

A Case of Canine Dermal Melanoma: A Nutraceutical Approach

Sergio Canello¹

Gianandrea Guidetti²

Alessandro Di Cerbo^{3*}

Raffaella Cocco⁴

¹Forza10 USA Corp., Research and Development Department, Orlando, 6450 Kingspointe Pkwy Orlando FL 32819, USA; E-mail. sergio@forza10usa.com,

²Research and Development Department, SANYpet S.p.a., 35023 Bagnoli di Sopra, Padua, Italy; E-mail. Gianandrea@forza10.com

³Department of Medical, Oral and Biotechnological Sciences, Dental School, University G. d' Annunzio of Chieti-Pescara, Chieti, Italy; E-mail Alessandro811@hotmail.it

⁴Department of Veterinary Medicine, Pathology and Veterinary Clinic Section, University of Sassari, 07100 Sassari, Italy; E-mail. Rafco@uniss.it

(*) Corresponding author: Alessandro Di Cerbo, Department of Medical, Oral and Biotechnological Sciences, Dental School, University G. D' Annunzio of Chieti-Pescara, Chieti, Italy; E-mail. alessandro811@hotmail.it; Ph. +393923731318

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ABSTRACT

The aim of this work was to evaluate the possible beneficial effects of a nutraceutical diet on a careless dermal melanoma in an elderly dog. Hemato-biochemical and metabolic parameters as well as clinical symptoms evaluations were performed to monitor the possible improvements of the clinical picture of the dog following a nutraceutical diet supplementation. Hemato-biochemical analyzes and clinical symptoms before nutraceutical diet and after specific diet suspension showed an overall improvement. Moreover, no strong evidence of metastasis after radiographic investigations was observed.

This study suggests that clinical status and quality of life (QoL) of an elderly dog affected by dermal melanoma can be

positively influenced by a nutraceutical diet supplementation.

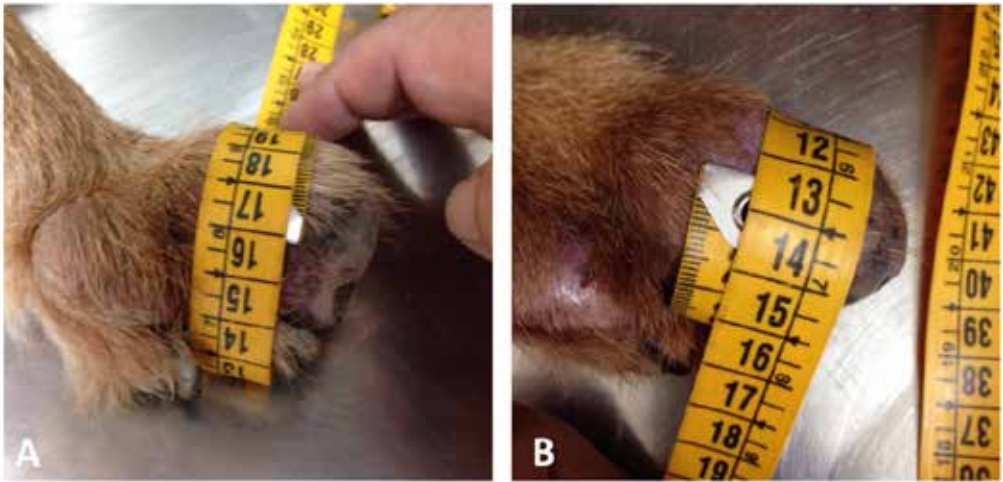
INTRODUCTION

Among canine skin tumors, cutaneous melanomas represent 0.8–2%.¹ Multiple factors affect biological behavior and prognosis of the melanomas such as:

- tumor site,²
- the mitotic index (three or more mitotic figures per 10 high-powered fields indicate malignancy),³
- degree of pigmentation,
- necrosis,
- ulceration,
- inflammation presence²

Most of cutaneous melanomas in dogs are benign, with a low mortality rate compared with those occurring in other districts such as eye, feet/digit and mucosa.^{4,5} Digit melanomas have an intermediate prognosis and are generally benign. However, an

Figure 1. Clinical pictures of right hind paw melanoma. (a) A 17 cm haired, stiff and homogeneous mass before and (B) after (13 cm) 2 months of nutraceutical treatment.



epidemiologic survey from Spangler et al (2006) revealed that feet melanomas have a diagnosis of malignancy in 74% of the cases, a recurrence or possibility to metastasize of 38% and a median survival time of 158 days.

Elective treatments for melanomas are surgical excision or systemic chemotherapy.⁶ However, molecular targeted therapies, e.g, receptor tyrosine kinase (RTK) inhibitors,⁷ IFN- α ⁸, and cancer vaccines^{9,10} have gained great attention.

To the best of our knowledge, this is the first case of an elderly dog treated with a commercially available nutraceutical diet for a right hind paw malignant melanoma. The nutraceutical diet consisted in a commercial mixed formula based on fish proteins, rice carbohydrates, *Cucumis melo*, *Ascophyllum nodosum*, *Hematococcus pluvialis*, *Aloe vera*, *Carica papaya*, *Punica granatum*, *Camellia sinensis*, *Polygonum cuspidatum*, *Curcuma longa*, *Piper nigrum*, zinc, and a Omega3/6 ratio of 1:0.8, which was already proven to significantly decrease type 1 helper T lymphocyte (Th1) cells and increase T regulatory (Treg) cells in dogs affected by *Leishmania infantum*¹¹, significantly improve clinical signs and symptoms of canine keratoconjunctivitis sicca¹² and exert a significant anti-inflammatory activity

in vitro.¹³

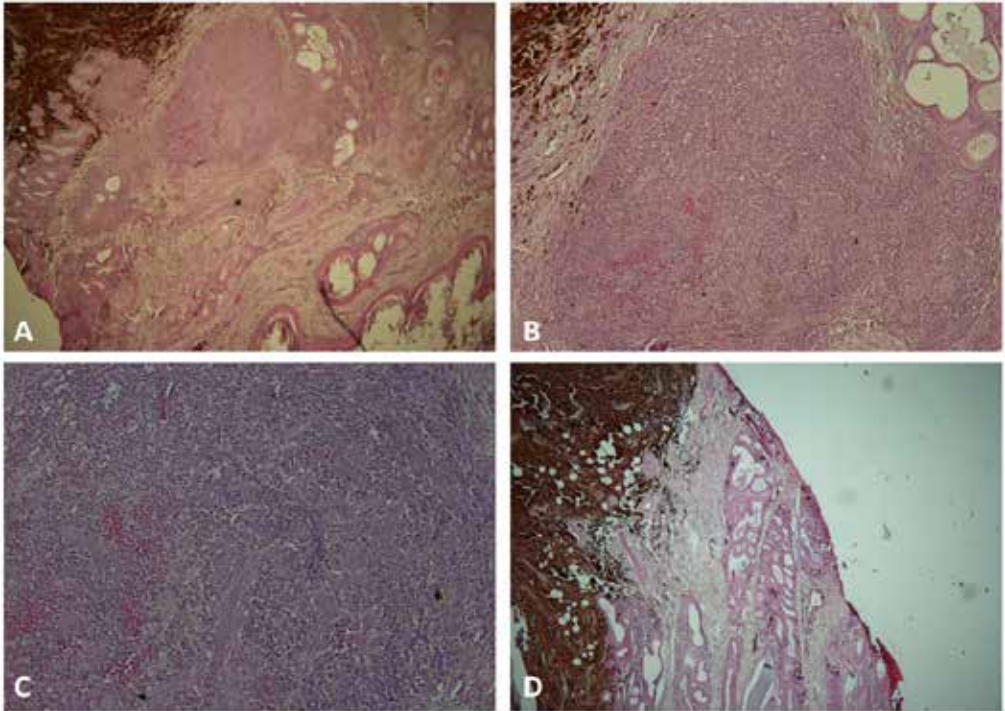
CASE PRESENTATION

On September 2014, a 13-years-old male mixed breed dog presented to the veterinary Hospital of the University of Sassari for treatment of asthenia, increased weight, and appetite loss.

Physical examination revealed brightness, poor responsiveness and altered vital parameters (T = 37.6 °C, P = 65 bpm, RR = 18 brpm). A 17 cm, haired mass raised over the dog's right hind paw was noted (Figure 1).

A biopsy revealed malignant melanoma with approximately 3 mitoses per 10 high-powered fields (HPF). Generally, mucocutaneous junctions and glabrous skin lesions refer to malignant forms, while the others are considered as benign. In this case the presence of atypical pleomorphic nuclei (multiple nucleoli) lay for a malignant form despite the low proliferative activity (Figure 2). The work-up for the dog also included hemato-biochemical and metabolic analysis, three-view thoracic radiographs, and abdominal ultrasound in order to obtain a base-line health status on the dog. Initial blood exam and serum proteins electrophoresis evidenced a slight lymphopenia (19.4%, ref. val. 25-50%) and an alfa2 and beta2 frac-

Figure 2. Photomicrograph of right hind paw melanoma. Presence of atypical pleomorphic nuclei (multiple nucleoli) at different magnifications (a-b) 4x, (c) 10x, (d) 20x.



tions increase (16.4%, ref. val. 7.9-13.0%; 36.3%, ref. val. 11.5 - 23.2%; respectively). None of the metabolic profile parameters resulted altered.

In spite of the need for surgical excision of the mass to reduce the risk of metastasis, the advanced age, the low survival rate after a surgical intervention, and the previous unsuccessful pharmacological treatments come out in favor of a nutraceutical approach.

After 1 month of nutraceutical diet administration, a normalization of lymphocytes was observed, while the alfa2 and beta2 fractions increase still persisted.

The same trend was observed after 3 months of nutraceutical diet supplementation. After 5 months, the metabolic profile showed a total bilirubin and CPK increase (1.18 mg/dl, ref. val. 0.11- 0.31 mg/dl; 279 U/l, ref. val. 42-155 U/l; respectively), while a decrease of alfa1 (2.2%, ref. val. 2.6 - 4.5%) and an increase in alfa2, beta, and gamma were observed (14.0, ref. val.

7.9 - 13.0; 33.0%, ref. val. 11.5 - 23.2% and 14.6%, ref. val. 6.5 - 14.0%; respectively).

Due to the reduced metabolic requirements of the dog, the nutraceutical diet was suspended and a specific diet for elderly dogs was administered. A further increase of CPK, creatinine, P, GOT, and Mg was observed (540 U/l, ref. val. 42-155 U/l; 1.69 mg/dl ref. val. 0.8- 1.42 mg/dl; 11.3 mg/dl, ref. val. 2- 3.5 mg/dl; 82 U/l ref. val. 21-44 U/l; 2.35 mg/dl ref. val. 0.67-0.94 mg/dl; respectively). Hence, the diet was suspended and the nutraceutical diet reintroduced. After 3 months CPK, creatinine, P, GOT, and Mg resulted decreased within normal range.

The three-view radiographs were clinically normal and negative for metastasis. The abdominal ultrasound revealed a diffusely, mildly enlarged spleen with normal echogenicity. Based on these findings, there was no strong evidence of metastasis and overall the dog appeared to be in good health.

Physical exams and diagnostic tests were also repeated 6, 12 and 24 months since nutraceutical diet supplementation begin.

Unfortunately, after 26 months since nutraceutical diet supplementation, the dog died due to a rapid worsening of clinical picture.

DISCUSSION

The initial lymphopenia might be ascribed to the right hind paw lesion. In fact, it is typical of an acute inflammatory status or infections, mostly viral. The metabolic profile did not evidence any alteration. Therefore, the appetite loss, the consequent slimming and asthenia, as well as the breath frequency increase might be the consequence of the pain/complaint derived by the lesion. Physical exam did not show any alteration of the cardiocirculatory and respiratory system. Also, the increase of alfa2 globulins might be referred to the presence of the lesion, while the increase of beta globulins was linked to the overall inflammatory status.

The significant reduction of the lesion dimensions (~24%) was a clear evidence of the anti-inflammatory activity exerted by the nutraceutical diet^{14,15}, as well as the normalization of the blood exam and appetite. After 5 months, the reduction of blood cells count and hemoglobin and the increase of bilirubin addressed toward the diagnosis of hemolytic anemia.

The metabolic parameters variations led to a suspension of the nutraceutical diet due to its metabolizable energy content, which was higher with respect to that recommended for an elderly dog. The new hematobiochemical analyzes revealed the onset of a kidney insufficiency, preannounced by clinical symptoms such as appetite loss, polyuria, and polydipsia. Therefore, the nutraceutical diet was reintroduced. After 3 months, all hematological parameters resulted improved along with clinical symptoms, thus demonstrating the good tolerability of the diet despite the high metabolizable energy content.

In conclusion, the introduction of a nutraceutical diet resulted particularly effective

in extending the median survival time of an elderly dog right hind paw melanoma, improving the hematological parameters and related clinical symptoms and consequently the QoL.

STATEMENT OF AUTHORSHIP

The authors hereby certify that all work contained in this article is original. The authors claim full responsibility for the contents of the article.

CONFLICT-OF-INTEREST STATEMENT

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript. This research was performed in collaboration with some scientists from the Division of Research and Development, Sanypet SpA, Padua, Italy (as indicated in the Author's affiliation) according to scientific and ethical principles of the scientific community.

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