SHORT CONTRIBUTION

Ataxia and paralysis in cats in Australia associated with exposure to an imported gamma-irradiated commercial dry pet food

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Between June 2008 and March 2009, 87 cats in Australia developed symmetrical hindlimb ataxia, paraparesis, tetraparesis, paraplegia or tetraplegia in association with eating an imported, irradiated dry pet food. This communication reports the clinical signs and outcomes of those cats.

Keywords cats; dry food; irradiation; leucoencephalopathy
Abbreviations CNS, central nervous system

Between June 2008 and March 2009, 87 cats in Australia developed symmetrical hindlimb ataxia, paraparesis, tetraparesis, paraplegia or tetraplegia. The affected cats ranged in age from 10 months to 15 years, and all were either indoor only or indoor/ outdoor domestic pets. In total, 69 affected cats came from Sydney and the remainder were reported from Newcastle, Melbourne, Canberra and Adelaide. Sixty-four of these cats were examined by one or more of the authors, a further 10 were reported by other veterinarians and 13 cats were reported to the authors by their owners. Both male and female cats were affected and all except two were neutered; 40 were Domestic Short-hairs, with other represented breeds including Domestic Long-hair, Burmese, Siamese, Himalayan type, Maine Coon, Spotted Mist, Cornish Rex, Devon Rex and Bengal. In households with more than one cat, multiple cats were affected, but the severity of clinical signs varied among them.

The majority (85/87) of cats were reported to have eaten Orijen® (Champion Petfoods Ltd, Morinville, Alberta, Canada) dry cat food in the months preceding the onset of neurological signs. Two cats ate only Orijen dry dog food. In households where cats were affected after eating Orijen dog food, dogs in the household have not shown any neurologic abnormalities to date. More than half of the affected cats were fed other food in addition to Orijen during the same period, but some cats were fed the dry food exclusively and others were fed Orijen® as a small part of their daily diet. Additional foods included other commercially available canned and/or dry foods, and raw or cooked meat. No single food product, except Orijen dry food, was fed to all affected cats. The period of time that Orijen was fed to the affected cats ranged from less than 1 month to 10 months. The total amount of Orijen fed has not been correlated with the severity of clinical signs.

The onset of clinical signs in all cats was at least 2.5 to > 6 months after the food was first fed. Onset of clinical signs was seen in some cats that had not been fed Orijen for more than 2 months. No other cats have been seen in this period of time that had similar clinical signs that have not been fed Orijen® dry food.

The initial presenting abnormalities have included difficulty in jumping, landing heavily and a swaying, often wide-based, crouching hindlimb gait. Symmetrical hindlimb paresis and ataxia progressed in more than 50 of the affected cats, to non-ambulatory severe paraparesis or paraplegia, and in 13 cases to tetraparesis or tetraplegia over a period of 4 to 8 weeks. Currently the worst affected cats have shown tetraparesis and either spastic paraplegia or tetraplegia.

The neurological abnormalities are indicative of an upper motor neuron abnormality with decreased or absent postural reactions in affected limbs, normal to increased spinal reflexes and normal to markedly increased muscle tone. No significant muscle atrophy has been seen unless the cat was paralysed and recumbent for extended periods. Spinal pain was reported initially in two cats, but has not been a typical feature. Several owners have commented that twitching or involuntary spasms occurred in either the hind- or forelimbs, especially when the cat was attempting to eat or urinate or defecate, and some paraplegic or tetraplegic cats have developed urinary incontinence. The most severely affected cats showed a subtle head tremor and/or difficulty eating (coordinating the prehension of food, constant licking of the nose), but all have remained seemingly alert and responsive to their owners. The menace response was absent in less than 10 affected cats and several of them have shown vision abnormalities. Many owners have reported that their cat’s behaviour changed, with the cat seeming to be more quiet or subdued than previously. Less than 10 cats have become temporarily inappetant, but this is also not typical. Generalised tonic–clonic seizures have occurred in two cats.

Because of the severity of their clinical signs 21 cats were euthanased, 2 cats died within 24 h of an acute onset of seizure activity and 1 cat died with no other cause established. Two cats were euthanased because of concurrent illness (chronic diabetes mellitus or renal insufficiency) and debility as a result of paraplegia.

Of the affected cats, 22 have improved clinically and 7 have recovered completely. Many of the affected cats were severely paraparetic or paraplegic for more than 6 weeks before any improvement was seen. One cat that was non-ambulatory and improved went on to show generalised seizure activity and died 3 months after initial presentation.

Affected cats have had different diagnostic evaluations, but in those tested, no abnormalities have been found on complete blood count, biochemistry profile, serologic testing (feline leukaemia virus, feline immunodeficiency virus, Toxoplasma gondii, Cryptococcus sp.), serum cholinesterase level, blood lead determination, spinal radiography,
computed tomography of the spine, myelography, magnetic resonance imaging of the spine and spinal cord, cerebrospinal fluid analysis or muscle biopsy. The earliest affected cats (approximately 20) were evaluated extensively for metabolic, toxic, infectious and compressive causes of spinal cord disease and no abnormalities were found. In later affected cats, a presumptive diagnosis was made based on clinical presentation and known exposure to Orijen dry food.

Treatment given to affected cats consisted of a change to another nutritionally balanced diet, nursing care and physiotherapy. No significant difference in the rate or degree of improvement in neurological function has been seen with treatment with vitamin and antioxidant supplements (including vitamins A, E, C, B and glutathione), minerals (e.g. copper and potassium), omega 3 fatty acids or empirical treatment with antibiotics, including clindamycin and/or prednisolone, compared with nursing care and a change in diet only.

Postmortem examination has been carried out in seven affected cats. No gross abnormalities were found. Histopathological abnormalities were confined to the nervous system in six cats. The seventh cat also showed chronic renal amyloidosis. The neuropathologic findings have been very similar in all cases and characterised by severe diffuse leucoencephalopathy. Degenerative changes were seen diffusely and symmetrically throughout all levels of the spinal cord, affecting the white matter of predominantly the lateral and ventral funiculi with moderate to severe spongiform vacuolation, occasional large swollen axons, prominent blood vessels and rare, occasional perivascular mononuclear cuffing. Similar diffuse and symmetrical changes were evident in the white matter tracts of the brainstem, but less severe than the changes within the spinal cord.

Mild spongiform degeneration was present in the cerebellar white matter of some cases. There was diffuse, symmetrical moderate to severe spongiform vacuolation, prominent plump branching blood vessels and diffuse gliosis, including prominent astrocytosis in some cases. Spinal nerve roots and sciatic nerves have shown no significant lesions. Heavy metal analysis of liver and brain samples has not shown any abnormalities.

Analysis of the imported dry food for trace elements, a volatile organic compound unknown screen and a semi-volatile organic compound unknown screen (Australian Government National Measurement Institute, Port Melbourne, VIC, Australia) have not identified a known toxin. Analysis of Orijen dry cat food imported into Australia has revealed some depletion of the vitamin A and B content after irradiation, but no nutritional deficiency.

Orijen is a recently imported pet food to Australia. Approximately 1300 kg of dry cat food was distributed in Sydney from February 2008, in Melbourne and Brisbane some months later and to online buyers in other areas by pet food suppliers. It has been available in North America and Europe for more than 2 years without any health problems reported. Only two shipments were distributed within Australia and lot numbers imported were also distributed in North America.

Orijen was subject to a total gamma irradiation dose ≥50 kGy on entry to Australia for biosecurity purposes. Australia is the only country where this pet food product was irradiated prior to distribution to retailers.

The histopathology in the seven cats examined does not suggest an infectious cause. A metabolic, nutritional or toxic cause is most likely, given the bilateral symmetric involvement of the white matter of the central nervous system (CNS). The histologic lesions are most consistent with acquired demyelination. Lesions are not typical of Wallerian degeneration; however, there is some evidence, although relatively minimal, of secondary axonal swelling. The grey matter and neurons are not affected.

No metabolic cause has been established in the affected cats. A nutritional deficiency is considered very unlikely in these cats as the majority of affected cats were also fed other foods and a nutritional deficiency has not been demonstrated in the Orijen food that was fed. The epidemiology suggests a delayed neurotoxicity; however, no specific toxin has been identified.

Leucoencephalopathy has been previously reported in colonies of cats in Ireland, Britain and New Zealand. Nutritional deficiency has been suggested as a possible cause, but a definitive cause has not been established. Irradiation of dry pet food has been implicated previously as a cause of leucoencephalopathy in one large group of cats. In that colony of specific-pathogen-free cats, ‘outbreaks’ of progressive hindlimb ataxia were seen in 190 of 540 at-risk animals in a period between 1998 and 2001 when they were fed a commercial dry food exposed to single-dose gamma radiation treatment at 36.3 to 47.3 kGy. It was not indicated whether the dry food fed to colony cats in the other reported ‘outbreaks’ of leucoencephalopathy had been subject to irradiation for pathogen control.

Irradiation results in the production of ions and free radicals, including high-energy oxygen radicals, that are used to kill or damage pathogenic organisms in food. Irradiation doses of foods for human consumption normally range from less than 1 up to 10 kGy. Larger doses (30 kGy) have been approved for dried herbs, spices and dehydrated vegetables. Oxygen radicals produced by irradiation will also cause the formation of lipid oxides by directly reacting with membrane lipids and other lipids in foods, and some foods such as fatty fish and meat are not considered good candidates for irradiation. Irradiation also induces chemical changes in carbohydrates and proteins by the action of hydroxyl radicals and hydrated electrons generated from water molecules to produce radiolytic products. These products are also generated in cooking or pasteurisation.

Depletion of vitamin A after gamma irradiation has been suggested as a possible contributing cause of leucoencephalopathy in cats, and other micronutrient deficiencies have also been postulated as possible contributing factors. However, vitamin A concentration has not been found to be deficient in the food in this ‘outbreak’ in Australia and the majority of cats were also fed other foods containing vitamin A that were nutritionally balanced. In a more recent study the peroxide content of commercial dry animal diets was increased 14- to 25-fold after high single-dose gamma irradiation of 38.4 to 48.7 kGy. Hydrogen peroxide is toxic to many cells if it comes into contact with reduced forms of certain metal ions, forming the highly reactive hydroxyl radical that acts to cause lipid peroxide formation and a process that can result in a chain reaction of lipid peroxidation.

The generally higher fat content of cat food and different species susceptibility to toxicity may be possible contributing factors to
oxidative damage to the CNS and the development of this disease in cats. However, the mechanism by which changes induced in foods then result in damage to the white matter of the spinal cord and brain is not clear. Whether a single insult to the CNS results in on-going damage or whether the damage is the result of cumulative or repeated insult remains speculative. The effect of irradiation on food packaging and the migration of components, such as plasticisers, into food may be important, but this has not been supported by toxicologic tests to date and packaging does not appear to be a common denominator in previously reported ‘outbreaks’. Various materials have been previously approved for irradiation of prepackaged foods at differing levels (0.5–60 kGy).9

Previously published data3,7 and strong circumstantial evidence in this outbreak suggest that single-dose gamma irradiation of dry pet food at high levels (>36.3 kGy) is associated with the development of leucoencephalopathy in cats. We suggest that food irradiated at high levels should not be fed to cats as it poses a significant risk of severe neurological disease.7

An epidemiologic study is underway and pathologic and toxicologic tests are ongoing. The prognosis for affected cats has been and still is extremely variable. The manufacturer withdrew both the cat and dog dry food from sale in late November 2008 and ceased shipment of pet food to Australia indefinitely. The dog food was withdrawn from the market, in addition to the dry cat food, because of the suspected toxicity to cats that are fed the dog food. A compensation fund has been established by the manufacturer to help owners whose cats have been affected. No new cases have been seen by the authors since the beginning of March 2009. Orijen pet food has not been commercially available in Australia since the end of November 2008.

The authors would welcome any information regarding any cats (affected or not) that have eaten Orijen pet food.

References

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