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# Surgical excision combined with electrochemotherapy in the treatment of squamous cell carcinoma in a feline: Case report

**Utilização de excisão cirúrgica associada a eletroquimioterapia no tratamento de carcinoma de células escamosas em felino: Relato de caso**

**Uso de excisión quirúrgica asociada a electroquimioterapia en el tratamiento de carcinoma de células escamosas en felinos: Reporte de caso**

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**Abstract**
Squamous cell carcinoma (SCC) is a malignant epithelial neoplasm derived from keratinocytes, commonly preceded by actinic (solar) keratosis, with unclear etiology but associated with host and environmental factors. The present study aimed to describe the therapeutic association of surgical resection with electrochemotherapy using carboplatin in a case of SCC. The work was conducted using qualitative methodology, providing a detailed case report of a domestic feline treated at a private hospital unit. The cat was of mixed breed, female, spayed, 12 years and 4 months old, with white and gray fur, weighing 5.1 kg. The patient presented with a unilateral ulcerative lesion on the lower right eyelid, which had been evolving for 2 years with a significant increase in size and ulceration for approximately 3 months. After an incisional biopsy for histopathological examination, the diagnosis of SCC was confirmed, and it was decided to perform surgical excision with 2 cm margins, along with two sessions of carboplatin electrochemotherapy. After 40 days from the second electrochemotherapy session, with no signs of recurrence, the patient was discharged.
**Keywords:** SCC; Feline; Electrochemotherapy; Surgical resection.

**Resumo**

O carcinoma de células escamosas (CCE) é uma neoplasia epitelial maligna, derivadas de queratinócitos, comumente antecedido por ceratose actínica (solar), de etiologia não clara, mas associada à fatores do hospedeiro e do ambiente. O presente estudo teve por objetivo descrever associação terapêutica da ressecção cirúrgica com eletroquimioterapia com carboplatina em um caso de CCE. O trabalho foi realizado com metodologia qualitativa, descrevendo detalhadamente, um relato de caso de um felino doméstico atendido em uma unidade hospitalar particular, sem raça definida (SRD), fêmea, castrada, 12 anos e 4 meses, pelagem branco e cinza, 5,1 Kg, apresentando lesão ulcerativa unilateral na pálpebra inferior direita, com evolução de 2 anos e aumento expressivo de tamanho e ulceração há aproximadamente 3 meses. Após biópsia incisional para exame histopatológico foi definido o diagnóstico de CCE e optou-se pela excisão cirúrgica com margens de 2cm associada a eletroquimioterapia com duas sessões com carboplatina. Após 40 dias da segunda sessão de eletroquimioterapia, por não haver sinais de recidiva, a paciente recebeu alta médica.
**Palavras-chave:** CCE; Felino; Eletroquimioterapia; Ressecção cirúrgica.

**Resumen**

El carcinoma de células escamosas (CCE) es una neoplasia epitelial maligna derivada de queratinocitos, comúnmente precedida por queratosis actínica (solar), de etiología no clara pero asociada a factores del hospedador y del ambiente. El presente estudio tuvo como objetivo describir la asociación terapéutica de la resección quirúrgica con electroquimioterapia con carboplatino en un caso de CCE. El trabajo se realizó con una metodología cualitativa, describiendo detalladamente un informe de un caso de un felino doméstico atendido en una unidad hospitalaria privada, de raza no definida (SRD), hembra, castrada, de 12 años y 4 meses, con pelaje blanco y gris, 5,1 Kg de peso, presentando una lesión ulcerativa unilateral en el párpado inferior derecho, con una evolución de 2 años y un aumento significativo de tamaño y ulceración desde hace aproximadamente 3 meses. Después de una biopsia incisional para examen histopatológico se confirmó el diagnóstico de CCE y se optó por la exéresis quirúrgica con márgenes de 2 cm asociada a electroquimioterapia con dos sesiones de carboplatino. Después de 40 días de la segunda sesión de electroquimioterapia, al no haber signos de recidiva, la paciente recibió el alta médica.
**Palabras clave:** CCE; Felino; Electroquimioterapia; Resección quirúrgica.

## 1. Introduction

In the broad field of veterinary medicine, feline specialty is becoming increasingly relevant in terms of market needs and demands, particularly regarding the specificities of this species. Ophthalmology plays a significant role in this context, considering that tumors affecting the eye region, orbit, or annexes can lead to destructive consequences for vision, as well as for the patient's aesthetics and comfort. Due to their location, tumoral tissues have the potential to cause blindness and loss of the eye, as well as to be at the forefront of potential diseases in other parts of the body (Fonsêca, 2022; Miller & Teixeira, 2020).

Squamous cell carcinomas (SCC), also known as squamous cell carcinoma (SCC) or epidermoid carcinoma, are malignant epithelial neoplasms derived from keratinocytes, commonly preceded by actinic (solar) keratosis. Based on the location and tissue invasion, the tumor can be classified as non-invasive when it remains in the epidermal layer and hair follicles, or invasive when it permeates the basal membrane and occupies the underlying dermis (Delisle & Devauchelle, 1999; Miller & Griffin & Campbell, 2013; Soltero-Rivera et al., 2014).

It is highly plausible that exposure to intense sunlight over long periods, lack of annexal pigmentation, and chronic irritation of the ocular surface can be considered risk factors for the incidence of SCC, typically occurring on the pinna margins, eyelids, nasal plane, and lips, which are areas of unpigmented skin, with a sparse, nonexistent, or thin hair coat. It is important to note that the etiology is not well defined, but there is an association with host and environmental factors. There is limited evidence of an association between papillomavirus and SCC; some in situ bowenoid carcinomas evolve from feline viral plaques induced by papilloma, however, it is more likely that mutations in the tumor suppressor gene p53, as well as overexpression of the p53 protein, are involved in the development of SCC (Delisle & Devauchelle, 1999; Miller et al., 2013; Miller & Teixeira, 2020).

Among the methods used in veterinary oncology, protocols involve treatment through medical methods, surgical excision, radiotherapy, chemotherapy, or less common therapies such as cryosurgery and photodynamic therapy. The recommended therapy should be carefully planned in order to fully benefit the patient (Calfee, 2014; Silveira et al., 2016). The

use of electrical current pulses for therapeutic purposes has been practiced since the 19th century and has become more frequent in the last 20 years, especially to enhance the localized cytotoxic effect of antineoplastic drugs. Currently, electrochemotherapy is recognized as an effective complex for drug administration in the treatment of cutaneous or subcutaneous neoplasms, and considering it as an assisted delivery modality, it has great potential for use in internal tumors (Oliveira & Telló, 2004; Larkin et al., 2007).

In general, the aim of this report is to describe the therapeutic combination of surgical resection with electrochemotherapy using carboplatin (FAULDCARBO®, Libbs, Libbs Farmacêutica Ltda, São Paulo – SP, Brazil) at a dose of 180mg/m² for the treatment of squamous cell carcinoma in a domestic feline.

## 2. Methodology

The present study was conducted using a qualitative methodology (Pereira, et al., 2018), providing a detailed description of a case of squamous cell carcinoma in a domestic feline treated with electrochemotherapy and surgical resection. Clinical, anesthetic, and surgical data from the feline patient were utilized to illustrate the case's progression and the treatment applied. In this manner, correspondences between the etiology and the outcomes of SCC were examined.

## 3. Case Report

A mixed-breed (domestic shorthair), spayed female cat, 12 years and 4 months old, with white and gray fur, weighing 5.1 kg, was seen at a private clinic. She presented with an ulcerative lesion on the lower right eyelid (Figure 1A), which had been progressing for 2 years, with a significant increase in size and ulceration over the past 3 months. The owner reported using a ointment containing fibrinolysin, deoxyribonuclease, and chloramphenicol (Fibrase®, Pfizer, Pfizer Laboratories Ltda, Guarulhos – SP, Brazil) with applications to the affected area, frequency and duration unspecified, without improvement in the clinical condition. The patient did not have free access to the streets, always staying indoors, in the company of two other cats of the same species, same gender, with no clinical signs of disease. Regarding vaccination and deworming status, they were overdue, and she was being fed a premium wet diet for neutered cats.

On physical examination, physiological parameters were within normal limits (alert animal; heart rate 210 bpm; temperature 37.8ºC; normal-colored mucous membranes, no apparent dehydration; strong and rhythmic pulse, non-reactive lymph nodes). The animal had a discontinuity in the lower eyelid of the right eye approximately 0.8 cm in length. Additional tests requested included a complete blood count, biochemical profile (GGT - gamma-glutamyl transferase, ALT - alanine aminotransferase, total proteins and fractions, urea, and creatinine), and cytology by imprint. The complete blood count showed no abnormalities, except for a profuse amount of platelet aggregates (3+). Cytology revealed high cellularity suggestive of bacterial blepharitis. As initial therapy, antibiotic treatment with amoxicillin and potassium clavulanate (Amox+Clavulanate Potassium, EMS S/A, Hortolândia - SP, Brazil) was instituted at a dose of 15mg/kg subcutaneously every 48 hours for 12 days, along with prednisolone (Prediderm 5mg, Ourofino, Vinhedo - SP, Brazil). In addition, endoparasitic and ectoparasitic treatment was administered, Vetmax Plus (Vetnil®, Vetnil Industria e Comercio de Produtos Veterin LTDA, Louveira - SP, Brazil) and Advocate (Advocate®, Bayer S.A, São Paulo - SP, Brazil), respectively.

**Figure 1 -** Photographic image of a feline with an ulcerative lesion on the lower right eyelid. A) Note the granulomatous appearance of the lesion and the bloody secretion. B) After tumor removal. C) Immediate post-operative. D. Medical release

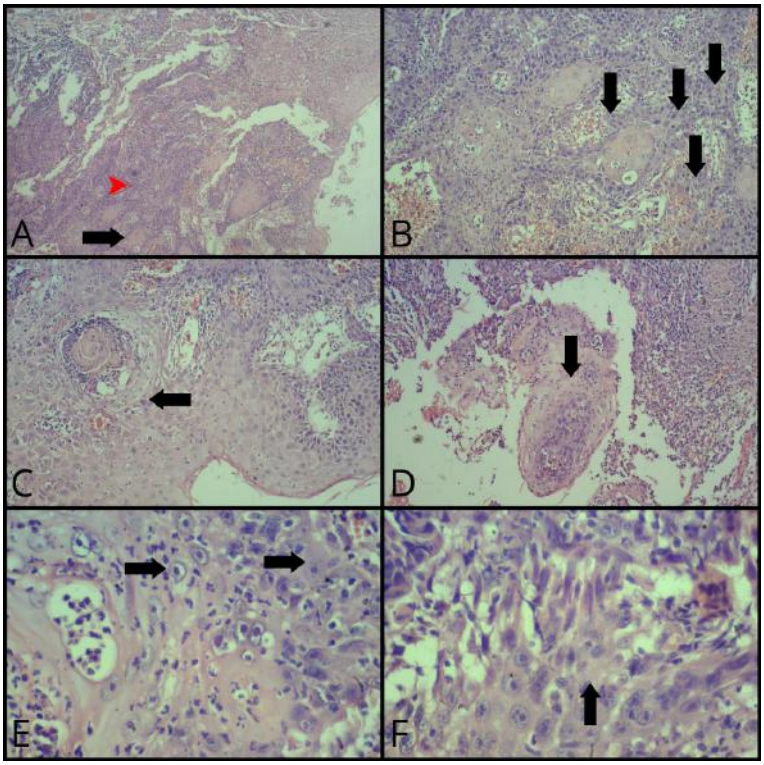

Source: Personal archive.

The images in Figure 1 show a feline with an ulcerative lesion on the lower right eyelid, presenting a granulomatous appearance and bloody secretion. After the tumor was removed, a corrective procedure was performed, and in the immediate postoperative period, the patient was discharged.

After 20 days, the tutor returned with the patient. An improvement in the clinical condition was reported, followed by a worsening after the completion of the therapy, where the discontinuity area continued to be ulcerated, with bloody secretion and crusts on the surface. Due to the persistence of the lesion, a veterinary ophthalmological evaluation and incisional biopsy for histopathological examination were requested. A therapeutic regimen was established with hylo-gel (HYLO®-GEL, FBM Indústria Farmacêutica Ltda, Itapevi– SP, Brazil) at a dose of 1 drop, topically, 4 times a day, pred-fort eye drops (Pred fort®, Allergan Produtos Farmacêuticos Ltda, Guarulhos - SP, Brazil) at a dose of 1 drop, topically, every 8 hours, for 5 consecutive days, and epitezan ointment (Epitezan®, Allergan Produtos Farmacêuticos Ltda, Guarulhos - SP, Brazil) with a thin layer applied every 12 hours, in addition to the full-time use of the Elizabethan collar until the histopathological result is obtained.

The histopathological sample, originating from the lower eyelid of the right eye, had a soft consistency and a brown coloration. The histological sections revealed a neoplastic proliferation of poorly defined, non-encapsulated, infiltrative epithelial cells (figure 2 a), supported by moderate fibrovascular stroma, forming islands and trabeculae (Figure 2 b-d). The cells were oval to polyhedral, closely packed, interconnected by desmosomal junctions, with ample eosinophilic cytoplasm, while the nuclei were oval, with loose chromatin and one to three prominent nucleoli, showing moderate anisocaryosis and anisocytosis, and two mitotic figures in 10 fields of higher magnification, with compromised lateral margin (Figure 2 e-f).

**Figure 2** - Photomicrographs of histopathological examinations of lower eyelid SCC samples in felines analyzed through HE histochemical reactions.




A: section 01 – Well-differentiated SCC, showing corneous pearl structures (arrow) and predominantly intense neutrophilic inflammatory infiltrate (arrowhead) (10x magnification); B: section 02 – Well-differentiated SCC, noting marked cellular pleomorphism (arrows) (40x magnification); C: section 03 – Well-differentiated SCC, demonstrating atypical mitotic figure in the field (arrow) (40x magnification); D: section 04 – Well-differentiated SCC, observing the arrangement of oncocytes in nests of cells in the dermal parenchyma (arrow) (40x magnification); E: section 05 – Well-differentiated SCC, noting the presence of oval to polyhedral cells (arrow) (100x magnification); F: section 06 – Well-differentiated SCC, observing wide and eosinophilic cytoplasm (arrow) (100x magnification). Source: Personal archive.

Figure 2 presents photomicrographs of histopathological examinations of samples from Squamous Cell Carcinoma (SCC) on the lower eyelid of felines, analyzed with H&E staining. It is possible to observe a well-differentiated SCC with structures resembling corneal pearls and a predominantly intense neutrophilic inflammatory infiltrate, as well as marked cellular pleomorphism.

Diagnosis of CCE was confirmed, and surgical excision with wide margin removal was chosen, along with two sessions of electrochemotherapy. To this end, an electrocardiogram was requested, which showed no alterations. After a 12-hour fast for solids and a 2-hour fast for water, pre-anesthetic medication was administered with morphine (Dimorf®, Cristália, Produtos Farmacêuticos Ltda., Itapira - SP, Brazil) at a dose of 0.2mg/kg, intramuscularly, in combination with acepromazine (Acepran®, Cristália, Produtos Farmacêuticos Ltda., Itapira - SP, Brazil) at a dose of 0.02mg/kg, intramuscularly. This was followed by vascular access and infusion of lactated Ringer's solution, anesthetic induction with ketamine (Dextrocetamine hydrochloride, Cristália, Produtos Farmacêuticos Ltda., Itapira - SP, Brazil) at a dose of 1mg/kg, intravenously, followed by slow administration of propofol (Propovan®, Cristália, Produtos Farmacêuticos Ltda., Itapira - SP, Brazil) at a dose of 2mg/kg, intravenously, in a dose-response manner.

The periorbital region was shaved with a grooming machine equipped with a #40 blade. Subsequently, the conjunctival fornices and the entire ocular surface were aseptically prepared with a 10% aqueous solution of povidone-iodine (PVP-I) diluted in 0.9% saline using a 5 ml syringe and cotton swabs. Preparation of the periocular skin surface continued with 10% PVP-I using sterile gauze compresses, followed by the placement of the surgical drape.

Surgical excision with approximately 2cm margins was performed, involving incision with a #15 scalpel blade and dissection with iris scissors. The resulting defect was corrected with a single-pedicle advancement flap (U-plasty) (Figure 1B), with suturing performed using 5-0 polyglactin 910 suture (Figure 1C).

Electrochemotherapy on the eyelid was administered by an oncology specialist, delivering carboplatin (FAULDCARBO®, Libbs, Libbs Farmacêutica Ltda, São Paulo – SP, Brazil) at a dose of 180mg/m², employing a technique involving localized administration of rectangular, low-duration, high-intensity electrical pulses, ranging from 1000 to 1300 volts, for 100 microseconds, achieving 16 amperes, thus ensuring more effective penetration of cell membranes (Larkin et al., 2007; Guiduce, 2011).

Following the procedure, the animal was released for home care, with a prescription for maxicam (Maxicam 0.2%, Ourofino Saúde Animal Ltda, Rod. Anhanguera - SP, Brazil) at a dose of 0.2mg/kg, intramuscularly, every 24 hours for 4 consecutive days, hylo-gel (HYLO®-GEL, FBM Indústria Farmacêutica Ltda, Itapevi – SP, Brazil) at a dose of 1 drop, topically, every 6 hours, and tobramycin eye drops (Tobramycin, Brainfarma Indústria Química e Farmacêutica S.A, Anápolis - GO, Brazil) at a dose of 1 drop in the right eye, topically, every 6 hours, for 15 consecutive days, with a 10-minute interval between eye drops and lubricant.

Additionally, six applications of amoxicillin trihydrate (Agemoxi injectable, União Química Farmacêutica Nacional S/A, Embu-Guaçu - SP, Brazil) were administered at a dose of 30mg/kg, intramuscularly, every 48 hours, for 12 days, along with the use of an Elizabethan collar full-time, 24 hours a day, until complete healing of the ocular lesion. After 20 days, the patient returned for a follow-up, presenting with a surgical wound in the process of healing, absence of entropion, unaltered palpebral incursions, no discharge, and no corneal ulcer. A second session of electrochemotherapy was performed. The patient was discharged 40 days after the second session of electrochemotherapy (Figure 1D).

## 4. Discussion

Compatible with the patient's profile, squamous cell carcinoma usually occurs in domestic cats with white or light-colored fur, whose predisposition is increased by 13 times in comparison to those with black or dark coloring. This factor is related to a higher tendency for actinic damage. The occurrence is most common in cats aged 9 to 12 years, with no predisposition based on breed or gender (Grant, 1991; Nishiya & Nardi, 2017). In contrast to studies by Newkirk (2009), Murphy (2013), and Pérez-Enriquez (2020), which indicate a higher incidence of squamous cell carcinoma in cats with significant exposure to ultraviolet rays (UV rays), the patient had no contact with outdoor environments or direct UV ray exposure.

In disagreement with the clinical examination findings suggestive of SCC, the initial diagnosis through cytology suggests an incorrect treatment. Bacterial blepharitis can primarily lead to changes in the conjunctiva and cornea, with signs such as erythema, edema, purulent exudate, and crust formation on the eyelid margin. In contrast, in SCC, the main macroscopic aspects are proliferative and erosive lesions, as observed in the above patient (Ferreira, 2009; Pinheiro, 2010; Rosolem et al., 2012; Murphy, 2013; Tozon et al., 2014).

According to Guedes (1998), Kraegel (2004), and Newkirk (2009), certain conditions can lead to the formation of squamous cell carcinoma, such as the folding disposition of the ears, resulting in a notched appearance, or regarding the facial area of the eyelid due to the absence of fur. In general, the complaint often mentioned by guardians is a non-healing wound on the skin, associated with the presence of a mass, thickening, or ulceration when observed. The lesion in the patient is located in the lower right eyelid, showing ulceration and an increase in size. This location is less common, as evidenced by Aquino (2007) and Newkirk (2009), who point out that cats commonly present squamous cell carcinoma among epithelial neoplasms, but the region of the face, eyelid, and eyeball has a lower prevalence, accounting for a sum of 28% among 3.6% of cutaneous tumors in

cats when compared to other affected areas.

Guerios (2003), Silveira et al. (2016), and Grandi e Rondelli (2016) indicate that surgical treatment in the early stage of the disease is more effective and aims primarily to remove all neoplastic tissue, ensuring clear margins, and is accompanied by adjuvant and complementary therapies. In the described case, surgical resection with electrochemotherapy was chosen, considering the tumor's dimensions, the absence of evident systemic alterations, as well as the affected anatomical region, providing a satisfactory aesthetic result and a good prognosis. As pointed out by Murphy (2013) and Conceição (2016), evaluating the patient's condition, classifying the carcinoma, and analyzing the occurrence of metastases or not are of paramount importance in determining the most appropriate treatment for the situation. Additionally, the collaboration of the guardian, availability of equipment and medications directly influence the prognosis and the quality of life of the animal.

Cytology of the neoplastic lesion through the excisional biopsy technique with deep incision is the best option for establishing a diagnosis (Cowell et al., 2002; Guérios et al., 2005). The method used in this patient aligns with the author's guidelines, making it possible to obtain a definitive diagnosis. Among the fundamental characteristics of SCC and in line with the histopathological findings of the biopsy, Cowell et al. (2002) observed the presence of many cells with abundant cytoplasm and angular borders, directly influencing the nuclear maturation of the cells. Similarly, Goldschmidt and Goldschmidt (2017) and Jie et al. (2021) showed that the arrangement of cells related to SCC is in islands or cords, closely associated with the epidermal surface, with the occurrence of concentric lamellae of keratin in the central region of the islands. Regarding the measurement and grading properties of the tumor, Delisle e Devauchelle (1999) and Jie et al. (2021) mainly highlight the desmoplastic reaction of the affected structures, the intense capacity for variation in shape, loss of specialization characteristics of multinucleated cells, high mitotic index, and multiple prominent nucleoli.

The cytological examination in clinical identification is of utmost importance, considering that, in more remote areas or due to various conditions, histopathology is not available or its availability is restricted. Similarly, Oliveira et al. (2023) assert that presumably, the cytological examination enables the clinician to make assertive and prompt decisions regarding the clinical case, resulting in a favorable outcome for the patient. However, confirmation for a more appropriate therapeutic approach should be obtained through histopathological examination.

No recurrence was observed after one year of surgical resection and electrochemotherapy, demonstrating a satisfactory result of the instituted therapy.

## 5. Final Considerations

The achievement of an early and targeted diagnosis is of paramount importance for the success of squamous cell carcinoma therapy, considering the various treatment options contingent upon a precise staging of the tumor and the overall clinical aspect of the patient. It can be inferred that the use of electrochemotherapy combined with resection yields a positive response in the treatment of SCC, especially in regions with limited margins.

For progress, it is crucial to focus on new therapeutic approaches, such as immunotherapy and targeted therapies, and to explore molecular markers. Improving early diagnostic techniques, like biomarkers and more sensitive imaging methods, is also essential to enhance detection and intervention, potentially improving patients' quality of life.

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