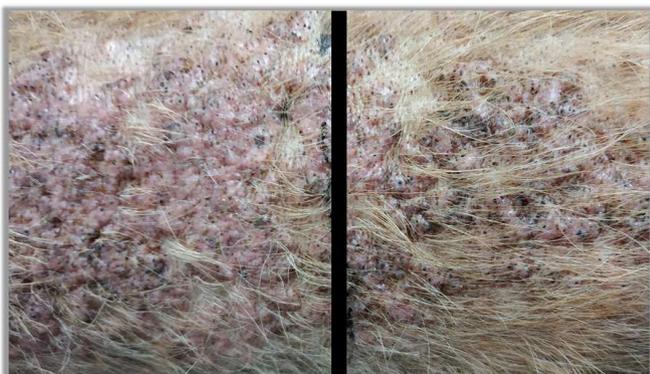
**Figure 3** Weekly cytology results.



**Figure 4** Application of Phovia. The control area is covered with a towel.

topically once weekly (two consecutive applications of 2 min each) to the calcinosis cutis lesions with bacterial infection, to accelerate clinical and cytological improvement and to reduce the duration of systemic antibiotics (figure 1). It is a quick and non-painful procedure, causing no distress and no sedation or anaesthesia is required. This approach has been previously described for management of superficial, deep and interdigital canine pyoderma,<sup>6–8</sup> in addition to the other topical therapies. The photoconverter gel (Phovia) was spread directly on the affected skin, forming a 2-mm-thick layer, and was then illuminated with the LED lamp for 2 min. The approximate distance between the lamp and the gel layer was 5 cm. Following the manufacturer's instructions, the residual gel was removed using gauze and a sterile saline solution at the end of each treatment. During the treatment course, there was hair regrowth and in order to better apply the gel, the hair overlying the calcinosis cutis lesions was carefully clipped, when necessary.

To evaluate the effect of Phovia, in aiding the resolution of the secondary bacterial skin infection of firm nodular papules and plaques (suspected calcinosis cutis), the lesions on the caudal half of the back and the rump were not exposed to the FLE system, serving as a control. To accomplish this, the control areas were covered with a towel during the illumination of all the other lesions (figure 4). The control areas still received the other topicals as described above using DMSO gel, a spray and shampoo. Physical and cytological examination were performed once weekly too (figures 1 and 3). The sample collection was performed from the same areas (cranial and caudal of the line on the back; see figure 5) as described previously. All samples were stained (Romanowsky stain) and examined cytologically by the



**Figure 5** Cytology sampling skin sites (on the back). Left side: illuminated (Phovia) area; right side: control area.

same investigator (NA), using a semiquantitative method, validated for monitoring antimicrobial treatment of skin lesions.<sup>10</sup> Briefly, cocci, rods, yeast, neutrophilic and eosinophilic granulocytes, and macrophages were evaluated, using scores ranging from 0 to 4 (0=not seen; 1=occasionally present but slide must be scanned carefully for detection; 2=present in low numbers, but detectable rapidly without difficulties; 3=present in larger numbers and detectable rapidly without any difficulties; 4=massively abundant), as previously described in the literature.<sup>10</sup> The areas additionally illuminated with Phovia were compared with those which were treated with systemic (cephalexin) and topical (spray and shampoo) treatment alone (figure 3).

#### OUTCOME AND FOLLOW-UP

During treatment, the skin improved. Fewer comedones and brown scales were visible. Furthermore, after the third week of therapy, the patient's hair started to slowly regrow (not visible in the pictures due to hair clipping, as described previously) in all areas (with and without Phovia) and no side effects were noticed. The pyoderma markedly improved by the fourth week of therapy and therefore the systemic antibiotic was discontinued and thereafter the patient was treated with topical therapy alone (figure 1). After 7 weeks of treatment, the pyoderma completely resolved and Phovia was discontinued (figure 1). The skin was less erythematous and seborrheic with fewer comedones. Furthermore, the calcinosis cutis improved, however very mildly, after 7 weeks of treatment. Although macroscopically there was no visible difference between the areas illuminated with and without Phovia, cytologically, we observed a faster improvement (figure 3) during the 7 weeks of therapy in the illuminated areas. From the fifth week, the Phovia-treated areas had no bacterial infection, whereas the other areas were still infected (figures 1 and 3). Topical treatment with antimicrobial spray, DMSO gel and shampoo was performed until the next recheck (week 10; figure 1), which had the first bacteria negative cytology in the Phovia-untreated sites (figure 3). At this recheck, the patient's hair had almost fully regrown and there were no clinical signs of pyoderma (figure 6). Blood examination was performed (CBC, biochemistry panel, T4 and TSH), to monitor the calcium levels during DMSO treatment and to evaluate for hypothyroidism. T4 and TSH values were within the normal RI, and hypothyroidism could be excluded. While calcium levels were within the RI, urea (31 mg/dL; RI: 9–29 mg/dL), potassium (6.4 mmol/L; RI: 3.9–5.8 mmol/L) and alkaline phosphatase (237 U/L; RI: 14–147 U/L) were increased. On the contrary, leucocytes (4.8 g/L; RI: 4.9–17.6 g/L), erythrocytes (4.3 T/L; RI: 5.4–8.7 T/L), haemoglobin (9.9 g/dL; RI: 13.4–20.7 g/dL) and haematocrit (33.3 per cent; RI: 38.3–56.5 per cent) were reduced. Although the levels of reticulocytes were 64.700/ $\mu$ L, mean corpuscular volume was increased (76.7 fL; RI: 59–76 fL) and mean corpuscular haemoglobin concentration was decreased (29.7 g/dL; RI: 32.6–39.2 g/dL) with present anisocytosis, indicating the presence of immature nucleated RBCs and regeneration of the anaemia. As a further diagnostic step, thoracic radiographs and ultrasound of the heart and abdomen were performed. A large cavernous inhomogeneous mass originating from the spleen (suspicion of haemangiosarcoma; differential diagnoses: lymphoma, splenic sarcoma, malignant histiocytosis, mast cell tumour, haemangioma, haematoma, nodular hyperplasia, granuloma) with lymphadenomegaly in the caudal abdomen was diagnosed. Furthermore, the dog had hyperechogenic foci in the liver, hypovolemia and a mitral valve



**Figure 6** (A) Dorsal caudal thorax, back, dorsal rump, (B) dorsal neck. Presentation at week 10. Hair almost fully regrown and there are no clinical signs of pyoderma.

insufficiency. The owner declined further diagnostic evaluation and treatment. The dog was euthanased after 2 days at home due to massive deterioration of clinical symptoms.

## DISCUSSION

Published guidelines for the treatment of canine pyoderma recommend early and frequent use of topical treatment to hasten resolution of the infection and to reduce the duration of systemic antimicrobial treatment, whenever these are indicated.<sup>4 5</sup> The most commonly used topical treatments are the traditional shampoos, gels, ointments, sprays and wipes.<sup>4</sup> Recently, however, another modern therapeutic modality of FLE using LED light (peak wavelength 440–460 nm) and a topical photoconverter gel has been described to be beneficial for the management of superficial, deep, interdigital canine pyoderma and canine otitis.<sup>6–8 11</sup> This approach has been described to promote wound healing of uncomplicated cutaneous incisional wounds in dogs,<sup>12</sup> and chronic wounds in humans,<sup>13</sup> and thus can be a beneficial adjunct in the management of wound healing.<sup>13</sup> The mode of action of this system is based on the ability of the chromophore molecules contained in the photoconverter gel to capture the light emissions of the LED lamp and convert them into photons with lower energy at different range wavelengths (fluorescence), affecting all three phases of healing.<sup>14</sup> Briefly, inflammatory

mediators are modulated (downregulation of pro-inflammatory cytokines, upregulation of anti-inflammatory cytokines), and tissue proliferation and angiogenesis are supported by elevated growth factors.<sup>12–14</sup> Collagen, which is important for remodeling, is also increased.<sup>12 14 15</sup> Finally, FLE also impacts new tissue maturation by increasing decorin.<sup>12 14</sup> Consequently, improved healing promotes faster resolution of infection and reduced duration of systemic treatment.<sup>6–8 11 12 14</sup> Furthermore, a bactericidal activity of the Phovia system could be postulated based on the clinical studies of pyoderma<sup>6–8</sup>; however, it has not been evaluated in vitro yet. Our diagnosis could not be further evaluated with diagnostics, including biopsy or ACTH stimulation test, due to the financial constraints of the owner. However, the diagnosis of calcinosis cutis was based on history, clinical signs and cytology and the suspicion of iatrogenic hypercortisolism was based on the striking 2-year history of steroid administration, clinical signs and blood biochemistry (as well as improvement of alkaline phosphatase after discontinuation of prednisolone and hair regrowth). This presumption is also supported by studies reporting that canine iatrogenic hypercortisolism is a major cause of calcinosis cutis.<sup>12</sup>

To the authors' knowledge, this is the first report where FLE using the Phovia system was used to manage pyoderma associated with calcinosis cutis plaques, showing accelerated cytological improvement, compared with lesions that were not managed with FLE. This finding is in accordance with other reports<sup>6–8 11</sup> and suggests that a FLE Phovia system could be used as an adjunctive therapy for many different forms of bacterial skin infection, helping reduce the usage of systemic antibiotics. Furthermore, studies should further evaluate and improve FLE protocols against bacterial skin infections, especially nowadays, in the era of multidrug-resistant bacteria.

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**Data availability statement** All data relevant to the study are included in the article.

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## Learning points

- ▶ Fluorescent light energy (Phovia system) may accelerate the improvement of skin infection and is an alternative modality of topical therapy.
- ▶ Early topical treatment against bacterial skin infection is important to hasten resolution and reduce the duration of systemic antimicrobial treatment.
- ▶ Patients treated with corticosteroids should be monitored for side effects like iatrogenic hypercortisolism and calcinosis cutis.

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