A Successful Nutraceutical Approach to Manage an Elderly Dog Presenting a Focal Granulomatous Dermatitis with a Concomitant Chronic Otitis

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ABSTRACT

We describe here the beneficial effects of two specific nutraceutical diets to relieve dermal and auricular disease in a clientowned, 9-years male Labrador Retriever suffering from focal granulomatous dermatitis, and chronic bilateral otitis. Due to the lack of significant and long-lasting effects with specific drugs reported by the owner, a 2-month course with two specific nutraceutical diets was opted. An overall significant improvement of clinical manifestations of both diseases was clearly visible at the end of the evaluation period. Moreover, no adverse reactions were reported.

This clinical evaluation suggests that a specific nutraceutical diet supplementation can significantly improve the clinical status of an elderly dog suffering from focal granulomatous dermatitis and chronic otitis, thus improving its quality of life along improving the final outcome.

CASE PRESENTATION

In June 2015, a client-owned, 9-year-old male Labrador Retriever was presented to the veterinary Hospital of the University of Sassari for treatment of dermal and auricular disturbances.

Physical examination revealed no altera-

Figure 1. Clinical pictures of head- and necklocalized skin lesions (a-b) before and (c-d) after 1 month of nutraceutical diet supplementation.



tion of vital parameters (T = $38.6 \circ C$, P = 75bpm, RR = 16 brpm). However, an extended skin lesion close to the neck, some other small skin lesion on the head and an excessive dirt in the ears was noted. A 3 mm skin biopsy revealed a marked hyperplasia with compact orthokeratotic hyperkeratosis, multifocal melanosis, dendritic elements, focal accumulation, and slight exocytosis phenomena at the epidermal level. At the dermal level, a superficial perivascular inflammatory infiltrated, mainly lymphoplasmacyticlike and secondary macrophage and mast cell-like, was observed. Deep granulomas, with dilated cytoplasm macrophages and neutrophile granulocytes surrounded by a lymphoplasmacytic component, were also noted.

The ear swab revealed a high number (> 10 per high power field) of Malassezia pachydermatis organisms. None of the meta-

bolic profile parameters resulted altered. The final diagnoses were focal granulomatous dermatitis and chronic bilateral otitis.

Due to the lack of significant and long-lasting effects with ketoconazole, Dexamethasone, Niacinamide, Gentamicin, Betamethasone, and Clotrimazole reported by the owner, a dietary approach with two specific nutraceutical diets was opted for.

Firstly, the specific nutraceutical diet for dermal manifestations was provided for 1 month and, at the end of the period, a significant reduction of head- and necklocalized skin lesions was observed (Fig 1). Secondly, the specific nutraceutical diet for auricular disease was provided for 1 month and, at the end of the period, a significant improvement of the ear clinical condition was observed (Fig 2).

Before and after the two diets supplementation 4 mL of blood were withdrawn and analyzed using an oxytetracycline specific ELISA kit for pets (Cat. # DE – 100430, Genemed Synthesis, Inc., San Antonio, USA). Interestingly, a slight decrease in oxytetracycline concentration, from 88.6 to 74.8 ng/ml, was observed.

Physical exams and diagnostic tests were also repeated at the end of the 2-month evaluation period, and showed a complete remission of all clinical manifestations.

DISCUSSION

Most of granulomatous skin lesions are known to manifest as papules, nodules, and/ or plaques, which can be either multiple or solitary, localized or generalized with a size ranging from few millimeters to several centimeters.^{1,2} Despite skin lesions, onset has been linked to infectious agents (i.e. bacteria, algae, fungi, parasites, and protozoa) or foreign bodies, idiopathic forms have been also documented.^{3,4} As to chronic otitis, it is one of the most frustrating disease affecting pets characterized by a 3-steps clinical evolution, i.e., acute inflammation and edema, chronic inflammation, and progressive stenosis and occlusion of the ear canal.5-7 The chronic process is usually generated by

Figure 2. Clinical pictures of ears (a-b) before and (c-d) after 1 month of nutraceutical diet supplementation.



microbial overgrowth, *Staphylococcus spp*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus mirabilis*, and mostly *Malassezia pachydermatis*.^{8,9}

Based on our previous clinical observations, we speculate that skin lesions and otitis onset in this dog were possibly due to high oxytetracyline serum concentration.^{10,11} We reported the widespread use of such antibiotic in intensive farming¹²⁻¹⁴ for its low cost and efficacy,¹⁵ but also its ability to strongly bind to calcium-rich tissues,¹⁶ e.g., bone, remaining fixed for extended periods even respecting withdrawal times.¹⁴ Moreover, we reported its presence within commercially available pet food ^{10,17} and showed its pro-apoptotic and pro-inflammatory effects *in vitro*.¹⁸⁻²⁰

Generally, a rapid and good to excellent response to glucocorticoids and other immunomodulating drugs is observed in both diseases.^{21,22} To the best of our knowledge, this is the first case of an elderly dog, poorly responsive to pharmacological treatments, supplemented with two commercially available nutraceutical diets for the treatment of focal granulomatous dermatitis and chronic otitis. The nutraceutical diet used to manage the focal granulomatous dermatitis consisted in a mixed formula of fish proteins, potato carbohydrates, Rosa canina, Salvia officinalis, and Vaccinium macrocarpon, while that used to manage the chronic otitis consisted in a mixed formula of fish proteins, rice carbohydrates, Melaleuca alternifolia, Tilia platyphyllos scapoli et cordata, Allium sativum L., Rosa canina L., and Zinc. Both diets have already proven to significantly ameliorate clinical symptoms of atopic dermatitis²³ such as flush, itch, dandruff, skin malodor, dry fur, and skin lesions, and clinical symptoms of chronic otitis7 such as occlusion of ear canal, erythema,

In conclusion, the introduction of a nutraceutical diet resulted particularly effective in significantly improving the clinical status of an elderly dog suffering from focal granulomatous dermatitis and chronic otitis, thus improving its quality of life along improving the final outcome.

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, Forza10USA Corp., Orlando (FL), USA (as indicated in the Author's affiliation) according to scientific and ethical principles of the scientific community.

REFERENCES

- Torres SM. Sterile nodular dermatitis in dogs. Vet Clin North Am Small Anim Pract. 1999;29(6):1311-1323.
- Panich R, Scott DW, Miller WH. Canine cutaneous sterile pyogranuloma/ granuloma syndrome: A retrospective analysis of 29 cases (1976 to 1988). J

Am Anim Hosp Assoc. 1991;27:519-528.

- Miller WH, Griffin CE, Campbell KL, Muller GH. Muller and Kirk's Small Animal Dermatology7: Muller and Kirk's Small Animal Dermatology. Elsevier; 2013.
- Fadok VA. Granulomatosis dermatitis in dogs and cats. Semin Vet Med Surg (Small Anim). 1987;2(3):186-194.
- 5. Logas DB. Diseases of the ear canal. Vet Clin North Am Small Anim Pract. 1994;24(5):905-919.
- Pietschmann S, Meyer M, Voget M, Cieslicki M. The joint in vitro action of polymyxin B and miconazole against pathogens associated with canine otitis externa from three European countries. *Vet Dermatol.* 2013;24(4):439-445, e496-437.
- Di Cerbo A, Centenaro S, Beribe F, et al. Clinical evaluation of an antiinflammatory and antioxidant diet effect in 30 dogs affected by chronic otitis externa: preliminary results. *Vet Res Commun.* 2016;40(1):29-38.
- Peano A, Beccati M, Chiavassa E, Pasquetti M. Evaluation of the antifungal susceptibility of Malassezia pachydermatis to clotrimazole, miconazole and thiabendazole using a modified CLSI M27-A3 microdilution method. *Vet Dermatol.* 2012;23(2):131-135, e129.
- Zamankhan Malayeri H, Jamshidi S, Zahraei Salehi T. Identification and antimicrobial susceptibility patterns of bacteria causing otitis externa in dogs. *Vet Res Commun.* 2010;34(5):435-444.
- 10. Di Cerbo A, Canello S, Guidetti G, et al. Adverse food reactions in dogs due to antibiotic residues in pet food: a preliminary study. *Vet Ital.* 2018.
- Mazzeranghi F, Zanotti C, Di Cerbo A, et al. Clinical efficacy of nutraceutical diet for cats with clinical signs of cutaneus adverse food reaction (CAFR). *Pol J Vet Sci.* 2017;20(2):269-276.
- Palmieri B, Di Cerbo A, Laurino C. Antibiotic treatments in zootechnology and effects induced on the food chain of domestic species and, comparatively, the human specie. *Nutr Hosp.* 2014;29(6):1427-1433.

- Chuah LO, Effarizah ME, Goni AM, Rusul G. Antibiotic Application and Emergence of Multiple Antibiotic Resistance (MAR) in Global Catfish Aquaculture. *Curr Environ Health Rep.* 2016;3(2):118-127.
- Odore R, De Marco M, Gasco L, et al. Cytotoxic effects of oxytetracycline residues in the bones of broiler chickens following therapeutic oral administration of a water formulation. *Poult Sci.* 2015;94(8):1979-1985.
- Chopra I, Roberts M. Tetracycline antibiotics: mode of action, applications, molecular biology, and epidemiology of bacterial resistance. *Microbiol Mol Biol Rev.* 2001;65(2):232-260 ; second page, table of contents.
- Milch RA, Rall DP, Tobie JE. Bone localization of the tetracyclines. J Natl Cancer Inst. 1957;19(1):87-93.
- Maine IR, Atterbury R, Chang KC. Investigation into the animal species contents of popular wet pet foods. *Acta Vet Scand*. 2015;57:7.
- Di Cerbo A, Rubino V, Morelli F, et al. Mechanical phenotyping of K562 cells by the Micropipette Aspiration Technique allows identifying mechanical changes induced by drugs. *Sci Rep.* 2018;8(1):1219.
- Gallo A, Landi R, Rubino V, et al. Oxytetracycline induces DNA damage and epigenetic changes: a possible risk for human and animal health? *PeerJ*. 2017;5:e3236.
- Di Cerbo A, Palatucci AT, Rubino V, et al. Toxicological Implications and Inflammatory Response in Human Lymphocytes Challenged with Oxytetracycline. J Biochem Mol Toxicol. 2016;30(4):170-177.
- Gross TL, Ihrke PJ, Walder EJ, Affolter VK. Skin Diseases of the Dog and Cat: *Clinical and Histopathologic Diagnosis*. Wiley; 2008.
- Guaguere E, Steffan J, Olivry T. Cyclosporin A: a new drug in the field of canine dermatology. *Vet Dermatol.* 2004;15(2):61-74.
- Di Cerbo A, Palmieri B, Chiavolelli F, Guidetti G, Canello S. Functional Foods in Pets and Humans. *Intern J Appl Res Vet Med.* 2014;12(3):192-199.