FELINE IDIOPATHIC HIPPOCAMPAL NECROSIS: FINDINGS IN A UK CASE

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HADAR YANAI, VIKTOR PALUS, ABBY CAINE, BRIAN SUMMERS, GIUNIO BRUTO CHERUBINI report on the clinical, MRI and pathological findings in a case of hippocampal necrosis in a cat presented with aggression and seizures

Summary

Behavioural abnormalities and seizures are common neurological disorders in feline patients. Cases due to hippocampal necrosis have been described initially in Switzerland, where two small temporal-geographic clusters suggested an environmental factor may be involved and a toxic (exo or endogenous) or metabolic cause was suspected. Since then, cases of hippocampal necrosis have been reported in Italy, Austria, Germany, Finland, Sweden and, very recently, in the UK as well. Different authors suggest different aetiologies for hippocampal necrosis: however, so far the aetiology remains unknown. The cases present common clinical features, MRI findings and pathology findings. A two-year-old female neutered Burmese, with no history of travelling out of the UK, was presented with behavioural changes followed by acute onset of seizures that were refractory to medical therapy. MRI features were consistent with hippocampal necrosis. Histopathological examination of the brain confirmed the clinical diagnosis. This clinical report describes a confirmed case of hippocampal necrosis in a cat in the UK, raising the importance of considering this condition as a differential diagnosis in cats presenting with severe seizure activity.

Key words

seizures, cat, hippocampal necrosis, UK, magnetic resonance imaging, clinical

A TWO-YEAR-OLD female neutered Burmese cat was referred to the neurology services at Dick White Referrals (DWR) for evaluation of acute onset behavioural changes, characterised by aggression, and seizures refractory to anticonvulsant medications (0.5mg/kg diazepam intrarectally). There was no history of travel, trauma or known toxin exposure, and the cat was fully vaccinated and dewormed.

The physical examination was unremarkable. The neurological exam presented bilateral absence of menace response and complex partial seizures with automatism and orofacial involvement – salivation, facial twitching, lip smacking, chewing and licking. The neurological signs and the history were consistent with a forebrain lesion. The differential diagnoses included metabolic disease, intoxication, inflammatory process (infectious or sterile), vascular disease, neoplastic disorder or degenerative process.

A haematology and biochemical panel, including electrolyte profile, were unremarkable. Magnetic resonance imaging (MRI) using a 0.4 Tesla permanent magnet was performed under inhalant general anaesthesia (isoflurane). The pulse sequences obtained were:

• T1-weighted pre and post-contrast;

• T2-weighted; and

• fluid-attenuated inversion recovery (FLAIR).

The images were acquired in transverse, dorsal and sagittal planes.

T2-weighted (Figure 1a) and FLAIR (Figure 1b) images revealed bilaterally symmetrical enlargement and hyperintensity of the hippocampus and piriform lobe. These areas are slightly hypointense on T1-weighted sequences (Figure 1c). The affected areas were enhanced following administration of intravenous non-ionic contrast agent (0.1mmol/kg of gadoteric acid) initially moderately and with a slightly patchy nature (Figure 1d), but progressively uniformly and strongly increased in enhancement (Figure 1e). Cerebrospinal fluid (CSF) analysis revealed elevated protein – 76mg/dl, (25-30mg/dl) and mildly elevated nucleated cell count of 11/ìl (>5 cells/ìl) with mixed pleocytosis and red blood cell count of 4/µl (0). Real-time PCR on CSF for feline leukaemia virus (FeLV), feline immunodeficiency virus (FIV), *Coronavirus* and *Toxoplasma gondii* were negative, but a very weak positivity for parvovirus (panleukopaenia) was detected.

Symptomatic therapy initiated to control the seizures consisted of phenobarbital 3mg/kg orally twice daily and diazepam 0.5mg/kg intravenously. When the cat poorly responded it was followed by continuous treatment with levetiracetam at 20mg/kg orally three times daily and, based on the inflammatory CSF results, also dexamethasone 0.2 mg/kg intramuscularly once daily.

Improvement in mental status was observed over the next three days and no seizure activity noted during this time. The cat was discharged for continuation of treatment and monitoring by the owners with the presumptive diagnosis of idiopathic hippocampal and piriform cortical disease.

Partial seizures

The cat was readmitted the following day due to another episode of complex partial seizures. The cat continued showing daily partial seizure activity and, following a clinical course of seven days, the owner elected humanitarian euthanasia and postmortem examination.

Gross pathology of the intact and sectioned brain was unremarkable. However, histology showed severe bilateral degenerative changes involving the hippocampus and extending into the parahippocampal gyrus and piriform lobe. The hippocampus showed extensive loss of pyramidal neurons (Figure 2a) and milder loss of granule neurons with pronounced reactive astrocytosis, microgliosis and light lymphocytic perivascular cuffing (Figure 2b). A final diagnosis of hippocampal necrosis was made.

Necrosis of the hippocampus and the piriform lobe was initially described in Switzerland as a disease of unknown aetiology, but suggested to be environmental or possibly toxicological in origin (Fatzer, 2000). The emergence of similar cases in Italy, Germany, Austria and recently Sweden and Finland, has suggested the cause is not environmental, but specific underlying aetiology was not found (Gandini, 2004; Brini, 2004; Schriefl, 2008; Pákozdy, 2010; Fors, 2010).

The MRI findings in our case are similar to those previously reported and include T2 hyperintensity and T1 hypointensity in the hippocampal region and the piriform lobe without mass effect (Schmied, 2008). The histopathological findings that are the hallmark of this feline syndrome are hippocampal and piriform lobe necrosis, pronounced astrogliosis and mild lymphocytic inflammation; they indicate a focused disease process in the brain – this process can only be speculated about and might be a novel toxin or infectious agent with very discrete neuronal targets or an autoimmune process affecting part of the limbic system.

Inflammatory CSF

One finding differed in our cat from those previously described and it is the inflammatory CSF. Mixed pleocytosis is observed in cats under several conditions including fungal infection, FIP, *Toxoplasma gondii* and ehrlichiosis, the latter rarely results in neurological signs and is included in differential diagnoses when haematological abnormalities are present and in endemic areas (Cowel, 2008).

No causative agent

Although our cat was negative for diseases associated with pleocytosis (Cowel, 2008), in a group of 30 cats investigated for recurrent seizures, all cats were found to have structural brain disease and 47 per cent of them had a nonsuppurative meningoencephalitis indicating viral infection, but a causative agent was not found (Quesnel, 1997).

Mixed pleocytosis in the CSF following seizures, although never been reported in cats, has been reported in dogs (Goncalves, 2010). The weak positivity for parvovirus is possibly due to sample contamination as the cat was vaccinated and the virus is ubiquitous (Greene, 2006). The emergence of cats with similar presentation in the UK (Marioni-Henry, 2012) might be contributing to the hypothesis that the structural changes to the brain are a consequence of the seizures rather than the other way around.

Unfortunately, our cat did not respond to aggressive antiepileptic treatment in the early stage of the disease and, in the past, it would seem most cats responded similarly.

However, a few authors have reported successful treatment of the condition when treated early and aggressively (Pákozdy, 2011; Marioni-Henry, 2012). More research should be conducted to investigate the aetiology of this syndrome.

This report illustrates a more widespread geographic distribution of feline hippocampal necrosis than previously thought, and suggests the disease should always be considered as a differential diagnosis in cats presenting with severe seizure activity.

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