Degenerative Changes in the Cerebral Cortex in Swayback Disease Lambs

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Summary

The study was undertaken to determine if there were differences in the degree of degeneration in different parts of the cerebral cortex in swayback disease in lambs. Histopathologic sections from the frontal, occipital, pyriform parietal lobes, the hippocampus, caudate nucleus showed that the hippocampus was the least affected.

Key words: neuropathology, hippocampus, caudate nucleus, necrosis, cavitation, vacuolation

Swayback is a disease of lambs and kids of worldwide distribution characterised by hindlimb incoordination. Severely affected lambs may be paraplegic at birth. Affected lambs may be paraplegic at birth. Affected lambs may be blind. Slighty affected lambs may have weakened hindlimbs and may be unable to stand but those that are able to move do so with an unsteady gait and swaying motion.

The association of copper deficiency with the pathologic changes in swayback disease has been established by several people. The low copper levels in the blood is either as a result of low copper content in pastures which the animals graze or due to interference with copper metabolism by some elements (molybdenum, sulphur and iron) [Mc Dowell et al., 1993]. In Trinidad swayback is a fairly common disease. Swayback disease in Trinidad is most likely as a result of low levels of copper in the pastures since copper levels of grasses in Trinidad have been found to be extremely low [Youssef and Brathwaite, 1987]. Some swayback cases develop in utero so that the animals die soon after birth. In other cases, the disease develops within the first six months of life. In Trinidad both types of swayback disease occurs.

Histopathologic diagnosis of swayback is usually based on lesions in the brainstem, the spinal cord and the cerebellum [Fell, 1987]. The lesions of this disease are found in the entire brain and spinal cord but the most remarkable lesions are found in the motor neurons of the brainstem, spinal cord and the cerebellum, [Roberts, et al. 1966, Seaman and Heartley 1981]. Even though lesions in the cerebral cortex have been well documented, it is not yet known if different parts of the cerebral cortex are equally affected. The objective of this study is to compare the histopathological lesions of this disease in different parts of the cerebral cortex.

Materials and Methods

Brains from four lambs affected by swayback were used for the study. The brains were fixed in 10% neutral buffered formalin for two weeks. Specimens were taken from the occipital, parietal, frontal, lobes, the hippocampus and pyriform lobes. The specimens were further fixed in 10% buffered neutral formalin for another two weeks before processing. The tissues were processed for normal histology and stained with haematoxylin and eosin. The main pathologic lesions which have been reported and which were found in swayback disease in this study are: (1) Vacuolation and cavitation; (2) Neuronal necrosis; (3) Glia infiltration; (4) Vascularisation; (5) Perineuronal vacuolation; (6) Perivascular necrosis. Of these the most common lesions are 1,2,3,5. These were the ones used for the evaluation. For each slide, five readings were taken from five parts of the slide. Each pathologic lesion is graded as: + (mild), ++ (moderate), +++ (severe), ++++ (very severe). The mean of the five readings for each lesion per slide was recorded as the score for that slide. The total of all the mean scores is recorded as the final score for the part of the brain. The score from different parts of the brain were then compared to determine the relative severity of the lesions.

Results

Neurodegeneration of the brain is manifested in several ways. The most common features of which are: cavitation and vacuolation. Others include, Neuronal necrosis; Glia infiltration; Vascularisation; Perineuronal necrosis; and Perivascular necrosis.
Fig. I shows vacuolation and cavitation of varying sizes in the neuropil. Cavitation is evidenced by slit-like areas of necrosis. In some cases this shows as cracks in the white matter. The molecular layer is usually less affected. The lesions are not confined to any particular layer or layers but the deeper areas of the cortex are usually more badly affected. These become more numerous and larger in the deeper parts of the gray matter bordering the white matter. In some cases there is radial necrosis. In severely affected cases, large cavities occur in the neuropil.

Necrosis of neurons occur in different forms. The pyramidal cells are usually more severely affected (fig. 2). These cells undergo coagulative necrosis in which the soma are homogeneously dark red. In some cases they lose their outline and disintegrate or lose their staining. Usually no nucleus or nucleoli can be differentiated. The granule cells lose clear nuclear boundaries. In some cases the cytoplasm loses its characteristic nissl stain. In severe cases the soma undergo liquefactive necrosis, is reabsorbed leaving empty cavities. The layers of the cortex containing pyramidal cells, i.e., the outer pyramidal layer and inner pyramidal layer are severely affected.

Glia infiltration is a very common feature of neurodegeneration in swayback. In mild cases, there is an increase in the number of glia cells in the area of degeneration. In most cases with severity of the condition gliosis become marked (fig. 3). Satellitosis is a common feature in which dead cells are surrounded by glia cells. In some cases the glia cells are plump an rounded and in other cases they

Table I: Mean scores for each of the lesions and the total scores of the lesions

<table>
<thead>
<tr>
<th></th>
<th>Brain I</th>
<th>Brain II</th>
<th>Brain III</th>
<th>Brain IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacuolation and Cavitiation</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Neuronal necrosis</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Glial infiltration</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Perineuronal vacuolation</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Total</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>
are dark and rod like. Satellite cells are usually plump and rounded. The satellite cells in some cases are surrounded by clear zones of necrosis indicating that they are elaborating substances that dissolve the tissue around them. In some severe cases the entire field is filled completely with glia cells masking the neurons in the field.

Table 2: Total scores from each of the brains and regions.

<table>
<thead>
<tr>
<th></th>
<th>Hippocampus</th>
<th>Pyramidal lobe</th>
<th>Caudate nucleus</th>
<th>Occipital lobe</th>
<th>Frontal lobe</th>
<th>Parietal lobe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain I</td>
<td>9</td>
<td>7.5</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>7.5</td>
</tr>
<tr>
<td>Brain II</td>
<td>5</td>
<td>10</td>
<td>10</td>
<td>8</td>
<td>6.5</td>
<td>8.5</td>
</tr>
<tr>
<td>Brain III</td>
<td>6</td>
<td>7</td>
<td>9</td>
<td>6</td>
<td>7</td>
<td>7.5</td>
</tr>
<tr>
<td>Brain IV</td>
<td>6</td>
<td>9</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>33.5</td>
<td>37</td>
<td>30</td>
<td>29.5</td>
<td>32.5</td>
</tr>
</tbody>
</table>

From table 2 above the total score for the hippocampus is the least and that of the caudate nucleus is the highest. The pyramidal, the occipital, the parietal and the frontal lobes seem to be fairly equally affected.

Vascularisation occurs but only in some cases. Where it occurs, there is a gradation. In several cases there are numerous capillaries in the gray matter. These do not seem to be confined to any layer or layers.

Perineuronal vacuolation ranges from a small space surrounding each neuron to marked spaces surrounding the cell bodies (fig. 4). In some cases the cell bodies are shrunken leaving large spaces.

Discussion

The association of degenerative changes in the central nervous system of swayback lambs and low levels of copper in the blood and liver has been established by many workers. Cavitation and vacuolation, extensive damage to cortical neurons, gliosis and perivenous and perineuronal vacuolation have been reported by several researchers [Roberts et al., 1966; Howell, 1968; Heartly, 1981; Inglis et al., 1986; Fell, 1987]. The vacuolation and cavitation give severely affected brains a spongy appearance. The vacuolation and cavitation are sometimes due to empty spaces left after
cell death and resorption; perivenous vacuolation and degeneration of the neuropil. Extensive damage to cortical neurons is a common feature of this disease (Seaman and Heartly, 1981). The pyramidal cells are more severely affected than the granule cells. The pyramidal cells are large cells which send their axons into the white matter and are responsible for the output from the cerebral cortex. The purkinje cells of the cerebellum, motor nuclei of the brainstem and the neurons of the ventral gray of the spinal cord are all efferent neurons and are all badly affected. Necrosis of neurons is accompanied by gliosis which is one of the most characteristic features of this disease. Astrogliosis has been frequently found in connection with swayback [Fell, 1987; Howell, 1968]. The role of glia cells has not been adequately investigated in swayback disease. Defective oligodendroglia as a result of the decrease in cytochrome oxidase has been proposed as the cause of myelin aphasia and demyelination that is seen in this disease but the role of microglia and astroglia in the disease has not been properly investigated. Microglia have been implicated in several central nervous system disorders such as stroke, multiple sclerosis and Alzheimer’s disease in man and may be involved in swayback as well.

Activation of microglial cells followed by reactive astrocyte changes has been known to contribute to brain inflammation and neuronal damage in neurodegenerative diseases by the release of reactive oxygen free radicals. The extensive damage to cortical neurons in swayback disease may be caused by the neurotoxic substances released by these glia as in Alzheimer disease.

Several hypothesis have been advanced to explain the pathophysiology of swayback disease. Impairment of oxygen diffusion due to cerebral edema combined with occlusive pressure on cerebral blood vessels has been proposed to account for some of the degenerative changes [Fell, 1987]. It has also been suggested that decreased activity of copper containing enzymes contribute largely to the pathophysiology of the disease. Cytochrome c - oxidase activity has been shown to be significantly lower in the brain tissue of swayback lambs than the brain from clinically normal lambs [Mills and Williams, 1962]. Copper is an essential component of several enzymes such as caeruloplasmin, dopaminine, superoxide dismutase, lysi oxidase, cytochrome c oxidase and tyrosinase. Superoxide dismutase is necessary to remove free radicals which can cause peroxidation in brain tissues a decrease of which can contribute to demyelination since dangerous free radicals can not be removed effectively from the brain tissue (Prohaska, 1987). Decreased cytochrome oxidase may result in reduced phospholipid synthesis which affects the integrity of cell and organelle membranes and also myelination (Mills and Williams, 1962).

The results of this study show that the hippocampus is the least affected and the caudate nucleus is most highly affected. The caudate nucleus is part of the extrapyramidal pathway which is severely affected in swayback. The pathognomonic lesions of this disease are vacuolation, chromatolysis and necrosis of these large motor neurons in the brainstem nuclei and ventral horn of the spinal cord (Barlow, 1991). The hipocampus is not a motor centre which may explain why it is not so badly affected. It can not be determined from this study whether the differences that exist between the cortical areas is significant or not. A more comprehensive study involving a larger number of brains and more areas of the cerebrum is currently being undertaken in order to determine the significance of the differences.

References


