

Case Report





Generalized canine demodicosis: case report

Abstract

The aim of this research was to evaluate the clinical condition of a case of generalized canine demodicosis and the effectiveness of the treatment applied. Theoretical methods used included deductive-inductive and analysis-synthesis. Among the empirical methods, the observation and survey methods were selected. In the latter, two techniques were deployed: documentary analysis, based on the dermatological medical history sheet records, which provided relevant information; and an interview of the caretaker of a male, mixed-breed, unneutered dog, 7 years old and weighing 8 kg live weight. The information collected led to the identification of Demodex through skin scraping. As a result, it is noted that the addition of Spirulina platensis combined with diphenhydramine 25 mg, linoleic and linolenic acids - marketed as omega 3 and omega 6, respectively - and ivermectin 1% at a dose of 0.2 mg/kg live weight with gradual increase, proved effective for the complete recovery of the animal. We concluded that generalized canine demodicosis has become an increasingly common disease, with a high degree of prevalence, and although there are several long-acting treatment options, they have the great disadvantage of being highly expensive. It was demonstrated that ivermectin 1%, when administered as described in this study, together with diphenhydramine, essential fatty acids and Spirulina platensis, is very effective and less expensive.

Keywords: canine demodicosis, treatment, ivermectin, diphenhydramine, *Spirulina* platensis

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Introduction

There are different factors that can favor the appearance of diseases affecting the skin of dogs (*Canis lupus familiaris*), such as demodicosis, which produces a dermatopathy with a high degree of prevalence. Demodex is a highly developed mite present in the microbiota of the skin of healthy dogs, inhabiting hair follicles and sebaceous glands, whose overpopulation is related to the development of dermatitis, which ranges from mild to severe, irregular hair loss and secondary bacterial infections. The increase in the population of *Demodex* acari mites may also be associated with genetic or immunological conditions.²⁻⁴

There are two clinical forms of demodicosis, depending on the extent and location of the lesions, localized or generalized, and the prognosis and treatment will be different for each stage of the disease.4 Transmission of this pathogen occurs through direct contact between the mother and her litter in the first hours postpartum. After this period it is not contagious between healthy animals in confined environments.⁵ It is considered localized when one to four lesions are present, mainly on the face, periocular area and corners of the mouth. In these areas, erythema and partial alopecia can appear, which may or may not involve pruritus and seborrhea, scaling and hyperpigmentation. Generalized demodicosis, on the other hand, is a severe disease characterized by the presence of five or more affected areas, with multiple lesions covering an entire region of the body and often accompanied by pododermatitis and secondary bacterial infections. Dogs may also develop generalized lymphadenopathy, lethargy and fever when deep pyoderma, furunculosis or cellulitis is manifested.⁵ Due to the high incidence of this disease in Cuba, the objective of this study was to evaluate the evolution of a clinical case of generalized canine demodicosis and the effectiveness of the treatment applied.

Materials and methods

This study was conducted in San Miguel del Padrón municipality, Havana province, in March 2018.

Case description

Following a request from the caretaker of a male, mixed-breed, unneutered dog, 7 years old and weighing 8 kg live weight, identified by the name of Feria, the dog was examined because of severe generalized skin lesions. The interview with Feria's caretaker showed that the animal had been adopted from the street, which made impossible to know its background and suggested that the vaccination and deworming scheme was not up to date. The animal's diet was based on food of animal origin protein, mixed with rice, malanga or sweet potato, twice a day and in copious amounts. Generalized skin lesions were the main reason for the consultation, accompanied by pruritus and sparse areas with scattered and hard fur (Figure 1).



Figure 1 Condition of the patient at the beginning of the treatment. Photo taken by the authors, March 9, 2018.





The physical examination revealed alopecia on almost the entire body of the animal, in which the color and texture of the skin was striking, with grayish scaling, mainly in the dorso-cranial region, covering both ears; erythema, in the glossopharyngeal area, abdomen and belly; as well as in the distal dorsal region of the four limbs at the level of the metacarpus and phalanges, where seborrhea was also detected. The skin, in general, was hyper pigmented and lichenified. The animal underwent a skin scraping, which confirmed the presence of an overpopulation of *Demodex* in all its stages, as the causal agent of the lesions.

Methods employed

The theoretical methods employed included the deductive-inductive and the analysis-synthesis methods. Among the empirical methods, the observation and survey methods were selected. In the latter, two techniques were deployed: documentary analysis, based on the dermatological medical history sheet records, which provided relevant information, and an interview with the animal's caretaker. The clinical method was applied using its three components: anamnesis or review, clinical examination and complementary tests.

Therapeutic protocol

The therapeutic protocol implemented included the weekly application of ivermectin 1%, at a dose of 1 ml/50kg of live weight, equivalent to 0.2 mg/kg, with a weekly increase of 0.05 ml for the duration of the treatment. The drug was administered subcutaneously with a 1 ml sterile syringe and a 26G, 0.45 x 12 mm sterile hypodermic needle. We added one pill of diphenhydramine 25 mg (3.1 mg/kg) for 7 days, two pills of *Spirulina platensis* and two gel capsules of linoleic and linolenic acids (180 mg/5kg), for 30 days. The *Spirulina platensis* was administered as 400 mg tablets doses. The frequency of administration of all these drugs was prescribed on a daily basis.

Results

For the analysis of the results, it was taken into consideration the dose formulated by the manufacturer of the pharmaceutical product, expressed in volume, of the solution per kg of live weight (1 ml/ 50 kg) and the concentration of ivermectin contained in each ml, equivalent to 10 mg. Therefore, it was necessary to carry out the following calculations:

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1 ml.......50 kg x ml......8 kg xi = 0.16 ml, total dose 10 mg.....1 ml x mg......0.16 ml xi = 1.6 mg, total dose (0.2 \text{ mg/kg}) xi = 1.6 mg x 10^3 = 1.600 \mu \text{g}, total dose (200 \mu \text{g/kg})
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Gradual increase of the total weekly dose, 0.05 ml.

$$10$$
 mg......1 ml
$$x$$
 mg......0.05 ml
$$xi = 0.5$$
 mg x $10^3 = 500$ µg, total dose (62.5 µg/kg)

This resulted in the data calculated and contained in table 1. To initiate the treatment, two important elements were considered; the first, to start with the dose indicated by the manufacturer and

evaluate its qualitative effect at the end of the first week, given the animal's severe condition. The second factor taken into account was the inclusion of Spirulina platensis as a nutritional supplement of extraordinary value for strengthening organic defenses and its role during inflammatory disorders, which represent a high risk during the occurrence of bacterial infections. For this reason, the evolution of the animal is expressed using qualitative parameters, such as Favorable (F), Unfavorable (D) or Equal (I). There were no favorable results during the first week. The total dose was increased on a weekly basis by 0.05 ml, equivalent to 500 μg, using a syringe with a precision of 10⁻² ml (minimum graduation of the scale), commonly used for the administration of insulin. As it appears at the end of table 1, the therapeutic dose was increased to approximately three times its initial value in the course of this prolonged treatment, since the calculations shown were made on the basis of the initial weight of the animal, which progressively acquired a greater body mass and a better general clinical condition. It was also considered that ivermectin has been widely used in the world in dogs suffering from generalized demodicosis up to doses of 300-600 µg/kg.6 This dewormer has been well tolerated, with no evidence of toxicity associated with the Central Nervous System (CNS) for doses up to 10 times greater than the highest approved by the FDA, which is $\leq 200 \,\mu\text{g/kg}$. Among the adverse effects of ivermectin, neurotoxicity is listed in patients with increased permeability of the blood-brain barrier associated with hyperinflammatory states,8 but it is an antiparasitic recognized for its wide range of activities, high efficacy and high margin of safety.9 The authors of this research acknowledge the addition of Spirulina platensis in the therapeutic protocol as a valuable contribution, which is recommended to be taken into account as a protective element associated with the sustained increase of the dose of the antiparasitic agent and the effects produced by the parasites on the skin. The weekly evolution of the results showed the predominance of an increasingly favorable condition.

Table I Qualitative effect of the treatment, with gradual increase of the normal (N) and modified (M) dose of ivermectin

Date (m/d/y)	Qualitative parameters			Total dose ivermectin		mg/kg	
	F	U	Е	ml	μg	N	M
03/09/2018			X	0.16	1600	0,2	
03/16/2018	X			0.21	2100		0,26
03/23/2018	X			0.26	2600		0.32
03/30/2018	X			0.31	3100		0.38
04/06/2018	X			0.36	3600		0.45
04/13/2018	X			0.41	4100		0.51
04/20/2018	X			0.46	4600		0.57
04/27/2018	X			0.51	5100		0.64
05/04/2018	X			0.56	5600		0.70

As shown in Table 2, clinical signs were evaluated qualitatively according to their severity, in the categories of Intense (I), Moderate (M), Light (L) and No Lesions (NL). The symptoms assessed included: erythema, alopecia, pruritus, comedones and desquamations. After the third week, a gradual improvement in the general clinical condition of the animal and a gradual disappearance of the symptoms were observed. The behavior of the animal's triad remained within the limits established for the species. The volume of the explorable lymph nodes and the coloration of the visible mucous membranes resulted to be normal.

Table 2 Weekly qualitative assessment of clinical signs

Date (m/d/y)	Erythema	Alopecia	Pruritus	Comedones	Desquamations	Scabs
03/09/2018	ı	I	М	М	I	1
03/16/2018	1	1	M	L	1	I
03/23/2018	M	1	L	L	1	1
03/30/2018	M	1	L	L	М	М
04/06/2018	M	1	L	L	М	М
04/13/2018	M	1	L	L	М	М
04/20/2018	M	М	L	L	L,	L
04/27/2018	M	М	L	L	L,	L
05/04/2018	L	М	L	L	L,	L
Animal's disch	arge					
05/11/2018	L	L	L	L	L,	L
05/18/2018	NL	NL	NL	NL	NL	NL

The therapeutic protocol applied required constant patient monitoring, due to the weekly increase of the ivermectin dose by 0.05~ml (62.5 µg/kg). Its application led to total recovery, which can serve as a reference for the establishment of a therapeutic conduct in cases of generalized canine demodicosis, always taking into account the particularities of each animal. In the eighth week of treatment, Feria was medically discharged, after obtaining negative results for *Demodex* in the second deep skin scraping, and taking into account the good general clinical condition, as shown in figure 2. Subsequently, Feria was subjected to a deworming and immunization program, which in the opinion of the authors of this study contributed to boost an optimal health condition.



Figure 2 Condition of the patient two months after starting treatment. Photo taken by the authors, May 18, 2018.

Discussion

There are several diseases associated with the breakdown of the skin barrier in canines, due to the damage produced in the epidermal layer by the physical and chemical effects caused by the excessive proliferation of mites, which promotes an inflammatory reaction that causes the rupture of the hair follicles and, consequently, alopecia. 10–12 It has been demonstrated that oral administration of ivermectin helps the drug to bind strongly with the digestive particles, which leads to a reduced potential for its subsequent absorption. However, injection by the subcutaneous route allows ivermectin to be distributed in better proportion in lipid reservoirs, which reduces the frequency of application, since by the oral route it is administered on daily basis, and by the subcutaneous route it is administered every seven days. 13,14

It has been reported that in dogs with generalized demodicosis, systemic antibiotics are not necessary unless a severe bacterial infection is present.⁵

Among the most commonly used antihistamines in cases of generalized canine demodicosis we find diphenhydramine, at a dose of 2.2 mg/kg, VO, 2 v/d, slightly lower than the one used in this clinical case. Diphenhydramine blocks the receptors responsible for pruritus (H receptors), as well as those responsible for increased vascular permeability and the release of inflammatory mediators. It is known that essential fatty acids (EFAs) act in synergy with antihistamines, increasing their effectiveness. Thus, the use of essential fatty acids is recommended at doses of 180 mg/5kg, VO., 1-2 v/d.⁴ Fatty acids are not only fundamental elements of the cell membrane, but they are also an integral component of the intercellular barrier in the stratum corneal, with linoleic and linolenic acids being the most important for the homeostasis of the dog's skin, which are popularly known as omega 3 and omega 6, respectively.¹⁵⁻¹⁷

No reports were found on the use of *Spirulina platensis* for the treatment of generalized canine demodicosis, but the authors included it in the therapeutic protocol taking into consideration its potential to prevent the development of pathogenic microorganisms, as well as its role in strengthening the immune system. ^{18,19} It is a source of bioactive substances of natural origin, obtained from *Arthrospira platensis*, an algae whose main active ingredient is phycocyanin, a photosynthetic pigment of protein nature, water-soluble, non-toxic and with proven therapeutic properties, including antioxidant, anti-inflammatory, antiallergic, immunomodulatory, neuroprotective, hepatoprotective and anticarcinogenic activity. ²⁰ It is also suggested that *Spirulina platensis* helps regulate overweight and obesity, has hypolipidemic and hypoglycemic effects, and helps treat anemia and certain deficiency diseases. The anti-infective effects of *Spirulina* extracts against human immunodeficiency virus have also been demonstrated in vitro. ¹⁹⁻²³

C-phycocyanin has been found to have an immunomodulatory effect on cytokines that enhance the activation of immune system cells, as well as the regulation of approximately 190 genes involved in immunity.²⁴ C-phycocyanin is a selective inhibitor of COX-2, and therefore intervenes in inflammatory reactions, which is a promising approach to prevent diseases accompanied by inflammatory processes.^{25–27} The anti-inflammatory environment in healthy people is a prophylactic measure to reduce the risk of developing certain types of cancer.²⁴

Based on what has been stated regarding the properties of Spirulina platensis and the way it has been used by the authors in the

treatment of generalized canine demodicosis, its use in combination with ivermectin is recommended to improve the therapeutic results.

Conclusion

The conclusion is that generalized canine demodicosis has become an increasingly common disease, with a high degree of prevalence in canines, and although there are several long-acting treatment options, they have the great disadvantage of being highly expensive. It was demonstrated that ivermectin 1%, administered as described in this study, in combination with diphenhydramine, essential fatty acids and Spirulina platensis, is very effective and less expensive to allow an optimal evolution of the treated animals.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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