



# A case of spongiform polioencephalomyelopathy in a cat with a history of behavioural problems

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## Abstract

A 7-month-old, entire female, domestic shorthair cat was referred to our behavioural service owing to soiling in the house and a play-related problem. The owners' complaints were that the cat had never used the litter tray, and it did not know how to play. After reviewing the behavioural history, a problem of substrate preferences acquisition was suspected with regard to the elimination problem. During the consultation, the physical examination was unremarkable, but the neurological examination revealed a moderate and hypermetric ataxic gait, and a bilateral lack of menace response. Some degree of visual impairment was suspected. The problem was located in the central nervous system (CNS); specifically, an intracranial and multifocal problem was diagnosed. After a complete work-up (complete ophthalmological examination, complete blood count and a complete biochemistry panel, feline immunodeficiency virus/feline leukaemia virus test, thorax radiographs, abdominal ultrasound, brain magnetic resonance imaging [0.2 T], cerebrospinal fluid analysis and a urinary metabolic screen test), a degenerative CNS problem was suspected. No treatment was prescribed for the neurological problem. Regarding the problem of soiling in the house, reward-based training with a clicker was used, and the cat partially improved in a few weeks. Three months later, the cat was referred to the neurology service in status epilepticus. A symptomatic treatment was prescribed, with a mild response. After 2 years of treatment and a progressive worsening, the cat was euthanased. Necropsy revealed spongiform polioencephalomyelopathy. In order to rule out prion aetiology a PrPsc immunohistochemistry assay was performed, and the results were negative. Congenital spongiform polioencephalomyelopathy (CSP) was diagnosed. We strongly suggest that the cat's behavioural clinical signs were caused by the CSP, causing learning impairment. To the best of our knowledge, this would be the first case in which a congenital degenerative disease affected a cat's capability to learn, leading to behavioural signs as the main complaint of the owners, even before neurological signs are detected by the owners.

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A 7-month-old, entire female, domestic shorthair cat was referred to our behavioural service owing to house soiling and a play-related problem. The owners' complaints were that the cat had never used the litter tray, and it did not know how to play. The environment consisted of two young adult humans with no children. They lived in a flat of 85 m<sup>2</sup>, with two terraces of 5 m<sup>2</sup> each. There were three separated litter boxes at home, all of which were non-covered with low sides. The owners had used clumping, non-clumping, silica-based and soil-based litter during the months between the adoption (when the

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cat was 4 months old) and the first visit. One of the latrines always had clumping substrate. There were three food and three water troughs, all of them far from the latrines.

The impression of the owners was that the cat eliminated where it was at any given moment. It eliminated many more times in front of the owner (90%) than when it was alone (10%). The cat never tried to cover its faeces or urine after depositions. Occasionally, the owners punished the cat verbally and physically, but only when it eliminated in front of them. The substrates used by the cat were ceramic tiles, the sofa and beds. It always adopted an emptying-body posture. Spots were always located on horizontal surfaces. The owners used bleach-based products in order to clean the spots, and just water in the case of the sofa and beds.

Regarding the play-related problem, the owners said that the cat did not understand the body language of other cats and commonly crashed into other cats or people. It also 'tried to bite, catch and scratch the air' when playing. It did not find balls or other toys when the owners threw them to the cat to play.

The rest of the cat's behavioural history was unremarkable.

The differential diagnoses of the house-soiling problem included problems with the litter trays, including insufficient number, incorrect type, competition with other cats for the latrines, incorrect location, acquired aversion, or inappropriate substrate; a preference for another location or substrate; a problem with preference acquisition (ie, because of a cognitive impairment, or a sensory impairment or an unavailability of appropriate latrines or substrate during the first few weeks of life); and marking behaviours. Finally, a medical illness can contribute to all of these problems or to be the main cause.<sup>1,2</sup>

We could rule out most of these problems after interviewing the owners. Firstly, it was unlikely that there was a problem with the litter tray because the number, type and location were correct. The locations were correct because the animal eliminated near the litter tray if it was there. Many different substrates had been used. Secondly, it was not a problem of preference because the cat eliminated in different locations and surfaces. The age of the animal, the distribution of the spots and the body posture during elimination ruled out marking behaviours.

Alterations in play behaviours described by the owners could have been due to a cognitive impairment, and/or a sensory impairment (ie, blindness). Play behaviours depend on learning capability and sensory systems.<sup>3</sup> Additionally, an enriched environment is necessary to learn and display play behaviours in a proper manner.<sup>4</sup> In that case, the social and instrumental environment was good.

Regarding elimination, a problem of substrate preferences acquisition was diagnosed. A cognitive impairment, a medical condition or both could have been the cause of the problem during the elimination habits acquisition. Moreover, cognitive impairment and some medical conditions also could explain the play-related behavioural problems.

During the consultation, the physical examination was unremarkable; however, the neurological examination revealed a moderate and hypermetric ataxic gait, and a bilateral lack of menace response. A complete ophthalmological examination was performed by the ophthalmological service in order to rule out ocular diseases. No ophthalmological abnormalities were detected. Additionally, based on the behaviours at home described by the owners (the inability to find some toys, and the behaviour of 'scratching and biting the air'), some degree of visual impairment was suspected but not confirmed with the neurological examination. The cat did not crash with objects either at home or at the consultation room. The problem was located in the central nervous system (CNS); specifically, an intracranial and multifocal problem was diagnosed. A complete blood count and a complete biochemistry panel were performed, and all of the results were within normal limits. The feline immunodeficiency virus/feline leukaemia virus test was negative. A thorax radiograph, abdominal ultrasound, brain magnetic resonance imaging (MRI; 0.2 T) and cerebrospinal fluid analysis showed no abnormalities. Although some small lesions could be missed with low-field MRI, we had to assume the absence of lesions obtained in the work-up. Thus, a degenerative condition such as a lysosomal storage disease, organic aciduria or mitochondrial encephalopathy was suspected. Samples of blood and urine were sent to the University of Pennsylvania School of Veterinary Medicine for metabolic screen tests. Amino acids, organic acids, carbohydrates, nitroprusside, ketone and mucopolysaccharide concentrations were analysed, as was  $\alpha$ -mannosidase,  $\beta$ -mannosidase, fucosidase and hexosaminidase A and B activity. All of these were within normal limits.

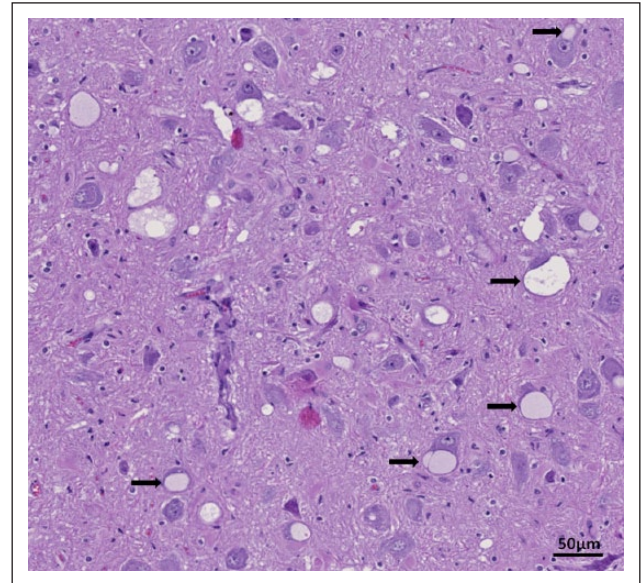
No treatment was prescribed for the neurological problem. The owners were given advice on correcting the soiling problem in the house using reward-based training with a clicker. During the first week, the clicker was conditioned by a food reward, and the entire floor was covered with newspaper. Each time that the cat eliminated, it was rewarded with a clicker and food. Newspaper was removed progressively. Three months later, the cat used a small newspaper-covered area to eliminate. This partial improvement suggests that there was a learning impairment during the acquisition of habits but not a total lack of learning capability.

After 3 months, the cat was referred to the neurology service again, in status epilepticus. Neurological

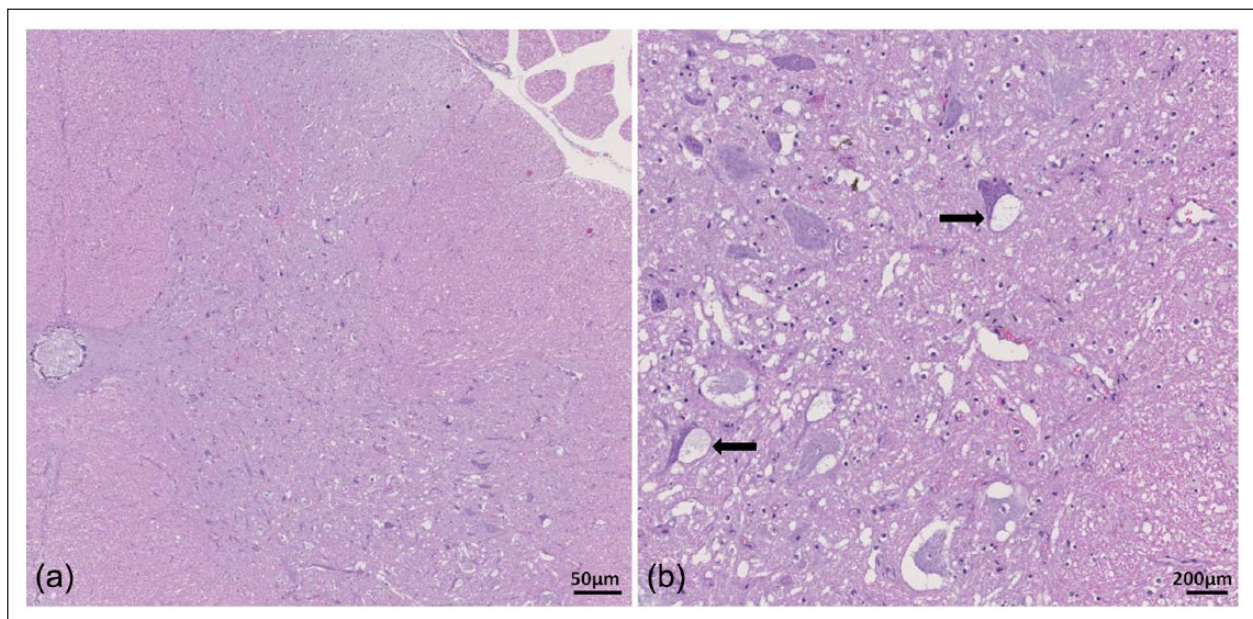
findings, after the postictal phase, included a lack of bilateral menace response and cerebellar ataxic gait. A bilateral carpal valgus that had already been found in the first visit and a visible suture line in the posterior capsule of both crystalline lenses were also detected. The owners reported progressive gait deficits over the previous month and compulsive running episodes with a partially impaired mental status (probably seizure activity). A symptomatic treatment with diazepam (1 mg/kg intrarectally only if seizures) and phenobarbital (2 mg/kg PO q24h) was started, with a very poor response. After 15 days of treatment, levetiracetam was added (10 mg/kg PO q8h) owing to an increase in seizure activity, with an initially good response. However, seizures reappeared after 2 months with 1–2 episodes every 15 days each lasting <2 mins. After 2 years of treatment and a progressive worsening, the cat was euthanased. A complete necropsy was immediately performed. No gross lesions were found, and based on the CNS histological lesions shown in Figures 1–4, a diagnosis of spongiform polioencephalomyelopathy was made. The spongiform degeneration of the grey matter was extensively distributed in the whole CNS. In order to rule out prion aetiology, a PrPsc immunohistochemistry assay was performed, and the results were negative. Thus, congenital spongiform polioencephalomyelopathy (CSP) was diagnosed postmortem.

Spongy vacuolation seen by light microscopy in the neural tissue is defined as spongy degeneration, and may take the form of vacuoles within processes of the

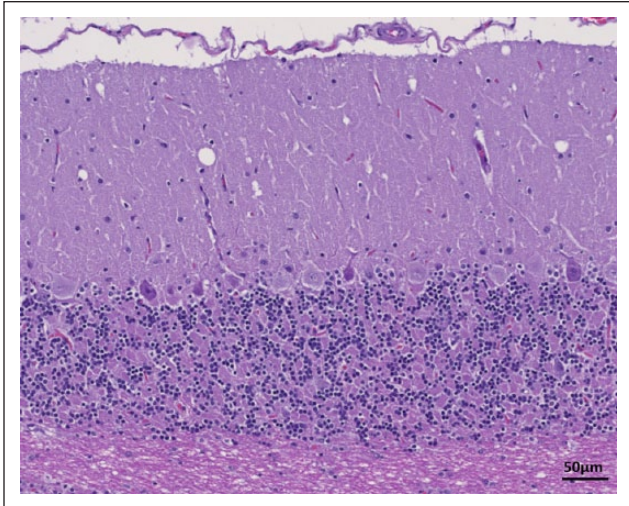
neuropil, vesiculation of myelin sheaths, or swelling of astrocyte or oligodendrocyte cytoplasm.<sup>5</sup> A congenital problem, retrovirus infection and prion disease have been suggested as possible aetiologies.<sup>6–10</sup> Congenital



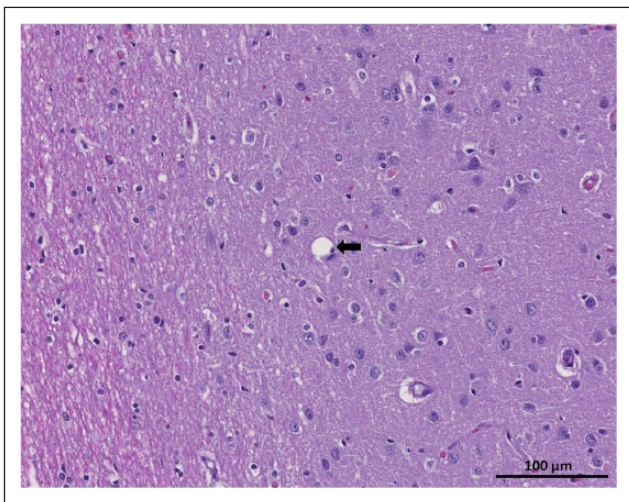
**Figure 1** Mesencephalon. Intraneuronal vacuolisation of the red nucleus. Prominent vacuoles of different sizes are located in the perikaryon of some neuronal bodies (arrows) occupying most of the perikaryon and displacing the neuronal nucleus to the periphery. Small vacuoles are also present in the neuropil together with a moderate gliosis (microgliosis)



**Figure 2** Lumbosacral spinal cord. (a) A general view of the lumbosacral spinal cord shows a generalised spongiform appearance of the grey matter in the dorsal and ventral spinal horns. (b) Detail of the ventral spinal horn showing a moderate spongiosis of the neuropil and the presence of vacuoles of different sizes with an irregular greyish content in most of the perikaryon of the neuronal bodies (arrows)



**Figure 3** Cerebellar cortex. High-power field view of the cerebellar cortex showing a generalised mild spongiosis of the molecular layer with round, empty spaces in the neuropil



**Figure 4** Cerebral cortex. Prominent and empty vacuoles are multifocally distributed throughout the neuropil of the parietal cortex (arrow). The lesion is located in the deeper layer of parietal cortex while no histopathological changes are observed in the subcortical white matter (left side)

spongiform degeneration of the grey matter has been previously described in a few cases of cats,<sup>6-8</sup> however, the cause remains still unknown. Common clinical signs include gait alteration, seizures, blindness, bilateral cataracts, behavioural changes and cranial nerve alterations. These signs appear during very early stages of development (just after birth), with a progressive fatal outcome in a few days or months. Behavioural signs are poorly described in animal science literature.<sup>6-8</sup> Although the degeneration usually affects diffusely all the grey matter, the behavioural alterations and the evolution of the clinical signs depend on the affected area of the brain in each

case. Nevertheless, the clinical signs do not always correlate with the degree of the histological lesions. A spongy degenerative problem of grey matter has also been described in humans, and occurs in isolated cases and in sibs.<sup>11-13</sup> In all of human cases reported, the problem appears early in infancy and the outcome is always fatal. All the affected children show learning disabilities (ie, retarded speech development) during the early periods of infancy. Additionally, they rapidly develop neurological signs, especially seizures. The clinical findings and neuropathological changes are very similar in humans and the present case. There are no studies regarding degeneration of grey matter and its effect on learning ability in animals. However, other neurodegenerative problems (ie, lysosomal storage diseases) and problems that lead to structural abnormalities of the forebrain (ie, hydrocephaly) may be correlated with learning disabilities in animals and humans.<sup>14-17</sup>

The acquisition of the elimination habits occurs during the first weeks of a kitten's life. Most kittens naturally seek out sand-like materials for elimination purposes. However, the preference for a substrate needs to be learnt during those first weeks of age. Learning disabilities and/or sensory impairments could modify the acquisition of these habits.

## Conclusions

We strongly suggest that the behavioural signs (elimination and the play-related problem) were caused by CSP, causing learning impairment.

This case contributes to scientific knowledge for two reasons. Firstly, it describes a CSP, which is a very rare condition described in cats. Secondly, to the best of our knowledge, this is the first case in which a congenital degenerative disease affects a cat's capability to learn, leading to behavioural signs as the main complaint, even before neurological signs are detected by the owner.

Finally, this case illustrates the importance of considering medical conditions in all behavioural cases and of using an accurate diagnostic protocol.

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