Case report

A CASE OF LEPORINE DYSAUTONOMIA FROM CROATIA

Doroteja HUBER*, Andrea GUDAN KURILJ, Ivan-Conrado ŠOŠTARIĆ-ZUCKERMANN

University of Zagreb, Faculty of Veterinary Medicine, Department of Veterinary Pathology, Vjekoslava Heinzela 55, 10000 Zagreb, Croatia

(Received 07 January, Accepted 10 March 2022)

Leporine dysautonomia (or dysautonomia of hares) is an idiopathic disorder associated with degeneration of neurons of the peripheral nervous system with loss of sympathetic and parasympathetic nerve function. The disease has so far been described in rabbits and hares from Great Britain, and a similar disorder has also been described in horses (grass sickness), dogs and cats (Key-Gaskell syndrome) throughout the world.

We describe a case of leporine dysautonomia in a rabbit from Croatia, characterized by gross findings of cachexia, dehydration, dilated intestines and urinary bladder. Histologic findings included severe vacuolation of neurons of the submucous and myenteric plexus in the intestinal tract.

This disease presents a rare disorder of rabbits, and based on current report, it should be considered as a possible differential diagnosis is rabbits with neurologic clinical signs and mild gross findings including cachexia and distension of intestine and urinary bladder.

Key words: Croatia, histology, leporine dysautonomia, pathology, rabbit

INTRODUCTION

Rabbits (*Oryctolagus cuniculus*) are a common laboratory and food production animal [1]. Furthermore, they are an increasingly popular pet species in Croatia, with only dogs and cats being more popular [2]. The increase in popularity is accompanied by a more frequent encounter of veterinarians with this exotic pet species. To raise awareness of veterinarians for rare diseases which can be encountered in such new patients, we describe a disorder of rabbits which has so far not been reported in Croatia.

^{*}Corresponding author: e-mail: dhuber@vef.hr

CASE PRESENTATION

A female pet rabbit (*Oryctolagus cuniculus*) of unknown age and breed was submitted to the Department of Veterinary Pathology for the determination of the cause of demise. No history data was provided except presence of unspecified neurologic signs. A full necropsy was performed. Grossly, the rabbit was thin, with no fat deposits in the subcutis, mesenterium and around the kidneys indicating cachexia. Mucoses and subcutis were dry and sticky, corresponding to dehydration. The whole intestine was mildly dilated. The small intestine was filled with small amounts of orange mushy content and gas. The large intestine was filled with moderate amount of mushy, green content and small amounts of gas, without presence of cecotrophs. The mucosa of the whole intestine was grossly normal. The urinary bladder was distended and filled with 40 ml of pale yellow, transparent urine. Other organs did not show gross lesions, but were dark red color indicating congestion. Due to the presence of all permanent teeth and partially atrophied thymus, the rabbit was presumed to be juvenile to young adult.

Representative samples of lungs, myocardium, liver, stomach, small and large intestine, pancreas, kidneys, spleen and brain were fixed in 10% neutral, buffered formalin, routinely dehydrated, embedded into paraffin, cut to thickness of 5 μ m and stained with hematoxylin and eosin (HE). Slides of intestine were routinely stained with Periodic acid-Schiff histochemical stain after microscopic investigation.

Informed consent: Informed consent has been obtained for client-owned animals included in this study.



Figure 1. Number and size of neurons within myenteric plexus are increased. Hematoxylin and eosin (HE).

Histology of the intestine revealed diffusely accentuated submucous and myenteric plexus (Fig. 1). The neurons were increased in size, with severely vacuolated cytoplasm and centrally located pyknotic nuclei (Fig. 2). Vacuolation of the cytoplasm did not



Figure 2. Neurons of the myenteric plexus show severely vacuolated cytoplasm and small, dark, pyknotic nuclei. HE.



Figure 3. The wall of the large intestine with PAS positive goblet cells and increased number and size of neurons within the myenteric plexus (red arrows). Periodic Acid-Schiff stain (PAS), objective magnification 20x.



Figure 4. The vacuolated cytoplasm of myenteric plexus neurons does not stain with PAS stain. PAS, 40x.

stain with Periodic acid-Schiff stain (Fig. 3 and Fig. 4). Apart from congestion of kidneys, myocardium and brain, other organs did not show any histologic lesions. Based on gross and microscopic pathologic findings, leporine dysautonomia was diagnosed.

Leporine dysautonomia (or dysautonomia of hares) is an idiopathic neurologic disorder associated with degeneration of neurons of the peripheral nerve system with loss of sympathetic and parasympathetic nerve function [3]. The disease is similar to dysautonomia in horses (grass sickness), dogs and cats (Key-Gaskell syndrome) [3]. To the authors' knowledge, the disorder has so far been described in rabbits and hares from the UK [4-7]. We present the first case in a rabbit from Croatia.

Based on similar gross and microscopic findings, it has been proposed that dysautonomia found in rabbits and hares is analogue to equine grass sickness [3-5,7]. Namely, in 1991 Whitwell diagnosed dysautonomia in hares which were found dead on one English estate where horses had died from grass sickness. Microscopic findings in the ganglia and alimentary tract of the dead hares and horses were similar, while two healthy hares from the same locality did not show such lesions [4]. Similarly, a possible cause of disease in both lagomorphs and horses was proposed to be a neurotoxin [9]. Clostridium botulinum toxin, apart from horses, has also been confirmed in the gastrointestinal content of one wild rabbit [10]. Apart from histologic examination of tissue, additional examination was not performed in the current case, hence neurotoxin as possible cause of disease was not investigated.

Dysautonomia is a disorder that rarely affects rabbits. Based on results of the current report, the disorder is present in Croatia and it should be considered as a possible differential diagnosis in animals with neurological symptoms and mild gross findings including cachexia and distension of intestine and urinary bladder. Further studies are needed to elucidate pathogenesis of this disease.

Authors' contributions

DH performed the necropsy, analysed histological slides and wrote the manuscript. AGK analysed histological slides and drafted the manuscript. ICŠZ made contributions to analysis and interpretation of data, critically revised the manuscript and, as a native speaker, made corrections to the English language. All authors read and approved the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- Artuković B, Grabarević Ž, Gudan Kurilj A, Beck A, Shirota K, Sakurada Y, Kawamura S, Džaja P: Clinical and pathological findings of an outbreak of Tyzzer's disease in a rabbit colony in Croatia. Vet Arhiv 2010, 80:761-770.
- 2. Blažinović A: Patofiziologija najčešćih neinfektivnih poremećaja probave kunića. Graduate thesis. Zagreb, Croatia: Faculty of Veterinary Medicine, University of Zagreb; 1-56.
- 3. Varga M: Digestive disorders. In: *Textbook of Rabbit Medicine*. Amsterdam, Netherlands: Butterworth Heinemann Elsevier; 2014, 303-349.
- 4. Whitwell KE: Do hares suffer from grass sickness? Vet Rec 1991, 128:395-396.
- 5. Griffiths IR, Whitwell KE: Leporine dysautonomia: further evidence that hares suffer from grass sickness. Vet Rec 1993, 132:376-377.
- 6. Hahn CN, Whitwell KE, Mayhew IG: Central nervous system pathology in cases of leporine dysautonomia. Vet Rec 2001, 149:745-746.
- 7. Hahn CN, Whitwell KE, Mayhew IG: Neuropathological lesions resembling equine grass sickness in rabbits. Vet Rec 2005, 156:778-779.
- 8. Miller AD, Zachary JF: Nervous System. In: *Pathologic basis of veterinary disease*. St. Louis, USA: Elsevier; 2017, 805-907.
- 9. Harcourt-Brown F: Digestive system disease. In: *BSAVA Manual of Rabbit Medicine*. Gloucester, UK: British Small Animal Veterinary Association; 2014, 168-190.
- 10. Barthold SW, Griffey SM, Percy DH: Rabbit. In: *Pathology of Laboratory Rodents and Rabbits*. Iowa, USA: Wiley Blackwell; 2016, 253-324.

SLUČAJ LEPORINSKE DISAUTONOMIJE KOD KUNIĆA U HRVATSKOJ

Doroteja HUBER, Andrea GUDAN KURILJ, Ivan-Conrado ŠOŠTARIĆ-ZUCKERMANN

Leporinska disautonomija je idiopatski poremećaj povezan sa degeneracijom neurona perifernog nervnog sistema sa gubitkom funkcije simpatikusa i parasimpatikusa. Bolest je do sada opisana kod kunića i zečeva u Velikoj Britaniji, a sličan poremećaj opisan je i kod konja (*grass sickness*), pasa i mačaka (*Key-Gaskell sindrom*) širom sveta.

U radu je prikazan slučaj leporinske disautonomije kod kunića iz Hrvatske, koji karakteriše makroskopski nalaz kaheksije, dehidracije, proširenih creva i mokraćne bešike. Histološki su ustanovljeni teška vakuolacija neurona submukoznog i mijenteričnog pleksusa u crevnom traktu.

Ova bolest predstavlja retku bolest kunića, a na osnovu aktuelnog izveštaja, kao moguću diferencijalnu dijagnozu treba je uzeti u obzir kod kunića sa neurološkim kliničkim znacima i blagim makroskopskim nalazima uključujući kaheksiju i distenziju creva i mokraćne bešike.