HEARTWATER IN ANGORA GOATS. II. A PATHOLOGICAL STUDY OF ARTIFICIALLY INFECTED, TREATED AND UNTREATED GOATS

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ABSTRACT


Pathological lesions in untreated Angora goats infected with the Ball, strain of *Cowdria ruminantium* corresponded with those previously reported. A severe nephrosis was the most prominent pathological lesion in the animals treated after the 1st day of the febrile reaction. Renal ischaemia appears to be central to the pathogenesis of the kidney lesions.

INTRODUCTION

The pathology of heartwater (HW) in cattle, sheep and goats has been described by Steck (1928), Alexander Pienaar (1970). Treatment after the 1st day of the febrile response.

Microscopical pathology

Various organs, including the kidneys, liver, spleen, brain, lungs and heart, were collected in 10% buffered formalin from each of the animals.

Paraffin sections were prepared from selected tissue blocks and stained with haematoxylin and eosin (HE), according to routine procedures. Special staining techniques, such as the Pickworth's benzidine method for haemoglobin, Perl's method for haemosiderin, Periodic acid Schiff's (PAS) reaction for mucopolysaccharides, Schmorl's technique for lipofuscin and Von Gieson's technique for collagen (Aron, 1968; Pearse, 1961), were applied to selected kidney sections.

Brain smears

Brain smears were prepared from the hippocampus of each animal according to the method described by Purchase (1945), and were stained with a 10% Giemsa solution for 45 min.

RESULTS

Clinical signs

Untreated goats

The incubation period ranged from 11-13 d (Table 1). During the febrile reactions, a gradual inappetence was noticed, and the goats were less inclined to move around. Respiration was costo-abdominal, and the respiratory rate gradually increased. A progressively unsteady gait was noticed, and the animals eventually stood with legs apart and head down. Terminally, the goats were hypothermic and dyspnoeic, and they died without showing pronounced nervous symptoms, although chewing movements and licking of the lips were noted.

Treated goats

The incubation period and maximum temperatures are recorded in Table 1. Inappetence was noted during the febrile reaction. After treatment, the goats gradually became lethargic and dehydrated, with congestion of the conjunctivae. They became comatose, hypothermic and dyspnoeic with occasional grinding of teeth and frothing at the mouth (Fig. 1).

Clinical pathology

The results are summarized in Table 1. BUN values in the 3 control goats ranged from 25-52 mg/100 ml. In untreated goats it measured from 143-144 mg/100 ml and in treated goats from 200-254 mg/100 ml. Proteinuria was evident in all the treated and untreated goats.

Gross pathology

Untreated goats

Respiratory system and heart: A moderate hydrothorax was present in both animals, the thoracic cavity containing c. 400 ml of pale yellow fluid. The lungs in both

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cases showed a diffuse oedema with widened interlobular septae and froth in the trachea and bronchi. The ventral borders of the diaphragmatic lobes showed atelectasis due to the hydrothorax. Oedema of the mediastinum was a constant lesion. Approximately 30-40 ml of pale-yellow fluid was present in the pericardial sac.

**Lymph nodes and spleen:** In both animals the spleen was moderately enlarged. The cut surface was pulpy in consistency and dark red. Oedema of the lymph nodes, especially the mediastinal and bronchial nodes, was seen in both goats.

**Kidneys:** The kidneys were slightly swollen and pale, but the medulla was congested. A moderate perirenal oedema was present in 1 goat.

**Other organs:** Apart from a mild hepatomegaly and oedema of the abomasum in 1 goat, no other noteworthy changes were observed.

### Treated goats

**Respiratory system and heart:** A mild lung oedema, affecting mainly the ventral borders of the diaphragmatic lobes, and a mild oedema of the mediastinum were present in 1 goat.

**Lymph nodes and spleen:** Oedema of the renal lymph nodes was a consistent finding in all the goats. In the goat with lung oedema, the mediastinal and bronchial lymph nodes were mildly enlarged. The spleen was normal in size in all the cases.

**Kidneys:** In all the goats the kidneys had a light-brown colour, were mottled and were markedly swollen (Fig. 2 & 3). Scattered, subcapsular ecchymoses were present in 2 goats. A few cysts, approximately 0.5 mm in diameter, were scattered throughout the cortex in most of the goats. On the cut surface, the pale cortex was clearly demarcated from the congested medulla. Oedema of the renal pelvis was a consistent finding in all the cases. A mild perirenal oedema was noted in 2 of the animals.

**Other organs:** Apart from a catarrhal enteritis in 2 goats, no other noteworthy lesions were present.

### Microscopical pathology

#### Untreated goats

**Lungs:** The alveolar spaces were filled with a protein-rich fluid. It had a patchy distribution, alternating with groups of empty, distended alveolar spaces. Macrophages, with abundant, eosinophilic, vacuolated cytoplasm, a few fibrin strands and red blood cells were present in some of the alveolar spaces.

Alveolar capillaries were congested and contained increased numbers of macrophages. Lymph vessels were dilated and some contained eosinophilic fluid. Subpleural and interlobular connective tissue appeared separated and contained fibrin strands and scattered groups of macrophages, lymphocytes and neutrophils. Some of these cells showed nuclear pyknosis or karyorrhexis.

**Kidneys:** The extent of the lesions varied in the 2 goats. Glomerular capillaries were congested and contained increased numbers of monocytes. In a few glomeruli, eosinophilic fluid was noted in Bowman's spaces. In 1 goat, tubular dilatation of the proximal and distal convoluted tubules and, to a lesser extent, the collecting tubules were in evidence. In both goats, the tubular epithelial cells were mildly swollen. Other changes included cloudy swelling, hydropic degeneration and occasional hyalin droplet degeneration of a few tubules. In 1 goat, a moderate amount of intratubular hyalin casts was noted (Fig. 5). A few colonies of *C. ruminantium* were present in the glomerular capillaries in 1 goat.

**Brain:** A mild to moderate brain oedema manifested as a *status spongiosus* with a predilection for the white matter was present in various areas of the brain in both goats. Neuroglica with enlarged, vesiculated nuclei and
FIG. 4 Kidney of a control goat: HE × 100
FIG. 5 Nephrosis with eosinophilic casts in an untreated goat: HE × 100
FIG. 6-12 Kidney lesions in goats treated after the 1st day of the febrile reaction
FIG. 6 Acute nephrosis with numerous eosinophilic casts: HE × 100
FIG. 7 Dilatation of Bowman’s spaces, tubules and ducts: HE × 60
FIG. 8 Numerous strongly eosinophilic hyalin and granular casts: HE × 60
FIG. 9 Pigment laden tubular epithelial cells. Note the flattened epithelium of dilated tubules and the presence of cellular casts: HE × 400
abundant eosinophilic cytoplasm were present in these areas. Small intracytoplasmic globules were noted within the processes of these cells. Groups of swollen axons were observed in different areas of the brain. A multifocal vasculitis, affecting primarily small vessels, was noted in 1 goat. The vessel walls were infiltrated with round cells and a few neutrophils. Scattered foci of macrophages lymphocytes and neutrophils were found in the perivascular spaces throughout the brain. Some of the blood vessels contained increased numbers of macrophages.

Other organs: The bronchial and mediastinal lymph nodes were oedematous. Hepatic lesions included a mild leukostasis, cloudy swelling and hydropic degeneration of hepatocytes. Abomasal oedema was confirmed microscopically.

Treated goats

Lungs: An increased number of macrophages, some of which contained a yellow-brown pigment which stained positive for haemosiderin, was present in the alveolar interstitial tissue. A few macrophages with abundant eosinophilic vacuolated cytoplasm were evident in the alveolar spaces. Some of the capillaries contained increased numbers of monocytes and neutrophils. One goat showed a mild interstitial and alveolar oedema.

Kidneys: There was a variation in the severity of the histopathological lesions among the goats. Dilatation of the proximal and distal convoluted tubules and collecting ducts, with flattening of the lining epithelium in some, was a constant finding in all the goats. These tubules were randomly distributed. The epithelial cells of nondilated tubules were swollen, and the tubular lumen was occasionally completely obliterated. The tubular epithelial cytoplasm was eosinophilic, had a finely granular to vacuolated appearance and frequently contained large quantities of light-brown lipofuscin pigment. The nuclei were often located near the cell borders. Necrosis of the tubular epithelial cells was evident in all the goats. Epithelial regeneration was apparent in 6 of them. Many of the tubules contained large quantities of pale to strongly eosinophilic (slightly to strongly PAS-positive), hyalin casts and smaller quantities of pale to strongly eosinophilic granular or cellular casts (Fig. 6-9). The latter consisted of desquamated epithelial cells (vide supra), neutrophils, macrophages and smaller numbers of red blood cells and nuclear fragments. A close association between neutrophils and granular or hyalin casts was noted (Fig. 10).

In all the goats, the Bowman’s spaces were dilated and contained variable amounts of a pale to strongly eosinophilic fluid and occasionally red blood cells (Fig. 11). Within each kidney, the glomeruli showed a variety of lesions. Many capillaries were devoid of erythrocytes. Necrotic glomerular epithelial cells with abundant eosinophilic cytoplasm and occasional intracytoplasmic hyalin droplets were evident in most of the goats.

Hypertrophy of the parietal epithelial layer of Bowman’s capsule, with thickening of the basement membrane and periglomerular fibrosis, was present in most of the goats.
<table>
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N/A: Not available
† - †††: Increasing severity (arbitrary relative units)
Neg: Negative
UT: Untreated
A mild to moderate interstitial fibrosis was noted in animals with more advanced lesions (Fig. 12). Apart from fibroblasts, single or groups of neutrophils, lymphocytes, red blood cells and a few pigment-laden macrophages were seen in the interstitial tissue.

**Brain:** Brain lesions were similar to those described in the untreated goats (*vide supra*). In 3 goats, the lesions were very mild.

**Other organs:** In all the goats the renal lymph nodes were oedematous. Lesions corresponded with those described in the bronchial and mediastinal lymph nodes of untreated goats. Apart from a mild oedema of the abomasum in 1 goat, no other noteworthy lesions were observed.

**Brain smears**

Colonies of *C. ruminantium* were present in the brain smears of both untreated and 3 treated goats (Table 1).

**DISCUSSION**

The clinical signs in the untreated goats corresponded closely with those previously described in cattle, sheep and goats with the acute form of HW (Alexander, 1931). Marked nervous symptoms were not present in the goats during this study. According to Alexander (1931), nervous symptoms are usually more pronounced in cattle than in sheep and goats. The most striking difference between untreated and treated Angora goats was the severe dehydration and comatose state during the terminal stages of the disease in the treated animals.

Gross lesions in the untreated Angoras corresponded to a large extent with those described in 82 untreated goats naturally infected with HW (Steck, 1928). A nephrosis was present in c. 25 % of the cattle, sheep and goats (Steck, 1928). Alexander (1931) confirmed these results, although the percentage of animals with gross kidney lesions in his survey is not known. Although a mild nephrosis was present in the 2 untreated Angoras in our study, the numbers are too limited for statistical comparison with the results of Steck (1928) and Alexander (1931).

A severe nephrosis was the most striking lesion in all the goats treated for HW. This corresponded with field observations where a marked nephrosis and a high mortality were reported in Angoras after treatment. Information related to the pathological lesions in HW-infected ruminants subsequent to specific chemotherapy is limited. Ilemobade & Adeoye (1976) reported a high mortality in HW-infected brown goats, treated after the 2nd day of the febrile reaction. According to these authors, the naturally and artificially infected goats that died without any treatment did not show a nephrosis. It is not clear, however, whether the treated animals that died were examined pathologically.

Histopathological lesions in the kidneys of the 2 untreated Angoras included protein-rich material in Bowman's spaces, swelling of tubular epithelial cells and intratubular hyaline casts. These mild lesions correspond to a large extent with those reported in cattle, sheep and goats by Steck (1928). He described these lesions as fairly characteristic, although not very marked. Contrary to these findings, a severe acute to subacute nephrosis was noted histologically in all the treated goats in our study. Lesions included swelling of glomerular epithelial cells, accumulation of protein-rich fluid in distended Bowman's spaces and tubular dilatation with the presence of numerous hyalin, granular and cellular casts. An interstitial fibrosis with a mild to moderate neutrophil infiltration of the interstitial tissue was noted in goats with more advanced lesions. The absence of pathological lesions in 2 uninfected Angora goats, treated at dose rates of 20-40 mg/kg live mass with the same long-acting oxytetracycline * used during this experiment, excluded the drug as the cause of the nephrosis (L. Prozesky & J. L. du Plessis, unpublished data, 1982).

The 2 main causes of tubular necrosis are nephrotoxins and ischaemia or a combined effect of the 2 (Dunhill, 1974). To assess the presence of ischaemia, endogenous serum creatinine levels can be used as an index of the glomerular filtration rate, since most of the urine creatinine is filtered by the glomeruli (Duncan & Prasse, 1981). According to Smith (1963), cited by Benson & Williams (1974), a rise in blood creatinine occurs when the functional capacity of the kidneys falls below 25 %. Furthermore, one of the causes of increased BUN is a diminished glomerular filtration rate (Duncan & Prasse, 1981). The high BUN levels recorded in this study, therefore, may indicate a diminished glomerular filtration rate associated with renal ischaemia. However, increased BUN may also result from passive diffusion of nitrogen from the tubular lumen back into the blood (Duncan & Prasse, 1981). A significant increase in both serum creatinine and BUN values were recorded in 4 untreated HW infected Angora goats 3-4 d after the height of the febrile reaction (L. Prozesky & J. L. Du Plessis, unpublished data, 1983). These findings suggest a reduced renal blood flow, although the increased values may also be attributed to other factors (Duncan & Prasse, 1981).

The nephrosis that features so prominently in the experimental animals used in this study may in all probability therefore be associated with a renal ischaemia. This conclusion, however, should be drawn with caution as the possible role of a "toxin" in the pathogenesis of HW cannot be excluded and may contribute to the nephrosis (L. Prozesky & J. L. Du Plessis, unpublished data, 1984).

Clark (1962) suggested that death in HW-infected sheep is due to a sudden loss of peripheral vascular resistance (sympatholysis). In treated animals which do not recover but pass into a state of collapse, he concluded that the specific chemotherapy eliminates the infection in time to prevent death from circulatory collapse, but that irreversible brain damage had occurred. Brain lesions in our untreated Angoras were indistinguishable from those in treated animals and corresponded with the lesions previously reported by Pienaar et al. (1966). Only mild brain oedema was present in 3 treated goats and therefore it appears unlikely that the comatose state of the goats during the terminal stages of the disease could be attributed to irreversible brain damage, as suggested by Clark (1962). The decline in peripheral resistance recorded in HW-infected sheep by Clark (1962) and Owen, Littlejohn, Kruger & Erasmus (1973) may inevitably result in a decreased blood supply to the kidneys.

Although prompt elimination of the infection by means of specific chemotherapy prevents the death of the goats from circulatory collapse, our findings suggest that irreversible kidney damage may lead to the death of the treated animals.

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REFERENCES


