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NEUROPATHOLOGY OF OVINE CEROID-LIPOFUSCINOSIS

A thesis presented in partial fulfilment (30%) of
the requirements for the degree of
Master of Philosophy in Veterinary Pathology at
Massey University

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1987

From

A handwritten signature in black ink, appearing to be 'A. Shimada' or similar, written in a cursive style.

ABSTRACT

The purposes of this study were to describe the neuropathology of ovine ceroid-lipofuscinosis, to compare findings with those of the related entities in humans and other domestic animals, and to provide morphological information that might help elucidate the pathogenesis of these diseases. An established flock of South Hampshire sheep carrying the ceroid-lipofuscinosis gene have made it possible to perform a longitudinal study on the central nervous system of affected sheep of various ages including fetuses.

The most striking gross pathological change of affected sheep was brain atrophy. At terminal disease, the brain weights of affected sheep were 55% of those of normal sheep. Atrophy affected mainly the cerebrum.

Sudan black and luxol fast blue positive autofluorescent neuronal pigment granules were detected by light microscopy as early as the mid stage of foetal development, the earliest stage examined. Postnatally there were topographical differences in the quantity of accumulated lipopigments in neurones of various areas. Similarly, there were age related topographical differences in secondary degenerative changes. Neuronal loss was most severe in the parietal lobe cortex showing an initial laminar distribution. This pattern was well demonstrated by a concomitant astrocytosis.

In addition to the complex electron dense cytosomes similar to those reported in the human syndromes, there were less complex cytosomes of smaller size in affected foetal brains. The latter were clearly bounded by a trilaminar membrane and contained whorls or loose stacks of trilaminar membranes resembling those of the limiting membranes. In some electronmicrographs there was a suggestion of continuity between the surrounding membrane and

the internal membranes, but this was not definitely demonstrated. This is provisionally interpreted as being due to an internalization of surrounding limiting membrane rather than a recycling of membrane. Some of these small cytosomes also showed complex multilamellar profiles similar to those of large complex cytosomes. These latter appeared to be formed by coalescence of smaller complex ones. There thus appeared to be a sequence of changes in the development of storage cytosomes.

This study revealed that the ovine disease has not only many neuropathological findings in common with analogous human diseases, but also some pathological features which have not been reported in affected humans or animals. Ovine ceroid-lipofuscinosis is thus a useful animal model for the study of the human ceroid-lipofuscinoses.

ACKNOWLEDGEMENTS

This study was performed using the facilities of the Department of Veterinary Pathology and Public Health at Massey University. I would like to thank Professor B.W. Manktelow, Head of the Department, for making these available. I am particularly grateful to Professor R.D. Jolly, my supervisor, for providing me with the opportunity to undertake this project and his continuous help and encouragement throughout the study.

Advice on the interpretation of light and electron microscopy was also provided by Dr. W.J. Hartley, pathologist at Taronga Zoo, Australia. Dr. D.N. Palmer and Mr. R.D. Martinus, who are members of the team working on ovine ceroid-lipofuscinosis in this laboratory, have also provided help in my understanding of biochemical aspects of the disease. Their encouragement was greatly appreciated.

I also wish to acknowledge the help of Mr. M.J. Birtles of the Department of Physiology and Anatomy in the preparation of tissues for the immunocytochemical study, Dr. A.S. Davies of the Department of Physiology and Anatomy in the study of ovine neuroanatomy, and Mrs. L.R. Dickson of the Department of Veterinary Clinical Science and fifth year B.V.Sc. students in the caesarean sections which provided fetuses for the study.

Special thanks are also due to Mr. D.H. Hopcroft and Mr. R.J. Bennett of the Department of Scientific and Industrial Research who gave advice on the preparation of tissues for electron microscopy and printed the electronmicrographs, and Mr. T.G. Law and the staff at the Central Photographic Unit who printed the lightmicrographs.

I would like to thank Mrs. P.M. Slack and Mrs. P.M. Davey for their great help in the preparation of tissues for light and fluorescent microscopy, Mr. F.K. Sharpe for his assistance

in post-mortem room, and Mrs. A.A. Scott for her assistance in the use of word processing program and in printing the final copy.

Finally I would also like to express thankfulness to my family in Japan for their continuous encouragement, and my wife, Naoko, and my son, Kentaro, for their patience and help.

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