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Short communication

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Renal (Uremic) Encephalopathy in a Goat

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With 6 figures

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Summary

Renal encephalopathy was diagnosed in a 2-year-old male boar goat with a history of chronic weight loss and ataxia. Histopathological examination of the brain revealed a striking myelin vacuolation distributed mainly in two patterns: (i) along the junction of the neocortex and corona radiata, and (ii) in the bundles of the internal capsule as it dissects through the basal nuclei. The kidneys had diffuse severe tubular and glomerular necrosis and degeneration. The neural lesions are consistent with renal (uremic) encephalopathy. To the authors' knowledge, this is the first report of renal encephalopathy in a goat.

Introduction

In large ruminants, such as cattle, spongiform changes in the central nervous system (CNS) have various causes including prions (bovine spongiform encephalopathy), rabies infection (Foley and Zachary, 1995), hepatic and renal encephalopathy, and metabolic disorders with enzyme deficiencies (i.e. Maple Syrup urine disease), or can be artifacts of inappropriate tissue handling or fixation (Wells and Wells, 1989).

Renal or uremic encephalopathy is a well-recognized syndrome of CNS dysfunction and is one of the most common neurologic consequences of acute or chronic uremia in humans (Raskin and Fishman, 1976a). Common symptoms of uremic encephalopathy in humans include a flapping tremor (asterixis), fatigue, alterations of alertness of sensorium and convulsions (Raskin and Fishman, 1976a). Although less common in veterinary medicine (Mahoney and Arieff, 1982; Fraser and Arieff, 1994), renal encephalopathy syndrome has been observed in cows, dogs, horses, rats and woodchucks (Wolf, 1980; Jeppsson et al., 1982; Summers and Smith, 1985; Anderson et al., 1990; Bouchard et al., 1994; Dunigan et al., 1996; Frye et al., 2001) and is associated with seizures, tremors, abnormal behaviour, ataxia or weight loss (Wolf, 1980; Frye et al., 2001). However, renal encephalopathy has not been previously reported in small ruminants, such as goats. In this brief communication, we describe spongiform encephalopathy and severe diffuse renal tubular and glomerular necrosis and degeneration in a boar goat.

Materials and Methods

Tissues of various organs from the postmortem examination of a 2-year-old male boar goat were submitted for histopathological examination. The referring veterinarian reported that the animal had a history of chronic weight loss, an inability to rise/ambulate, and ataxia. The animal was killed, postmortem examination was performed and tissues of various organs were collected by the referring veterinarian. No gross pathological changes were observed at the time of necropsy. Scrapie and neurotoxicosis were suspected.

Tissues from multiple organs, including the brain (no spinal cord), heart, liver, lung, spleen, kidney, intestine, and forestomachs and were either fresh or fixed in buffered 10% formalin were examined. Paraffin sections, 4–5 μm thick, were prepared and processed routinely and stained with haematoxylin and eosin (H&E) for histopathologic examination. Brain tissue was sent to the National Veterinary Services Laboratories for protease resistant prion protein (scrapie) testing by immunohistochemistry. Fresh liver and kidney samples were submitted to the toxicology laboratory for copper and lead levels analysis. Prussian blue pigment staining for iron was performed on spleen, liver, and kidney sections. Intestinal contents were submitted for detection of viruses by direct electron microscopy and for parasitological examination.

Results

By light microscopy, the brain had a striking myelin vacuolation distributed in two primary patterns: (i) along the junction of the neocortex and corona radiata and (ii) in the bundles of the internal capsule as it dissects through the basal nuclei (Figs 1–4). Alzheimer type II astrocytes were not observed in the neocortex or basal nuclei. The kidney had severe diffuse glomerular and tubular cellular injury (degeneration), necrosis and haemorrhage of tubular epithelial cells with tubules consisting of hypereosinophilic and brown granular cytoplasm and nuclear karyorrhexis (Fig. 5). Multifocally, the interstitium was expanded by mild numbers of lymphocytes and plasma cells. Scattered tubules were ectatic and contained karyorrhectic cell debris and eosinophilic casts. Some renal blood vessels had degeneration with mural haemorrhage (Fig. 6). There were no significant microscopic abnormalities in other organ systems. Protease-resistant prion

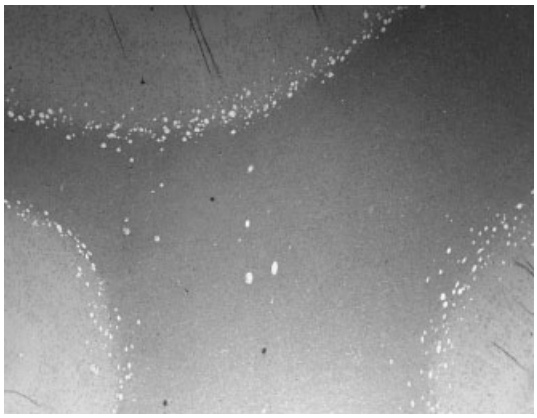

Fig. 1. Severe myelin vacuolation distributed mainly along the junction of the neocortex and corona radiata in a 2-year-old male boar goat with renal encephalopathy; haematoxylin and eosin stain (magnification ×20).

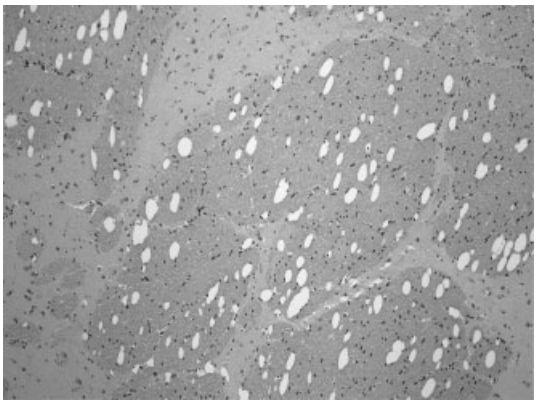

Fig. 4. Higher magnification of Fig. 2. Notice that the spongy change is confined to white matter and spares the grey matter neurophils; haematoxylin and eosin stain (magnification ×100).

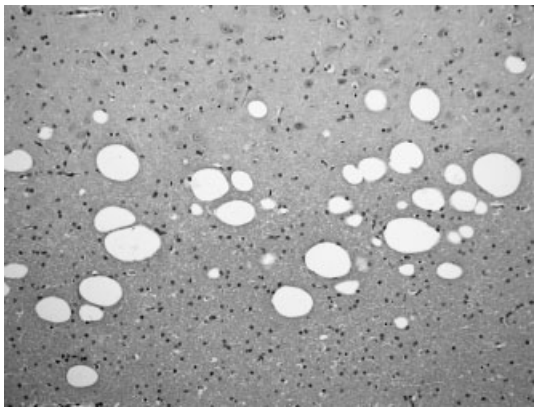

Fig. 2. Higher magnification of Fig. 1. There is no evidence of swollen astrocytes in the neocortex; haematoxylin and eosin stain (magnification ×200).

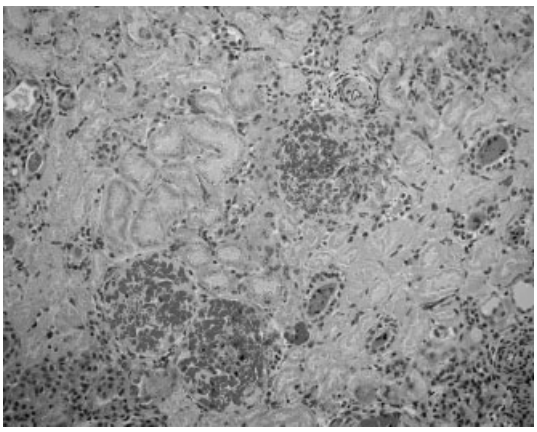

Fig. 5. Severe diffuse renal tubular and glomerular necrosis and glomerular haemorrhage in a 2-year-old male boar goat with renal encephalopathy; haematoxylin and eosin stain (magnification ×200).

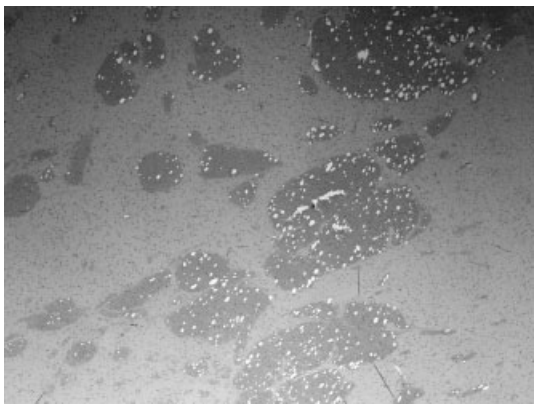

Fig. 3. Severe myelin vacuolation distributed in the bundles of the internal capsule as it dissects through the basal nuclei in a 2-year-old male boar goat with renal encephalopathy; haematoxylin and eosin stain (magnification ×20).

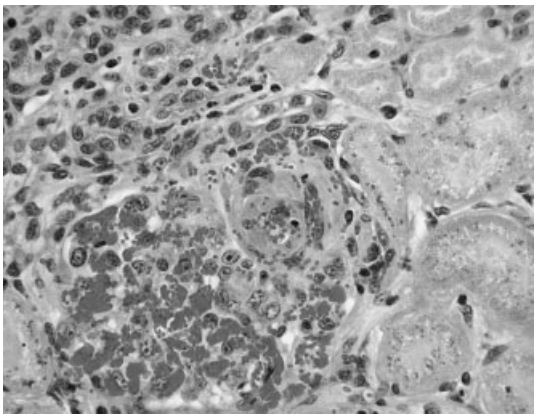

Fig. 6. Renal vascular degeneration with haemorrhage in a 2-year-old male boar goat with renal encephalopathy; haematoxylin and eosin stain (magnification ×600).

protein was not detected by immunohistochemistry on brain sections.

Toxicological analysis of the kidney for lead by atomic absorption spectroscopy was negative (< 0.5 ppm of lead, wet weight basis). Liver copper concentration was 40.01 ppm (wet weight basis). Direct electron microscopy and parasitological examination of intestinal contents were negative for viruses and parasites.

Discussion

To the best of our knowledge, this is the first report of renal encephalopathy in a goat. The differential diagnoses for CNS disease in goats included hepatic encephalopathy and renal encephalopathy, scrapie, heavy-metal toxicosis (lead), copper deficiency, storage diseases (mannosidosis), polioencephalomalacia, listeriosis, *Haemophilus somnus* infection, and viral diseases [caprine arthritis encephalitis virus (CAE); rabies virus].

The distribution of spongiform lesions in the brain of this goat is characteristic of hepatic or renal encephalopathy in ruminants (Summers et al., 1995b). No hepatic lesions were seen, but severe renal lesions observed were consistent with renal encephalopathy. Alzheimer type II cells have been reported in horses with renal encephalopathy (Frye et al., 2001), but none were present in this case.

In humans, renal or uremic encephalopathy can occur in patients with acute or chronic renal failure. The exact pathogenesis is not fully understood, but several factors have been postulated to be involved (Fraser and Arieff, 1994), including a marked increase in calcium content in the cerebral cortex in patients with acute or chronic renal failure. Recently, toxic effects of the parathyroid hormone on the CNS have also been suggested (Fraser and Arieff, 1994). This hypothesis is supported by demonstrated prevention of brain calcium content abnormalities in dogs with renal failure can be prevented by parathyroidectomy (Guisado et al., 1975).

The exact cause of the nephrosis and vasculopathy in this case is not known. Iron was found in considerable amounts in the spleen as demonstrated by prussian blue pigment staining. Mild amounts of iron were present in Kupffer cells in the liver and within the cytoplasm of a few tubules and in the interstitium (probably in macrophages) in the kidney. These findings suggest that a hemolytic process may have been involved in the pathogenesis of the renal changes. Possible causes could be: (1) *Leptospira* infection, (2) plant intoxication, (3) eperythrozoonosis, and (4) drug toxicosis (e.g. phenothiazine). The renal vascular changes may also represent a secondary hypertension that had resulted from renal dysfunction. The hypertension can be attributed to decreased renal excretion of sodium, retention of excess sodium, blood volume expansion and vasoconstriction.

In humans, uremic encephalopathy develops more frequently in males than females (Raskin and Fishman, 1976b). While gender predisposition in renal encephalopathy in veterinary medicine is not known and has not been investigated, it should be noted that the affected animal in this study was a male.

Another characteristic of human uremic patients is muscle cramping (Nielsen, 1971). As previously mentioned, the goat was unable to stand. This symptom may represent either a shift of fluids into muscle or the effects of uremic toxins on the neuromuscular junction (Nielsen, 1971).

Scrapie in goats is characterized by a spongiform change with intracytoplasmic vacuoles within neurones in the brain stem grey matter, astrocytosis and neuronal degeneration (Hadlow et al., 1980). The lesion in this case involved primarily the white matter and no protease-resistant prion proteins were detected by immunohistochemistry.

Lead toxicosis usually causes neuropil spongiosis and pallor, capillary endothelial swelling, and cerebrocortical neuronal degeneration and necrosis (Summers et al., 1995b). These microscopic features were not present in this animal and toxicological analysis of the kidney for lead was within normal limits.

Swayback or enzootic ataxia is a well-known neurological disorder of young sheep that is caused by copper deficiency (Summers et al., 1995b). Enzootic ataxia caused by copper deficiency has been reported in goat kids. Purkinje cell chromatolysis, astrogliosis, cerebellar granular cell layer depletion and thinning of the molecular layer are usually seen by light microscopy (Summers et al., 1995b). These features were lacking in this case and liver copper concentration was within normal limits. Copper values < 10 ppm wet weight are considered evidence of copper deficiency and copper values > 250 ppm wet weight are considered evidence of excess copper (Puls, 1994).

Rabies-induced spongiform encephalopathy has been described in a cow (Foley and Zachary, 1995). Rabies infection causes a lymphocytic encephalitis and inflammatory changes, neither of which were present in this case. CAE is usually associated with marked non-suppurative inflammation (Summers et al., 1995a). No histopathologic changes suggestive of bacterial or viral aetiology were found, and direct electron microscopy of intestinal contents was negative for viruses.

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