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MALASSEZIA INFECTIONS IN THE DOG

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The decision making in the treatment of the malassezia affections (dermatitis/otitis) in the dog is based in the reckoning of the pathology and the grade of affection.

Illnesses caused by Malassezia yeasts in dogs, first described in 1983 by Dufait, are inflammatory dermatoses associated with an overgrowth of these in certain anatomic locations and / or a hypersensitivity reaction to the yeast that does not always depend on its quantity. The Malassezia involved in the canine dermatoses is almost always of pachydermatis species characterised for being the only non-dependent of lipids in culture 15, consisting of four genotypes 20 and that colonizes skin and mucosal sites of healthy dogs as part of their natural microflora 15 and not affecting the hair follicle.

It’s ovaly shaped, with a size of 2-3 microns by 4-7 microns. At the time of gemation they acquire their characteristic peanut or sole of a shoe. (Figure 1)

This yeast is distributed throughout the body, preferably in the anal area (including anal sacs), lips and external auditory canal. The dorsal and periocular region are less densely populated 2. Certain canine breeds have a genetic predisposition to suffer these dermatoses 9 such as West Highland White Terrier, Basset Hound, Dachshund, Cocker sp. Terranova, Shih Tzu, Shar Pei, English Setter, German Shepherd 2,7,9,10.

Biological characteristics and the response of the body:

Not yet fully understood the mechanism by which yeast changes its commensal to pathologic feature. In this mechanism there would be involved biological characteristics specific to the yeast like the lipidic wall, adhesion to corneocytes trypsin-sensitive protein molecules and the products of its enzymatic cytoplasm consisting mainly of the pro-enzyme zimogen, lipases and proteases 2. The defences provided by the body can be classified as:
- Natural or innate-type formed by the components that make up the ecosystem of the skin such as ceramides, transferrin 5, dendritic cells, the keratinocyte desquamation and its bacterial flora.
- Acquired: including immunoglobulins A, E and G and all cell mediated immunity 15.

Clinical features:
The conditions for Malassezia in dogs can be classified into:
- Localized
- Generalized

Within these can be included by Malassezia otitis externa which may be part of a systemic condition or a localised condition.
It can occur in dogs of any sex, breed or age, but appears to be most common among one and three years of age1.
The skin reaction to the Malassezia aggression is characterised by erythema, fat exudate with rotten smell, desquamation, hyperkeratosis, lichenification, hyperpigmentation and reddish hair and nails 5.
In the otitis the ceruminal exudate is profuse and wet brown.
The affected areas more frequently are:
External auditory canal (60% of dogs with otitis externa1), face, ventral neck, axilla, thighs, interdigital spaces, nail folds and areas of intertrigo.
According to Mason classification 21 there are three systemic syndromes:
- Primary Dermatitis by Malassezia (no recurrence after a rapid therapeutic response)
- Secondary Dermatitis by Malassezia (recurrent and associated with an underlying disease)
- Nose and anal area acute pruritus, with self-harming. (rare)
Therefore processes are described as scaly seborrhoeic with mild pruritus 17, processes fat seborrhoicus processes ,intertrigo, pododermatitis, paronychia, anitis, folliculitis and otitis externa 17.

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Diagnostic:

Today is well known that Malassezia is capable of producing the clinical signs by a combination of biological characteristics and flaws in the physical, chemical and immunological defences of the organism. These clinical signs can also be presented by a hypersensitivity reaction to the antigenic components (protein 45, 52, 56 and 63 kDa) in the yeast.

It is therefore difficult to assess the weight of each mechanism, direct or hypersensitivity in the clinical setting.

This makes relative the value of quantification Malassezia in diagnostic tests. Moreover, recalling that in most cases there is an underlying disease, we must evaluate the weight of yeast as a pathogen in the general clinical setting. However, the observation of many forms in the budding stage would be suggesting an active state of overgrowth.

The differential diagnosis in this dermatitis must be done of the following diseases which in many cases are its origin:
· keratinization disorders,
· endocrinopathies
· allergies
· ectoparasites
· bacterial overgrowth
· epitheliotropic lymphoma

The more usual complementary methods for the diagnosis of Malassezia dermatitis are cytology (tape, impression, swabs), culture and biopsy. Intradermoreaction and IgE serology may have some utility in the event accompanied by clear clinical signs and want to check the presence of hypersensitivity to it.

However, to date, the therapeutic diagnosis remains the best tool, since in animals with a low burden of Malassezia, almost undetectable, the response to it, would confirm the presence of this hypersensitivity, also taking into account the antiinflammatory effect of these azoles treatments.

Measurement of αTNF that is a pro-inflammatory cytokine produced by various cells in peripheral blood may be an interesting tool for the future to know the sensitivity level of the organism in the presence of Malassezia (M. Beccati).

Treatment

We have to remember that there are three variable that affect it:

· Clinical signs
· Scientific evidence of the treatment to use
· Owner´s compliance

After a detailed diagnosis in which determine the presence of an underlying condition, the therapeutic focus should be pointed to three key points:

· Underlying condition treatment
· Reinforcement of the natural or immunological defences of the individual
· Direct action against Malassezia

Improving the skin ecosystem can help the physical, chemical and immunological mechanisms to normalize the population of yeast.
It is very important to keep balanced skin components such as intercellular ceramides and essential fatty acids that act as fungistatic. It is also important to encourage the proper moist of the skin and the balance of bacterial flora, since it is known that excess staphylococci can produce a symbiosis with Malassezia produce B complex vitamins. Wax secretion normalisation in the ears allows the balance in the population of Malassezia preventing their proliferation and that of the substrates for feeding and reproduction. Practically no in vitro resistances by Malassezia have been described to the more used anti fungal except one study which described the resistance of some strains to fluconazole and the majority to flucytosine. With regard to direct action on the yeast, the treatment will depend on the circumstances. We can define it by its topical or systemic action. Systemic therapy is always used as diagnostic plan. In local and mild systemic processes, treatment, in general, leans toward the use of topical drugs. In case of systemic serious or local difficult to treat processes systemic therapy is the usual choice, normally in combination with the topical. We refer first to the treatments in the body except the ears. Topical treatments can be applied in a localized or widespread as shampoos, lotions, foams, sprays, wipes, creams or ointments.

Antiseptics with good degree of effectiveness can be enumerated:
- Clorhexidine 3-4%
- Selenium sulphide 1%
- Sulfurated lime 2%
- Acetic Acid + water 1:1
- Boric acid combined with acetic acid
Topical anti-fungal for the body:
- Ketoconazole
- Miconazole
- Chlotrimazole
- Enilconazole
- Nystatin
- Piroctone Olamine

Combinations between clorhexidine and azoles are very interesting, where the anti fungal and bacterial action are empowered. They are applied twice a week as average, maintaining the frequency until the condition is controlled, usually in 4-6 weeks. After that we move into once a week dosage. Some topical treatments like the melaleuca alternofilia essential oils (fine leaf tea tree) has shown in vitro effectiveness against malassezia. Other studies haven proven the in-vitro efficiency of the oregano, thyme and propolis.

The azole based products are normally used by the systemic route, being the most used:
- Ketoconazole 10 mgs./kg/day
- Itraconazole 5 mgs./kg/day or 2 days a week

Terbinafine at a dose of 30 mgs./kg/day 12 is an allylamine of which there are studies backing its use 7, with the advantage of having a metabolism outside the cytochrome P450 enzyme, good tolerance and time remaining in tissues. It could be interesting its use in dogs treated with cyclosporine. The systemic treatments will last an average of 3 weeks. Relapsing cases, treatment in pulses can be indicated, using either ketoconazole or itraconazole, twice a week, as long as necessary at the indicated dose. A recent systemic revision by Ameliè Negre et al, regarding the scientific evidences that exist for the recommendation of the most efficient treatments for the malassezia dermatitis, have concluded that there is a good evidence of the efficacy of the topical application of a combination of clorhexidine 2% and miconazole nitrate 2%, twice a week for 3 weeks. This revision also recommends with substantial evidence the systemic use of itraconazole and ketoconazole for 3 weeks. The improvement of the skin environment in general, can be achieved by controlling the underlying diseases, a good nutrition and substances that improve the composition of the intercellular cement, among them there are the phytosphingosines and essential fatty acids. The antibiotics, controlling the bacterial overgrowth, and the corticosteroids, inhibiting the excessive production of fat can favour the ecosystem normalisation.

Regarding the otitis by malassezia, the efficient substances are the same than mentioned before, changing in many cases the presentation and concentration respect the general topical treatments.
- Clorhexidine 0,05 %
- Acetic acid 2%+ boric acid 2%
- Acetic acid 1:1 in water
- Miconazole
- Chlotrimazole
- Nystatin
- Nystatin
The lipidic vehicles can favour the malassezia proliferation. To improve the ear environment and allow the correct epithelial migration and wax production effective in amount and quality, corticosteroids and antibiotics may be necessary, which indirectly can normalise the ear microflora.

**Immunotherapy:**

There are allergens available produced with malassezia extracts used for intradermoreaction tests or IgE specific serological tests. In these cases the immunotherapy generally is performed using other allergens besides the malassezia and, also, in many cases of atopic dogs azole based therapies are used that include antiinflammatory effects, which makes assessing the sensibility therapy for yeasts difficult to determine.

**Bibliography**

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