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A retrospective-cohort study on the development of cataracts in dogs with diabetes mellitus: 200 cases

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Abstract

The objective of the study was to determine the incidence and estimated median time to cataract formation in dogs with diabetes mellitus. The animals studied were 200 dogs with diabetes mellitus which were referred to a university teaching hospital between 1985 and 1995. Medical records from dogs with a diagnosis of diabetes mellitus were reviewed and, where necessary, further follow-up information was gathered from the referring veterinarian. Incidence rate and median time to diabetic cataract formation was calculated using survival-analysis techniques in a retrospective cohort study design. Among the 200 dogs in the study population, 23 had cataracts at the time of diabetes diagnosis that were presumed to be related to other disease processes. Of the remaining 177 dogs, 132 had documented cataract development with features suggestive as being secondary to diabetes. Twenty-three dogs did not have obvious cataracts at the time of their last examination while 22 dogs did not have cataracts at the time they were lost to follow-up. These 55 cases contributed to the statistical models as noncases of cataracts until the last date for which an examination was available. Half of the population had developed cataracts by the 170th day postdiagnosis of diabetes mellitus, while 75% and 80% of the population developed cataracts by 370 days and 470 days, respectively. The results of this study suggest that the majority of dogs with diabetes will develop cataracts within 5–6 months from the time of diagnosis of the disease, and that approximately 80% of dogs will develop cataracts within 16 months of diagnosis.

Key Words: aldose reductase, cataract, diabetes mellitus, dog, survival analysis

INTRODUCTION

Cataract formation is a common complication of canine diabetes mellitus, occurring through a well-characterized alteration in glucose metabolism by the lens metabolic pathways.[1,2] The dog has a relatively high prevalence of naturally occurring diabetes mellitus. Moreover, it appears to have a unique susceptibility to subsequently develop cataract from this disease.[3] In this study, we determined the time to cataract development in a group of dogs referred to a teaching hospital for diabetes mellitus, using survival-analysis techniques.

STUDY DESIGN

Design

Medical records of all dogs in which diabetes mellitus, defined as a resting blood glucose that exceeded 250 mg/dL and for which insulin therapy was subsequently recommended, were evaluated. Cases were seen at the North Carolina State University, Veterinary Teaching Hospital between 1985 and 1995. A case was excluded from the survival-analysis described below if, at the time of evaluation at the teaching hospital, a cataract was present that the attending ophthalmologist felt was attributable to another disease process (e.g. progressive retinal atrophy, characteristic genetic cataract, trauma, or age-related cataract) based on morphologic features or historical information. A retrospective-cohort study design was used to determine whether dogs diagnosed with diabetes developed cataract related to the disease. Dogs that fulfilled the criteria and for which follow-up information was available were included in the analyses that consisted of a statistical estimation of median time to cataract development using the Kaplan–Meier technique.[4] The risk of cataract development when different factors were considered was evaluated using Cox's proportional hazards models (EGRET Version 1, Cytel Software Corporation, 1997, Seattle, WA, USA).[5]

Information on the animal's status and any cataract formation was obtained through the patient's medical record if the cataract was evident on initial examination or if repeat

examination visits were performed at the teaching hospital. If no repeat visits were made to the teaching hospital, information was gathered by telephone contact with the referring veterinarian, who was asked to comment on the presence of clinically apparent cataracts (i.e. those detectable without pharmacological mydriasis or critical inspection of the lens with a biomicroscope). Signalment, date of diagnosis of diabetes, estimated date of cataract formation, and date of last examination in which the animal was free of clinically apparent cataracts were recorded. Animals were considered as lost to follow-up when a confirmation of their cataract status could not be made. For these animals, the last date of examination in which no cataract was evident was used. This group, along with the animals for which a confirmation of the absence of clinically apparent cataracts at the last date of the examination was available, both contributed to the survival-analysis as 'noncases' of cataracts. Median time to diabetic cataract formation was stratified by age, breed, and gender. Age groups were defined as less than or equal to 7 years or more than 7 years of age. Breed was defined using standard American Kennel Club breeds or breed groups, while gender included males and females independent of the spay–neuter status. Similarly, risk of cataract development was estimated for the different age, breed, and gender groups.

RESULTS

Two hundred cases of canine diabetes for which a complete medical record was available were identified during the study period. The population included 65 males and 135 females with a mean $\pm$ SD age of 8.9 $\pm$ 2.8 years and ranging from 2 to 16 years. Eight breed groups of dogs were represented with mixed breed ($n = 51$), toy and miniature poodles ($n = 41$), and sporting and hound breeds ($n = 41$) being most commonly represented (Table 1).

One hundred and thirty-two dogs developed diabetic cataracts (Table 2). Twenty-three dogs had no obvious cataract development at their last examination, and 22 dogs were lost to follow-up. Twenty-three dogs had pre-existing cataracts at the time of diagnosis which were suggestive of another etiology.

Of the 132 dogs that ultimately developed cataracts, 19 of these cases were noted at the time of diagnosis of diabetes mellitus. Forty cases were diagnosed between the 2nd and 100th day, 30 cases were diagnosed between days 101 and 200, and 26 cases were diagnosed between days 201 and 400 after diagnosis. Finally, 17 cases were diagnosed at a time period equal to or greater than 400 days after diabetes mellitus diagnosis and one case was diagnosed 70 months after the initial diagnosis. The estimated median time between diagnosis of diabetes mellitus and cataract formation was 170 days for all dogs (Fig. 1). The time interval for 25%, 75%, and 80% of the study population to develop cataract was 60, 370, and 470 days, respectively.

Nonsporting and other breeds were 2.7 times more likely to develop cataracts than terriers (the comparison group) with a median time of 10 days. All other breeds were less likely than terriers to develop cataracts and the median times ranged between 139 and 238 days. Gender or age group did not have any effect on cataract development (Tables 3 and 4).

Table 1 Breed distribution in 200 dogs with diabetes mellitus

Breed	Frequency (*n*)	Percentage
Terriers	9	4.5
Poodles	41	20.5
Schnauzers	21	10.5
Mixed breeds	51	25.5
Sporting and hound breeds	41	20.5
Working and herding breeds	16	8.0
Toy breeds	11	5.5
Nonsporting and other breeds	10	5.0

Table 2 Incidence of cataract development in 200 dogs with diabetes mellitus

Category	Frequency (*n*)	Incidence (%)
No cataract development at last examination	23	11.5
Cataract attributed to diabetes mellitus	132	66.0
Pre-existing cataract attributed to other etiology	23	11.5
Losses to follow-up (no cataract development at time of last examination)	22	11.0

DISCUSSION

The results of this study confirmed that approximately 50% of dogs with diabetes mellitus that were referred to a teaching hospital developed cataracts within 5 and 6 months of the time of diagnosis. Progressively more dogs developed cataract with increasing time, such that the interval in which cataract was noted in 75% and 80% of the dogs was approximately 12 months and 16 months, respectively. A previous study of 56 dogs with diabetes noted a 68% incidence rate of cataracts.[6] However, the authors of this study calculated a rate of cataract at or near the time of diagnosis, with a relatively small follow-up interval following diagnosis.

In the current study, some breed-dependent variation in the likelihood of cataract development was noted, with the nonsporting breeds of dogs, which included the brachycephalic breeds and Shar Peis, having a median time of cataract of 10 days. The factors responsible for this finding could not be ascertained but may have reflected relative severity of the diabetes mellitus or relative ability to regulate blood glucose levels with insulin therapy in the different breeds. No attempt was made in this study to account for therapeutic control of the diabetes mellitus with cataract formation. Alternatively, a small sample size and great variability in the risk estimate could also explain these results.

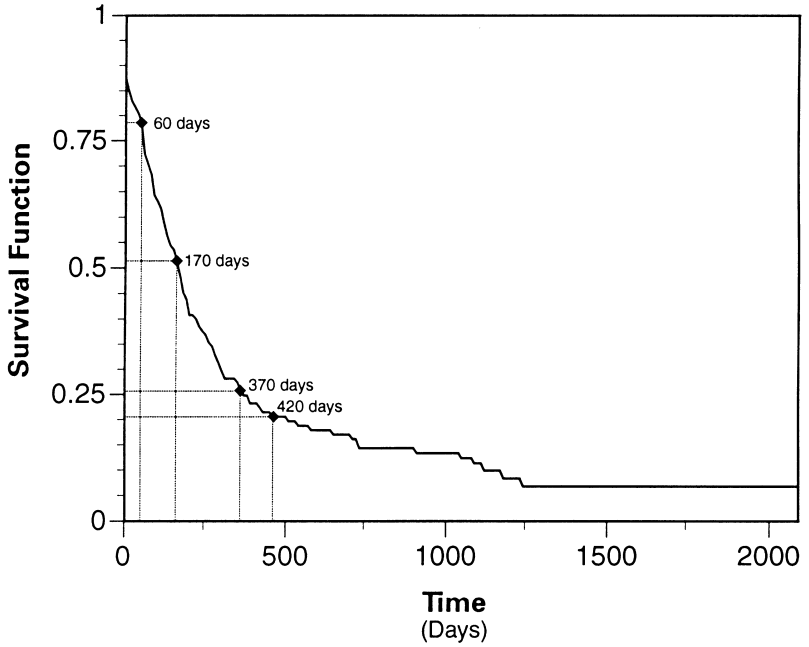

Figure 1. Estimated time course of development of cataract in 177 dogs with diabetes mellitus (Kaplan–Meier technique). The survival plots represent the percentage of dogs who were free of cataract at the beginning of a time interval (*x*-axis).

Table 3 Median time to diabetic cataract development for 177 dogs with diabetes mellitus

Category	Median time (days)
All breeds	170
Terriers	70
Poodles	184
Schnauzers	238
Mixed breeds	151
Sporting and hound breeds	145
Working and herding breeds	139
Toy breeds	180
Nonsporting and other breeds	10
Gender: male	194
Gender: female	151
Age group less or equal to 7 years	201
Age group more than 7 years	145

Several limitations in study design should be noted. The cases were referred to a teaching hospital and may have included patients who had relatively poorly controlled diabetes, not necessarily representative of the canine diabetic population as a whole. Conversely, clients who consult with a veterinary teaching hospital are often highly motivated with regard to treatment of their pets, and might be expected to administer therapy for diabetes mellitus to their animal to a more stringent degree than most pet owners. Additionally, because much of the follow-up evaluation was performed by the referring veterinarian, subtle degrees of early cataract formation related to diabetes mellitus may have gone undetected. Therefore, the results here can only be interpreted to represent the incidence and time-course of development of advanced diabetic cataracts i.e. those apparent without pharmacological mydriasis and biomicroscopy.

The dog appears to have a unique susceptibility to the development of cataracts secondary to diabetes mellitus (for

Table 4 Results from Cox's proportional hazards model on the development of cataracts in 177 dogs with diabetes mellitus

	Hazard ratio	*P*-value	95% confidence limits
Putative risk factor			
Poodles vs. Terriers*	0.38	0.02	0.17–0.86
Schnauzers vs. Terriers	0.35	0.02	0.14–0.85
Mixed breeds vs. Terriers	0.46	0.05	0.21–0.99
Sporting and hound breeds vs. Terriers	0.53	0.12	0.24–1.17
Working and herding breeds vs. Terriers	0.65	0.37	0.26–1.64
Toy breeds vs. Terriers	0.20	0.01	0.06–0.68
Nonsporting and other breeds vs. Terriers	2.66	0.09	0.87–8.16
Female vs. males	1.10	0.65	0.74–1.62
Age group more than 7 years vs. less or equal to 7	1.24	0.27	0.85–1.80

*Terriers were used as the comparison group.

example, when compared with humans and cats). Dogs also readily develop experimental hypergalactosemic cataracts with, presumably, a similar pathogenesis to the rapid onset cataract typically seen in the diabetic dog.[2] This susceptibility may reflect a difficulty in strictly administering insulin therapy to the diabetic dog to a sufficient degree to maintain euglycemia and prevent cataract formation. However, feline diabetes mellitus is often difficult to manage with insulin therapy, yet diabetic cataracts appear to be relatively uncommon in cats.[3] Alternatively, the high prevalence may be the result of species differences in lens metabolic pathways. The level of aldose reductase activity in the lens varies among different species, and some correlation can be made between the level of this enzyme and the likelihood of cataract formation.[1,7] For example, the rat, a species with extreme sensitivity to galactosemic cataracts, has a lens aldose reductase activity level approximately 14 × that of the dog.[1] Additionally, the NADPH-dependent aldose reductase activity in the canine lens is 0.745 ± 0.061 units/min/g lens protein, significantly higher than the cat lens at 0.667 ± 0.049.[8] Lenticular aldose reductase activity decreases with increasing age and younger dogs are more susceptible to experimental galactosemic cataracts when compared with older dogs.[9] However, lens aldose reductase levels are similar in dogs and humans (0.39 nm/min/mg lens protein),[1] despite a relatively low incidence of cataract in humans with diabetes.

Recently, alternative mechanisms of diabetic cataract formation, including glycosylation of lens proteins and oxidative stress, have been proposed.[6] As such, the varying rates of diabetic cataract formation in different species may also be attributable to species-dependent differences in lens metabolic pathways, independent of aldose reductase.

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