CEROID-LIPOFUSCINOSIS IN TWO SALUKI DOGS

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INTRODUCTION

The ceroid-lipofuscinoses form a group of inheritable diseases occurring in man in which ceroid-lipofuscin pigment accumulates in cells, particularly in neurones and glial cells of the central nervous system, retina and ganglia. Nervous signs are seen at varying ages from infancy to adulthood in association with these findings and the syndromes have various eponymous designations e.g. Jansky-Bielchowsky's disease, Batten's disease and Kuf's disease (Dustin, Tondeur and Libert, 1978).

Neuronal ceroid-lipofuscinosis occurs as an inheritable disease in English Setters and has been compared with the juvenile form of familial amaurotic idiocy (Batten's disease) in man (Hagan, 1953; Koppang, 1970). A similar condition has been reported in Chihuahuas in New Zealand and Australia (Rac and Giesecke, 1975; Jolly and Hartley, 1977) and Cummings and De Lahunta (1977) described a single case in an adult wire-haired Dachshund, and compared the condition with Kuf's disease in man.

Similar diseases have also been described in cattle (Read and Bridges, 1969) and sheep (Jolly, Janmaat, West and Morrison, 1980).

The purpose of this contribution is to present two cases of neuronal ceroid-lipofuscinosis in related Saluki dogs. The findings closely resemble those described in the English Setter and appear to be the first such cases described in the Saluki breed. Many Saluki breeders are aware of the problem and are attempting to modify their breeding programmes accordingly.

CLINICAL HISTORY

Two, pure-bred, 2-year-old animals, one male and one female, were presented for clinical examination. They were from related litters and were said to have shown increasing signs of hyperaesthesia and blindness from one year of age. The male came from a litter of seven and at least two of his litter mates were also affected clinically.

On examination, both showed inco-ordination and "swimming" movements associated with paresis of neck and limb muscles. They were unable to stand,

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even when supported, but showed no evidence of pain or obvious impairment of vision. No other clinical abnormalities were observed. The male, examined on two occasions, showed slight depression of blood glucose and a normal concentration of blood urea. Liver function tests showed no abnormality.

The familial relationships of the group from which these dogs came are indicated diagrammatically in Fig. 1, which shows only mated animals and offspring known to be affected. More distantly related animals are indicated by a double symbol. All breeding took place between clinically normal dogs.

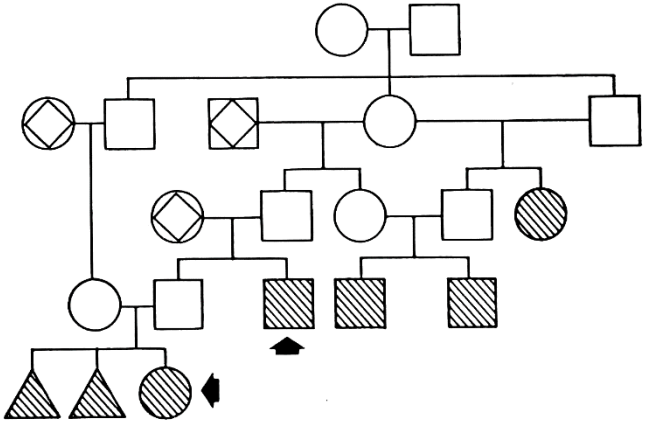

Fig. 1. Familial relationships of the two cases studied and of other affected animals. □, male; ○, female; △, sex unknown; ◇, distant relatives; ▩, affected animals; →, cases reported.

RESULTS

Pathological Examination

Following euthanasia the two affected animals were examined and no significant, gross abnormalities were found in either.

Histological examination of haematoxylin and eosin-stained paraffin sections prepared by standard methods shows marked changes in the cerebrum, thalamus, hippocampus, cerebellum and medulla of both animals. The most obvious change is seen in large neurones which show numerous, prominent and closely packed pinkish masses resembling ceroid which replace much of the cytoplasm (Figs 2 and 3). Small neurones and other cells resembling glia are also affected.

The cytoplasmic masses stain densely with Sudan Black and with Luxol Fast Blue. They are periodic acid–Schiff-positive and show autofluorescence with ultraviolet light. Similar material is present in enteric ganglion cells and in the ganglion cell layer of the retina. Many of the neurones retain their normal form but evidence of damage is seen, especially in the cerebellum where some Purkinje cells are lost. Large clumps of pigment, evidently representing degenerate cells, are present in the granular cell layer and elsewhere.

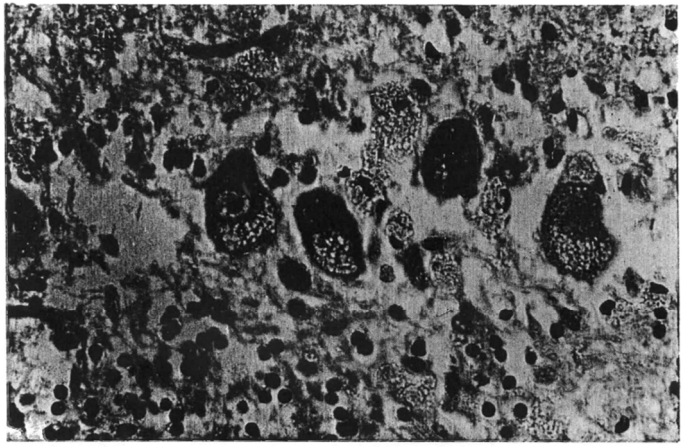

Fig. 2. Cerebellar folium. Pigment in Purkinje cells and degenerating cells. HE ×400.

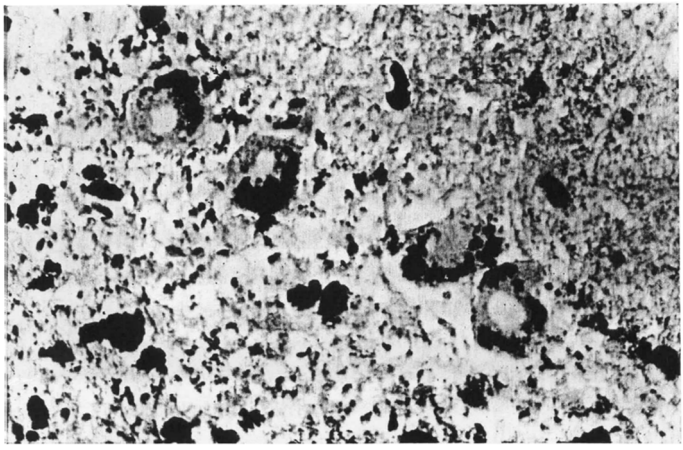

Fig. 3. Cerebellar folium. Pigment in Purkinje cells, molecular layer and granular layer. Sudan Black ×400.

Electron micrographs of brain tissue (fixed in glutaraldehyde and osmium tetroxide following extended formalin fixation) show masses of laminar inclusions in the cytoplasm of neurones: these masses have a whorl or "finger-print" pattern in some instances and resemble bundles or stacks of sectioned plates in others. The photographs show some evidence of a single membrane surrounding the inclusions. (Fig. 4.)

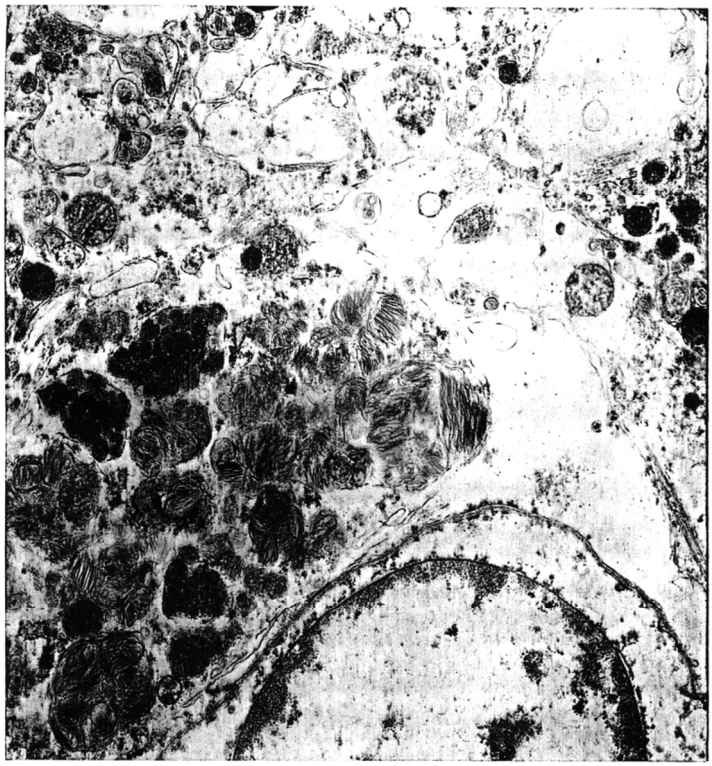

Fig. 4. Hippocampal neurone. Membrane-bound, laminated inclusions adjacent to nucleus. ×12 715.

DISCUSSION

The clinical history suggests an inherited disturbance of the central nervous system associated with an autosomal recessive factor. The light microscope findings and, in particular, the appearance of the inclusions on electron micrography correspond closely with descriptions of neuronal ceroid-lipo-

fuscinosis in the literature, especially Koppang's (1970) account of the disease in English Setters.

According to Zeman and Siakotos (1973), a detailed study of the electron-micrographic appearance of the neuronal inclusions may prove an unsatisfactory basis for distinguishing between the different syndromes associated with human ceroid-lipofuscinosis. In our cases, the age of onset of the disease suggests a parallel with the juvenile form of familial amaurotic idiocy (Batten's disease), thus resembling the condition described in the English Setter and Chihuahua, rather than with the adult form (Kuf's disease) with which the case reported in a Dachshund may be compared.

Other forms of neuronal lipidosis in dogs have been reported, for example, GM_2 gangliosidosis in German Short-haired Pointers (Karbe, 1973) and a possibly related condition in Cocker Spaniels (Ribelin and Kinter, 1956; Fankhauser and Luginbühl, 1968; Koppang, 1970). In contrast to GM_2 gangliosidosis, ceroid-lipofuscinosis is considered not to be a primary lysosomal disorder. Zeman and Siakotos (1973) suggest that, in the latter condition, the pigment is formed in the cytoplasm and only later incorporated into the lysosomes by autophagy. They also suggest that whereas lipofuscin can be formed from lipids and fatty acids in the cytoplasmic pool and causes little interference with cell function, ceroid formation may involve damage to intracellular membrane structures and lead eventually to cell death.

The underlying mechanism may involve the excessive peroxidation of polyunsaturated fatty acids. Following studies on Batten's disease in man (Armstrong, Dimmit and Van Wormer, 1974), Patel, Koppang, Patel and Zeman (1974) found a similar marked reduction in *p*-phenylenediamine-mediated peroxidase in the circulating leucocytes of English Setters homozygous for ceroid-lipofuscinosis and an intermediate activity in heterozygotic animals.

Zeman and Siakotos (1973) suggest that different mechanisms may be involved in the different forms of human ceroid-lipofuscinosis and so animal models may still be of value in comparative research.

SUMMARY

Two 2-year-old Saluki dogs from related litters developed nervous signs from 1 year of age and showed inco-ordination, swimming movements and inability to stand.

The principal pathological finding was the presence of intracytoplasmic, lipoid pigment masses in large neurones of the brain, retina and enteric ganglia. The pigment was autofluorescent, stained positively with Sudan Black and Luxol Fast Blue and with HE staining resembled ceroid. Electron micrography showed membrane-bound masses of laminar inclusions in patterns of whorls or bundles in the cytoplasm of neurones.

The clinical history and pathological appearances resemble those of an inheritable type of neuronal ceroid-lipofuscinosis (juvenile familial amaurotic idiocy, Batten's disease) described in man and in the English Setter. This is believed to be the first report in the Saluki breed.