Op – Ophthalmology
HEREDITARY RETINAL DISEASES

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INTRODUCTION

The spectrum of hereditary retinal disease in the dog is well defined and closely related to the intensive breeding patterns which are used in some breeds. Many retinopathies are often detected as the result of routine screening in the absence of dramatic clinical features or noticeable disturbance of sight for, while our clients may notice the painful or discoloured eye, few recognise the subtle variation in pupil size and many do not suspect sight deficiency until it is well established. The pathognomic features of retinal disease defined by ophthalmoscopic examination are changes in tapetal reflectivity and pigmentation, blood vessel congestion or attenuation, haemorrhage and retinal non-attachment. Thus, a combination of reduced tapetal reflectivity and intraretinal haemorrhage indicates active inflammation, whereas a zone of increased tapetal reflectivity or a patch of reduced pigmentation signifies post-inflammatory degeneration. Unfortunately, retinal pathology does not automatically flag its cause and, as such, dilemma in diagnosis is always possible. For example, the retinal degeneration which accompanies retinal dysplasia can be confused with post-inflammatory retinal degeneration and, without history, sudden acquired retinal degeneration (SARD) can look like progressive retinal atrophy (PRA).

The range of retinopathy in the dog has been largely defined and new retinopathies are relatively few and far between. Central PRA appears to be a misnomer because the condition is a secondary photoreceptor degeneration due to abnormal retinal pigment epithelial activity, which appears to be governed by environmental or metabolic factors to some extent. Thus, a classical ocular diagnosis becomes an ocular feature of a condition of unspecified aetiology, yet one that demonstrates breed predisposition. Sadly more canine breeds become involved in the PRA story of inherited photoreceptor degeneration. Similarly more breeds are becoming involved in retinal dysplasia; the multifocal and total forms of this condition have been joined by a geographical lesion in the Cavalier King Charles and Retriever breeds. Collie Eye Anomaly is still the commonest inherited ocular disease in dogs in the United Kingdom but its recent appearance in the Lancashire Heeler suggests that a change in nomenclature would be appropriate.

THE RETINOPATHIES

Retinal Dysplasia

The term is applied to those inherited neuroretinal conditions which are seen clinically as either neuroretinal folds and rosettes or retinal non-attachment. The simplest manifestation of retinal dysplasia (R.D.) is a fold in the neuroretina, the affected dog demonstrating no associated visual impairment. Complicated folds in which there is proliferation of photoreceptor and RPE elements are also referred to as rosettes. This form of R.D. is inherited in the Cavalier King Charles Spaniel, the Hungarian Puli and the Rottweiler as a recessive trait. In the English Springer Spaniel the neuroretinal folds may be accompanied by retinal degeneration, these lesions taking on the appearance of post-inflammatory retinopathy due to the presence of melanin pigmentation. Occasionally retinal detachment complicates the clinical picture and both intraocular haemorrhage and cataract formation may be seen.

Collie Eye Anomaly

During organogenesis it is the cells of the posterior wall of the invaginating optic vesicle which form the primordial retinal pigment epithelium. Failure to express growth hormone by these cells affects the subsequent differentiation of the ocular tissues. In Collie Eye Anomaly (CEA) the choroid remains hypoplastic in an area lateral to the optic disc and there may be failure of the foetal fissure to close leaving a colobomatous defect involving either papillary or peripapillary tissue. The degree of choroidal hypoplasia and the size of the colobomata vary considerably between affected individuals and even between the eyes of the

same individual. All affected puppies demonstrate choroidal hypoplasia but by the age of twelve to sixteen weeks many may have masked the smaller lesions by melanin pigmentation. The estimates vary but in the U.K. it is likely that some thirty per cent of affected puppies demonstrate this masking procedure: somewhat confusingly this process is described as "go normal" status. The phenotype thus appears ophthalmoscopically normal but genetically these dogs are affected and must be avoided in disease control programmes. It is of considerable significance, underlying the necessity for screening all litters in the affected breeds

The diagnostic picture is understood well and painted in the above terms it would appear to be straightforward. However, like most things in life the story is not as black and white as it may seem and we do see problems which, at the very least, should provide discussion. I believe that there is a possible ten per cent error in diagnosis due to several features : the small papillary coloboma in the six week old puppy, the significance of the pale pink patch in the six week old fundus, the reduction of peripapillary pigmentation in the sable and white or colour dilute dog and the merle eye. Add to this the "go normal" phenomenon and the significance of the coloboma which is unaccompanied by choroidal hypoplasia. Thus life behind the ophthalmoscope can become difficult! Fortunately a mutation based DNA test for choroidal hypoplasia is now available.

A recent publication reported CEA in the Lancashire Heeler breed of terrier, and this puts the cat amongst the nomenclature pigeons! The author suggests that new terminology is required and suggests that "Congenital Posterior Segment Anomaly" (CPSA) might fit the bill.

Progressive Retinal Atrophy

Progressive retinal atrophy (PRA) is the umbrella term used to describe a number of inherited neuroretinal degenerations. Generalised PRA, or simply PRA, describes those degenerations in which the primary focus of disease is the photoreceptor unit. Such degenerations are characterised by a nyctalopia which progresses to total blindness and involves a high incidence of secondary cataract formation. All these diseases bar one are inherited as simple autosomal recessive traits.

The ophthalmoscopic signs are similar for each type of PRA, but the aetiologies vary considerably. For example dysplasia of the rod and cone photoreceptors has been described in the Irish Setter and Rough Collie breeds. As such this type of PRA is an early onset disease with severe impairment of vision being present at eight months of age and total blindness at twelve months. The photoreceptor defect is an enzyme abnormality within the phototransduction cascade. Specifically the retinal level of the nucleotide cyclic guanosine monophosphate (cGMP) is elevated to approximately ten times its normal value due to reduced cGMP-phosphodiesterase activity.

A second form of PRA in which the rod photoreceptor unit is dysplastic and there is subsequent degeneration of normal cone photoreceptors has been described in the Norwegian Elkhound. The initiatory rod defect remains undermined, as does the cause of a third form of PRA, a disease seen classically in the Miniature and Toy Poodle breeds, the English Cocker Spaniel and the Labrador Retriever. Here there is normal development of both photoreceptor units but blindness is caused by their premature degeneration in middle age. Fortunately the disease control picture for all types of PRA is improving in that several DNA based tests are now available and others are in the development stages.

Retinal Pigment Epithelial Dystrophy

Originally considered to be a primary photoreceptor degeneration, this disease is due to defect of the RPE. One of the many important functions of RPE cells is the degradation of utilised photoreceptor outer segment (POS). Dystrophic RPE cells can neither degrade utilised POS quickly enough nor effectively participate in POS production. Their cytoplasm accumulates phagocytosed POS material and their many other functions in terms of neuroretinal support cease. Thus the rod and cone photoreceptors degenerate and sight is affected. Affected dogs therefore lose their central field of vision but maintain peripheral sight. There is undoubtedly genetic predisposition to this disease as witnessed by specific breed involvement but many factors influence the course of degeneration, most significantly vitamin E.