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Abstract: Captive cheetahs have larger adrenal cortices (adrenal hyperplasia) and higher level of fecal corticoids than free-ranging cheetahs, suggesting that chronic stress may contribute to many health problems of captive cheetahs (Terio, 2004). Among the neurological diseases, the cheetah ataxia, caused by a degenerative spinal cord disorder affecting young and adult cheetahs, represents a serious threat for a sustainable captive cheetah population in Europe. Furthermore several cases of FSE have been diagnosed in European cheetahs. Although the disease has been reported in several large cat species, the relatively high incidence in cheetahs suggests that they may be more susceptible than other zoo felids. In North America, a neurological disease of undetermined aetiology and known as leucoencephalopathy has been reported in numerous adult cheetahs

NEUROLOGICAL DISEASES IN CHEETAH

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Extended abstract

Low reproductive success as well as high prevalence of diseases that are rare in other feline species, including neurological disorders, has been documented in captive North American, South-African, European, and Japanese cheetah populations (Kotsch et al., 2002; Munson et al., 1993, 1999; Une et al., 2001). The cheetah appears to have a low genetic variability, therefore a genetic basis for disease predisposition has long been considered (O'Brien, 1985). However, Namibian free-ranging cheetahs have been shown to have a very low incidence of diseases, and considering the same genetic base as the captive cheetah population, extrinsic factors causing chronic stress must be considered to play a significant role in disease pathogenesis (Munson, 2005a). Captive cheetahs have larger adrenal cortices (adrenal hyperplasia) and higher level of fecal corticoids than free-ranging cheetahs, suggesting that chronic stress may contribute to many health problems of captive cheetahs (Terio, 2004).

Among the neurological diseases, the cheetah ataxia, caused by a degenerative spinal cord disorder affecting young and adult cheetahs, represents a serious threat for a sustainable captive cheetah population in Europe. Furthermore several cases of FSE have been diagnosed in European cheetahs. Although the disease has been reported in several large cat species, the relatively high incidence in cheetahs suggests that they may be more susceptible than other zoo felids. In North America, a neurological disease of undetermined aetiology and known as leucoencephalopathy has been reported in numerous adult cheetahs since 1996.

Cheetah myelopathy

The cheetah myelopathy is a distinct neurological disorder characterized by degenerative lesions of the spinal cord causing ataxia and paresis. The disease has emerged in the last twenty years and represents today a limiting factor in the growth of the European captive population (Walzer 2005). To date more than 60 cases have been registered in at least 16 different locations in Europe and in the United Arab Emirates and resulted in the euthanasia of many cheetahs that were part of the EEP breeding program. There is no apparent sex predilection and the age of onset of the ataxia ranges from 2.5 months to 12 years. All affected cheetahs have been captive bred in a European, Middle-Eastern or South-African institution from captive born or wild caught parents, belonging to the South-African subspecies (*Acinonyx jubatus jubatus*) or East-African subspecies (*Acinonyx jubatus soemmeringii*). Some of the parents are known to have produced other healthy litters prior or subsequent to the ataxic litters, and individual parents developed ataxia themselves at a later stage. Often several or all siblings of the same litter will eventually develop the disease, either simultaneously or successively over a period of several months or years interval.

In cubs and in adults, onset of ataxia is usually acute, and can occur spontaneously or following a stressful experience for the individual or for the litter, such as capture and restraint for examination and treatment, or subsequent to enclosure translocation. In cubs, clinical signs are often temporally associated with sneezing and ocular discharge typical of FHV-1 infection. The course of the disease is variable; ataxia and paresis may develop rapidly to hind limb dragging or recumbency, or progress slowly and stabilize to moderate symptoms for several months or years, with possible acute relapsing episodes. The severity of the symptoms may vary considerably among individuals; the clinical signs however always indicate an upper motor neuron lesion and proprioceptive deficits with involvement of the long-tract sensory pathways in all cases. After an onset of hind limb ataxia, sometimes with involvement of the forelimbs, further symptoms include paresis, staggering, knuckling, swaying high stepping gait (hypermetria), falling over while turning, dragging of the paws or hind limbs, difficulties rising to a standing position and finally recumbency in the most severe cases, usually accompanied by slowly developing wasting (disuse atrophy) of the muscle of the hind limbs. In the standing position, the hind legs are typically kept abducted and the support of the tail is reduced. Although clinical improvement following tentative treatment was observed in a few cases, relapsing bouts of ataxia or paresis eventually reappeared in most cases. Throughout the disease progression, the affected cheetahs had a normal appetite, did not seem to experience pain, remained alert and responded to visual and auditory stimuli (Palmer 2001; Walzer 1995, 1998, 2003).

The aetiology of the disease is still unknown and several causes has been considered, including genetic, environmental / toxic, nutritional (specially copper) and viral factors (Burger 2004; Palmer 2001; Shibly 2005; Walzer 1995, 1998, 2003). The first cases of cheetah ataxia were described in South Africa in 1981 (Brand 1981), and then later in two litters in the Netherlands (Zwart 1985). The disease was ascribed to copper deficiency, based on the copper levels in the organs and to the fact that one cheetah completely recovered after copper supplementation. It is however not clear from the description of the cases, whether pathological lesions were similar to the later outbreaks. This copper deficiency hypothesis could not be confirmed by other authors or in our experience. The captive management and holding conditions vary among institutions that have reported ataxic cheetahs and no "common denominator" could be identified to date. Vaccination and deworming of the young and adult cheetahs, using different vaccines and antiparasitic products, occur on a routine basis in all institutions that have reported ataxic animals. A few cubs developed clinical signs before vaccination, but most of the affected cheetahs were routinely vaccinated against FPV, FHV-1 and FCV using inactivated or modified live vaccines (Palmer 2001; Walzer 1995, 2003).

Thorough clinical investigations (including imaging methods, hematology, blood chemistry, CSF examination) have been carried out in most reported ataxia cases, but, although the disease has often been temporally associated with clinical herpes virus infection in cubs, no definitive etiologic factor could be determined. Serum copper values revealed no significant difference between ataxic cheetahs and domestic dogs and cats. Serologic examinations revealed negative or low titers against FIP, CDV, PLV, FCV, FeLV, FIV, Borna disease virus, encephalomyocarditis virus, tick-borne encephalitis virus, mucosal disease complex virus, Teschen-Talfan disease virus, *Listeria monocytogenes* and *Chlamydomphila psittaci*. Antibody titers against FHV-1 and *Toxoplasma gondii* were elevated in several cases, but negative in another institution. The tests for FIP revealed also negative (Palmer 2001; Walzer 1995, 1998, 2003).

Pathological lesions are restricted to the white matter of the spinal cord and consist of continuous columns of white matter degeneration with only occasional presence of chromatolytic neurons in the gray matter. The degenerative lesions are characterized by ballooning of myelin sheaths, either devoid of axons, or containing intact or fragmented axons, or macrophages (gitter cells, myelinophages), and distribution and severity may vary among individuals. At necropsy, ataxic cheetahs are frequently diagnosed with mostly mild or moderate lesions in non-CNS organs. Most of these non-CNS diseases are "classical" diseases frequently observed in captive cheetahs, such as gastritis, enterocolitis,

glomerulosclerosis/glomerulonephritis, hepatic and/or renal amyloidosis, and myelolipoma. However, no correlation could be made with the myelopathy.

As the etiology of the disease is unknown, no treatment beside supportive care as appropriate can be recommended. Numerous treatment attempts have been reported. Products used include the NSAIDs tolfenamine, flunixin meglumine, carprofen; the steroids dexamethasone and prednisolon, and various supplementary drugs such as acyclovir, vitamin B complex, α -tocopherole, selenium CuSO_4 , a paraimmunity inducer, and/or serum neutralizing antibodies against FPV, FHV-1 and FCV, but, beside occasional temporary improvement, the disease progress could not be influenced by the drug therapy (Palmer 2001; Walzer 1995, 1998).

Further characterization of the lesions using molecular biological techniques, as well analytic and epidemiologic investigations of the environmental status of captive cheetahs, e.g. nutrition and standard medication, are in progress and may provide clue to the pathogenesis of this unique disease entity.

Spongiform encephalopathy

Feline spongiform encephalopathy (FSE) affecting domestic and captive feline species is a prion disease considered to be related to bovine spongiform encephalopathy (BSE). FSE has been reported in several non-domestic cat species, including cheetah, puma, ocelot, tiger, lion and cougar, but the relatively high incidence in cheetahs suggests that they may be more susceptible than other zoo felids. To date 10 cases of FSE have been diagnosed in cheetahs (Baron 1997; Kirkwood 1995; Lezmi 2003; Peet 1992; Vitaud 1998; Petit, pers. obs.). All affected cheetahs were older than 5 yr and born in the U.K., with the exception of 2 cheetahs born in France. Typically, clinical signs have a slow onset and progressive ataxia, initially involving the hind limbs but later also the forelimbs, is consistently observed. Further symptoms appear with variable frequency and include postural difficulties, hypermetria, muscle tremors (particularly affecting the head), changes in behaviour (specially increased aggressiveness or anxiety), hyperesthesia and hyper-reaction to sounds, ptialism, prominent nictitating membranes, central blindness, alimentary disorders (polyphagia or polydypsia), and/or loss of condition. The clinical signs usually develop over a period of about 8 weeks. One affected female had a litter when the clinical signs appeared and she continued to suckle the cubs throughout the disease period until she was humanely euthanased. One of the three cubs developed the disease later at the age of 6 yr (Petit, pers. obs.). It is important to note that this animal was born after the implementation of meat control and sanitary measures concerning BSE, and had been fed with chicken, rabbits and beef meat that was validated for human consumption. Clinically, the disease cannot be differentiated from other CNS-disorders and the definitive diagnosis of FSE requires histopathological examination of the brain and finding the characteristic vacuolation in the neuropil and neurons. It is broadly accepted that FSE is the result of BSE infection in felids and the incubation period appears to be 4.5-8 yr in cheetah. However, the occurrence of FSE in an offspring of an affected cheetah in France raises the question about a possible vertical transmission.

Leucoencephalopathy

Leucoencephalopathy is a unique degenerative disease of the brain affecting adult (>10 yr old) North American cheetahs (Munson 2005b). With one exception in the U.K., the disease has never been observed in the European and South-African populations despite thorough investigations. The most distinctive clinical signs are blindness or visual abnormalities, lack of responsiveness to the environment, behavioural change, incoordination or convulsions. The first cases were diagnosed in 1996, with a peak of incidence between 1998-2001, and the caseload is now declining. About seventy animals have been affected to date at about 30 different facilities. The pathological lesions are restricted to the cerebral cortex and characterized by loss of white matter with associated bizarre astrocytosis. The cause is unknown, but epidemiological features suggest exposure to an exogenous agent through diet or medical management. For clinical diagnosis MRI is the most sensitive method, but

confirmation of the disease is based on histopathological investigations. The disease appears to be irreversible and treatment is limited to supportive therapy.

Other neurological diseases

Vitamin A deficiency has been incriminated as cause of a neurological disease in two adult cheetahs. Pathologically there was evidence of coning of the cerebellum and ischemic necrosis of the spinal cord (Palmer and Franklin, 1999).

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