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CASE REPORT
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Canine Oral Papillomatosis - Treatment with Association of Azithromycin and Meloxicam

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ABSTRACT

***Background*:** Canine oral papillomatosis is an infectious disease that usually affects dogs with immune deficiencies, but can eventually regress without treatment. However, this regression without treatment can be time-consuming, taking up to 12 months for complete regression, thus causing more suffering for the dogs and difficulties in the maintenance and hygiene of the animal. Many treatments have been proposed, but most without scientific references, which has often led to frustrating results. The aim of this report is to describe the response to the treatment of a bitch with oral papillomatosis, using Azithromycin associated with Meloxicam.

***Case*:** A 6-month-old bitch Pug with skin lesions consistent with canine oral papillomatosis, presenting typical clinical lesions such as exophytic vegetative formations, cauliflower-like lesions and verrucous and hyperkeratotic papules around the mouth and on the internal oral mucosa. The treatment protocol included Azithromycin (10 mg/kg) in combination with Meloxicam (0.1 mg/kg), administered orally every 24 h for 10 days. This therapeutic management protocol was in accordance with the dosage recommendations provided by the manufacturer of the drug approved and commercially available in Brazil. The animal maintained normal appetite and behavior and showed no clinical signs other than the aforementioned lesions. This treatment resulted in complete resolution of the papillomatous lesions. Follow-up monitoring over 12 months showed no recurrence, indicating sustained clinical remission.

***Discussion*:** Azithromycin is widely used in Veterinary Medicine to treat various bacterial infections, and it is well tolerated and effective in treating papillomatosis in humans; however, the precise mechanism of its antiviral activity is not fully understood. In the present case, the lesions completely regressed after 10 days of treatment with Azithromycin and Meloxicam. Possibly Meloxicam improved the quality of life during treatment by reducing the discomfort associated with the oral lesions, since other studies have shown that Meloxicam was effective *in vitro* in reducing cell proliferation, inducing apoptosis and improving the human patient's quality of life by relieving the pain and discomfort caused by the papillomatosis lesions. The combined treatment of Azithromycin and Meloxicam carried out in this case was effective for the rapid resolution of canine oral papillomatosis and without recurrence, indicating sustained clinical remission. Effective treatment is particularly important to avoid a prolonged course of the disease, which can increase the spread of the infection to other canines. Tumor recurrence after apparently successful treatment is also common and, in addition, the possible malignancy of papillomatous lesions requires prompt and effective treatment. Reducing the incidence of clinical cases of oral papillomatosis in dogs requires strategic management, including appropriate treatment to contain the spread of the virus. Further studies are needed to investigate any specific antiviral activity of these 2 drugs used on the animal in the present report.

Keywords: dog, bitch, papillomavirus, wart, disease.

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INTRODUCTION

Canine oral papillomatosis is a viral disease transmitted mainly by direct contact; however, indirect transmission is also possible, due to the ability of the papillomavirus to persist in the environment [10,13]. Canine papillomatosis is common in young puppies and is characterized by multiple, invasive, cauliflower-like hyperkeratotic masses on the tongue, lips, palate, gingiva, buccal mucosa, and pharynx [17]. Although the lesions are typically benign, they can progress to squamous cell carcinoma [5].

It is a self-limiting infectious disease that can regress without treatment [12], but the complete regression of these lesions can take up to 12 months, and this long waiting period often causes suffering in dogs and serious disruption to the animal's maintenance. Dogs with immunosuppressive disorders are more prone to developing canine papillomatosis [13,16] and Pug dogs are considered particularly susceptible to immunological disorders and papillomavirus infections [7,11]. Furthermore, the underlying mechanisms are not fully understood. Therefore, considering the complexity and difficulties related to the treatment of canine oral papillomatosis, the aim of this manuscript is to report the response to treatment with Azithromycin-based medication associated with Meloxicam in a case of canine oral papillomatosis.

CASE

A 6-month-old bitch Pug, weighing 2 kg, from Itabirito, Minas Gerais State, Brazil (20.2482° S, 43.8044° W), was clinically diagnosed with skin lesions characteristic of canine oral papillomatosis, observed around the mouth and on the internal oral mucosa (Figure 1). The diagnosis of papilloma infections in the Pug was based on typical clinical signs, including observation of exophytic vegetative formations, cauliflower-like lesions, and verrucous and hyperkeratotic papules. Due to typical gross features, the diagnosis of oral papillomatosis can often be made based on the appearance of the lesions [8,14,21]. Considering the dog's young age, the rapid growth of warts, and the potential complications such as difficulty eating, breathing, anorexia, and halitosis that can arise from the exacerbated growth of oral warts in dogs [9,22], treatment was promptly planned and started.

The treatment plan involved administering a 200 mg dose on the 1st day (D=1), followed by a half tablet of medication composed of Azithromycin+Meloxicam[1] [Azicox-2® - 10 mg/kg and 0.1 mg/kg, respectively, QD, PO, for 10 days]

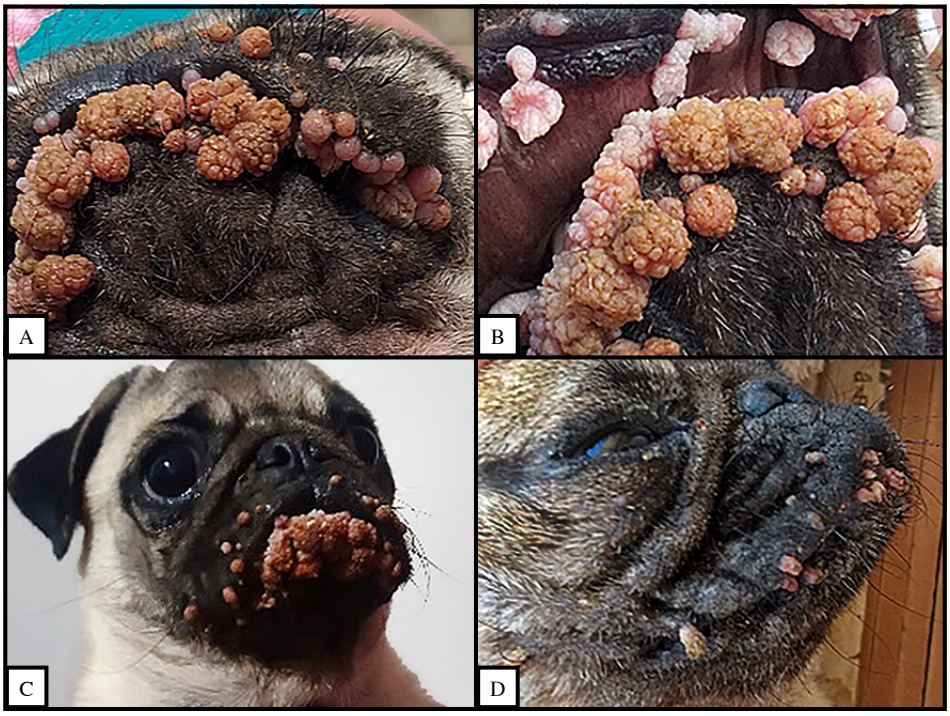

Figure 1. A & B- Canine oral papillomas in a bitch Pug at the time of diagnosis (July 26, 2022). C- Initial regression of papillomas observed after 3 days of treatment (August 3, 2022). D- Continued regression of papillomas observed after 7 days of treatment (August 7, 2022).

(Figure 2). This therapeutic management protocol was under the dosage recommendations provided by the manufacturer of Brazil's approved and commercially available drug, and as previously proposed by Azithromycin [21] and the manufacturer's recommended use for Meloxicam. The selection of the commercial product approved by the Brazilian government ensured adherence to the appropriate veterinary dosage. Within a few days of initiating treatment, noticeable regression of the lesions was observed (Figure 1), with progressive and complete resolution of the lesions over the treatment period in D=10 (Figure 3).

In this case, to meet the need to use a commercial product approved by the Brazilian government for veterinary use and for use in dogs, the commercial product used and available on the market is a combination of Azithromycin with Meloxicam. Meloxicam for dogs is a non-steroidal anti-inflammatory drug commonly prescribed by veterinarians to help reduce pain caused by arthritis, soft tissue injuries or surgical pain. No side effects have been reported in the treated animal.

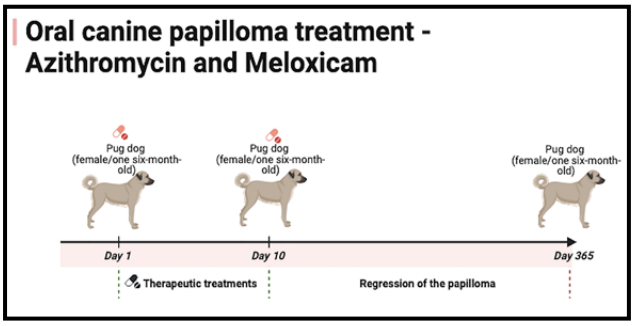

Figure 2. Graphical and temporal scheme of the treatment for papillomatosis in a bitch Pug, utilizing Azithromycin+Meloxicam.

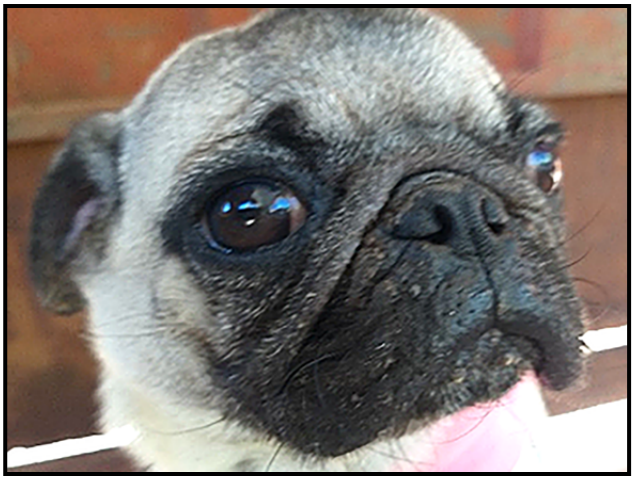

Figure 3. Full papilloma's regression in a bitch Pug after 10 days of treatment (August 10, 2022).

DISCUSSION

Papillomatosis is a classical but enigmatic disease in veterinary medicine, with various treatments suggested, many of which remain controversial. This condition poses a significant challenge for veterinarians, as pet owners are often distressed by the critical appearance of the lesions in their dogs' mouths. Consequently, there is an increasing demand among veterinarians for rapid resolution of canine oral papillomatosis cases. Therapeutic interventions, including invasive and surgical procedures, are frequently proposed depending on the lesions' size and extent of tissue invasion.

Although canine oral papillomatosis is a self-limiting disease, with spontaneous regression of the lesions that usually occurs within 12 months [15,20], there is a need for safe therapeutic protocols that promote the regression of the lesions more quickly and effectively, considerably reducing the inconvenience to the affected animals, and returning the animal's well-being quickly. This is particularly important to prevent the prolonged course of the disease, which can increase the spread of infection to other canines. Furthermore, the potential malignancy of papillomatous lesions necessitates prompt and effective treatment, and reducing the incidence of clinical cases of oral papillomatosis in dogs requires strategic management, including proper treatment to curb the spread of the virus [8,18].

Other canine oral papillomavirus treatments have been documented and have also led to the regression of papillomatous lesions, but have taken longer to resolve the lesions, such as a case of canine oral papillomatosis treated with autohemotherapy (AHT) [4], in which it was reported that the lesions regressed after 24 days of treatment, but there is no information on whether the regression of the lesions was sustained and for how long, or whether there was a recurrence. Autologous vaccines combined with immune support was effective after treatment for 21 to 30 days has also been reported [8]. In contrast, ineffective treatment was reported after a another dog received a combination of autoimmune therapy (serum), topical application of podowart apple cider vinegar, and Thuja (homeopathy). Lesion regression in this last case only occurred after applying lithium antimony thiomolate [6].

In present case, the treatment with Azithromycin it was consistent with the effective and

safe treatment outcomes for canine papillomatosis as proposed [21], and Azithromycin also is widely used in veterinary medicine to treat various bacterial infections, including dermatological, urogenital, respiratory, and otitis, and it is an approved drug for canine use [21]. In addition, Azithromycin is well tolerated and effective in treating papillomatosis in humans, but its precise mechanism of antiviral activity is not fully understood [3,19].

Regarding Meloxicam, it may have improved the quality of life during treatment by reducing the discomfort associated with the oral lesions. Meloxicam is a drug approved for use in dogs, is a non-steroidal anti-inflammatory drug (NSAID) that inhibits the enzyme cyclooxygenase 2 (COX-2), thereby reducing prostaglandin production. Meloxicam possesses anti--exudative, analgesic, and anti-inflammatory properties and inhibits leukocyte infiltration in inflamed bone and cartilage tissues [23]. Beyond its common use for inflammatory conditions, we consider the use of the combined drug, also since Meloxicam has been investigated in humans for treating cancers such as urinary bladder cancer and for managing pain associated with anal cancer. It has demonstrated *in vitro* efficacy in reducing cell proliferation, inducing apoptosis, and improving patient quality of life by alleviating pain and discomfort caused by lesions [1,2].

This case report demonstrates the efficacy of a combined treatment regimen of Azithromycin and Meloxicam for rapidly resolving canine oral papillomatosis within a short period, and no recurrence of papillomas, indicating sustained clinical remission. However, further studies are needed to investigate whether Azithromycin and Meloxicam have any specific antiviral activity and to elucidate their mechanisms of action against papillomatosis in dogs.

MANUFACTURER

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