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Abstract: The clinical signs shown by four cheetahs which were diagnosed as having spongiform encephalopathy are presented. Chronic, progressive ataxia initially involving the hindlimbs, but later the forelimbs also was consistently seen. Some of the animals also had postural difficulties, hypermetria and muscle tremors. All showed some degree of central nervous involvement, but the pattern of signs varied. The signs observed included a change in behaviour, hyperaesthesia to sounds, ptyalism, prominent nictitating membranes and blindness. No abnormalities were detected on clinical examination, routine haematological and biochemical investigations. Radiography and myelography were carried out on three animals. Two showed no abnormalities and one had fused thoracic vertebrae, but these did not impede passage of contrast medium in the spinal canal.

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CLINICAL OBSERVATIONS IN FOUR CASES OF FELINE SPONGIFORM ENCEPHALOPATHY IN CHEETAHS (*ACINONYX JUBATUS*)

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Summary

The clinical signs shown by four cheetahs which were diagnosed as having spongiform encephalopathy are presented. Chronic, progressive ataxia initially involving the hindlimbs, but later the forelimbs also was consistently seen. Some of the animals also had postural difficulties, hypermetria and muscle tremors. All showed some degree of central nervous involvement, but the pattern of signs varied. The signs observed included a change in behaviour, hyperaesthesia to sounds, ptyalism, prominent nictitating membranes and blindness. No abnormalities were detected on clinical examination, routine haematological and biochemical investigations. Radiography and myelography were carried out on three animals. Two showed no abnormalities and one had fused thoracic vertebrae, but these did not impede passage of contrast medium in the spinal canal.

Zusammenfassung

Dievon vier Geparden gezeigten und als spongiforme Enzephalopathie diagnostisierten klinischen Symptome werden dargestellt. Ein chronische, vortschreitende Ataxie, die im Anfangsstadium die Hintergliedmassen betraf, später aber auch die Vorderbeine miteinbezog, wurde stets beobachtet. Einige Tieren hatten Gleichgewichtstörungen, Hypermetrie und Muskelzittern. Allen zeigten mehr oder weniger ausgeprägte zentralnervöse Symptome, wenn auch in unterschiedlicher Ausprägung. Die beobachteten Erscheinungen umfassten: eine Veränderung im verhalten, Hyperästhesie in Bezug auf Geräusche, Speichelfluss, Nickhautvorfall und Blindheit. Die klinische Untersuchung ergab keine klinisch fassbare Abnormitäten, bei normalen Blutwerten und biochemischen Bestimmungen.Drei Tieren wurdenr röntgenologisch und myelographisch untersucht. Zwei davon zeigten keinerlei Veränderungen, bei einem wurden verwachsene Brustwirbel festgestellt, die allerdings die Passage des Kontrastmittels im Rückenmarkskanal nicht beeinflußten.

Résumé

Les signes cliniques présentés par 4 guépards atteints d'encéphalopathie spongiforme sont décrits. Une ataxie progressive chronique des membres postérieurs puis des membres antérieurs a été observée sur tous les animaux. Certains ont aussi présenté des troubles de l'équilibre, une hypermétrie et des

tremblements musculaires. Tous ont montré différents stades d'une atteinte nerveuse centrale mais l'expression des signes cliniques différait entre les sujets. Les symptômes incluent une modification de comportement, une hypereactivité aux sons, du ptyalisme, une protusion de la troisième paupière et de l'amaurose. Aucune anomalie n'a pu être détecté à l'examen clinique, ni lors des analyses hematologiques et biochimiques. Des radiographies et myelographies ont été réalisées sur 3 des 4 animaux. Deux d'entre eux ne présentaient aucune anomalie ; une fusion des vertèbres thoraciques a été décelée sur le troisième mais sans modification du passage du produit de contraste.

Keywords
Cheetah, *Acinonyx jubatus*, feline spongiform encephalopathy, progressive ataxia.

Introduction

At the present time, seven cases of feline spongiform encephalopathy (FSE) have been diagnosed in captive cheetahs (*Acinonyx jubatus*). All of the animals were born in the United Kingdom, but three developed the disease after being exported, one to Australia (9) and two to France. We present here personal observations on the development of clinical signs in four cheetahs with confirmed FSE, the two cases in France and the last two cases to be diagnosed in the UK. Three of these cases have been reported (1,3,6), but clinical details were only summarised.

History

Case 1. Michelle.

Michelle was born at Whipsnade Wild Animal Park in June 1986 and remained there throughout her life. She had two litters of cubs, but she only reared successfully the second litter of three. In October 1993 she showed signs of loss of body condition and hindlimb ataxia. The ataxia progressed to all four limbs and this, and other central nervous signs, worsened over eight weeks, although her appetite and body condition improved. She was euthanased in December 1993 aged 91 months and FSE was diagnosed at the Central Veterinary Laboratory (CVL), Weybridge, UK, by histological appearance of the central nervous system and by the presence of scrapie-associated fibrils on electron microscopy of fresh brain material (6).

Case 2. Jason II.

This male cheetah was born in September 1987 at Whipsnade. He had the same father as Michelle, Herero, but a different mother, Susie. In April 1993 Jason II was sent to the Safari of Peaugres along with its mother. Both animals were examined under anaesthesia before export and no clinical or haematological abnormalities were detected. Susie, who was born in 1980, is still alive at Peaugres and, despite advanced age, is in excellent shape!

Jason was euthanased in January 1997 after seven weeks of progressive nervous disease, and aged 111 months. A diagnosis of spongiform encephalopathy was subsequently established at the Centre National d'Etude Veterinaire et Alimentaire (CNEVA) in Lyon France by histopathology and immunohistochemistry (1).

Case 3. Daphne.

Daphne, a female, was born at another British zoo, in April 1991. She moved to Whipsnade in July 1995 and was mixed with two males, but failed to breed. Behavioural changes were observed in December 1996, but initial examination suggested that this was due to a severe infection with ear mites. There was moderate improvement after treatment against mites, but behaviour did not return to normal. Five months after the initial record of change in behaviour, hindlimb ataxia was noted. Locomotor abnormalities were progressive, and central nervous signs were also seen (3). The animal deteriorated rapidly after the myelography and was euthanased in April 1997, aged 72 months. Feline SE was diagnosed by the CVL, Weybridge.

Case 4. Domino.

This female was a full sister and litter-mate of Daphne (Case 3). She remained at her place of birth until May 1993 when she was transferred directly to Peaugres. Spongiform encephalopathy was suspected in mid-June 1997, but because she was rearing three youngsters born at the end of April 1997 she was left to raise the litter for as long as possible. After five weeks of disease development she was euthanased on humanitarian grounds on the 17th July 1997, aged 75 months. She continued to suckle the youngsters throughout this period. The diagnosis was confirmed by CNEVA, Lyon.

Clinical signs

The opportunities for, and means of performing a neurological examination of zoo animals are extremely limited. Feline and other spongiform encephalopathies can only be confirmed post-mortem, but the observation of neurological signs is strongly suggestive when all other diseases are ruled out.

Kirkwood and Cunningham (5) documented the clinical signs suggestive of transmissible spongiform encephalopathies of zoo animals which were diagnosed as having died of the disease. These include a) nervous signs and b) wasting of body condition. The following signs, which are also related to the nervous system and body condition, were seen in the four cheetahs:

1. Locomotor abnormalities. In all four cases problems with locomotion were the principal sign, and in cases 1,2 and 4 it was the first thing noted by the keepers. Initially there was a mild posterior paresis giving the impression of hindquarter stiffness and causing slight difficulty standing. The keepers at Peaugres mentioned that "the animal seemed to have arthritis". However, when one of the animals, Daphne, was observed by one of the authors she started to run and the stiffness disappeared. Within a short period, three weeks for Jason and Domino, the simple incoordination progressed to symmetrical hindlimb ataxia with staggering or swaying gait, and even collapse when changing direction or on uneven ground. At full development, Jason and Domino's gait was characteristic: robotic movements of the forelimbs with accentuated and accelerated forward extension, thought to represent hypermetria, plus swaying of the hindquarters with crossing of the hindlegs. The two animals also had cutaneous erosions of the pads of the forefeet on the day they were euthanased. Hindlimb ataxia in Michelle and Daphne was bilateral and there appeared to be a defect of proprioception because they were not placing the feet correctly and they occasionally jerked the hindlegs from an abnormal to a more normal position. Another possible proprioceptive deficit which was noted towards the end of Michelle’s clinical development was a lack of awareness of the head position, leading to repeated attempts to place the lower jaw on a log. Each time the log was missed the attempt was repeated until another stimulus ended the sequence. Daphne was also noted to have hindquarters which seemed to act independently of the rest of the body. Her hindquarters were observed to sway and hit trees as she walked past. The forelimbs were involved subsequently.

2. Abnormalities of balance.

It was noted that Jason and Domino had postural difficulties, they kept their limbs wide apart to remain balanced when standing, and had difficulties sitting and then lying down. The male, Jason, could not get into position to urine mark trees and neither animal was able to stand on their hindlegs to scratch trees, even though they tried regularly.

3. Muscular disorders

All four animals showed muscle tremors which affected particularly the head, but also the rest of the body at rest. Occasionally the tremors became spasms of the sub-cutaneous muscles. In Jason these spasms gave the face an almost grinning appearance, the cheek raised to one side exposing the upper canine.

It was also noted that there were very frequent ear movements in all directions and Jason also had blepharospasm.

4. Other nervous signs

a) Hyperaesthesia. Jason was hyper-reactive to sounds. Michelle was hyperaesthetic to touch when anaesthetised. This made judgement of the depth of anaesthesia difficult.

b) Ptyalism. Three animals, Daphney, Michelle and Domino were noted to have saliva drooling from the corners of the mouth, and strings of saliva were almost a constant feature in Domino towards the end.

c) Behavioural changes. Initially Daphne presented a change of behaviour. She was very aggressive towards her keepers and earned herself the nickname "spitfire". This then changed and she became more placid towards the keepers, although she still reacted strongly to strangers. Domino appeared anxious for several months before giving birth in April 1997. She yelped occasionally which she had never done before. Her maternal behaviour was also completely different from that expressed with her first litter, when she had been an excellent mother. She was often impatient with her three offspring and, although not exactly aggressive, she was much rougher and clumsy in her movements. When trying to move one of the cubs in her mouth she used inappropriate jaw pressure and fractured three ribs. Another cub was found one morning with a double fracture of the radius and ulna for which the cause was not established. The growth curve of these cubs was irregular, whereas her previous litter had grown steadily

d) Daphne had a prominent nictitating membrane in the right eye which remained until she was euthanased. This started after general anesthesia for myelography.

e) Michelle, Jason and Daphne appeared to have some form of central blindness, although in the case of Daphne it followed shortly after having a myelogram. Michelle and Daphne were aware of people but looked in the wrong direction. Michelle would go where food was usually placed but was unable to find food if it was displaced even slightly.

5. Alimentary disorders.

a) The two cheetahs at Peaugres, Jason and Domino, presented with polydypsia. Each day they drank, on average, every quarter of an hour.

b) Polyphagia. The rations for Jason and Domino were doubled and yet they always seemed to be hungry. Despite this the female lost condition. It was recorded that Michelle had an increased appetite, but she did increase in weight.

c) Jason defaecated uncontrollably during the final stages.

6. Loss of condition. Michelle was initially reported as having lost body condition, but when she was hospitalised and monitored more closely she actually increased in weight. Domino was over-weight, but from eight months before the onset of nervous signs she slowly lost weight without any other clinical signs and despite continuing to eat normally. Daphne was also overweight when she arrived at Whipsnade, but she was given restricted food until her weight had dropped. However, there was no subsequent change before or during her illness.

7. Results of clinical examinations. All four cheetahs were examined at least once under general anaesthesia. No additional clinical signs were detected, except for an ear mite infection in Daphne. Daphne's eyes were examined with an ophthalmoscope, but no lesions were found. Routine and contrast radiological examinations were carried out on Michelle, Jason and Daphne, but no spinal lesions could be detected. Daphne had fused thoracic vertebrae, but the spinal canal was not affected and contrast medium passed unimpeded. Haematological and biochemical results were unremarkable. Tests for feline leukaemia virus (FeLV), feline immunodeficiency virus (FIV) and feline infectious peritonitis virus (FIPV) were negative in all four cases. Toxoplasma serology was performed in one case, Daphne, and was negative. There were no abnormalities in the cerebrospinal fluid collected from any of the four animals.

Differential diagnosis

The history and clinical signs indicated chronic and progressive ataxia, especially of the hindlimbs, with various additional central nervous signs. In the absence of central signs, hindlimb ataxia has been reported in cheetahs associated with vertebral fractures (10), and spinal cord degeneration (12) which can be due to copper deficiency (14). However, the progression to central nervous signs and the variety of these suggest a central origin. Interestingly none of the animals showed depression, head pressing, fits, nystagmus or evidence of disequilibrium, such as a head tilt or circling.

Infectious causes of encephalitis or meningoencephalitis would usually also affect the animal more generally with, for example, depression, pyrexia and changes in haematological parameters. The most important infections reported in cheetahs are viral; feline infectious peritonitis can occur as effusive or chronic granulomatous forms (8, 11), but has not presented as primarily a neurological disease. Feline panleucopaenia can occur naturally or due to vaccination with live attenuated virus, but all four cheetahs had been vaccinated with killed vaccine regularly. Rabies might be considered in an endemic region with a history of exposure to an infected animal, and Aujesky's disease would be a differential if the animals had been fed pork, which these had not. Bacteria such as *Staphylococcus, Streptococcus*, *Listeria* and *Erysipelothix* species, and generalized fungal infections like cryptococcosis, can involve the brain and/or meninges, but usually with other non-nervous clinical signs. Toxoplasmosis was considered, and one animal was tested serologically. However, the presence of antibodies might indicate a carrier state.

Nutritional and metabolic diseases which can cause nervous signs in cats were considered. Thiamine deficiency was unlikely because the animals were not fed fish and were given a vitamin supplement containing the vitamin. Hepatic encephalopathy is important because veno-occlusive liver disease is a common finding in cheetahs in the USA (8). However, there were no other signs of liver failure and no increases in liver enzymes. Similarly, nervous signs

and loss of condition may be seen in chronic renal failure, another common disease of cheetahs (8), but uraemia and/or raised serum creatinine were not detected. Poisoning was discounted because of lack of exposure to known poisons and the slow, progressive nature of the nervous signs. Lead poisoning might be considered if the animals had been moved to an enclosure which had old lead-based paint.

Other possible diagnoses, for instance neoplasia of primary nervous origin and granulomatous meningoencephalitis (2) could not be discounted on clinical signs alone, at least at the onset of the disease.

Discussion

The diagnosis of FSE requires histopathological examination of the brain and the finding of characteristic vacuolation. Therefore it is important that the brain and rostral spinal cord of any suspicious case in saved in formalin and submitted to a laboratory which performs histopathological examination of the nervous system (4). Additional information can be achieved if some brain tissue is sent fresh, or frozen, for electron microscopical examination for the presence of scrapie-associated fibrils. Nevertheless, a provisional diagnosis could be made on the basis of the characteristic development of clinical signs seen in these four cheetahs, notably the chronic and progressive ataxia affecting particularly the hindlimbs, and varied central nervous signs, and by eliminating other possible causes. Ataxia was also the principle nervous sign reported in the first three cheetahs affected with spongiform encephalopathy (5,9). One of these was also hyperaesthetic and lost weight (9).

The initial reports of the disease in domestic cats also highlighted the progressive ataxia , hypermetria and behavioural changes. The first case (13) showed postural difficulties causing the animal to fall over and fail to rise, as was shown by the two Peaugres cheetahs. The cat reported by Leggett et al (7) also salivated profusely, as did three of the cheetahs and was hyperaesthetic to loud noises, like Jason. Additionally it showed an intention tremor of the head and dilated unresponsive pupils, signs which were not seen in the cheetahs.

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