PHOTODYNAMIC THERAPY OF FELINE SUPERFICIAL SQUAMOUS CELL CARCINOMA OF THE NASAL PLANUM

De fotodynamische behandeling van een oppervlakkig plaveiselcelcarcinoom van de neusspiegel bij een kat

E. Vinck¹, H. Vinck², B. Cagnie¹, D. Cambier¹

¹Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, Ghent University, University Hospital, De Pintelaan 185 (6K3), 9000 Gent, Belgium
²Dendermondesteenweg 624, 9070 Destelbergen, Belgium
elke.vinck@UGent.be

ABSTRACT

The objective of this case report was to demonstrate the feasibility of photodynamic therapy for the treatment of feline superficial squamous cell carcinoma and to illustrate its approachability in veterinarian practice.

Photodynamic therapy using topical 5-aminolaevulinic acid was applied on a superficial squamous cell carcinoma at the nasal planum of a cat. After applying of the cream, the irradiation was performed with a red Light Emitting Diode contrivance with a wavelength of 660 nm.

The following day, the tumour area was erythematous and oedematous. On the second day after the treatment a scab was formed. The response rate was encouraging as visual observation of the tumour area revealed a removal of the malignant cells. The recovery of the normal epithelialised skin structure was observed two months after the treatment. A follow-up period up to two years revealed no recurrence.

These promising results demonstrate that photodynamic therapy should be considered as treatment modality for early stage superficial squamous cell carcinoma.

INTRODUCTION

In clinical practice, feline squamous cell carcinoma (SCC) of the skin is traditionally treated by surgery, cryosurgery, intrallesional chemotherapy and/or radiotherapy (Lana et al., 1997; Moore and Ogilvie, 2001). Though the success ratios of these treatments are relatively high, they do involve a number of disadvantages. These forms of therapy are costly and potentially harmful. They can leave a scar
and hypo- or hyperpigmentation, and may have other side effects such as pain, severe inflammation and irritation (De Rosa and Bentley, 2000; Moore and Ogilvie, 2001).

The search for a more acceptable treatment that is capable of killing cancerous cells in a more selective way has led to the development of photodynamic therapy (PDT). PDT is a treatment modality based on the interaction between a photosensitizer (precursor), light and oxygen, which causes photochemically induced selective cell death (De Rosa and Bentley, 2000; Guillen et al., 2000; Maier et al., 2001; Morton et al., 2002). The selective toxicity of PDT is based on the preferential uptake or retention of the photosensitive agent at higher concentrations in tumor tissue than in the surrounding normal tissue. Application of the photosensitizer is followed by exposure to light of a wavelength corresponding to one of the absorption maxima of the photosensitizer. Light absorption transforms the sensitizing agent from its ground state into an excited triplet state molecule. The excited triplet can undergo two types of reaction. It can transfer its energy to oxygen directly to form reactive singlet oxygen. Alternatively, it can transfer its energy to intermediate molecules, which then react with oxygen to produce free radicals. As a result of the activation of reactive singlet oxygen or free radical production, subsequent tissue damage is generated. Without exposure of the photosensitizer to light of the appropriate wavelength, the photosensitizer is not activated and so there is no effect on the tumor tissue (Cairnduff et al., 1994; Lucroy et al., 2000; Lucroy et al. 2002; Morton et al., 2002; Peng et al., 1997; Stell et al., 2001). This case report, which is aimed at familiarizing practitioners with the use of PDT and providing the necessary information for eventual clinical application, deals with recent clinical progress in topical PDT of skin cancer using 5-amino laevulinic acid (5-ALA) and Light Emitting Diodes (LEDs).

**MATERIALS AND METHODS**

A neutered male cat (domestic longhair, 18 months, 4 kg, FeLV negative and FIV negative) with cytologically confirmed superficial SCC of the nasal planum and the transition to the bridge of the nose, and tumor grade T1 (Figure 1) (Owen, 1980; Hahn and Richardson, 1995; Moore and Ogilvie, 2001) was selected for photodynamic treatment with 5-ALA and LED. Macroscopically, a grade T1 tumor (Owen, 1980; Hahn and Richardson, 1995; Moore and Ogilvie, 2001) is characterized by a crusting lesion with erythemic tissue beneath the crust. According to the TNM classification system, a T1 tumor is superficial and non-invasive (Owen, 1980; Hahn and Richardson, 1995; Moore and Ogilvie, 2001). Figure 2 pictures the corresponding cytological appearance. The diameter of the lesion (Figure 1) was approximately 1.2 cm. Clinical and routine blood examinations confirmed the good general health of the cat and no palpable regional lymph node enlargements were detected. Sensitization with 5-ALA cream was preceded by cleaning of the SCC with sterile polyvidon-iodine 10% solution (iso-BETADINE; Asta Medica) and removal of the crust. Two millimeters of Porphin 5-ALA cream 20% (Aladerm; Crawford Pharmaceuticals) was applied topically to the lesion and to a 2 mm margin of apparently normal skin tissue. Application occurred by means of a cotton swab. The cream was applied over a period of five hours. Every 30 minutes the presence of the cream was examined and, if necessary, more cream was applied. The cat was anesthetized throughout the entire procedure to avoid attempts to remove the cream by licking or rubbing and to avoid discomfort. Sedation was done with Medetomidine HCl 1 mg/ml (Domitor, Pfizer Animal Health) at 0.05 mg/kg intramuscular and anesthesia with Ketamine HCI 100 mg/ml (Alesketin, Eurovet) at 2.5 mg/kg intramuscular. Propofol 10 mg/ml (Rapinovet, Schering-Plough), which served as maintenance anesthesia, was administered intravenously as needed throughout the procedure. An insulin was used to prevent hypothermia during anesthesia. After removal of the photosensitizing agent, irradiation was accomplished using a red Light Emitting Diode contrivance (BIO-DIO preprototype; MDB-Laser Belgium) with a wavelength of 660 nm. LED irradiation at continuous mode was administered for a period of 20 minutes at a power output of 80 mW, resulting in a radiant exposure of 38 J/cm². During irradiation, the distance from light source to treatment area was 0.6 cm and aluminized tape was used to protect the eyes of the cat from irradiation (Figure 3). Immediately before irradiation, the tumor area was exposed to the ultraviolet light of a Wood lamp, verifying the presence of the typical red fluorescent spectrum of protoporphyrin IX (PPIX).

**RESULTS**

Besides normal distress after anesthesia, no adverse effects were monitored during a hospitalization...
of 48 hours following the treatment. Consequently, no local anesthesia was administrated, though as a precautionary measure an Elizabethan collar was applied for 24 hours to prevent licking, rubbing and scratching.

The day following irradiation, the tumor area became erythematous and somewhat edematous. The cat did not attempt to lick or scratch the treated area. Two days after the treatment, a scab developed. Response to the therapy was assessed by visual observation of the tumor area at 1 month (Figure 4), 2 months, 6 months and 2 years post-treatment. The second observation, at two months post-treatment, revealed a complete response, which is defined as the disappearance of the malignant cells (based on macroscopic observations) and the complete disappearance of the crusting lesion, which relates to the recovery of normal re-epithelialized skin structure. No recurrence was noted up to two years post-treatment.

**DISCUSSION**

In the perspective of this case, PDT using topical 5-ALA and LED can be considered as safe and effective in treating early stage SCC of the skin. The initial response rate was encouraging, as normal tissue was...
spared and healing occurred very fast. There also was an excellent cosmetic result, thanks to the small amount of crust formation. In accordance with some studies (Reeds et al., 2004) and in contradiction to others (Peaston et al., 1993; Frimberger et al., 1998; Stell et al., 2001; Touma et al., 2004), this study did not reveal adverse effects such as local discomfort, lack of appetite or vomiting. Thanks to the topical use of the cream, systemic effects and generalized photosensitization leading to cutaneous sensitivity, which has been noted in cases of intravenously administered photosensitizing agent (Hahn et al., 1998), was absent and the cat could be exposed to sunlight within 24 hours after the treatment (Savary et al., 1998; Maier et al., 2001).

Apart from the convincing outcome, several points should be noted. First of all it should be noted that during the follow up period the cat was exposed to nearly no direct sunlight as the owners live in an apartment. As sun avoidance and protection from sunlight are important precautionary measures to prevent recurrence of superficial squamous cell carcinomas, one essential risk factor for possible recurrence was eliminated (Anonymous, 2003; Alam and Ratner, 2001; Moore and Ogilvie, 2001). Secondly, the lesion was rather superficial (T1) (Owen, 1980; Hahn and Richardson, 1995; Moore and Ogilvie, 2001) and, as Peaston et al. (Peaston et al., 1993) state, treatment is more effective in tumors at stage T2 and earlier. A third and final remark relates to the fact that only one case, and hence one type of lesion, was considered at one specific location. Consequently, the extrapolation of the results to various types of tumors, tumors located elsewhere than the nasal planum, and tumors with deeper dermal involvement (stages T3-T4) (Owen, 1980; Hahn and Richardson, 1995; Moore and Ogilvie, 2001) is only permitted after the treatment of a large number of various different tumors at different stages and at various different locations in the body.

The above mentioned points, which provide ample material for future investigations, do not lower the considerable value of this study, which has proved that PDT can lead to beneficial results in the treatment of superficial SCC of the nasal planum in cats. Since this innovative procedure is a valuable alternative to conventional treatment (Reeds et al., 2004), it is necessary to inform practitioners about it and to familiarize them with the use of PDT. By drawing up an elaborate description of the materials and methods, the investigators have endeavored to make the procedure accessible for daily veterinary practice, or at least to encourage veterinarians to refer patients to colleagues where PDT is available.

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REFERENCES


