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A DISSERTATION  
FOR THE DEGREE OF MASTER

**Clinical Manifestations and Therapeutic Outcomes of  
Sudden Acquired Retinal Degeneration Syndrome in Dogs:  
A Retrospective Study**

급성 후천성 망막 변성증을 가진 개에서 임상적 특징과  
치료 결과에 대한 후향적 연구

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**Clinical Manifestations and Therapeutic Outcomes of  
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## **ABSTRACT**

The purpose of this study was to investigate clinical manifestations in dogs with sudden acquired retinal degeneration syndrome (SARDS), and to evaluate the therapeutic outcomes. One hundred dogs presented with SARDS between January 2005 and December 2016 at the Veterinary Medical Teaching Hospital of Seoul National University. This study included dogs with a history of acute vision loss and, absence of ophthalmic lesions consistent with the degree of vision loss. Among them, SARDS was diagnosed by using electroretinogram, clinical signs and ophthalmic examination. Medical records including breed, age, gender, weight, serum biochemistry, season of diagnosis, and clinical signs were reviewed when available.

The incidence rate of SARDS was 2.4%. The most frequently affected breeds were the Maltese (40), Schnauzer (23), Cocker Spaniel (10), and Shih-Tzu (9) in order. The gender of SARDS-affected dogs comprised 55 male dogs and 45 female dogs. The mean age of SARDS patients was  $8.3 \pm 2.6$  yr. Of the dogs diagnosed with SARDS, Cushing's-like signs were observed in 35 dogs. The median body weight of SARDS patients was  $6.5 \pm 3.5$  kg; approximately 72.9% weighed less than 9 kg. Forty-four dogs were prescribed systemic steroids; of those, 4 dogs regained vision (4/44, 9.1%). In conclusions, middle-aged to older dogs were commonly affected by SARDS. Smaller dogs, less than 9 kg, appeared overrepresented. There were no significant gender-related differences. Also, if the patient is confirmed as SARDS, high-dose steroid can be a good therapeutic trial for regaining the patient's vision.

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**Key words:** dogs, retrospective study, sudden acquired retinal degeneration syndrome, vision loss

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## **Introduction**

Acute vision loss is a very frustrating condition in dogs that can severely impair quality of life (Grozdanic *et al.*, 2008; Stuckey *et al.*, 2013). If there are no apparent lesions that can cause vision loss in the affected eye, retinal dysfunction or neurological disease may be suspected (Montgomery *et al.*, 2008). Sudden acquired retinal degeneration syndrome (SARDS) is a disease that occurs only in dogs and can cause acute vision loss in both eyes due to apoptosis of the photoreceptor layer of the retina (Acland *et al.*, 1984; Font *et al.*, 1987; Gilmour *et al.*, 2006). In several studies, apoptosis of the photoreceptor layer is assumed to be caused by metabolic or hormonal abnormalities (Carter *et al.*, 2009; Vainisi *et al.*, 1983). Glutamate toxicity has also been reported as a possible cause of retinal apoptosis in patients with SARDS (Abrams and Dreyer, 1993). However, despite these hypotheses, the etiology of SARDS remain poorly understood.

SARDS is known to occur most frequently in female and middle-aged to older dogs (Acland and Aguirre, 1986; Komáromy *et al.*, 2015; Stuckey *et al.*, 2013). However, another study reported that there was no significant gender-related difference in incidence (Heller *et al.*, 2014). Another study reported that the Miniature Schnauzer, Dachshund, American Cocker Spaniel, and Maltese breeds were most frequently affected (Stuckey *et al.*, 2013). However, the mixed-breed was the most affected breed in another retrospective study (Heller *et al.*, 2014). Some authors have suggested that the diagnosis of SARDS is most common in winter

(Acland *et al.*, 1984).

On ophthalmic examination, SARDS-affected dogs typically have a mydriatic pupil at rest with a sluggish or nonresponsive pupillary light reflex (PLR) and unexplained mild to moderate hyperemia is detected (Gilmour *et al.*, 2006; Montgomery *et al.*, 2008). The fundus of SARDS patients appears normal or shows subtle degeneration that does not impair vision (Acland *et al.*, 1984; Vainisi *et al.*, 1983; Van der Woerdt *et al.*, 1991). In another aspect, SARDS is commonly accompanied by Cushing's-like signs such as polyuria (PU), polydipsia (PD), polyphagia (PP), and weight gain (Gilmour *et al.*, 2006; Komáromy *et al.*, 2015; Montgomery *et al.*, 2008). Biochemical abnormalities including elevated serum cholesterol, serum alkaline phosphatase (ALP), and serum alanine aminotransferase (ALT) levels were also commonly observed in SARDS patients (Komáromy *et al.*, 2015; Mattson *et al.*, 1992; Van der Woerdt *et al.*, 1991).

The diagnosis of SARDS is based on history, clinical signs, and the findings of a nonrecordable electroretinogram (ERG). In addition, the fact that the pupils of SARDS patients react only to high-intensity wavelength blue light can be helpful for diagnosis (Grozdanic *et al.*, 2007; Heller *et al.*, 2014; Komáromy *et al.*, 2015; Montgomery *et al.*, 2008).

As the cause of SARDS is uncertain and the clinical signs are variable, the etiopathogenesis of SARDS is still a matter of debate. These features also raise questions about whether SARDS is a single disease entity. Some diagnostic “labels”

such as immune-mediated retinitis (IMR), autoimmune retinopathy (AIR) and cancer-associated retinopathy (CAR) in humans could be used instead of SARDS, as the clinical presentations of these diseases are similar to SARDS (Grozdanic *et al.*, 2008).

Although a treatment for SARDS is not yet known, many treatment options have been tried in recent studies (Grozdanic *et al.*, 2008; Stuckey *et al.*, 2013). Administration of high-dose systemic steroids and intravenous immunoglobulin (IVIg) has been reported to be effective in some SARDS-affected dogs (Grozdanic *et al.*, 2008).

The aim of this retrospective study was to investigate the incidence rate, age, body weight, clinical signs, serum biochemistry, season of diagnosis, gender, and breed distribution of SARDS cases, and to discuss the therapeutic outcome of high-dose steroid therapy.

## **Materials and Methods**

### **1. Animals**

Medical records of 4109 dogs that presented with ophthalmic disorders to the Veterinary Medical Teaching Hospital of Seoul National University between January 2005 and December 2016 were reviewed. Complete ocular examinations including neuro-ophthalmic examination, tear production (Schirmer tear test®, Intervet Inc., Sumit, NJ, USA), intraocular pressure measurement (TONOVET, Icare®, Vantaa, Finland), slit-lamp biomicroscopy (DC3®, Topcon Corp., Tokyo, Japan) and indirect ophthalmoscopy (Vantage Plus®, Keeler Instruments Inc., Broomall, PA, USA) were performed in all ophthalmic patients. Patients were included in the study if the main symptom was acute vision loss without other causes such as cataracts, glaucoma or retinal detachment. Scotopic ERG (RETIcom®, Roland Consult, Brandenburg, Germany) was performed. A diagnosis of SARDS was made when the ERG amplitudes were very low to nonrecordable.

Clinical signs including polyuria, polydipsia, polyphagia and weight gain were reported by owners. Patients were assessed based on the presence or absence of clinical signs. Medical records including breed, age, gender, body weight, serum biochemistry, season of diagnosis, and therapeutic outcome were reviewed when available. Body weight and biochemical

profiles were documented in 59 dogs and 27 dogs, respectively. SARDS patients were classified into three groups according to body weight as described by a previous study (Hayes *et al.*, 1994): small group (< 9 kg), medium group (9 ~ 18 kg) and large group (18 ~ 36 kg).

## **2. Therapeutic trials**

High-dose systemic steroids were prescribed for SARDS-affected dogs with no systemic problems. Prednisolone at a dose of 1–2 mg/kg was orally administered twice per day for 2 weeks and then tapered slowly for 1 month. To prevent adverse effects of steroid therapy, famotidine 0.5 mg/kg, misoprostol 5 mg/kg and silymarin 10 mg/kg were also prescribed.

### **3. Statistical analyses**

Categorical data such as incidence rate and breed distribution were listed as proportions. Continuous data such as age and body weight were presented as median or mean with standard deviation. Statistical evaluations were performed using SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA). A chi-square test was used to compare gender proportion. For breeds with more than 5 cases, a Student's *t*-test was used to compare the age at onset in each breed with the age of other SARDS patients, and a Mann-Whitney *U*-test was used to compare the body weight of each breed with other SARDS patients. A value of  $P < 0.05$  was considered significantly different.

## Results

During the reference period, 4109 dogs were presented with ophthalmic disorders. Of the ophthalmic patients, 100 dogs were diagnosed as having SARDS by using scotopic ERG, clinical signs and ophthalmic examination. The overall incidence of SARDS was 2.4%.

Among SARDS patients, the most frequently affected breeds were the Maltese (40/100, 40.0%), followed by Schnauzer (23/100, 23.0%), Cocker Spaniel (10/100, 10.0%), Shih-Tzu (9/100, 9.7%), Yorkshire terrier (6/100, 6.0%), mixed (5/100, 5.0%), and Dachshund (3/100, 3.0%) in order. One case each (1.0%) was diagnosed in the Poodle, Pug, Miniature Pinscher and Pomeranian (Table 1).

Of the SARDS-affected dogs, 55 were male and 45 were female. There were no significant differences between male and female dogs ( $P = 0.130$ ; Table 2). The mean age was  $8.3 \pm 2.6$  years. Among patients, the youngest dog was 1-year-old; the oldest was 15 years old. When comparing age among breeds that were affected by more than 5 cases, the breed with the highest mean age was the mixed breed ( $9.8 \pm 1.9$  years) followed by the Cocker Spaniel ( $8.8 \pm 2.3$  years), Schnauzer ( $8.5 \pm 2.4$  years), Shih-Tzu ( $8.3 \pm 3.3$  years), Yorkshire Terrier ( $8.0 \pm 4.0$  years), and Maltese ( $7.8 \pm 2.3$  years). However, the differences in each breed were not statistically significant. (Table 3).

The median weight of patients with SARDS was 6.5 kg, with a standard

deviation of 3.5 kg. The median weight in the Schnauzer ( $9.6 \pm 2.5$  kg) and Cocker Spaniel ( $11.5 \pm 2.9$  kg) groups were significantly higher than that in the other breeds. The median weight in the Maltese ( $3.8 \pm 1.1$  kg) was significantly lower than that in the other breeds. The small-breed group contained 43 dogs (72.9%); 16 dogs weighed between 9 kg and 18 kg (27.1%). There were no dogs classified as large among the patients (Table 4).

SARDS was most frequently diagnosed during spring (29/100, 29.0%), followed by autumn (26/100, 26.0%), winter (23/100, 23.0%) and summer (22/100, 22.0%).

Of the dogs diagnosed with SARDS, clinical signs including PU, PD, PP, or weight gain appeared in 35 dogs (35/100, 35.0%). Serum biochemistry was recorded in 27 dogs. Twenty dogs had biochemical abnormalities including elevated ALT, ALP, AST or cholesterol levels (20/27, 74.1%).

Of patients diagnosed with SARDS, 44 dogs were prescribed steroids; 4 of them experienced unilateral vision recovery (4/44, 9.1%). These 4 dogs were followed up for 2 weeks, 1 month, 2.5 months, and 15 months, respectively. During the follow-up period, 3 dogs maintained their vision, and 1 dog lost vision again 10 months after diagnosis.

**Table 1.** Incidence rate and breed distribution in SARDS patients

Breed	Ophthalmic patients	SARDs		
		No. of dogs	Incidence rate (%)	Breed distribution (%)
Maltese	624	40	6.41	40
Schnauzer	244	23	9.43	23
Shih Tzu	1137	10	0.88	10
Cocker Spaniel	364	9	2.47	9
Yorkshire Terrier	444	6	1.35	6
Mixed	199	5	2.51	5
Dachshund	39	3	7.69	3
Poodle	325	1	0.31	1
Pug	33	1	3.03	1
Miniature pinscher	86	1	1.16	1
Pomeranian	56	1	1.79	1
Other breeds	558	0	0.00	0
Total	4109	100	2.43	100

**Table 2.** Gender distribution of SARDS patients

Breed	No. of dogs	Male	Female
Maltese	40	23	17
Schnauzer	23	9	14
Shih Tzu	10	8	2
Cocker Spaniel	9	3	6
Yorkshire Terrier	6	5	1
Mixed	5	4	1
Dachshund	3	1	2
Poodle	1	0	1
Pug	1	0	1
Miniature pinscher	1	1	0
Pomeranian	1	1	0
Total	100	55	45

**Table 3.** Mean ages of SARDS patients

Breed	Age	
	Mean $\pm$ SD (years)	No. of dogs
Maltese	7.8 $\pm$ 2.3	40
Schnauzer	8.5 $\pm$ 2.4	23
Shih Tzu	8.3 $\pm$ 3.3	10
Cocker Spaniel	8.8 $\pm$ 2.3	9
Yorkshire Terrier	8.0 $\pm$ 4.0	6
Mixed	9.8 $\pm$ 1.9	5
Dachshund	7.3 $\pm$ 1.2	3
Poodle	6.0	1
Pug	12.0	1
Miniature pinscher	6.5	1
Pomeranian	13.0	1
Total	8.3 $\pm$ 2.6	100

**Table 4.** Median body weight of SARDS patients

Breed	Body weight				
	Median ± SD (kg)	No. of dogs	<9 kg	9~18 kg	18~36 kg
Maltese <sup>‡</sup>	3.8 ± 1.1	23	23	0	0
Schnauzer <sup>†</sup>	9.6 ± 2.5	12	4	8	0
Shih Tzu	7.2 ± 1.6	6	5	1	0
Cocker Spaniel <sup>†</sup>	11.5 ± 2.9	5	1	4	0
Yorkshire Terrier	7.5 ± 3.1	3	2	1	0
Mixed	6.5 ± 3.3	5	4	1	0
Dachshund	7.3 ± 0.5	2	2	0	0
Poodle	3.0	1	1	0	0
Pug	9.7	1	0	1	0
Miniature pinscher	5.5	1	1	0	0
Total	6.5 ± 3.5	59	43	16	0

<sup>†</sup> Significantly higher than the weight in the other SARDS patients

<sup>‡</sup> Significantly lower than the weight in the other SARDS patients

## **Discussion**

A number of retrospective studies of SARDS-affected dogs have been conducted to identify SARDS and its clinical manifestations (Montgomery *et al.*, 2008; Stuckey *et al.*, 2013).

According to recent studies, the mixed breed, Schnauzer, Dachshund, Pug, and Maltese breeds were commonly diagnosed with SARDS (Heller *et al.*, 2014; Keller *et al.*, 2006, Montgomery *et al.*, 2008). Similarly, many cases occurred in the Maltese, Schnauzer, Shih Tzu, and Cocker Spaniel breeds in this study. Although a previous study identified the Bichon Frise as an at risk breed, there were no Bichon Frises in the SARDS population in this study (Stuckey *et al.*, 2013). The reason for the higher proportion of Maltese and Shih Tzus among the SARDS patients compared to the previous study was probably due to high proportion of Maltese and Shih Tzu dogs among the ophthalmic patients in this study.

The mean age of SARDS patients was  $8.3 \pm 2.6$  years, which corresponded to the age of middle-aged to older dogs. Although the age was not significantly different in each breed, it was confirmed that the Maltese ( $7.8 \pm 2.3$  years) was affected to SARDS at a younger age than other breeds. In some previous studies, females were overrepresented than males (Keller *et al.*, 2006; Montgomery *et al.*, 2008). Conversely, in this study, males were more affected than females with no statistical difference.

Regarding the correlation between body weight and SARDS development, it was suggested that SARDS occurred more often in smaller dogs of less than 25 lbs (Heller *et al.*, 2014). In this study, dogs weighing less than 9 kg accounted for the majority of SARDS patients (72.9%). This result was thought to be due to the fact that most of the SARDS patients were small breed group. Although direct comparison between the small and large dog group was difficult because there were no affected dogs in the large dog group in this study, the tendency to represent more in smaller dogs was identified.

Several studies have investigated the relationship between occurrence of SARDS and season (Acland *et al.*, 1984; Stuckey *et al.*, 2013). According to a previous study, SARDS was most common in the winter, with 46% of cases diagnosed in that season (Acland *et al.*, 1984). However, Stuckey *et al.*, 2013 suggested that there is no appreciable association between season and incidence. There was not relationship between season and incidence in this study.

SARDS patients generally have systemic signs such as PU, PD, PP, and weight gain. In addition, serum biochemical abnormalities such as elevated liver enzyme levels or cholesterolemia are also detected due to the increase in adrenal steroid hormones. These changes are similar to those observed in certain endocrinopathies such as Cushing's disease (Acland *et al.*, 1986; Braus *et al.*, 2008; Carter *et al.*, 2009; Vainisi *et al.*, 1985). It was reported that more than 90% of SARDS patients showed an increase in adrenal sex hormone which can exhibit glucocorticoid-like activity (Carter *et al.*, 2009). According to previous studies, approximately 20% of SARDS

patients were diagnosed with Cushing's disease, and systemic signs resolved spontaneously over time if the cause was not typical Cushing's disease (Acland and Aguirre, 1986; Acland *et al.*, 1984; Holt *et al.*, 1999; Mattson *et al.*, 1992; Van der Woerdt *et al.*, 1991). In this study, Cushing's-like signs including PU, PD, PP, and weight gain appeared in 35% of cases, similar to the 28-39% reported in a previous study (Montgomery *et al.*, 2008). Elevation of liver enzyme levels or hypercholesterolemia was identified in most dogs undergoing blood analysis (20/27). However, it was not possible to investigate how many cases were diagnosed with Cushing's disease and whether systemic signs were resolved in SARDS patients due to the lack of medical records.

In humans, several treatment strategies including administration of high doses of systemic steroids, intravenous immunoglobulins (IVIg), and immunosuppressive drugs have been tried in patients with AIR, CAR and IMR, and have been reported to be effective in a number of patient (Grewal *et al.*, 2014; Guy and Aptsiauri, 1999; Heckenlively and Ferreyra, 2008; Subhadra *et al.*, 2008). Similarly, in veterinary ophthalmology, it was reported that high-dose systemic steroids and IVIg were effective treatments for SARDS patients (Grozdanic *et al.*, 2008). Nevertheless, IVIg therapy is still controversial because of the lack of peer-reviewed reports, and side effects such as anaphylactic reaction, renal failure, cardiac failure and hemolytic anemia reported in humans (Gaines, 2000; Orbach *et al.*, 2004; Schiavotto *et al.*, 1992; Stenton *et al.*, 2005). High-dose systemic steroids were prescribed to 44 SARDS patients in this study, and 4 of them regained vision.

According to the current study, patients with a positive response to high-dose steroid therapy have been reported to require long-term treatment and may lose vision again if the steroid dose is reduced (Grozdanic *et al.*, 2008). If a tapered dose of steroids causes loss of vision, an increase in the dose could restore vision within 1 to 2 days (Grozdanic *et al.*, 2008). However, steroid therapy was not maintained for a long duration in this study due to adverse effects such as gastrointestinal ulceration, infection, or hyperglycemia. Despite the use of short-term steroid therapy, 3 dogs with follow-up periods longer than 1 month maintained vision after tapering the dose. One dog was lost to follow up during steroid tapering, making it difficult to assess the persistence of vision after tapering the medication dose.

It is generally known that while SARDS patients have a normal fundus at an early stage, retinal degeneration such as attenuation of retinal vessels and hyperreflectivity is typically seen after a few weeks to years after diagnosis (Montgomery *et al.*, 2008). In this study, 1 of the 4 dogs with a positive response to high-dose steroid therapy was found to have retinal degeneration approximately 10 months after diagnosis, and the remaining 3 dogs had early retinal degeneration at the time of diagnosis.

There were several limitations to this study that deserve consideration. Firstly, the sample size was small and medical records of some patients were not available. Body weight was not reported for 41 dogs, and serum biochemistry profiles were not documented for 73 dogs. At second, SARDS patients could not be identified by categorizing them based on diseases such as IMR, AIR and CAR. It has been

reported that AIR and CAR are mediated by autoimmune mechanisms associated with antiretinal antibodies in humans (Grange *et al.*, 2014). Therefore, serum antibody analysis might be a good diagnostic indicator of AIR and CAR, but it was not performed in this study. Finally, the follow-up period of patients who recovered after high-dose steroid treatment was short. It was found that vision loss occurred after 10 months in a dog with a follow-up period of 15 months. However, it was not possible to confirm whether the remaining 3 dogs with short follow-up periods were able to maintain their vision and whether retinal degeneration had progressed. In addition, as the scotopic ERG was not performed after regaining vision, it could not confirm whether there was a change in the ERG amplitudes compared to when the diagnosis was made.

In this study, etiopathogenesis, additional clinical manifestations of SARDS, and other therapeutic trials were not determined. Further studies are needed to identify etiopathogenesis, additional clinical signs, biochemical abnormalities, seasonality and treatment of SARDS in dogs.

In conclusion, SARDS was most common in middle aged to older dogs, and often accompanied biochemical abnormalities, showing clinical signs similar to Cushing's disease. The most common breed affected was the Maltese, and SARDS tended to develop more often in smaller dogs. Also, if the patient is confirmed as SARDS, high-dose steroid can be a good therapeutic trial for regaining the patient's vision.

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# 국문 초록

## 개에서 급성 후천성 망막변성증의 임상적 특징과 치료 결과에 대한 후향적 연구

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본 연구에서는 급성 후천성 망막변성증을 가진 개에서 임상적 특징 조사와 치료 후 효과를 평가하였다. 2005년 1월부터 2016년 12월 사이에 서울대학교 동물병원에 내원한 환자 중 시력 상실을 일으킬만한 다른 안과적 질환이 없음에도 불구하고 급성 시력 소실을 주증으로 하는 개들을 대상으로 하였다. 이들 중 망막 전위도 검사, 증상 및 안과 검사를 통하

여 급성 후천성 망막변성증을 진단하였다. 종, 나이, 성별, 체중, 혈청 생화학 검사, 진단된 계절과 임상 증상과 같은 의료 기록이 사용되었다.

내원한 환자들 중 100마리가 급성 후천성 망막변성증으로 진단되었고, 발생률은 2.4% 였다. 가장 호발하는 품종은 말티즈(40), 슈나우저(23), 코카스파니엘(10), 시츄(9) 순이었다. 성별로 보면, 55마리는 수컷이었고, 45마리는 암컷이었다. 평균 나이는  $8.25 \pm 2.55$  살 이었다. 35마리에 서는 쿠싱병과 같은 유사한 증상을 나타내었다. 몸무게의 중간값은  $6.50 \pm 3.49$  kg 이었으며 약 72.9%가 9kg 이하였다. 44마리의 개에서 전신 적 스테로이드 치료법이 시행되었으며, 그 중 4마리에서 시력의 회복이 확인되었다.

결론적으로 급성 후천성 망막변성증은 중년에서 노년령의 개에서 흔하게 발생하는 것이 확인되었다. 그리고 9 kg 이하의 소형견종에서 더 흔하게 발생하며 말티즈에서 가장 흔하게 발생하는 것으로 확인되었다. 성별 간 발생에는 유의적인 차이가 없는 것으로 확인되었다. 또한 환자가 만약 급성 후천성 망막변성증으로 진단된다면, 고용량의 스테로이드 치료가 환자의 시력 회복에 도움을 줄 수 있다.

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주요어: 개, 후향적 연구, 급성 후천성 망막변성증, 시력 상실

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