

Risk Factors for *Malassezia pachydermatis*-associated Dermatitis in dogs: a Case-control Study

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개에서 *Malassezia pachydermatis*에 의한 피부염의 위험요인에 관한 Case-control 연구

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요 약 : *Malassezia(Pityrosoprum) pachydermatis*에 의한 피부염의 위험요인을 파악하고자 1997년 1월에서 1998년 12월까지 서울대학교 수의과대학 부속동물병원에 내원하여 본 질환으로 진단된 29두와 동일한 기간 동안 피부과 검사에서 임상적으로 건강한 개로 확인된 97두의 대조군을 대상으로 분석하였다. 각 설명변수에 대한 교차비(odds ratio, OR)와 신뢰구간(confidence interval, CI)은 변수보정법을 사용하여 계산하였다. 다른 공변수를 보정한 상태에서 다중 로지스틱 회귀분석(multiple logistic regression analysis)을 시행한 결과 피부병 기왕력($p=0.0059$; OR, 4.44; CI, 1.5~12.8)과 비만($p=0.0013$; OR, 5.38; CI, 1.9~14.9)은 유의한 위험요인으로 나타났다. 단변량 분석(univariate analysis)에서 주 사료로 고기를 섭취하는 경우 피부염의 위험이 높은 변수로 작용하였지만($p=0.0398$; OR, 6.38; CI, 1.1~37.3) 다른 공변수를 보정한 분석에서는 유의하지 않은 것으로 나타났다. 성별, 품종, 및 예방접종은 위험요인으로 작용하지 않았다.

Key words : canine, *Malassezia pachydermatis*, risk factor, case-control study

Introduction

Malassezia pachydermatis is a nonobligatory lipophilic, commensal yeast from mammalian skin and mucosa that, under certain circumstances, shows exacerbated development leading to subsequent clinical disease¹. In veterinary clinic, *M. pachydermatis* is often isolated from otitis and dermatitis cases, particularly in dogs²⁻⁷. This yeast may also be found on humans⁸⁻⁹ and are emerging as opportunistic nosocomial pathogens in animal and man¹⁰⁻¹¹.

The definite diagnostic criteria has not been established, because it is extremely difficult to differentiate skin microbial populations as abnormally high prev-

alence from the skin of the clinically normal dog. This is attributed to the difference on the number of organism by the various anatomic locations and sampling method; Bond *et al.*¹² and Kennis *et al.*¹³ reported that *Malassezia* organisms were identified more frequently by use of adhesive tape and fungal culturing than by the methods used for cytologic examination, with the highest number on chin and the lowest number at inguinal and axillary regions.

Although studies on the microbiology, morphology, and physiology of *Malassezia* species have been investigated^{4,14-17} the risk factor for infection with *M. pachydermatis* has not been completely elucidated. The purpose of this retrospective study was to define the prevalence of the infection in a large referral hospital and to exploit varying potential risk factors in

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dogs related to the clinical diagnosis of *M. pachydermatis*.

Materials and Methods

Medical records

The records of all dogs examined between January 1, 1997 and December 31, 1998 at Seoul National University, College of Veterinary Medicine (SNU-CVM) teaching hospital were reviewed. The case population (n=29) consisted of all dogs with a atopic dermatitis or hypersensitivity that were receiving medication for dermatitis and were confirmed as *Malassezia* dermatitis by attending veterinarian. A control population (n=97) was selected from canine patients for which key variables were recorded suitable for the study during that period and whose diagnosis was confirmed as those disorders other than dermatitic problem. Demographic data (breed, age, and gender) were collected from the medical record of each dog in the case and control populations.

Statistical analysis

The median test was used to evaluate that age was homogeneous among groups. The potential association of age, breed, gender, weight, vaccination, and dietary habit was evaluated by logistic regression. Nominal groupings were created for continuous variables and were coded as dummy variables by the package with a value of zero. An independent assessment of each variable with *M. pachydermatis* by logistic regression analysis was used as a baseline for assessment of confounding. Statistical significance of the effect of a variable on risk was assessed by the ratio of the coefficient to its standard error (Wald statistic). A positive coefficient indicated that as the value of the variables changed, the risk of the event changed in the same direction; the opposite relationship existed for a negative coefficient. Adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were derived from the maximum likelihood coefficient of each model¹⁸. An OR greater than unity (1.00) and corresponding CIs greater than 1.00 were interpreted as meaning that a dog with that variable had an increased likelihood of concurrent *M.*

pachydermatis infection. ORs and CIs less than 1.00 were interpreted as meaning there was a decreased likelihood of concurrent *Malassezia* dermatitis. Interaction terms such as age/gender and age/breed were included based on the biologic relevance¹⁹. Because of small sample in each age category age was just used as confounding factor to be adjusted. Multivariate interrelationships among significant univariate factors were explored using multiple logistic regression. All logistic regression models were generated

Table 1. Summary statistics of demographics of dogs in the *Malassezia pachydermatis* and control populations

Variable	<i>Malassezia pachydermatis</i> (n=29)		Control (n=97)	
	Mean±SD*(Median)	Mean±SD(Median)	Mean±SD(Median)	
Age (month)	51.6±42.2 (36)		44.7±38.9 (33)	
Variable	No.	%	No.	%
Age				
36	15	51.7	39	54.2
37-72	7	24.1	17	23.6
73-108	3	10.3	12	16.7
109	4	13.8	4	5.6
Gender				
Male	15	51.7	26	36.1
Female	14	48.3	46	63.9
Breed				
Toy	23	79.4	64	88.9
sporting	3	10.3	5	6.9
others	3	10.3	3	4.2
Obesity				
Yes	16	55.2	16	22.2
No	13	44.8	56	77.8
Vaccination				
Yes	18	62.1	34	47.2
No	7	24.1	25	34.7
Incomplete	4	13.8	13	18.1
Prior history of skin problem				
Yes	19	65.5	15	20.8
No	10	34.5	4	5.6
Incomplete	—	—	53	73.6
Diet				
Pellet	21	72.4	67	93.1
Rice	4	13.8	3	4.2
Meat	4	13.8	2	2.7

SD: standard deviation

using the software package SAS (release 6.04; SAS Institute, Cary, NC, U.S.A.)²⁰. A statistical significance level of 0.05 was used for analyses.

Results

During January 1997-December 1998, a total of 753 medical records were retrieved from the medical records available. Of these, 29 met the criteria established for *M. pachydermatis*, indicating a prevalence of 3.6% at the SNU-CVM teaching hospital. Demographic characteristics of both population are presented in Table 1. Dogs in the patient and control populations ranged in age from 2 months to 12 years and from 2 months to 14 years, respectively (Table 1). The median age among groups was not significantly different ($p=0.8247$). Affected dogs included 4 Maltese, 4 Yorkshire Terriers, 3 each Shih Tzu dogs,

Table 2. Independent evaluation of the potential association of demographic factors with a diagnosis of *Malassezia pachydermatis*

Variable	Parameter estimate	Odds Ratio	95% CI*	p-value
Gender				
Male	0.6395	1.90	0.8-4.5	0.1509
Female	-	1.00	-	
Breed				
Toy	-	1.00	-	
Sporting	0.5126	2.78	0.4-7.6	0.5055
Others	1.0234	1.67	0.5-14.8	0.2296
Vaccination				
Yes	-	1.00	-	
No	-0.6370	0.52	0.2-1.5	0.2184
Incomplete	-0.5427	0.58	0.2-2.0	0.3978
Prior history of skin problem				
No	-	1.00	-	
Yes	1.9769	7.22	2.8-18.7	0.0001
Obesity				
No	-	1.00	-	
Yes	1.4604	4.31	1.7-10.8	0.0018
Diet				
Pellet	-	1.00	-	
Rice	1.4479	4.25	0.9-20.6	0.0716
Meat	1.8533	6.38	1.1-37.3	0.0398

*CI: confidence interval

Table 3. Final effects of potential factors on the risk of *Malassezia pachydermatis* as determined by logistic regression analysis

Variable	Parameter estimate	Odds Ratio	95% CI*	p-value
Prior history of skin problem				
No	-	1.00	-	
Yes	1.4903	4.44	1.5-12.8	0.0059
Obesity				
No	-	1.00	-	
Yes	1.6820	5.38	1.9-14.9	0.0013

*CI: confidence interval

Pugs, Poodles, and other 12 toy breeds. The proportion of toy breeds in case and control group was 79.4% and 88.9%, respectively. Table 2 lists the variables evaluated independently as risk factors for *Malassezia dermatitis*. Prior history of skin problem (OR, 7.22; 95% CI, 2.8~18.7), obesity (OR, 4.31; 95% CI, 1.7~10.8) and diet (OR, 6.38; 95% CI, 1.1~37.3) differed from those in the control population. These three variables showing significant at the initial independent analysis were entered into the final model. Multivariate analysis suggested that prior history of skin problem (OR, 4.44; 95% CI, 1.5~12.8) and obesity (OR, 5.38; 95% CI, 1.9~14.9) were found to be associated with *Malassezia dermatitis* (Table 3). All interaction terms tested were not significant.

Discussion

The factors that favor proliferation of *M. pachydermatis* and its transition from a commensal organism to an apparent pathogen on canine skin are poorly understood but presumably reflect disturbances of the normal physical, chemical or immunological mechanisms that restrict microbial colonization of skin. Although geographical differences are apparent a number of breeds appear predisposed to *M. pachydermatis*, including Basset hounds, Dachshunds, Cocker spaniels, West highland White terriers, Miniature poodles and Australian Silky terriers, and *M. pachydermatis*-associated skin disease may develop in both young and old dogs^{1,21-23}. Bond and Lloyd²⁴ reported strong positive relationship between Basset

hounds with skin disease associated with *M. pachydermatis* and increases in skin population densities in comparison with healthy dogs, which may reflect the susceptibility of this breed to the disease. We could not demonstrate breed predilection because of small case population in each breed in the study. Male dog was more likely to acquire *Malassezia* dermatitis; however, this difference was not statistically significant (OR, 1.9; 95% CI, 0.8~4.5). This finding is supported by other studies^{1,24,25} showing no gender predilection.

In relation to canine otitis, several authors comprehensively reviewed factors that may predispose an animal to ear infections^{14,26}. Amongst included the presence of hair and polyps in the ear canal, type of pinnae, allergy, seborrhea, nutritional and hormonal factors, amount of fatty acid produced by the glands lining the ear canal, and neoplastic diseases. Cerumen⁵, carbon dioxide accumulate²⁷ and some climatic factors such as humidity and temperature²⁸ were reported to be enabling factors to promote the growth of the organism. In a study on human beings, Chang *et al.*¹⁰ implied that a greater severity of illness, arterial catheterization, and exposure to a certain nurse were independent risk factors for infection or colonization of *Malassezia*.

It is of interest to note that prior history of skin problem ($p=0.0059$) and obesity ($p=0.0013$) were found to be significant risk factors for *Malassezia* dermatitis. These factors have been debated over the years in the literature. Midgley¹⁷ have failed in demonstrating the temporal relationship between *Malassezia* and seborrhoeic dermatitis^{17,29}. The primary seborrhea possibly does not predispose the dogs in getting the *Malassezia* dermatitis²⁵. However, authors implied that the seborrhea can occur as the secondary manifestation of the yeastic infection.

Because SNU-CVM teaching hospital is a referral hospital, the cases reviewed in this study may not accurately represent the majority of cases of *M. pachydermatis* observed in routine clinical practice. Additional validation of the potential association of prior history of skin problem and meat diet with *Malassezia* dermatitis is needed before these variables can be considered important in veterinary clinic.

Further studies are indicated to evaluate some other predisposing and/or reinforcing factors associated with an increased prevalence of *Malassezia* species such as recent antibiotic treatment, more specifically defined diet, age and breed. Dufait²¹, Larsson *et al.*²⁵ and Lukman³⁰ reported that the percentage of *Malassezia* dermatitis was increased with age. In addition, concurrent diseases such as hypersensitivity, endocrine and keratinization disorders, which are believed to favor the development of canine pyoderma, are recognized in many, but not all, cases of *Malassezia* dermatitis^{2,23}. In recent years there has been increasing interest in gaining a better understanding of the epidemiology of *M. pachydermatis* dermatitis as showing that the skin of an animal may be colonized by more than one type of *M. pachydermatis* by the partial sequencing of ribosomal RNA³¹. This finding indicates that a variety of epidemiologic study on the *M. pachydermatis* would be of great value provided that resolution of sequence types of the organism is available from extensive research.

Conclusion

The records of 29 dogs presented to the Veterinary Medical Teaching Hospital, college of veterinary medicine of Seoul National University between January 1997 to December 1998 were analyzed to determine risk factors associated with *Malassezia (Pityrosporum) pachydermatis*. These cases were compared with a control population consisting of 97 clinically normal dogs in dermatologic examination. Cases comprised known atopic dermatitis and/or hypersensitivity that were receiving medication for dermatitis and were confirmed as *Malassezia* dermatitis by attending veterinarian. The odds ratios (OR) and confidence intervals (CI) associated with each explanatory variable were calculated by variable-adjusting methods.

Multiple logistic regression analysis showed that prior history of skin problem ($p=0.0059$; OR, 4.44; CI, 1.5~12.8) and obesity ($p=0.0013$; OR, 5.38; CI, 1.9~14.9) were significant risk factors for acquiring *M. pachydermatis* after adjusting for other confounding covariates. Although dietary habit for eating meat ($p=0.0398$; OR, 6.38; CI, 1.1~37.3) was significant

risk factor when analyzed univariately, this variable was not significant after adjusting for other covariates. Gender, breed and routine vaccination were beyond the reach of statistical significance as risk factors to *M. pachydermatis* in our sample. These findings may have certain implications with regard to the understanding of the disease.

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