Photodynamic therapy in the treatment of canine oral papillomatosis.

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Abstract

Canine papillomatosis is an infectious viral disease that is characterised by the formation of usually benign oral, skin or eye papillomas. The persistence of oral formations may produce dysphagia, prostration, pharyngeal obstruction, anorexia, inanition and death. Treatment is indicated when the lesions do not voluntarily regress, which leads to a deterioration in clinical symptoms. A mixed breed adult canine patient was treated. A clinical protocol using photodynamic therapy was established for the treatment of canine oral papillomatosis. A complete reduction in the buccal and tongue lesions was observed after 30 days. A clinical protocol using photodynamic therapy was established as a successful therapeutic procedure for this disease.

Keywords: Photodynamic Therapy, Papillomatosis, Laser, Dog, Treatment.

Introduction

Photodynamic therapy (PDT) is a therapeutic method used to destroy tumour cells [1]and microorganisms (bacteria, viruses and fungi) [2]. This therapy uses oxygen free radicals to produce cytotoxicity in proliferating tumour cells without genotoxic or mutagenic effects, and it also inhibits the development of microbial resistance [3]. The use of PDT in veterinary medicine is under investigation [3-6]because this technique has considerable clinical potential in the treatment of various diseases. Canine papillomatosis exhibits high morbidity in kennels, veterinary hospitals, clinics and similar environments that have a large rotation of animals, and it can affect entire litters. A virus in the genus *Papillomavirus*, family *Papovaviridae*, causes the disease, and it generally produces tumorous lesions (papillomas) in the oral cavity of canines. These lesions are generally benign and often spontaneously regress within a few weeks. However, the lesions may become chronic and malignant. Therefore, mortality from this disease is low, except when secondary complications that affect the overall health of the animal develop. The prognosis is good once an animal recovers from the lesions, and the animal is immune for the rest of its life [7].

Surgical removal and cryosurgery are effective treatments for cutaneous, oral and conjunctive papillomas. However, these procedures are not indicated for corneal papillomas. The relationship between clinical resolution and surgical intervention is difficult to determine due to the frequent spontaneous regression of these lesions. Systemic or local chemotherapy using agents, such as vincristine, cyclophosphamide or doxorubicin, have yielded controversial or inefficient results in the majority of canine therapeutic trials [7]. Therefore, this report investigated the efficacy of PDT for the treatment of canine oral papillomatosis.
Materials and methods

A mixed breed adult canine patient was treated. The patient presented with dysphagia, halitosis and multiple verrucous oral lesions and was diagnosed with canine oral papillomatosis.

Major lesions in the buccal mucosa, excluding the tongue lesions, were injected with an aqueous methylene blue solution (300 µM) under general anaesthesia, and after five minutes, the lesions were irradiated with a diode laser ($\lambda = 660$ nm) perpendicular to the lesion for 3 minutes ($40$ mW, $0.4$ J per point, $10$ J/cm$^2$). After 15 days, a second application was performed, including tongue lesions underwent the same protocol as the buccal lesions.

Results

The irradiated lesions were significantly smaller at the two-week follow-up. The lesions on the tongue, which were not injected with methylene blue and irradiated, did not show visible changes. A complete reduction in the buccal and tongue lesions was observed 15 days after the second application, as might see at Figures 1, 2, 3, 4 and 5.

Figure 1: Canine oral papillomatosis before treatment.

Figure 2: Lesions injected with methylene blue.
Figure 3: First laser irradiation

Figure 4: Lesions after two weeks of the first application.

Figure 5: Complete reduction in the buccal and tongue lesions, 15 days after the second application.
Discussion

Canine oral papillomatosis is a common disease in small animals. Several therapeutic methods have been described previously, but treatment remains an open question. Many studies have been performed to elucidate and design an effective and less invasive therapy.

Oral manifestations of this disease generally occur on the lips, tongue, soft palate, pharynx and oesophagus. Lesion size ranges from small round nodules less than 0.5 cm in diameter to large uneven masses known as “cauliflowers,” “warts” or “papillomas.” Papillomas typically appear as warts, and the lesions are hard. Coloration varies from greyish-white to black, and the lesions exhibit a rough and crumbling surface that is easily removed, which causes bleeding [8]. Ocular papillomas occur in the conjunctiva, cornea and eyelid margin [7]. Lesions generally develop over one to five months in dogs and regress between four to eight months after the lesion appears in the majority of cases. However, lesions occasionally become chronic [9]. Benign cancerous lesions, such as a squamous cell carcinoma, may also become malignant, but this transformation is a rare clinical outcome [10]. Infected animals are generally resistant to new infections after the complete regression of papillomas. However, papilloma relapse may be caused by an inadequate immune response or immunodeficiency in susceptible animals [7].

Papillomas rarely cause severe problems. However, these lesions may affect the overall health of the animal by obstructing the pharynx and producing dysphagia [8]. Common clinical complications in dogs include drooling, halitosis, bleeding, secondary bacterial infections and purulent discharge near the papillomas [7].

Papillomatosis therapy is a controversial subject among researchers. A wide variety of drugs and treatment methods are available, but a therapeutic protocol that is highly effective and produces reproducible results has not been identified. However, most animals are not treated because the disease is self-limiting. Several treatment options, including surgical resection, antiviral drugs, autochthonous vaccines and immunomodulatory drugs, are available in complicated clinical cases, such as tumour ulceration or pharyngeal obstruction, or in cases where aesthetics are important [11].

PDT uses a light source and a photosensitising agent to produce cytotoxicity in proliferating cancer cells, through molecular oxygen [5]. The photosensitising agent in PDT is taken up by cancer cells and activated by light at a specific wavelength. This activation raises the photosensitiser from a ground state to an excited state. The molecules return to a ground state by emitting energy through fluorescence or the release of photons, or the molecules may undergo a series of chemical reactions to create a reactive species called a triplet. Molecules in a triplet state interact directly with biological substrates to form free radicals, a type I reaction, or the molecules may transfer their energy to cellular oxygen and form singlet oxygen, a type II reaction, which is highly reactive and causes cell death [12-14].

Therefore, treatment of the reported patient encompasses many factors, such as the aetiology of the disease and its behaviour in the patient, which prevents the direct conclusion that PDT was successful. However, the lesions on the tongue, which were not treated in the initial application, were the only lesions that did not regress after the initial PDT treatment. These results suggest that the therapy was successful.

Combinations of novel techniques, such as PDT, may create novel options for the treatment of this disease. The case reported herein warrants the further investigation of this novel and rarely used treatment. The development of novel photosensitising agents and cost-effective light sources will promote PDT as an important veterinary tool.

Conclusions

PDT is a novel candidate for canine oral papillomatosis treatment, and further studies are warranted to elucidate its use as a veterinary oncological treatment and to understand the pathophysiology of this disease.
References


