Pectinate ligament dysplasia and narrowing of the iridocorneal angle associated with glaucoma in the English Springer Spaniel

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Abstract

Objective The aim of the study was to evaluate if tonometry and gonioscopy could serve as predictors of later glaucoma development in the English Springer Spaniel, a breed prone to developing primary glaucoma.

Animals studied Gonioscopy was performed on 279 English Springer Spaniel dogs, 119 males and 160 females, with clinically normal eyes. In addition, 14 dogs, five males and nine females were examined for glaucoma.

Results A positive relation between pectinate ligament dysplasia (PLD) and narrowing of the relative width of the ciliary cleft (RWOCC) and also between PLD, RWOCC and age was demonstrated. The prevalence of PLD was 25.5%, which is higher than in other breeds reported. A positive association was demonstrated between PLD and glaucoma, as well as between narrowing of the RWOCC and glaucoma. Glaucoma was not observed in dogs with normal appearance of the iridocorneal angle. English Springer Spaniels related to dogs with glaucoma show more narrowing of the RWOCC and more PLD than unrelated dogs.

Conclusion This study demonstrates the positive association between PLD and glaucoma, between narrowing of the iridocorneal angle and glaucoma and the effect of age on the iridocorneal angle. Mating of dogs with normal iridocorneal angles appears to reduce the presence and degree of abnormal appearance of the iridocorneal angle in the offspring. However, breeding only dogs with normal iridocorneal angles without consideration of their relationship to dogs with glaucoma is not a guarantee for preventing glaucoma in the offspring.

Key Words: dogs, English Springer Spaniel, glaucoma, gonioscopy

INTRODUCTION

Primary glaucoma in the English Springer Spaniel has frequently been diagnosed in Norway and Sweden, but the disease seems to be less frequent in this breed in other parts of the world. Gustafsson1 reported 28 cases of primary glaucoma in the English Springer Spaniel in Sweden in 1986, of which 22 dogs were related and could be traced back to common ancestors. Males and females were equally affected. Abnormal pectinate ligament was diagnosed upon histopathology of two eyes, but gonioscopy was not routinely performed on the affected dogs. The English Springer Spaniel was listed as one of the breeds affected with angle-closure glaucoma in England.2,3 However, only one English Springer Spaniel was included in the list of breeds affected by glaucoma in an American study by Smith et al.4

Cottrell and Barnet5 reported 28 cases of glaucoma related to abnormalities of the iridocorneal angle in a related breed, the Welsh Springer Spaniel, and suggested a dominant mode of inheritance. They also found that females were more frequently affected than males, although this difference was not statistically confirmed.

Pectinate ligament dysplasia (PLD) has been associated with glaucoma in many breeds, including the Flat Coated Retriever,6,7 Samoyed,8,9 Bouvier des Flandres,10,11 Siberian Husky,12 Basset Hound13 and American Cocker Spaniel.14 Anecdotal cases of glaucoma considered to be related to PLD have also been reported in other breeds.2,3 There seems to be an interesting difference in breed incidence in different parts of the world. Whereas goniodysgenesis was not diagnosed in the American Cocker Spaniels studied in England15 and primary glaucoma is infrequently found in
this breed in Norway and Sweden, the American Cocker Spaniel has been one of the most frequently affected breeds in the USA.

Several cases of glaucoma have been diagnosed in the English Springer Spaniel in Norway. The disease has initially been unilateral in all cases. Gonioscopy of the normotensive eye of affected dogs has been performed when possible, and has shown narrow or closed iridocorneal angles with or without concurrent PLD. Based on these findings a screening program for eye examinations was established, in which tonometry and gonioscopy were included. The aim of this study was to evaluate if tonometry and gonioscopy could serve as predictors of later glaucoma development in the English Springer Spaniel.

**MATERIALS AND METHODS**

Routine eye examination as part of the Norwegian screening program for hereditary eye diseases was performed on 279 English Springer Spaniel dogs, 119 males and 160 females, with clinically normal eyes. Examination included indirect ophthalmoscopy, slit-lamp biomicroscopy and gonioscopy. The ages at examination ranged between 1 and 10 years. One dog was only 8 months old at the time of examination, but was grouped as a 1-year-old dog in the statistical analyzes. The mean age at examination for males was 5.5 years compared to 4.0 years in the females. Pedigrees were obtained for all except five dogs. The majority of the dogs came from different parts of Norway and represented most of the Norwegian breeding lines. However, some of the sires had previously been examined by one of the authors in Sweden. Five of the examined dogs later developed glaucoma. In addition, nine glaucomatous dogs were examined. Gonioscopy of the other (normotensive) eye was performed in six out of the nine dogs already diagnosed with glaucoma prior to this study.

Intraocular pressures were initially measured in all dogs with clinically normal eyes, but as preliminary data showed no relation between PLD, width of the iridocorneal angle and intraocular pressure, this procedure was later not considered in the examination protocol in dogs with clinically normal eyes. Thus, data for intraocular pressures are included in 153 of the 279 dogs. All the dogs were examined by two of the authors, apart from 20 dogs, which were examined by other members of the Norwegian eye panel. The opening of the ICA was inspected after indirect ophthalmoscopy and tonometry (Oculab Tono-Pen, Bio-Rad Laboratories, Santa Ana, CA, USA) on examined dogs.

Gonioscopy was performed in both parents of 99 of the examined dogs by other members of the Norwegian eye panel. In addition, nine glaucomatous dogs were examined. Gonioscopy of the other (normotensive) eye was performed in six out of the nine dogs already diagnosed with glaucoma prior to this study. After indirect ophthalmoscopy and tonometry (Oculab Tono-Pen, Bio-Rad Laboratories, Santa Ana, CA, USA) on the unilaterally blind eye, examination of the iridocorneal angle (ICA) by gonioscopy (Barkan Lo-vac goniolens, Medical Workshop, Groningen, the Netherlands) was performed after instillation of topical anesthesia on unsedated dogs. In a few dogs, sedation with 10 μg/kg medetomidine was however necessary. The opening of the ICA was inspected with an otoscope lamp with magnification, scanning an angle of 360°. Both eyes were examined, and the width of the ICA and the degree of PLD were evaluated according to the method described by Ekested and Narfström with a slight modification in which wide-open angles and normal-open angles were given the same scoring value (0). The anterior width of the ciliary cleft (the distance from the origin to the insertion of the pectinate ligament) and the total distance from the origin of the pectinate ligament to the anterior corneal surface were subjectively evaluated. The ratio between these two variables was then estimated subjectively and used as an estimate of the relative width of the opening of the ciliary cleft (RIWCC). The RIWCC was graded according to the following scale: 0: open, 1: slightly narrowed, 2: narrow and 3: closed. A pectinate ligament was considered to be dysplastic if it extended over more than 1/16 of the circumference without being interrupted by normal interligamentary spaces. The extent of dysplasia of the pectinate ligament was graded from 0 to 4 according to a previously described method where 4 represented dysplasia affecting the whole ligament with only occasional small flow holes and 0 represented a normal pectinate ligament.

The tendency of dogs related to glaucomatous dogs to have PLD and/or narrowing of RIWCC was evaluated by dividing the dogs into groups according to the following criteria:

(0) Littermate of dog affected by glaucoma.
(1) One parent affected by glaucoma or a littermate had produced offspring with glaucoma.
(2) One grandparent affected by glaucoma or one parent had produced offspring with glaucoma in another combination.
(3) One grandparent or one sibling to a parent had produced offspring with glaucoma.
(4) Dogs unrelated to dogs affected by glaucoma in the first two generations.

Statistical analyzes were performed on JMP statistic package, SAS Institute, Inc. Relation between age on PLD and RIWCC, and between intraocular pressures and the iridocorneal parameters in normal-eyed dogs were investigated using ANOVA, while Chi-square tests were used to analyze the relation between sex and iridocorneal angle parameters. The relation between RIWCC and PLD was evaluated by ANOVA. A general linear model was used for evaluating the RIWCC as a function of age and PLD (\(Y = \beta_0 + \beta_1 \cdot \text{age} + \beta_2 \cdot \text{PLD} + \gamma_1 \cdot \text{age} \cdot \text{PLD}\)). The relation between glaucoma and narrowing of the RIWCC and glaucoma and PLD was evaluated by ANOVA. The effect of kinship with glaucomatous dogs on the iridocorneal angle parameters of dogs with glaucoma was evaluated by ANOVA. A result was considered statistically significant if \(P < 0.001\).

**RESULTS**

**Normotensive dogs**

The results of the gonioscopy are given in Table 1. The degree of pigmentation in the superficial and deep bands of the
RWOCC (age and PLD. Both factors had a significant effect on the model was used for evaluating the RWOCC as a function of PLD (\( P < 0.001 \) for both findings). There was also a relationship between both PLD and narrowing of the RWOCC and kinship with affected dogs, closer relatives showing more abnormal appearance of the iridocorneal angles than unrelated dogs (ANOVA, \( P < 0.001 \) for both findings).

### Dogs with glaucoma

Fourteen dogs were examined for glaucoma: five males and nine females. Pedigree analyzes showed that they were all related. There was a statistically significant difference in gender susceptibility (Chi-square, \( P = 0.008 \)). The age of the dogs when the diagnosis was established ranged from 3 to 12 years, with a mean age of 6.3 years. All the affected dogs showed unilateral signs of glaucoma.

Three female littermates and their dam had been examined at the ages of 3 and 7 years, respectively, showing narrowed RWOCC and only moderate PLD. The fourth littermate was examined at the same time and was found to have very narrow RWOCC, but at the age of 9 years had not developed glaucoma. On gonioscopy, the dam had pectinate ligament dysplasia (grade 3) but only moderately narrowed RWOCC (grade 1), while the sire of this litter had very narrow RWOCC (grade 2) with PLD (grade 3). The combination of the dam with a different, unexamined sire resulted in eight pups of which six were examined. Five of these pups had normal RWOCC, the sixth had narrowed angles with some pectinate ligament dysplasia when examined. A full sister of the dam, which at examination had shown narrowed RWOCC and PLD, also developed glaucoma at a later stage.

The other nine glaucomatous dogs in the study were presented with advanced glaucoma. Two of the dogs were dam and son. Gonioscopy was performed on the normotensive eye in six of the dogs, and all had very narrowed or closed RWOCC. Evaluation of the pectinate ligament of the glaucomatous eye was possible only in two dogs, of which one showed extensive PLD with only occasional flow holes; the other only moderate PLD (grade 2). Histology of the iridocorneal angle of one of the glaucomatous eyes is shown in Fig. 5.

### DISCUSSION

Pectinate ligament dysplasia (PLD) and narrowing of the iridocorneal angle (ICA) have been considered predictors of glaucoma in certain breeds of dog. The present study shows a positive relationship between both PLD and glaucoma as well as between narrowed RWOCC and glaucoma.

<table>
<thead>
<tr>
<th>RWOCC</th>
<th>n</th>
<th>%</th>
<th>PLD</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>229</td>
<td>82.1</td>
<td>Normal</td>
<td>208</td>
<td>74.5</td>
</tr>
<tr>
<td>Moderately narrow</td>
<td>42</td>
<td>15.0</td>
<td>Grade 1</td>
<td>44</td>
<td>15.8</td>
</tr>
<tr>
<td>Very narrow</td>
<td>8</td>
<td>2.9</td>
<td>Grade 2</td>
<td>19</td>
<td>6.8</td>
</tr>
<tr>
<td>Closed</td>
<td>0</td>
<td>0</td>
<td>Grade 3</td>
<td>5</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grade 4</td>
<td>3</td>
<td>1.1</td>
</tr>
</tbody>
</table>

There was also a relationship between both PLD and narrowing of the RWOCC and kinship with affected dogs, closer relatives showing more abnormal appearance of the iridocorneal angles than unrelated dogs (ANOVA, \( P < 0.001 \) for both findings).

| Table 1 The distribution of the relative width of the ciliary cleft (RWOCC) and pectinate ligament dysplasia (PLD) in 279 normotensive English Springer Spaniel dogs |
|---|---|---|---|---|---|
| Normal | 229 | 82.1 | Normal | 208 | 74.5 |
| Moderately narrow | 42 | 15.0 | Grade 1 | 44 | 15.8 |
| Very narrow | 8 | 2.9 | Grade 2 | 19 | 6.8 |
| Closed | 0 | 0 | Grade 3 | 5 | 1.8 |
|             |    |     | Grade 4 | 3 | 1.1 |

There was also a relationship between both PLD and narrowing of the RWOCC and kinship with affected dogs, closer relatives showing more abnormal appearance of the iridocorneal angles than unrelated dogs (ANOVA, \( P < 0.001 \) for both findings).

### Discussion

Pectinate ligament dysplasia (PLD) and narrowing of the iridocorneal angle (ICA) have been considered predictors of glaucoma in certain breeds of dog. The present study shows a positive relationship between both PLD and glaucoma as well as between narrowed RWOCC and glaucoma.

<table>
<thead>
<tr>
<th>Normal offspring</th>
<th>Abnormal offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal sire × normal dam</td>
<td>44</td>
</tr>
<tr>
<td>Normal sire × abnormal dam</td>
<td>16</td>
</tr>
<tr>
<td>Abnormal sire × normal dam</td>
<td>7</td>
</tr>
<tr>
<td>Abnormal sire × abnormal dam</td>
<td>3</td>
</tr>
</tbody>
</table>

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prevalence of PLD on gonioscopy in normotensive dogs from breeds where hereditary primary glaucoma is known to occur, varies between 22.4% in the Samoyed to 37.5% in the Bouvier des Flandres. In a study of the Bouvier des Flandres based on histology, the majority of the examined eyes, 75%, showed some degree of PLD. The report, however, does not state if this represents a random sample from the Bouvier des Flandres breed or a selected group. In
comparison, the prevalence of PLD was only 6% in a study comprising a group of 100 dogs in Britain representing 30 different breeds with no history of primary glaucoma.7

The results in the present study show a frequency of 25.5% of PLD in normotensive English Springer Spaniels, which is higher than the reported value from Great Britain in a normal population of other breeds.6 Narrowed RWOCC was diagnosed in 17.9% of the normotensive dogs. There was also a relationship between these two findings, although both entities could be observed independently in both normal dogs and dogs later affected with glaucoma. Consequently, both factors may contribute additively or synergistically as well as independently to the development of primary glaucoma in this breed, or they may serve as markers of abnormalities in the outflow pathways that cannot be visualized using gonioscopy.

In the present study a narrowing of the RWOCC with increasing age was demonstrated. A narrowing of the iridocorneal angle caused by an anterior displacement of the iris due to a relative increase of the pressure in the posterior chamber, or by an age-related increase in the size of the lens, has been suggested. These factors may eventually lead to the final closure of an abnormal iridocorneal angle.1 The latter theory was demonstrated in a group of Samoyeds17,18 where it was found that age-related changes, mainly in lens thickness, reduces the depth of the axial anterior chamber. It has also been established that the thickness of Descemet's membrane increases throughout life, because of a continuous addition of new basement membrane material by the endothelium.19 This may also contribute to a thickening of the fibers in the pectinate ligament and a narrowing of the RWOCC.

In the present study there was also a change in the degree of PLD with increasing age, resulting in higher scores in older dogs. Similar changes in the pectinate ligament with increasing age could not be demonstrated in the Samoyed16 but were demonstrated in the Flat Coated Retriever by Wood et al.7 In the Flat Coated Retriever this was considered as not significant enough to be of biological importance. As the pectinate ligament has already developed between 19 and 28 days after birth20 a later thickening of the pectinate fibers must be caused by other factors. This could be either as a response to repeated subclinical inflammatory events, or as a response to other secondary changes. Another possibility is that the difference between PLD in dogs of different ages is a result of (unintended) selection of the dogs used for breeding. Change in the pectinate ligament is also demonstrated in the pigmented glaucoma in the Cairn Terrier.21 The influence of age on the appearance of the iridocorneal angle may be significant. Thus, gonioscopy, if performed, should ideally be carried out at the same age in dogs screened for inherited eye diseases if the results are to be comparable.

Although more females than males were affected by glaucoma in the present study, there was no sex difference in the RWOCC or in the morphology of the pectinate ligament in normotensive dogs. This corresponds with findings in the Samoyed16 and the Flat Coated Retriever.5 A gender difference has been described in PLD in other breeds, including the American Cocker Spaniel,22 Welsh Springer Spaniel1 and Siberian Husky,2 with females being more frequently affected with PLD than males. Statistical analyzes were not performed in any of these studies, but there may be breed-specific differences for clinically similar findings.

The parents' status may affect the status of the offspring, as mating of two normal dogs produces predominantly normal offspring (Table 2). It is interesting to note, however, that mating of two dogs with abnormal iridocorneal angles resulted in the same percentage of normal-eyed dogs as mating of a dog with normal ICA with a dog with abnormal ICA.

More females than males developed glaucoma in this study. Although statistically significant, this result should be interpreted with caution, as the total number of dogs with glaucoma was relatively small. It might, however, reflect a gender difference in factors involved in glaucoma development in the English Springer Spaniel. Similar gender difference has been described in glaucoma in the Welsh Springer Spaniel, but statistical evaluation of the findings was not performed in the study.2

Intraocular pressures (IOP) were measured in 153 normotensive dogs. There was no statistically significant relationship between IOP and the RWOCC or degree of PLD. Thus, measuring of the IOP on a single occasion cannot be used to evaluate the appearance of the drainage angle, nor be used as a predictor of whether an English Springer Spaniel dog will develop primary glaucoma in the future.

Although primary glaucoma is commonly considered to be an inherited disease in certain dog breeds, an exact mode of inheritance is yet to be demonstrated in affected breeds. Only a small number of dogs with PLD or narrowed RWOCC will develop glaucoma, suggesting that more than one factor may be involved. An autosomal recessive mode of inheritance of PLD in the Siberian Husky has been suggested.15 The results of mating of English Springer Spaniels with normal or abnormal iridocorneal angles does not show this mode of inheritance, as mating of sires and dams with PLD resulted in three normal and four abnormal offspring of which none have developed glaucoma so far.

Furthermore, we believe that a trait such as PLD or the RWOCC, which can vary continuously between 0 and 100%, is unlikely to be determined by only one gene. It is likely that such a trait, if inherited, will depend on multiple genes and the trait would then be inherited in a polygenic mode. As an increase in thickness of the pectinate fibers with age was found, it is also possible that other factors, such as low-grade intraocular inflammation, may render certain dogs more susceptible to changes in the iridocorneal angle than others.

The obstruction of flow through the trabecular meshwork by small macromolecules occurs in humans24 and accumulation of basal lamina-like material seems to be involved in the development of late onset goniodysgenetic glaucoma in humans.24 Although not investigated, similar factors may be involved in the increasing degree of PLD in the English Springer Spaniel with increasing age.
The number of dogs with glaucoma is too restricted to establish the mode of inheritance in primary glaucoma in the English Springer Spaniel. A dam that later developed glaucoma, produced four examined offspring with narrowed RWOCC. Three of these offspring also later developed glaucoma. The dam, however, did not produce any affected offspring in a combination with another male. The mother of one of the other dogs presented with glaucoma later developed glaucoma herself. The rest of the dogs with glaucoma in the present study were the single affected dogs within their litters, and although not examined, the parents had no history of glaucoma themselves. Thus, it is crucial to understand that the manifest disease, glaucoma, may have a different mode of inheritance than the factors involved that can be visualized using gonioscopy. Understanding of the relationship between PLD and RWOCC and between PLD and glaucoma is still poor.

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