Abstract. Canine anal sac gland carcinoma (ASGC) is a frequently described neoplasm that is highly aggressive and can frequently lead to metastatic spread. In this paper, we describe the successful treatment of an incompletely excised ASGC by using cisplatin selectively driven within the tumor cells by trains of biphasic pulses. The dog received two courses of electrochemotherapy 14 days apart. Neither systemic nor local toxicities were detected during the whole course of therapy. The dog is still in complete remission after 18 months. Electrochemotherapy is a safe and efficacious adjuvant therapy for ASGC and warrants further investigation in order to standardize its protocols.

Electrochemotherapy (ECT) is an anticancer treatment that involves the association of chemotherapy drugs with the delivery of permeabilizing electrical pulses, leading to improved local control, with lack of systemic toxicities (1). Several cohorts of companion animals with spontaneous neoplasms have been treated by selectively driving anticancer agents by means of trains of biphasic pulses (2-13). To date, the use of ECT has been of significant importance for the treatment of locoregional disease; however, its application has been mostly limited to the therapy of melanoma, sarcoma and mast cell tumors (2-8). In this article, we describe the long-term control of an incompletely excised canine sac gland carcinoma (ASGC) treated with adjuvant ECT. ASGC account for 2% of all skin tumors in dogs and are treated with different combinations of surgery, chemotherapy and radiation therapy (14-18). Recently, a therapeutic algorithm has been proposed for the management of these neoplasms.

Case Report

A fourteen-year-old male intact giant schnauzer dog was referred for the adjuvant treatment of an incompletely excised ASGC involving the left anal sac. The tumor was excised surgically by BM and GG, however the large size of the neoplasm (5x3x3 cm) and the spatial relationship with deep underlying structures prevented a wide excision for fear of inducing fecal incontinence. For these reasons, the tumor was classified as T4N0M0, and the surgeons performed a conservative surgery of the primary neoplasm (18, 19). The excised tumour specimens were fixed in 10% buffered-formalin and paraffin embedded. Sections of 5 μm were stained with haematoxylin-eosin, haematoxylin van Gieson, and PAS-haematoxylin. The histopathology examination showed that the neoplasm was a tubular type anal sac gland carcinoma displaying large lumens lined by cuboidal cells with abundant cytoplasm and hyperchromatic nuclei (Figure 1). At this time, the owner elected the dog to be treated with adjuvant ECT. The tumor was re-staged with a complete blood cell count, serum biochemical profile, urinalysis, chest radiographs (three projections) and abdominal ultrasonography. All the tests were within reference limits and the imaging studies showed no evidence of metastatic spread (data not shown).

Anesthesia was induced with a combination of medetomidine (Domitor 10 ml vial; Pfizer Italia, Pomezia, Italy) and propofol (Diprivan 10 mg/ml; Astra Zeneca, Milan, Italy) as per manufacturers’ instructions and the tumor bed was pretreated with a combination of hyaluronidase and lidocaine (LIDO-HYAL B; Laboratori Farmaceutici Giovanni Ogna & Figli S.p.A., Milan, Italy), to dissolve the ground substance and to increase local
analgesia (5-10). Five minutes after the injection of hyaluronidase, the tumor bed and 1 cm of normally appearing margins were infiltrated with cisplatin (CDDP) (Platinex vial 50 mg/100 ml, Bristol-Myers Squibb, Sermoneta (LT), Italy) at a concentration of 0.5 mg/ml (total dose 8 mg). Five more minutes after the infiltration of the antiblastic agent, trains of 8 biphasic electric pulses (EP) lasting 50 + 50 Ìs each, with 1 ms interpulse intervals, were delivered by means of caliper electrodes at a voltage of 1300 V/cm (3). The dog recovered from the treatment and received a second session two weeks later. During both sessions, the adherence of the electrodes was increased by using an electroconductive gel (2-10). The dog has remained in complete remission for 18 months and is still monitored by two of the authors (BM and GG).

Discussion

Apocrine gland carcinomas of the anal sacs have been frequently described in veterinary medicine (14-18) and their treatment is based on surgical excision, eventually followed by adjuvant radiation therapy (especially for invasive tumors) with an average survival time of 540 days. Chemotherapy has been confined to the treatment of metastatic ASGC in dogs using platinum compounds (15, 16, 18) and its role can currently be considered as palliative with median survivals ranging from 6 to 7 months (15, 16). At present, the proposed standard approach for ASGC involves a careful staging process leading to the surgery ± radiation therapy ± chemotherapy, however radiation therapy to the pelvis can be associated with several degrees of colitis, especially if coupled with radiosensitizers (18, 20). To the best of our knowledge, this is the first report of successful treatment of a canine T₄ ASGC by a combination of surgery and adjuvant ECT. To date, ECT has been confined to the palliation of metastatic spread of apocrine carcinoma of the anal sac in a cat that experienced a partial remission (2). The choice of cisplatin was made in consideration of the lower risk of local toxicity of this agent compared to bleomycin, which could induce Raynaud-like phenomena (2) and on the basis of an ongoing clinical trial testing CDDP-based electrochemotherapy. The tolerability of this ECT protocol and the successful response observed in our patient with advanced disease (T₄N₀M₀) suggests a potential role of this therapy for the treatment of infiltrative carcinomas. Further studies in this field are warranted, also in consideration of the possible translation of data to humans.

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References


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