CAECAL IMPACTION IN THE RABBIT : RELATIONSHIPS WITH DYSAUTONOMIA

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Abstract - In rabbits a disease occurs that is characterised by caecal impaction, dilatation of the bladder, aspiration pneumonia and a high mortality. No etiologic agent can be isolated. In histology and with transmission electron microscopy changes can be found in the neurones of parasympathetic and sympathetic ganglia and also in the central nervous system. The lesions are similar to the lesions in other animal species (horse, dog, cat and hare) suffering from dysautonomia.

INTRODUCTION

Dysautonomia is defined as a dysfunction of the sympathetic and parasympathetic autonomic nervous system.
Primary dysautonomias have been described in the horse (grass sickness; OBEL, 1955 ; GILMOUR, 1973 ; DOXEY *et al.*, 1992 ; JOHNSON 1995), the cat (Key-Gaskell syndrome; KEY and GASKELL, 1982 ; NASH *et al.*, 1994 ; SYMONDS *et al.*, 1995), the dog (canine dysautonomia ; SCHRAUWEN *et al.*, 1991 ; WISE and LAPPIN, 1991 ; POLLIN and GRIFFTH, 1992) and the hare (leporine dysautonomia ; WHITWELL, 1991 ; GRIFFITH and WHITWELL, 1993 ; WHITWELL, 1994, 1995a). In the horse acute and chronic forms are distinguished, but in the dog and the cat only the chronic form is seen (WHITWELL, 1991 ; SHARP *et al.*, 1984).
The most important symptoms in these animals are related to malfunction of the digestive tract. In horse, dog and cat a mega-oesophagus may be found, and as a consequence of paresis of the gut in horse, cat and hare hard dehydrated caecal contents are often described (WHITWELL, 1991 ; POLLIN and GRIFFITH, 1992). In dog, cat and hare also dilated (paralysed) bladders are mentioned (WHITWELL, 1991, 1994). The dysfunction of the intestinal system often causes gastric regurgitation. A pneumonia by choking and aspiration of food as a result of disturbed swallowing mechanism is seen primarily in dog and hare and mentioned for horse (WHITWELL, 1995b). Dilated pupils are only observed in cats with the disease (BLAXTER *et al.*, 1987, SCHRAUWEN *et al.*, 1991, WISE *et al.*, 1991, DOXEY *et al.*, 1991).
The main clinical symptoms in all these animals are that they stop eating, regurgitate and hardly are able to drink (UZAL, 1992). Hares are usually found dead, so only limited clinical symptoms have been seen. Most prominent feature is a dull emaciated animal with a grass filled mouth (WHITWELL, 1995b).
At necropsy a general feature is a dilated, atonic, gut and an obstipation of the large intestine in most cases. Several animals show aspiration pneumonia (WHITWELL, 1994, 1995b).
In man different forms of dysautonomia are known and some of them are comparable to the disease that is described in animals (MATHIAS, 1987).
In the present study a disease syndrome in rabbits is discussed that has many similarities with dysautonomia syndrome as was described for the other species above and has been outlined at a German rabbit symposium (HAGE and DORRESTEIN, 1995). In the last ten years rabbits were frequently brought to the Diagnostic Laboratory of Veterinary Pathology with a history of large losses in commercial rabbit-farming. The regular finding in these animals was a caecal obstipation syndrome. This was the motive to start a more systemic diagnostic approach, sampling for the autonomic innervation of the enteric system.

MATERIAL AND METHODS

Nineteen animals of about 6 weeks from three rabbit-farms were selected. From each farm pelleted food was collected for examination. The farms had a history of periods with a high mortality caused by caecal impaction and periods of "normal" losses. The selection was based on a simple history, looking for the following parameters: emaciation, respiratory distress, distended abdomen with a palpable, obstipated caecum or a distended bladder.

These animals were clinically examined, euthanised, necropsied and sampled for histology (4% buffered formaldehyde for Haematoxylin & Eosin staining) and transmission electron microscopy (Karnovsky's). The following organs were sampled: the wall of the caecum, the lungs, the brain, the coeliac ganglia and, if they could be found, the stellate ganglia.
Routine microbiology (aerobic culturing, blood agar, serum broth, at 37°C for 24-48 hrs) was performed from liver and intestine.
The food was suspended 1:1 (w/v) in 1% pept on water and checked for the presence of bacterial inhibiting substances using the well-diffusion test in DST-agar. A sample was also inoculated on Malt-agar for growth of fungi.
Livers of five animals were sent to the ID-DLO (Lelystad) and checked for viruses.
Samples of livers and food were investigated for the presence of aflatoxins and their metabolites (ELISA-method, Department of Veterinary Pharmacology, Utrecht University).

RESULTS

History

All three farms had a history of periods with a high mortality caused by caecal impaction and periods of "normal" losses. One of the farms had a death rate of 40% of animals around the age of eight weeks (three to six weeks after weaning). Not only young but also adult, full-grown does were affected with the syndrome. Lately the farmer had taken 400 young rabbits immediately after weaning to an other rabbit-farm where the disease was not seen. These rabbits were raised normally, without signs of the disease. Of the 100 young animals that stayed at the original farm approximately 40% developed caecal impaction.

Clinical examination

All selected rabbits showed anorexia, lethargy, dehydration, obstipation or meteorismus. Some animals suffered from extreme respiratory distress. When palpating the abdomen the obstipation of the caecum and often an enlarged (overfilled) bladder could be found. Sometimes, when a animal was allowed to walk around, clear mucus was found to be lost from the anus.
Usually the animals die shortly after the onset of the respiratory distress caused by aspiration pneumonia. When this does not happen, they suffer from anorexia and dehydration for a week, before dying.

Post-mortem examination

In ten animals (53%) the caeca were filled with dry contents. The colon was empty in most cases or contained some mucus. The bladder was distended in twelve rabbits (63%), although in three animals this was not very extensive.
An aspiration pneumonia was recognised in five cases (26%). The pneumonia was always located in the cranial part of the lung.
Two rabbits (11%) showed none of the specific abnormalities.

Histology

In the rabbits it appeared to be very difficult to locate sympathetic ganglia other then the coeliac ganglion. The ganglia are very small and just as pale as the adipose tissue they are imbedded in. In the sixteen rabbits of this study the ganglia were recognised histologically. Abnormal pericarya were found in the coeliac ganglia of twelve rabbits (75%), and in the spinal cord of ten cases (62%). Some pericarya were shrunken. Homogenous eosinophilic cytoplasm was often present as was vacuolisation. The nucleus was often shrivelled and pyknotic, while it was eccentrically localised.
In the brain many astrocytes were present that seemed to be activated. These cells had enlarged cloudy nuclei and a sharply defined cytoplasm that under normal circumstances can not be discerned.
The enteric plexuses of Meissner and Auerbach were difficult to locate and therefore not taken into account in this study.
In the lungs with gross aspiration pneumonia, particles of vegetable matter could be found in the bronchi and bronchioli surrounded with an acute exudative inflammatory reaction.
The two animals that showed no specific gross pathology had no microscopic lesions either.

Transmission Electron Microscopy

In several of the rabbits many neurones in the coeliac ganglia were found to be degenerated, as recognised by loss of rough endoplasmatic reticulum and free ribosomes. The endoplasmatic reticulum showed widened cisterns and larger clear vacuoles.

Other findings

The microbiology of the intestine of the rabbits was negative for infectious agents as tested sofar, food analysis was negative for growth inhibiting substances and fungi. Aflatoxins or metabolites of aflatoxin could not be found in the livers of these rabbits, nor in the food samples. No virus was isolated on the cell cultures.

DISCUSSION

In dysautonomia of other animal species than rabbit the clinical features, gross pathology and histopathological lesions are very specific and similar in all species investigated. Characteristic is neuronal degeneration in the sympathetic ganglia and in more chronic cases a decrease of the total amount of ganglionic neurones. Neuronal lesions are seen not only in peripheral ganglia, but also in the brain-stem, spinal cord and in the plexus of MEISSNER and AUERBACH in the wall of the digestive tract (SCHOLES *et al.*, 1993 a,b). The degeneration is expressed as a loss of NISSL substance and this manifests itself as chromatolysis. Sometimes vacuolisation is mentioned. The pericarya are rounded and shrivelled, and the nucleus can be pyknotic and eccentrically located (POGSON *et al.*, 1992 ; GUSCETTI *et al.*, 1991 ; SCHOLES *et al.*, 1993 a,b). The main ultrastructural findings in the sympathetic neurones of other animals are loss of ribosomes of the rough endoplasmatic reticulum and distension of its cisternae, while the Golgi apparatus is no longer recognisable in affected neurones. In hares and cats moreover, vacuoles filled with membranous stacks are found in neurones of dysautonomia cases (GRIFFITHS and WHITWELL, 1993)

The present history, clinical findings, pathological lesions and microscopical and transmission electron microscopical features of the coeliac ganglion fit well with the diagnosis of a similar dysautomomia syndrome in the rabbit.

This study is not the first publication on this syndrome. In 1967 MARCATO and SJABAN described degenerated ganglionic neurones in rabbits with a mucoid enteritis-like syndrome. This finding has not been repeated by others, until in 1982 MORISSE described a disease in rabbits which he called "caecal paresis-pulmonary edema syndrome". The disease was characterised by caecal impaction with a lot of dry matter, pulmonary congestion and often retention of urine. PEETERS described the disease in 1989 as "caecal paresis-pneumonia syndrome". He saw corpora aliena (food particles) in the lungs with a polymorphonuclear inflammatory reaction. He also mentioned bladder paralysis. The cause of the disease was not found.

All tests to reveal a possible aetiology in the cases published up to now, including the present cases, were negative. These negative findings also makes this rabbit syndrome fit in with the dysautonomias as described in other animal species.

In horses with grass sickness no conventional infectious agent has been found. Intraperitoneal injection, however, of serum of patients suffering from grass sickness could cause lesions in healthy ponies (GILMOUR, 1973). When the serum was injected into the parotid gland of experimental ponies, the ipsilateral cranial cervical ganglion showed chromatolysis of neurones (GRIFFITHS et al., 1994). The cause of this disease is unknown. Possibly, a naturally produced neurotoxin may be responsible.

CONCLUSION

The clinical symptoms, gross lesions and the microscopical findings in our rabbits are comparable to those seen in dysautonomia syndromes of other animal species. Therefore, it is feasible to call this "caecal-paresis, pneumonia syndrome" the next example of dysautonomia.

REFERENCES

BLAXTER A., GRUFFYDD-JONES T., 1987. Feline Dysautonomia. *In practice*, **9**, 58-61.

DOXEY D., ROBB J., MILNE E., GILMOUR J., 1991. Clinical and biochemical features of grass sickness (equine dysautonomia). *Equine Vet. J.*, **23**, 360-364.

DOXEY D., POGSON D., MILNE E., 1992. Clinical equine dysautonomia and autonomic neuron damage. *Res. in Vet. Sci.*, **53**, 106-109.

GILMOUR J., 1973. Observations on neuronal changes in grass sickness of horses. *Res. in Vet. Sci.*, **15**, 197-200.

GRIFFITH I., WHITWELL K., 1993. Leporine dysautonomia: further evidence that hares suffer from grass sickness. *Vet. Rec.*, **131**, 376-377.

GRIFFITHS I., SMITH S., DOXEY D., WHITWELL K., LOVE S., 1994. Evidence that the agent of equine grass sickness may reach neurons by retrograde axonal transport. *Vet. Rec.*, **135**, 520-523.

GUSCETTI F., POSPISCHIL A., LAUCHLI Ch., EHRENSPERGER F., 1991. Pathomorphologie der felinen Dysautonomie (Key-Gaskell-Syndrom). *Tierarztl. Prax.*, **19**, 296-301.

HAGE M.H. VAN DER , DORRESTEIN G.M., 1995. Dysautonomia in Rabbits. in: *Proceedings 9. Arbeitstagung über Haltung und Krankheiten der Kaninchen, Pelztiere und Heimtieren, Celle 1995. ed. German Vet. Med. Ass., Giessen*, 283-287.

JOHNSON Ph., 1995. Equine Dysautonomia. *Equine Practice*, **17**, 25-32.

KEY T., GASKELL C., 1982. Puzzeling syndrome in cats associated with pupillary dilation. *Vet. Rec.*, **110**, 160-162.

MATHIAS C., 1987. Human dysautonomia. Waltham symposion no 6, *J.Small Anim. Prac.*, **28**, 333-416.

MARCATO P., SJA'BAN M., 1967. *Nuova Veterinaria*, **43**, 546.

MORISSE J-P., 1982. Le syndrome "parésie caecale-oedème pulmonaire". *Cuniculture*, **45**, 141-143.

NASH A., THOMPSON H., ROSENGURT N., SYMONDS H., GASKELL C., HUGHES K., 1994. Feline Dysautonomia in group-housed cats. *Vet. Rec.*, **134**, 175-176.

OBEL A., 1955. Studies on grass disease. The morphological picture with special reference to the vegetative nervous *system. J. of Comp. Path*, **65**, 334-346.

PEETERS J., 1989. Het caecale parese-pneumonie syndroom. *Diergeneeskundig Memorandum*, **3**, 108.

POGSON D., DOXEY D., GILMOUR J., MILNE E., CHISHOLM H., 1992. Autonomic neurone degeneration in equine dysautonomia (Grass sickness). *J. Comp. Path.*, **107**, 271-283.

POLLIN M., GRIFFITH I., 1992. A Review of the Primary Dysautonomias of Domestic Animals. *J. Comp. Path.*, **106**, 99-119.

SCHOLES S., VAILLANT C., PEACOCK P., EDWARDS G., KELLY D., 1993a. Enteric neuropathy in horses with grass sickness. *Vet. Rec.*, **132**, 647-651.

SCHOLES S., VAILLANT C., PEACOCK P., EDWARDS G., KELLY D., 1993b. Diagnosis of grass sickness by ileal biopsy. *Vet Rec*, **133**, 7-10.

SCHRAUWEN E., VAN HAM L., MAENHOUT T., DESMIDT M., 1991. Canine dysautonomia: a case report. *Vet. Rec.*, **128**, 524-525.

SHARP N., NASH A., GRIFFITHS I., 1984. Feline dysautonomia (the Key-Gaskell syndrome): a clinical and pathological study of forty cases. *J. Small Anim. Pract.*, **25**, 599-615.

SYMONDS H., McWILLIAMS P., THOMSON H., NASH A., SANCHEZ S., ROZENGURT N., 1995. A cluster of cases of feline dysautonomia (Key-Gaskell syndrome) in a closed colony of cats. *Vet. Rec.*, **136**, 353-355.

UZAL F., ROBLES C. OLAECHEA F., 1992. Histopathological changes in the coeliaco-mesenteric ganglia of horses with 'mal seco', a grass sickness-like syndrome, in Argentina. *Vet. Rec.*, **130**, 244-246.

WISE L., LAPPIN M., 1991. A syndrome resembling feline dysautonomia (Key-Gaskell syndrome) in a dog. *JAVMA*, **198**, 2103-2106.

WHITWELL K., 1991. Do hares suffer from grass sickness? *Vet. Rec.*, **128**, 395-396.

WHITWELL K., 1994. More cases of leporine dysautonomia. *Vet. Rec.*, **134**, 223-224.

WHITWELL K., 1995a. Pathological findings in wild hares suffering from a disease resembling equine grass sickness. in: *Abstr. 13th European Congr. on Vet. Path. Edinburgh 1995, 3A-6, H.M. Pirie, Glasgow ed.*

WHITWELL K., 1995b. Histopathology of GS- comparative aspects of "dysautonomias" in various species (hares, cats,dogs).in: *Abstr. 1th Intern. workshop on Equine motor neuron disease and equine dysautonomia, Bern 1995, H.Gerber, Bern ed.*

La parésie caecale chez le lapin : relations avec la dysautonomie - Chez les lapins, une maladie se produit qui est caractérisée par une obstruction du coecum, une dilatation de la vessie, une pneumonie et par une mortalité considérable.

On n'a pas réussi à isoler un agent pathogène.

Dans l'histologie et dans la microscopie électronique par transmission, on peut trouver des transformations des neurones des ganglions parasympathiques et sympathiques et aussi dans le système nerveux central.

Les lésions sont similaires aux lésions observées chez d'autres espèces animales (le cheval, le chien, le chat et le lièvre) étant sujets à la dysautonomie.