OVINE CEROID-LIPOFUSCINOSIS

A thesis presented in partial fulfilment (70%)
of the requirements for the degree of
Master of Veterinary Science
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Antonie Janmaat
1979

to my parents

..."Ie hebt 't good edôan"...

ABSTRACT

Ovine ceroid-lipofuscinosis is a rare inherited neurological disease which has only been diagnosed in one family of the South Hampshire breed of sheep. This breed is of relative recent origin and was established from an initial cross between Southdown and Hampshire Down sheep. Affected sheep show loss of vision and behavioural abnormalities starting at 11-12 months of age, with motor dysfunction commencing soon afterwards. The clinical signs increase in severity as the disease progresses and under field conditions affected animals are not expected to live beyond 2 years.

Ovine ceroid-lipofuscinosis is characterized histologically by the intracytoplasmic accumulation of PAS and Sudan black positive autofluorescent lipopigment material in neurons and a wide variety of other cell types. The process leading to the accumulation of lipopigment seems only to damage neurons and there is degeneration and loss of neurons, especially in the cerebral cortex and the visual neuroepithelium of the retina i.e. retinal atrophy. Grossly, affected brains show reduction in size and weigh on average 66% of those of normal sheep.

Ultrastructurally, the typical lipopigment inclusion is a round or oval body 0.2 - 5.0 µm in size, of varying electron density, in which a wide variety of membranous profiles may be seen. Some of the membranous patterns have received special names such as curvilinear, fingerprint and crystalloid.

Pathological examination of liver, skin and rectal biopsy material of lambs at 4 - 5 months of age shows the presence of accumulated lipopigment, and is a means of early diagnosis before the onset of clinical signs. This observation and the fact that lipopigment has been demonstrated in affected lambs at birth, show ovine ceroid-lipofuscinosis to be associated with a true inborn error of metabolism.

The family tree of all affected sheep and the results of sire-daughter matings of a heterozygous ram show the disease to be inherited as a simple autosomal recessive trait. The deleterious gene for ovine ceroid-lipofuscinosis is unlikely to be of economic importance to the sheep industry as the South Hampshire breed was developed to supply sires for terminal crosses associated with table lamb production.

The objects of this study were to define ovine ceroid-lipofuscinosis in clinical, pathological and genetic terms, and to compare it with similar diseases in man and domestic animals. It is concluded that the ovine disease does indeed belong to the heterogeneous group of diseases of man and domestic animals known as Batten's disease or the neuronal or generalised ceroid-lipofuscinoses. Of these the ovine entity most closely resembles the late infantile and the juvenile forms of the human syndrome, and the canine disease. It is proposed that ovine ceroid-lipofuscinosis would make a useful experimental model for Batten's disease.

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