Veterinary Ophthalmology (2016) 1–10 DOI:10.1111/vop.12448

Characterization of a novel form of progressive retinal atrophy in Whippet dogs: a clinical, electroretinographic, and breeding study

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Abstract

Objective To describe a form of progressive retinal atrophy (PRA) in Whippets including clinical, electroretinographic, optical coherence tomographic changes and pedigree analysis.

Animals studied Client-owned Whippet dogs (n = 51) living in Brazil.

Procedures All animals were submitted for routine ophthalmic screening for presumed inherited ocular disease, which included the following: visual tests, such as obstacle course tests, in scotopic and photopic conditions, cotton ball test, dazzle reflex, ocular fundus evaluation by indirect ophthalmoscopy followed by fundus photography. Additionally, electroretinography (ERG) and optical coherence tomography (OCT) were performed in 24 and four dogs, respectively.

Results Sixteen dogs were diagnosed with PRA. Vision deficits in dim light were detected in dogs examined at a young age associated with nystagmus. Funduscopic changes included the development of multifocal retinal bullae from 6 months of age. Retinal thinning became apparent later, at which time the bullae were no longer detected. OCT examination of selected young dogs revealed that the retinal bullae were due to separation between photoreceptors and the retinal pigment epithelium, and of dogs with more advanced disease confirmed the development of retinal thinning. Electroretinography in young dogs revealed a negative ERG due to a lack of b-wave in both scotopic and photopic recordings. With progression, the ERG became unrecordable. Pedigree analysis suggested an autosomal recessive mode of inheritance.

Conclusion The retinal dystrophy reported here in Whippet dogs has a unique phenotype of an initial lack of ERG b-wave, development of retinal bullae then a progressive generalized retinal degeneration.

Key Words: electroretinography, optical coherence tomography, progressive retinal atrophy, retina, Whippet

INTRODUCTION

The canine Whippet breed was developed in the north of United Kingdom and was mainly used for rabbit coursing and track racing, being recognized by the UK Kennel Club as an official breed in 1890.[1,2] In Brazil, the breed has become more popular over the last few decades with a total of 1083 Whippets being registered by the Brazilian Canine Breeders Confederation (CBKC) between 1999 and 2003 (CBKC, personal communication).

Hereditary and suspected hereditary eye diseases reported in the breed include narrow angle glaucoma, corneal dystrophy, dermoid, heterochromia iridis, persistent pupillary membranes, cataract, micropapilla, vitreous degeneration, and progressive retinal atrophy (PRA).[2,3] There are only a few reports of the incidence of PRA in

the breed[3], and none of them provides detailed phenotypic information.

Hereditary retinal diseases are an important cause of blindness in both humans and animals[4]. Detailed studies of the wide spectrum of retinal dystrophies, including PRA, that affect different breeds of dogs are important not only for the affected dogs but also for comparative purposes as they can provide valuable models for studies focused on the development and testing of therapeutic approaches for the equivalent human disease.[4,5]

The purpose of this study was to provide a clinical and functional description of the phenotype of a unique form of retinal dystrophy in the Whippet.

MATERIALS AND METHODS

Animals

Fifty-one Whippet dogs, (28 females and 23 males) varying in age from one to 167 months were examined. Informed consent was obtained from the owners, and the study conducted in accordance with ARVO's Statement for Use of Animals in Ophthalmic and Vision Research and with that of the Federal University of Paraná's Animal Use Committee. All dogs included in the study and investigations performed on each one are shown in Table 1. Pedigree information was collected for the examined dogs, and in some families, dogs were followed over two generations enabling the assessment of young, potentially affected dogs for early stage retinal changes.

Clinical examination

All dogs underwent a complete physical examination and a complete blood panel before ocular examinations to exclude animals with indications of systemic disease. Vision testing was performed including ability to track falling cotton wool balls and to negotiate an obstacle course test in both bright and dim light. Ophthalmic examination included assessment of the menace response, dazzle reflex, and pupillary light reflex. The anterior segment was examined by slit-lamp biomicroscopy (Hawk Eye, Dioptrix, L'Union, France). The fundus was examined by indirect ophthalmoscopy (Eyetec Equipamentos Oftálmicos, São Carlos, Brazil). Additionally, several fundus photographs (ClearView® optical imaging system, Eickemeyer, Tuttlingen, Germany) were obtained from both center and mid-peripheral retinal areas, from all affected dogs and selected age-matched clinically unaffected dogs, Sequential fundus photographs were taken for six age-matched dogs, three being affected, and three clinically unaffected. Several dogs were reexamined to monitor disease progression (Table 1).

Electroretinography (ERG)

ERGs were recorded from both eyes of 13 affected and nine clinically unaffected Whippets. Pupils were dilated using 1% tropicamide (Mydriacyl; AlconTM, São Paulo, SP, Brazil) combined with 10% phenylephrine (Frumtost, São Paulo, SP, Brazil).[6] Dogs were sedated with acepromazine (0.03 mg/Kg; Acepran, 0.2%—Vetnil Indústria e Comércio de Produtos Veterinários Ltda, São Paulo—SP, Brazil), induced with propofol (5 mg/kg; Propovan 1%, Cristália Produtos Químicos e Farmacêuticos Ltda, Itapira—SP, Brazil), intubated and maintained with isoflurane (1– 1.5% Isoforine, Cristália Produtos Químicos e Farmacêuticos Ltda, Itapira—SP, Brazil) delivered in oxygen (30 mL/kg/min) using a semi-closed system. For dogs weighing less than 4 kg, a Jackson Rees modified Ayre's T-piece with fresh gas flow of 250 ml/kg/min was used. Heart and respiratory rates, electrocardiographic trace, noninvasive blood pressure, end-tidal CO_2, pulse oximetry, and esophageal temperature were continuously evaluated by a multiparameter monitor (LifeWindow LW9*x*Vet, Digicare Animal Health, Boynton Beach—Florida, USA). A topical corneal anesthetic was applied (proparacaine hydrochloride 0.5% ophthalmic solution USP; Alcon Laboratories, Forth Worth, TX, USA), and eyes were positioned using a lid speculum and stay suture in the superior perilimbal conjunctiva. A corneal contact recording electrode was used (ERG-Jet, Fabrinal SA, La Chaux-de-Fonds, Switzerland) with reference (2 cm from lateral canthus) and ground (over base of neck) platinum subdermal needles (Model E2, Grass Technologies, Warwick, USA). A portable mini Ganzfield ERG unit (HMsERG model 1000, RetVet Corp, Columbia, MO, USA) was used to record the ERGs from one eye under scotopic and then photopic conditions. Electrode impedance was maintained at <5 kΩ, and bandpass was 0.3–300 Hz. The eyes were positioned centrally in the palpebral fissure and the mini Ganzfield was carefully positioned with the aid of a tripod to be centered over the cornea and 1 cm from the corneal surface. Electroretinography was performed with a preprogrammed protocol previously used to describe a novel dog retinopathy[6] consisting of the following stimuli: (i) Rod function was tested every 4 min during the period of 20 min of dark adaptation using a dim stimulus (average of 10 flashes, 0.5 Hz, −2 log cds/m^2); (ii) combined rod–cone response to a standard intensity (average of four flashes, 0.1 Hz, 0.47 log cds/m^2) and a high-intensity (average of four flashes, 0.05 Hz, 1 log cds/m^2) flashes under scotopic conditions; (iii) cone function following light adaptation (10 min at 30 cd/m^2) using a standard intensity flash (average of 32 flashes, 2 Hz, 1 log cds/m^2) and a cone flicker test (128 flashes, 31 Hz, 1 log cds/m^2).[7]

Optical Coherence Tomography (OCT)

Spectral domain optical coherence tomography (SD-OCT, Spectralis® HRA+OCT; Heidelberg Engineering Inc., Heidelberg, Germany) was performed to obtain *in vivo* high-resolution cross-section images of the retina and optic nerve head (ONH) of four dogs (one 5-month-old affected, one 5-month-old clinically unaffected animal,

Table 1. Individual details of the Whippets included in the study and tests performed

Dog number	Sex	Age at first examination (months)	Age at diagnosis (months)	Reexamination age (months)	ERG age (months)	Repeated ERG age (months)	OCT age (months)
Early funduscopic changes							
#1	M	1	1	2, 3, 4, 5, 10	1	2,3	
#2	M	3	3	5, 6, 9, 12	3		5
#3	F	3	3	6, 8, 9	3		8
Moderate funduscopic changes							
#4	F	3	9	9, 12, 18	12		18
#5	M	3	12	9, 12	12		
#6	F	15	15	15, 21,24,30	17		
#7	F	16	16				
End-stage retinal atrophy							
#8	M	24	24		24		
#9	M	29	29				
#10	F	33	33				
#11	M	34	34		36		
#12	F	36	36		36		
#13	M	36	36		52		
#14	F	40	40	52	38		
#15	F	46	46		55		
#16	F	72	72		72	96	
Unaffected dogs							
#17	M	1		2, 3, 4,	1	2,3	
#18	F	1		2, 3, 4,	1	2	
#19	M	2		3,6,9	6		
#20	M	3		5, 6,9	3		5
#21	F	6			6		
#22	M	9					
#23	M	12			13		
#24	F	16			17		
#25	M	17					
#26	M	20					
#27	F	23					
#28	M	24					
#29	M	24					
#30	F	24					
#31	M	27					
#32	F	28					
#33	M	30					
#34	M	32			40		
#35	F	32					
#36	M	36					
#37	F	37					
#38	F	42					
#39	F	46					
#40	F	60					
#41	M	57			57		
#42	F	64					
#43	F	66					
#44	F	68					
#45	F	67					
#46	F	72					
#47	M	87					
#48	M	120					
#49	F	126					
#50	F	144					
#51	F	167					

one 8-month-old affected, and one 18-month-old affected; animals #2, #20, #3 and #4, respectively) (Table 1). This procedure was performed at a separate examination session. The pupils were dilated, and anesthesia protocol was the same as previously described for the ERGs. The eyes were positioned using a lid speculum and stay suture

in the superior perilimbal conjunctiva. In sequence, 10 retinal cross-sectional images were obtained for each eye examined, including tapetal, nontapetal, and papillary areas. Total retinal thicknesses were compared between affected and clinically unaffected dogs using the optic disk as a landmark.

RESULTS

Animals

All 51 of the dogs studied were in good physical condition, and no abnormalities were detected on the complete blood count (CBC). Sixteen of the 51 dogs (31.37%) (10 females and six males) were diagnosed as affected with retinal changes upon ophthalmoscopic examination and/or abnormal retinal function by ERG. The age of the affected dogs (at the time of the diagnosis) ranged from 30 days of age (animal #1—diagnosed by ERG) to 72 months of age (animal #16—diagnosed by funduscopy) with a median of 38.5 months.

Clinical examination

Owners of the affected dogs typically did not report ocular abnormalities until the dogs were one to 2 years of age. Then, the two most frequent observations were visual impairment in dim-light or dark conditions and some owners noticed increased 'eye shine'. At early stages, between one and 6 months of age, affected dogs usually had a greater resting pupillary diameter than clinically unaffected dogs under ambient lighting and showed some difficulty in negotiating an obstacle course in dim lighting. This difficulty in negotiating an obstacle in the maze test was somewhat more evident in 6- to 12-month-old dogs in dim lighting and even in bright light for a few of the dogs examined. Pupil diameters were accessed as a qualitative observation transcribed the medical record or directly compared with normal littermates under the same lighting conditions. PLRs were present and apparently normal, but dazzle reflex, cotton ball tracking, and menace response were either markedly reduced or absent. The young affected dogs (from 1 to 6 months of age) also exhibited an oscillatory nystagmus, although this became less apparent with age. Dogs with moderate stage disease, aged between 12 and 24 months, noticeably had a more decreased ability to negotiate an obstacle course in dim-light conditions, and a few also had difficulty in bright lighting conditions. PLRs were still present, but slower than normal. Yet, dazzle reflex, cotton ball tracking, and menace response were absent. The dogs with more advanced disease, aged between 24 and 72 month of age, had marked visual impairment apparent during obstacle course testing, both in dim and bright light. There was a minimal PLR, and the dazzle reflex, cotton ball tracking, and menace response were all absent. Two of the affected dogs (animals #3 and #16) developed posterior subcapsular cataracts. Dog #3 was diagnosed with incipient posterior cortical cataract at 6 months of age, suggesting it may not have been secondary to retinal degeneration. Cataract was also diagnosed in one of the clinically unaffected dogs (animal #41).

Funduscopic changes

Funduscopic findings followed a consistent chronological pattern of retinal deterioration and were divided as follows: (i) early funduscopic changes; (ii) moderate funduscopic changes; and (iii) end-stage retinal changes. The older the animal the most severe retinal changes were detected. At one month of age, it was impossible to differentiate the affected animal from the two unaffected animals examined by funduscopy alone. By three months of age, a mild/early vascular attenuation was present already in the affected animals. Between six months of age up to 12 months of age, the animals presented moderate funduscopic changes typical of a progressive retinal atrophy. Those between 24 and 72 months of age showed signs of a marked generalized retinal degeneration and retinal vascular attenuation and were classified as having an end-stage retinal atrophy (Fig. 1). Curiously, multiple small retinal bullae were apparent in affected dogs ($n = 2$; dogs #2 and #3) between 5 and 8 months of age (Fig. 2). With further progression of disease and development of a more intense tapetal hyper-reflectivity (about 12 months of age), the bullae became less apparent. Affected dogs between 12 and 18 months of age showed marked vascular attenuation and generalized tapetal hyper-reflectivity.

Electroretinography

The morphology of the ERGs of the affected Whippets was abnormal from the earliest age tested (1 month of age): The b-wave was not detectable above background noise in response to a scotopic stimulus of -2 log cds/m^2 under scotopic conditions (Fig. 3a). In responses to stronger stimuli, only the a-wave was discernible from the background noise (scotopic stimulus of 0.47 log cds/m^2 under scotopic conditions; Fig. 3b). The morphology of the ERG elicited with a photopic single flash under photopic conditions revealed a residual a-wave and a lack of the b-wave (Fig. 3c). The photopic 30 Hz flicker was barely recordable in the 1-month-old affected dog and not recordable in the older affected animal (Fig. 3d). In all affected dogs, the residual ERG responses decreased from 1to 3 months of age and were severely diminished at 12 months of age (data not shown) and completely extinguished in all affected dogs by 72 months of age (Fig. 3).

Optical coherence tomography

Four dogs (three affected and one unaffected control) underwent OCT examination. OCT imaging of the retina of two dogs, one 5 month old and one 8 month old (animals #2 and #3) confirmed the presence of multiple retinal bullae (Fig. 4) as previously detected by funduscopy (Fig. 1). The OCT images revealed that the bullae were

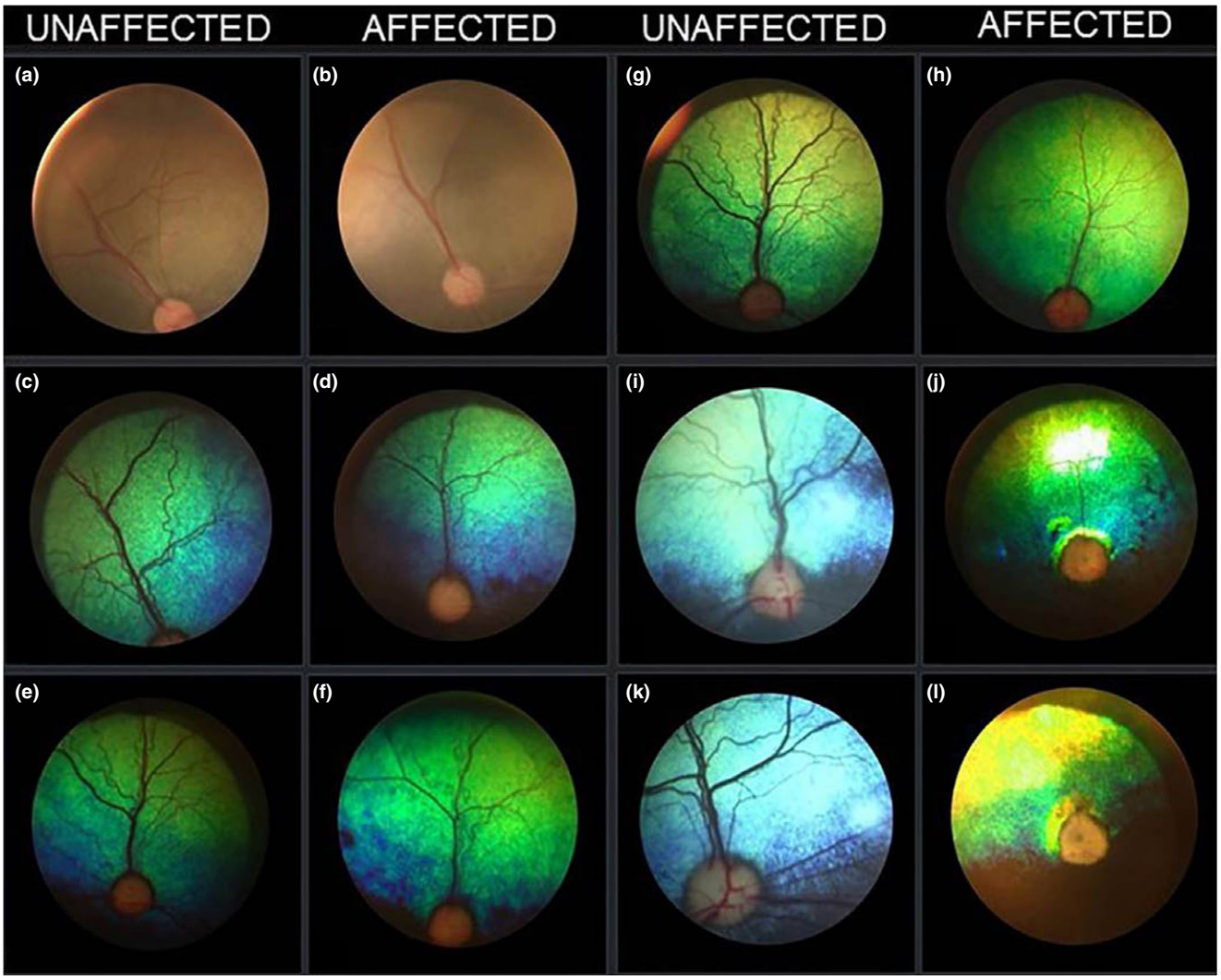

Figure 1. Clinically unaffected (a, c, e, g, i, and k) and affected (b, d, f, h, j, and l) dogs. Selected fundus photographs of age-matched unaffected and affected dogs at the following ages: 1-month (a and b)—(dogs #17 and #1). Note that the affected dog (diagnosed by ERG) appears ophthalmoscopically normal at this age; 3 months of age (c and d)—(dogs #18 and #2). Dog #2 mild/early vascular attenuation when compared to an age-matched dog #18; 6 months of age (e and f)—(dogs #20 and #3), retinal bullae and vascular attenuation were present in #3; twelve months of age (g and h)—(dogs #23 and #4). At this age in dog #4, tapetal hyper-reflectivity and mild retinal blood vessel attenuation are present (moderate funduscopic changes); 36 months of age (i and j)—(dogs #36 and #12) and 72 months of age (k and l)—(dogs #46 and #16). Dogs #12 and #16 at these ages had marked progressive generalized retinal degeneration and retinal vascular attenuation classified in Table 1 as end-stage retinal atrophy.

due to separation between the photoreceptors and the retinal pigment epithelium. OCT cross-section imaging of the retina of an 18-month-old affected dog (dog #4) did not detect the bullae, which were present in the younger affected dogs. At this age, there was a notable thinning of the retina, predominantly of the outer nuclear layer, compared to that of the unaffected control dog (dog #20) (Fig. 5). The full retinal thickness comparison showed that there was a progressive decrease in retinal thickness in affected dogs (data not shown).

Pedigree analysis

To characterize the inheritance pattern of the disease, all available related dogs were clinically examined and pedigrees constructed. A similar number of males (7) to females (9) were diagnosed as affected, ruling out an X-linked mode of inheritance. Additionally, the crossing of two clinically unaffected dogs (#47 and #49) resulted in an affected offspring (#16), suggesting an autosomal recessive mode of inheritance. Figure 6 depicts the largest and most complete pedigree constructed.

DISCUSSION

Retinal dystrophies represent an important group of heterogenic ophthalmic disorders in dogs.[8] The commonest category of dystrophies is the progressive retinal atrophies (PRA). These share a similar phenotype of a

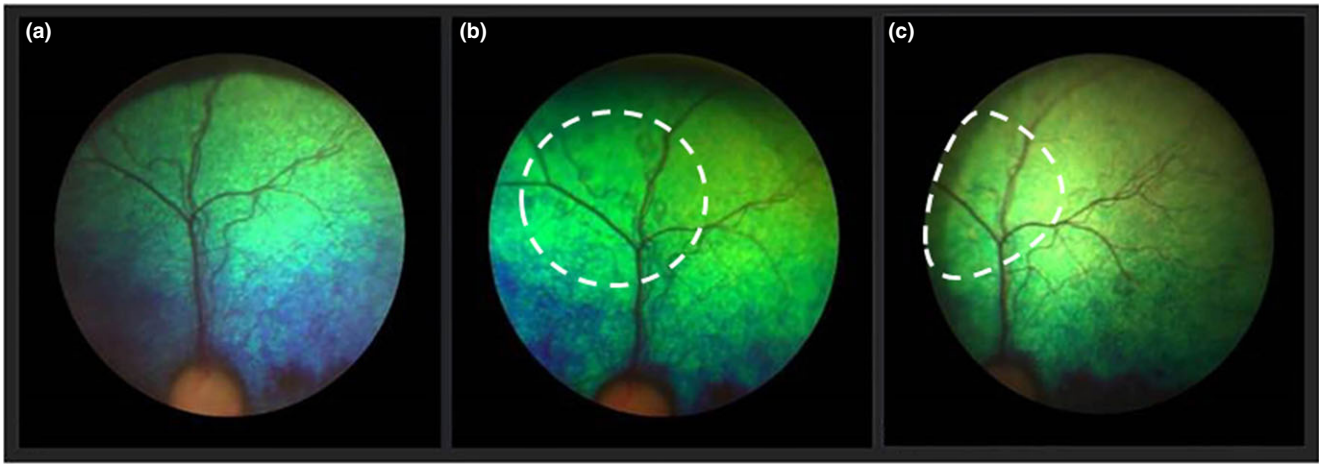

Figure 2. Sequential fundus photographs of an affected male (dog #2). a: At 3 months of age, the fundus appeared close to normal. b: At 6 months of age, multifocal retinal bullae had developed, mainly in the tapetal area. c: At 12 months of age, there was generalized hyperreflectivity. Even though this fundus picture was taken in slightly different angle, there were no perceptible retinal bullae (compare the dashed line areas of the pictures b and c).

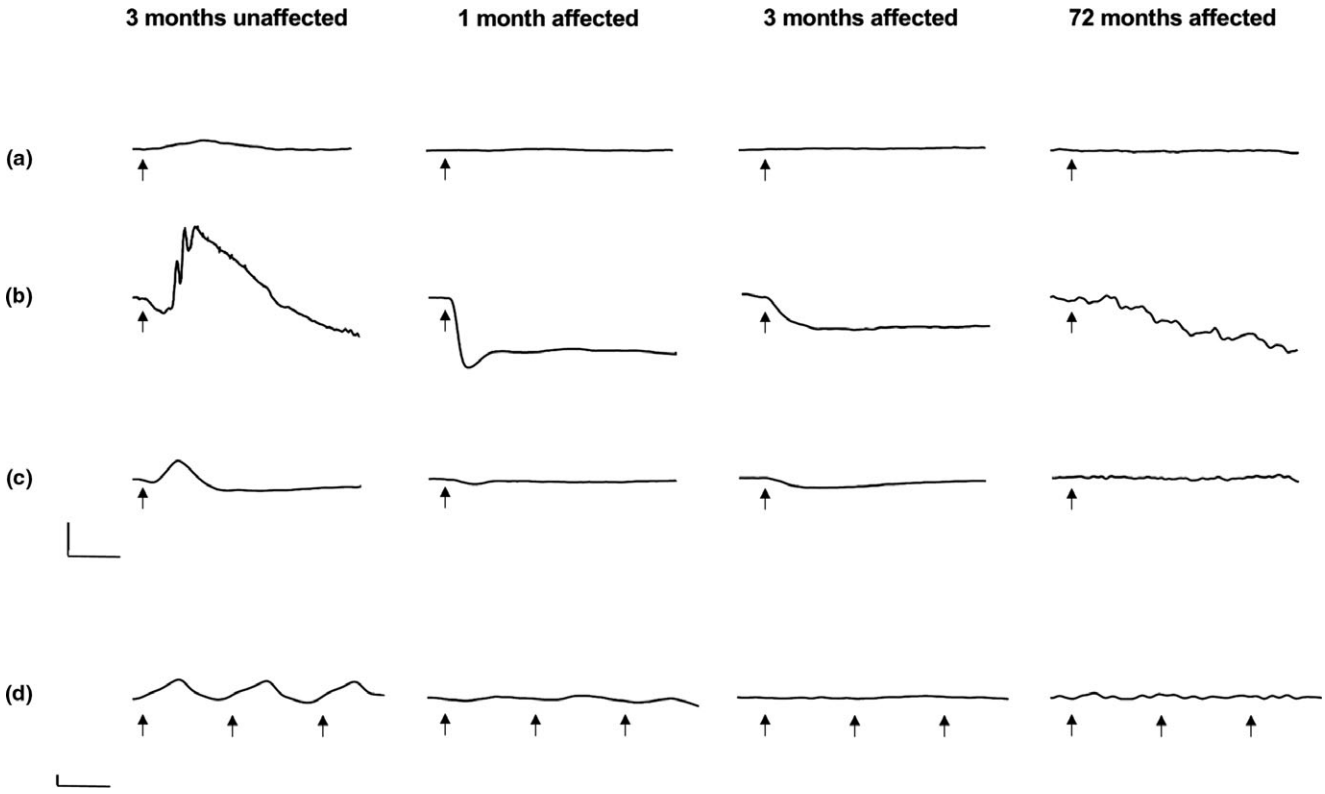

Figure 3. Representative standard ERGs recorded from normal and affected Whippet dogs. In a, animals were dark-adapted for 20 min and stimulated with a flash of −2 log cds/m^2 (rod-driven response); b, animals were stimulated with a flash of 0.47 log cds/m^2 (combined rod–cone-driven response); c, animals were light-adapted for 10 min and stimulated with a higher intensity flash of 1 log cds/m^2 (cone driven response); and d, animals were stimulated with a 30 Hz flicker at the same intensity of 1 log cds/m^2. Note that the ERG morphology of the affected dogs consisted of an a-wave discernable only in response to the brighter stimulus. Flicker responses are decreased in amplitude compared to unaffected controls. Note that all ERG responses decrease with age in affected dogs being almost completely extinguished by 72 months. Size bars: vertical = 100 μV (a–d); horizontal = 50 ms (a–c) and 20 ms (d). Arrows = stimulus flash.

progressive, typically rod-led photoreceptor degeneration, resulting in an initial loss of night vision and a generalized, bilateral retinal thinning and eventual complete vision loss. PRA has been reported in more than 100 breeds of dog.[9] Clinical, electrophysiological[9–15] morphological,[10–15] and molecular[16–22] aspects were characterized

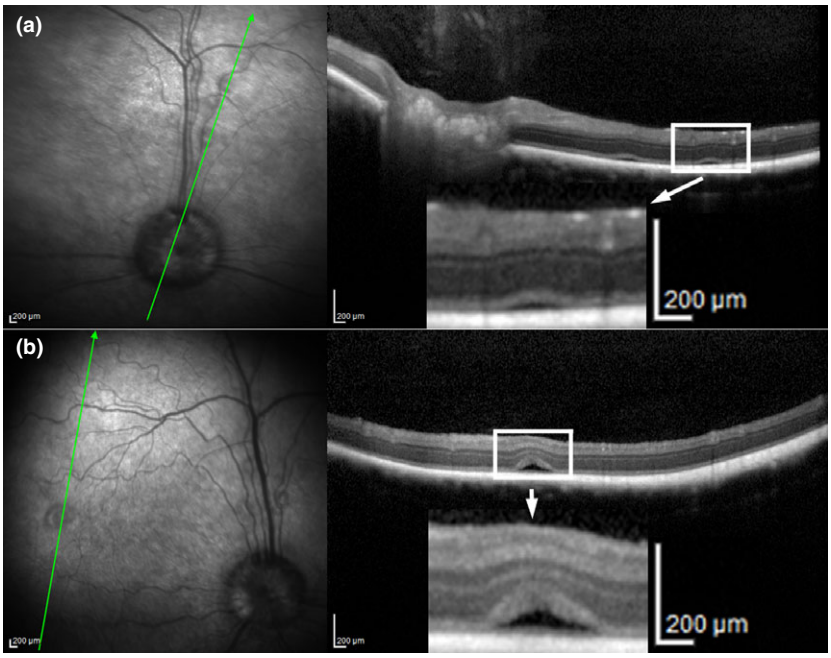

Figure 4. cSLO fundus image and OCT high resolution cross-section retinal images of a. a 5-month-old affected dog #2 and b. an 8-month-old affected dog #3. Multiple small retinal bullous detachments (bullae) are present. On the magnified images, some separation between the photoreceptors and the retinal pigmentary epithelium can be seen. Additionally, photoreceptor layer (IS/OS) appears thickened and ONL and INL appear somewhat thinner in the detached area.

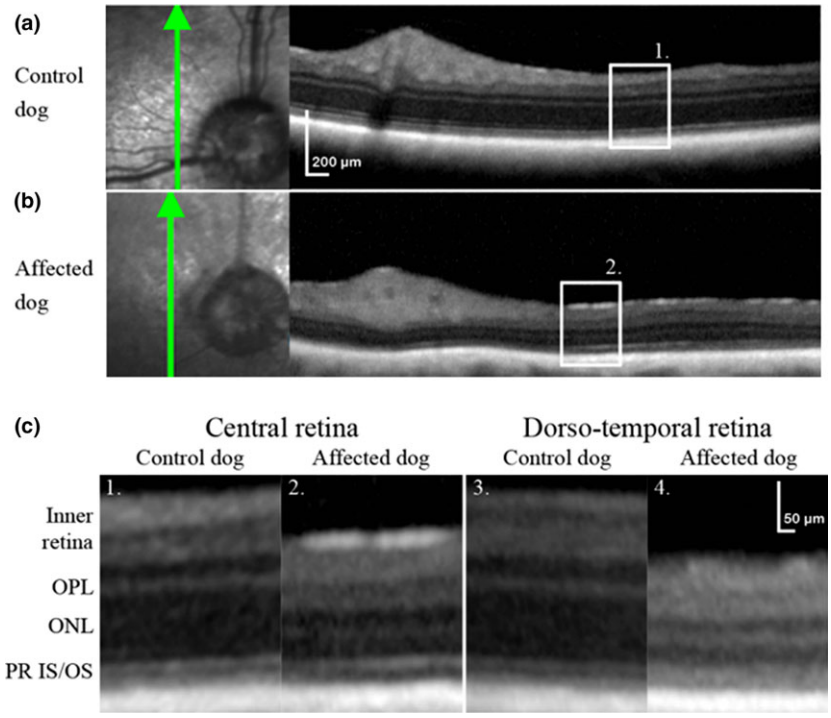

Figure 5. cSLO fundus images and OCT high-resolution cross-section retinal images of a. a 5-month-old unaffected dog #20 and b. an 18-month-old affected dog #4. c. Magnified view of OCT images of the central retina from the control (c1) and affected dog (c2) (site indicated by white boxes in a. and b.). c3 and c4 are OCT images from the peripheral (dorso-temporal) retina of the same control and affected dogs. Note that there is severe thinning of the outer nuclear layer and also of the total retina in both retinal regions in the affected animal. Key: OPL—outer plexiform layer; ONL—outer nuclear layer; PR IS/OS—photoreceptor inner segment and outer segment layer.

in several of these breeds. PRA is an important condition because it is a common cause of vision loss in dogs, but it also has value from a comparative point of view being the counterpart of human retinal dystrophies such as retinitis pigmentosa (RP) and some forms of Leber congenital amaurosis.[22]

Here, we report the phenotype of an inherited progressive retinal degeneration in Whippets, which has features quite distinct from previously described canine retinal dystrophies. PRA has been previously reported in related sight hounds including the Greyhound and Italian Greyhound[23,24], but there are only a few reports of this disease in Whippets.[3,9] Although Whippets are related closely to those two breeds[25] the phenotype of the PRA that we describe in this study is markedly different from that in the other sight hounds. Retinal degeneration due to PRA in Greyhounds becomes apparent between 12 and 18 months of age[22], and in the Italian Greyhounds, clinical signs develop between 5 and 8 years of age.[23] In this study, we showed that affected Whippets had an early loss

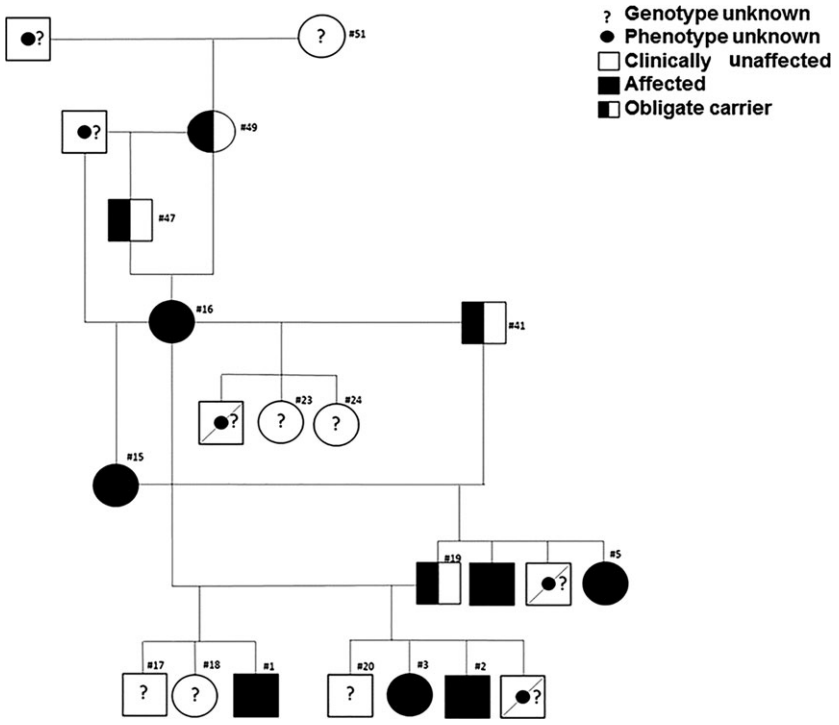

Figure 6. Pedigree of one Whippet dog family in which PRA was segregating. All dogs classified as clinically unaffected and affected were examined by indirect ophthalmoscopy at an age at which retinal thinning was well developed in all the affected dogs. The pedigree supports an autosomal recessive mode of inheritance with both males and females being affected, and in this lineage, an affected dog (#16) is produced from the mating of two phenotypically normal dogs (#47 and #49).

of rod-mediated vision and had abnormal ERG changes from the earliest time point assessed (1 month of age), prior to complete retinal maturation.

The youngest affected Whippets examined (from 1 to 6 months of age) had an oscillatory nystagmus, similar to that previously described in RPE65-mutant Briards[26] and as seen in humans with severe early-onset vision loss such as Leber Congenital Amaurosis.[22] Interestingly, affected adult dogs with advanced retinal degeneration and total blindness did not show nystagmus. In common with typical PRA in dogs[5,27–29] and RP in humans[30,31] rod-mediated vision was reduced initially (detectable from 1 month of age). Although impaired dim-light vision could be demonstrated by vision testing, owners did not usually notice it until the dogs were 1 to even 2 years of age at which stage there was advanced retinal degeneration. The reason for this disparity between owners′ perception and actual progression of the disease is not clear, but conceivably vision loss may not have been detected by owners until cone vision was compromised and the range of lighting levels to which cones were responding was reduced. The authors have noted similar disparities between owner assessment of their dog's vision and that detected by careful vision testing in dogs with forms of PRA associated with a lack of development of rod function.

Fundus examination of two young animals (animals #2 and #3) revealed the development of multiple small retinal bullae (small retinal detachments) prior to detectable retinal atrophy. With progression of retinal atrophy, the bullae became less apparent and eventually were not detectable. Retinal bullae were not detected in older dogs with end-stage retinal atrophy, and as these dogs had not been examined ophthalmoscopically at a younger age, it was not possible to tell whether similar lesions had been present in all dogs at early disease stages.

In scotopic conditions with a dim flash, the a-wave reflects hyperpolarization of rods while the b-wave reflects the rod (ON) bipolar cell depolarization.[32] In scotopic conditions with the use of a photopic flash, the a-wave reflects hyperpolarization of both cones and rods while b-wave reflects depolarization of both ON rod bipolar cells and ON cone bipolar cells.[33] In photopic conditions with the use of flash stimulus, the a-wave reflects the hyperpolarization of cones plus hyperpolarization of OFF cone bipolar cells[34] while the b-wave reflects the depolarization of all cone ON bipolar cells limited by hyperpolarization of cone OFF bipolar cells.[35] With the use of a 30 Hz flicker, waves reflect hyperpolarization plus depolarization of diffuse cone ON and OFF bipolar cells.[36,37] Thus, a lack of b-wave and a decrease in flicker wave could be related to postsynaptic changes.

There are several retinal dystrophies that result in an ERG with a reduced or absent b-wave. Many of these are stationary conditions (congenital stationary night blindness: CSNB) that result from mutations in either genes encoding presynaptic photoreceptor proteins or in those expressed in the synaptic tips of bipolar cells. CSNB is well recognized in human ophthalmology and divided into different categories based on the details of the ERG and fundus changes.[38] Several spontaneous and engineered mouse models have also been characterized and are commonly referred to as *nob* (no b-wave) mice.[39]

Recently, a phenotype similar to the Schubert-Bornschein form of complete CSNB in humans was described in Beagles and, despite screening candidate genes, the causal gene mutation was not identified.[38] CSNB has been recognized for many years in the Appaloosa horse and more recently was shown to be due to a mutation in *Trpm1* which encodes a channel protein important in bipolar cell function and melanocyte biology.[40] Most dystrophies characterized by altered ON bipolar cell function are stationary. The loss of both scotopic and photopic b-wave suggests that an ON bipolar cell defect may be responsible for the condition in the Whippets, but the affected dogs went on to develop a progressive retinal degeneration which is not reported for known ON bipolar cell gene mutations. The three Whippets in which ERGs were recorded and were found to have a lack of b-wave all developed a progressive retinal degeneration, whereas the littermates with a normal ERG did not. While it seems highly likely that the ERG changes represent the earliest abnormalities due to the gene mutation that causes retinal degeneration, there is still a slight possibility that two separate hereditary conditions are segregating within the same family.

Further breeding studies will enable this possibility to be explored. The young affected Whippets also had multiple small retinal bullae. OCT examination showed these to be small bullous retinal detachments. This feature distinguishes the retinal lesions in the Whippets from the fundus spots seen in human patients with fundus albipunctatus, which was an initial comparative suspicion because these human patients can also have a CSNB and an ERG with a reduced b-wave.[41] The small bullae seen in the Whippets in this study appear clinically distinct from the lesions described in canine multifocal retinopathy (CMR) where lesions are usually larger and will often be characterized by having tan-colored subretinal fluid. Furthermore, CMR is not associated with the ERG changes seen in the young affected Whippets and does not typically lead to a generalized retinal degeneration, rather a patchy degeneration of the affected retinal regions.[42]

Pedigree analysis is supportive of an autosomal recessive mode of inheritance for the retinal degeneration. Similar numbers of affected males and females have been identified, and affected offspring were produced from the mating of two clinically normal dogs. However, establishment of a breeding colony would allow confirmation of the suspected mode of inheritance, as well provide subjects for further electrophysiologic and histopathological characterization.

In conclusion, we report an apparently unique retinal dystrophy leading to a generalized retinal degeneration typical of PRA. The phenotype of an ERG that lacks a b-wave coupled with the development of small retinal bullae then with progression loss of photoreceptors, an extinguished ERG and blindness is unlike previously characterized PRAs in dogs. Molecular studies to identify the causal gene mutation will allow for further understanding of disease mechanism in this condition.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Cecília Vargas da Costa for all the essential support since from the very beginning of this study, Dr. Luana Lins and Dr. Alexandre Luiz Pereira, for all the engagement during the ERG data acquisition, Dr. Naoye Shiokawa for kindly conducting the OCT procedures, and all participating Whippet owners.

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