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Absence seizures with myoclonic features in a juvenile Chihuahua dog

Roberto Poma[1], Ayako Ochi[2], Miguel A. Cortez[2]

[1] Dept. of Clinical Studies, Ontario Veterinary College, University of Guelph
[2] Division of Neurology, Department of Paediatrics, Hospital for Sick Children, University of Toronto, Canada

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ABSTRACT – Long-term video-EEG was recorded for an eight-month-old Chihuahua dog with recurrent episodes of altered behaviour associated with head and nose twitching. Each episode lasted one to two seconds, multiple times per day before treatment. Ictal EEG showed generalised bilaterally synchronous 4 Hz spike-and-wave complexes during the "absence-like" event, along with rhythmically correlated head and nose twitching. We present video documentation of such attacks and discuss their similarities to human epilepsy with myoclonic absences. *[Published with video sequences]*

Key words: canine, myoclonic absence epilepsy, video-EEG, seizures

Epilepsy is the most common neurological disorder in dogs, with an incidence that ranges from 0.5% to 5.7% (Chandler, 2006). The current classification of canine seizures is mainly based on seizure phenotypes, the majority of which are motor activities, either focal or generalized (Berendt and Gram, 1999). There are only a few epileptic syndromes described in canine epilepsy (Lohi *et al.*, 2005; Morita *et al.*, 2002, Srenk and Jaggy, 1996). In this study, we report the first case of canine absence epilepsy with myoclonias which presents similar clinical and EEG characteristics to those reported in childhood absence epilepsy (Sadleir *et al.*, 2009).

Correspondence:
R. Poma
Dept. of Clinical Studies,
Ontario Veterinary College,
University of Guelph, Guelph,
ON, N1G 2W1, Canada
<rpoma@uoguelph.ca>

Case study

An eight-month-old male intact Chihuahua dog was admitted for evaluation of recurrent episodes of suspected focal seizures. The dog had a four-month history of recurrent episodes of head and nose twitching associated with intermittent hind limb jerking and suspected staring for a duration of a few seconds. Although the duration of these episodes remained unchanged the frequency continued to increase to three or four episodes witnessed in a day. There were no other abnormalities reported in his medical and physical history. At the time of admission, the completed blood count and a serum biochemistry profile were normal. On neurological examination, no significant findings were observed. Brain MRI was normal. Five-hour long-term video-EEG monitoring documented multiple clinical events.

At four months of age, the dog owner observed intermittent head and nose twitching along with occasional hind limb jerking especially when the dog was lying down in a quiet state

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(see video sequence 1). At that time, baseline metabolic investigations were normal and no treatment was administered by the referring veterinarian.

Multiple daily staring episodes with cessation of motor activity continued to be noticed along with intermittent head and/or nose twitching. A few seconds after each episode, the dog was reported to be quieter than usual and slower to respond to commands. Hind limb jerking episodes were occasionally seen and often in association with the facial twitching.

Upon admission to our canine epilepsy monitoring unit (Ontario Veterinary College, University of Guelph), the dog was sedated with intravenous propofol to set up a standardized montage with nine subdermal wiring electrodes located as follows: two frontal (F3, F4), one central (Cz), two occipital (O1, O2), two temporal (T3, T4) a ground and a reference. The reference was located 2 cm rostral to the Fz electrode. All electrodes were secured with a bandage and the dog was placed in a crate for long-term video-EEG monitoring, performed with a digital Stellate Harmonie EEG system using a referential montage.

Video-EEG documented multiple staring episodes either alone or in association with head and/or nose myoclonic jerks *(see video sequence 2A and B)*. There were no episodes of hind limbs jerking during this five-hour video-EEG session. The ictal EEG showed generalised bilaterally synchronous 4 Hz spike-and-wave complexes with rhythmic twitching of the head and/or nose, time locked to the abnormal EEG frequency *(figure 1)*. No photic stimulation or hyperventilation tests were performed. Immediately afterwards, treatment with phenobarbital 7.5 mg bd (6 mg/kg/day) was initiated. Five months later, a significant decrease in the number of episodes was reported and a follow-up five-hour long-term video-EEG recording did not detect any clinical or EEG abnormalities.

Discussion

Our clinical and EEG findings described in this case report appear to be similar to human absence seizures with myoclonic features (Hirsch *et al.*, 2008; Tassinari, 2008). Absence seizures are clinically described as a transient cessation of activity with staring, unresponsiveness and "blanking out" episodes. Our canine patient displayed similar features appearing somehow "disconnected" and transiently impaired in his behavioural attitude. Other clinical features usually reported in human patients with myoclonic features include motor activity characterized by bilateral myoclonic jerks mainly involving the muscles of the shoulders, arms, and legs but also facial muscles more evident around the chin and the mouth. In this case, the patient presented with a history of intermittent hind limb jerks, transient impairment of consciousness

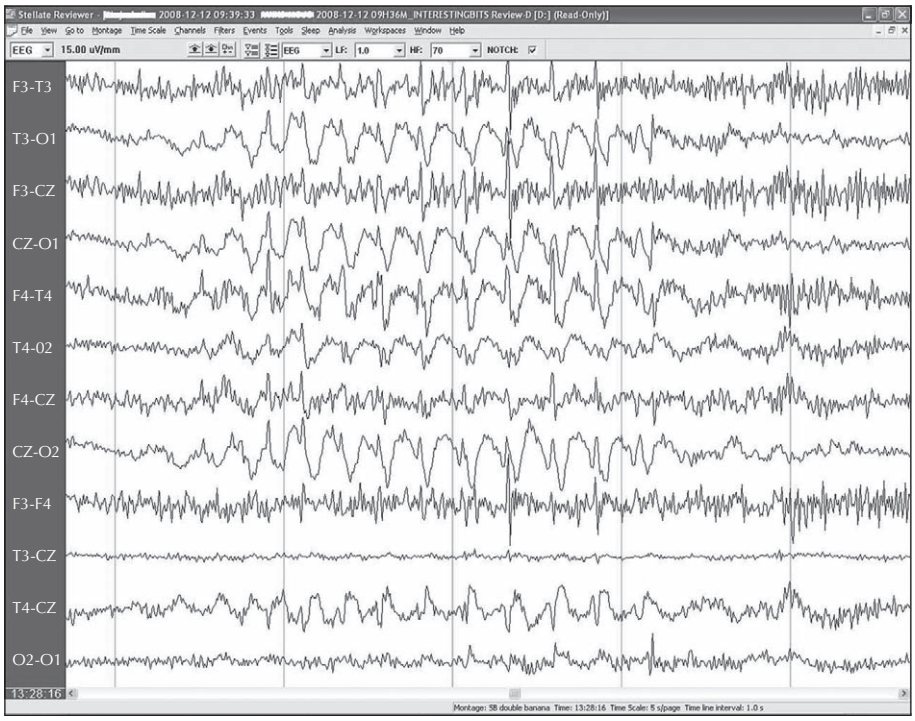

Figure 1. Ictal EEG. This epoch shows a 2-second run of 4 Hz spike-and-wave complexes during the absence episodes, time locked with the associated myoclonic head and nose twitching.

and motor manifestations characterized by head twitching along with nose twitching, both rhythmically correlated with the 4 Hz generalized spike-and-wave complexes, indicative of epilepsy with myoclonic absences. The jerking hind limb reported by the owner was not captured during the baseline and follow-up long-term video-EEG recordings, although several episodes were videotaped by the owner suggesting an abrupt, bilateral and synchronous myoclonic jerk involving both hind limbs and occurring at the same time as the head and nose twitching. These hind limb jerks resembled those observed in human patients with myoclonic absence epilepsy, a rare form of generalized cryptogenic/symptomatic epilepsy where severe bilateral rhythmic clonic jerks occur during an absence episode. The ictal EEG pattern recorded in our canine patient showed multiple runs of generalised bilaterally synchronous 4 Hz spike-wave complexes that correlated with head and/or nose twitching as documented in the video-EEG sequence.

Our patient responded partially to phenobarbital treatment exhibiting an overall decrease of myoclonic events. Human typical absences tend to respond well to sodium valproate and ethosuximide at high doses. In individual cases, good seizure control was achieved by using a combination of phenobarbitone, valproic acid and benzodiazepines (Tassinari, 2008). Unfortunately, the use of sodium valproate for dogs is not appropriate since its pharmacokinetic profile reveals a very short half-life, precluding the possibility to maintain a therapeutic concentration over the long term. The use of ethosuximide in dogs with seizure activity is so far unreported, and we reason that this could be an ideal treatment for future similar cases. We believe that the partial response to phenobarbital treatment in our case included spontaneous remission of the myoclonic absences, as observed in certain types of typical absences in humans. Since our patient is currently on a decreasing course of phenobarbitone, further considerations regarding efficacy of long-term response to treatment *versus* spontaneous improvement will be made according to his clinical neurological status and presence of eventual relapses.

Human absence seizures with and without myoclonic features are epileptic seizures manifested by impairment of consciousness during the occurrence of high amplitude 2.5- to 4-Hz generalised spike-and-slow-wave discharges. An absence seizure without myoclonic features is clinically described as the transient cessation of activity with staring, unresponsiveness and "blanking out" episodes. Absence seizures with myoclonia are characterized by motor activity including bilateral myoclonic jerks mainly involving the muscles of the shoulders, arms, and legs but also facial muscles, more evident around the chin and the mouth. Human epileptic syndromes with absence seizures that display electro-clinical manifestations similar to those observed in our patient include childhood absence epilepsy (CAE) and juvenile absence epilepsy (JAE). Children with CAE are usually aged 4-8 years old while JAE is more commonly seen around puberty (10-12 years).

Clinically, CAE is characterized by very frequent absences (from several to many per day) and generalised tonic-clonic seizures during adolescence, while JAE has a much lower frequency of seizures with similar phenomenology. First-line drugs for CAE are ethosuximide, sodium valproate and lamotrigine, alone or in combination. The majority of patients have a good response to treatment, and in some cases, absence seizures may remit or, more rarely, persist as the only seizure type. Patients with JAE are usually treated with similar medications to those with CAE. The response to treatment is good overall, especially when absence seizures are the only manifested seizure type. A less favourable response to treatment, however, is noted when generalised tonic-clonic seizures are associated with absence seizures (Hirsch *et al.*, 2008).

The absence seizure phenotype is observed in mice, rats, dogs and primates and each species presents similar seizure characteristics including staring spells, blanking out, unresponsiveness, stiffening and myoclonic jerks (Snead, 1995; Cortez and Snead, 2006; Chandler, 2006). Currently, only a few epileptic syndromes have been described in canine epilepsy (Lohi *et al.*, 2005; Morita *et al.*, 2002; Srenk and Jaggy, 1996). Lohi and colleagues (Lohi *et al.*, 2005) discovered a mutation in the *Epm2b* gene as the cause of Lafora disease in miniature wire-haired dachshunds. The genetic predisposition in our canine patient is unknown, however, this case report suggests the potential existence of a breed-related canine epileptic syndrome, of pure-breed long hair Chihuahuas with seizure onset at four months of age.

The adult stage of a dog is usually reached at around one year of age. If we consider the most general assumption that one year of life for a dog is equal to seven years of age for humans, we can estimate that this dog started to have seizure episodes (noted by the owner) at an equivalent human age of 3.5 years, comparable to early onset childhood absence epilepsy. Since our patient is a pure breed dog which was purchased from a selected breeder, further investigations were made to retrieve information regarding littermates and previous generations, however, there was no significant evidence of similar neurological features. This lack of findings for sibling or littermates may reflect a polygenic inheritance of idiopathic generalised epilepsy. Based on the pure breed nature of our patient, it is possible that only a few members of the family would be affected. On the other hand, the lack of evidence within a selected breed is not a surprising finding in veterinary medicine since scientific collaboration with the vast majority of breeders is often precluded by personal and financial reasons. Since the owner of our dog owned one of the patient's littermates, long-term video-EEG recording was performed with the aim of discovering similar neurological and EEG features,

however, no abnormalities were detected by neurological examination or during a three-hour video-EEG recording. Based on these considerations, more work is warranted to identify patients with similar phenotypes that may lead to the determination of a breed-related syndrome in long hair Chihuahuas and characterize a consistent clinical pattern that may correlate with a specific human epileptic syndrome.

The adjuvant of long-term video-EEG monitoring for the diagnosis of canine seizures represents a significant step forward in the evaluation of seizure phenomenology and seizure classification in dogs (Berendt *et al.*, 1999). In the past, the classification of canine seizures was purely based on seizure phenotypes, of which the majority were either focal or generalised motor activities. The existence of other seizure types, without overt motor manifestations such as sensory or autonomic seizures, has been speculated in canine epilepsy, although never scientifically demonstrated by video-EEG or ambulatory recordings (Berendt *et al.*, 1999).

We reason that without the video-EEG monitoring system in our clinical veterinary centre, this type of seizure in our canine patient could easily have been misdiagnosed. The bilaterally synchronous 4 Hz spike-and-wave complexes formally excluded the possibility of either simple partial or complex partial seizures. This case illustrates a formal indication of video-EEG monitoring for diagnosis of subtle myoclonic absences with perioral myoclonia and head twitching in dogs.

Legends for video sequences

Video sequence 1
Multiple, intermittent, abrupt and bilaterally synchronous hind limb jerks were observed and reported to occur at the same time as the head and nose twitching.

Video sequences 2A and B
Six clinical episodes are shown using a referential *(video sequence 2A)* and bipolar montage *(video sequence 2B)*, with a real time EEG correlate of 4 Hz spike-and-wave complexes associated with head and/or nose twitching. Four episodes (1st, 2nd, 4th and 6th) showed head twitching alone while one episode (3rd) showed subtle nose twitching only. The fifth event in these video sequences was characterized by significant head twitching that was preceded by overt nose twitching. A consistent altered behaviour is visible throughout the recording with the canine patient appearing "absent" during the duration of the epileptogenic discharges.

To our knowledge, this is the first case report of canine epilepsy with myoclonic absences. The clinical and EEG features recorded for our patient may represent a basis for facilitating comparative studies between different species with spontaneous and naturally occurring epilepsies. Further diagnostic studies are warranted to determine the existence of novel canine epilepsy syndromes and possibly breed-related epileptic syndromes with specific genetic mutations which may be shared by their human counterpart. □

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Disclosure.
None of the authors has any conflict of interest to disclose.

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