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Case Report

Clinical use of an herbal-derived compound (Huperzine A) to treat putative complex partial seizures in a dog

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ABSTRACT

A Bernese mountain dog was diagnosed with complex partial seizures that were supported by electroencephalographic findings. Clinical signs of the problem included "star gazing," fly snapping, licking, vacuous chewing, and ongoing anxiety. Treatment with Huperzine A, a compound isolated from Chinese club moss with NMDA receptor blocking activity, anticholinesterase activity, and anticonvulsant properties, produced useful suppression of the abnormal behavior for more than months. A relapse occurred when the dog was treated with tramadol for joint pain and the improvement that had been made was not recaptured with Huperzine A. At this stage, phenobarbital therapy was instituted and the dog improved greatly. The role of Huperzine A in controlling seizures is discussed.

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1. Introduction

A dog was evaluated for daily bouts of repetitive behavior such as star gazing, fly snapping, air licking, chewing, and lip smacking. In addition, the dog also showed fearful behavior, for example, running and bolting from one area of the room to another during these episodes.

2. Case description

The 2-year 10-month-old, 52.6-kg (116 lb) castrated male Bernese mountain dog resided with a single female owner and another dog, a 7-year-old spayed female Akita. The Bernese mountain dog was obtained from a breeder at the age of 8 weeks. The owner noted episodes of bizarre behaviors for the first time when the dog was about 2 years old. The first odd behavior that became evident to the owner was a behavior she called "air kissing." During these episodes the dog looked up, licked the air, and smacked his lips afterward. The dog repeated this behavior, and bouts generally lasted several minutes. The severity and frequency slowly progressed. Over time the dog started to exhibit new and different behaviors during an episode. The additional behaviors included fly snapping, star gazing, vacuous chewing, and running from one corner of the room to another while

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appearing fearful. Between episodes the dog acted normally and interacted happily with his owner and the other dog in the household.

The dog that is the subject of this report developed a hot spot on his lower back about 9 months after the initial bizarre behaviors were noted. He was hospitalized to receive treatment and had to wear an Elizabethan collar to prevent him from licking that area. While hospitalized, the dog was treated with diphenhydramine 1 mg/kg (0.45 mg/lb) three to four times a day for 1 week. The owner noted significant exacerbation of the behavioral episodes following the dog's hospitalization. The frequency of the bouts increased to several times daily and, ultimately, to hourly for some days after the hospitalization. The duration of a single episode was between 10 and (about once every 3 months) 60 min.

One trigger of the episodic behavior was the presence of a fly in the house. Whenever the dog saw a fly, he started chasing it and continued searching and chasing behavior plus the aforementioned oral behaviors for up to an hour after the fly was removed. The owner was not always able to ascertain a trigger for an episode, but noted that the dog had more frequent and more intense episodes during stressful times (such as long car rides) and in the morning. It was also extremely difficult or sometimes even impossible for the owner to interrupt the dog when he was engaged in these behaviors, especially when bolting from one corner to another. The owner tried to reduce the dog's stress by keeping him busy and distracting him with obedience commands and talking to him in a soothing way during these episodes. She also took the dog to several classes on basic obedience and agility training.

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In addition, the owner had started to attend "Feisty Fido" classes because the dog had exhibited some mild aggression toward other dogs during the second year of his life. The owner worked with a trainer on desensitizing and counterconditioning her dog to other dogs.

2.1. Previous diagnoses, clinical findings, and laboratory results

The dog had been diagnosed with a variety of medical issues prior to the behavioral consultation. At the age of 6 months, he developed a mass on the right side of his abdomen. The mass was removed and found to be a benign granuloma. Subsequently, elbow and hip dysplasia was diagnosed within the first year of life. At the time of the behavioral consultation, the dog's orthopedic conditions were under treatment with carprofen 100 mg (1.9 mg/kg) once a day and acupuncture every 5-6 weeks. According to the owner, these treatments worked very well. Before the combination of pain medication and acupuncture, the dog reportedly was hardly able to walk. The owner also occasionally gave the dog a Chinese herbal combination called Du Huo Ji Sheng Wan and the joint supplement OsteoBiFlex. She was not sure how much these supplements helped with the joint issues. Bilateral cataracts were noted when the dog was 14 months old as he was being examined for apparent conjunctivitis. The cataracts appeared to be nonprogressive on regular eye examinations performed by the local veterinarian. A complete blood count and a chemistry profile were performed by the local veterinarian 2 weeks before the behavioral consultation. All values were within reference range except for marginally elevated alanine aminotransferase (ALT: 158 U/L on a scale of 5-107 U/L) and aspartate aminotransferase (AST: 70 U/L on a scale of 5-55 U/L) levels.

On presentation at the behavior clinic, the dog was found to be in overall good health. The cataracts, a slightly impaired gait, and obesity were noted. The dog appeared somewhat nervous in the consulting room. Two short (20-s) bouts of star gazing and fly snapping occurred during the appointment. According to the owner the episodes we observed were only mild.

2.2. Diagnosis

Previous blood work and physical examinations had ruled out several possible medical reasons for the dog's fly snapping, star gazing, vacuous chewing, and anxious behavior, such as inflammatory and infectious processes, organ dysfunction, and impaired vision. Abnormalities noted in the blood work were marginal and did not raise any concerns. However, the owner was asked to have the blood work repeated in 6 months. Attention-seeking behavior could be ruled out as the dog often separated himself from the owner by going into another room before air licking and star gazing, and his owner usually did not follow him. A compulsive disorder as the cause for the dog's repetitive bizarre behavior could not be ruled out completely.

Based on the boutlike presentation of the episodes and on the behaviors exhibited (star gazing, fly snapping, licking, chewing, and anxiety) and taking into account that the dog was a Bernese mountain dog, a preliminary diagnosis of an idiopathic focal seizure disorder was made. An EEG was recommended to confirm this diagnosis; however, for reasons of cost, the owner opted against it at that time.

The owner did not want to discuss her dog's aggression toward other dogs as she did not perceive it to be a major problem. During the consultation she wanted us to focus our attention on treating the bizarre episodic behavior. For this reason, no diagnosis in regard to the aggression toward other dogs was made.

3. Treatment

Treatment comprised several different components. First, the owner was advised to make a videotape of more intense episodes to share with the clinicians, help confirm the diagnosis, and allow posttherapeutic comparisons to be made. She was also asked to keep the stress level low for her dog by maintaining a structured, predictable daily routine with respect to feeding, walking, and playtime and was encouraged to continue attempting to distract the dog during the episodes. Furthermore, she was advised to try to avoid exposing the dog to potential triggers of the behavior as far as possible. Pharmacological options were discussed, and the owner was given the option of treating the dog with phenobarbital to control putative seizures or trying a new, holistic approach using Huperzine A. As the owner favored holistic treatment, she decided to try Huperzine A first. A starting dose of $1 \mu g/kg$ (0.45 $\mu g/lb$) twice a day was employed. The owner was notified that possible side effects of Huperzine A are ataxia, dizziness, vomiting, and diarrhea. She was asked to report back immediately if she observed any of these or other side effects. The owner was also asked to report back on a weekly basis to assess changes in the star gazing, air licking, fly snapping, chewing, and anxious behavior.

3.1. Follow-up

The owner picked the Huperzine A up from a pharmacy on the way home from the appointment and gave her dog the first dose that evening. Four days after the appointment, the owner called to report that the episodes had become considerably less intense over the past few days; they no longer lasted 10-60 min but instead lasted only 2-3 min. In addition, she had not witnessed any aimless running from one corner of the room to another. She described that her dog, in general, appeared more focused and responsive. A week later she checked in again to report that she had not witnessed a single episode for the last few days. She even took the dog on a long car ride to another state, and this did not trigger an episode. This type of activity had been stressful for the dog in the past and reliably triggered episodes. The owner was extremely pleased with her dog's progress and reported that he could easily be distracted with obedience training, toys, and games from minor episodes she witnessed at the beginning of the second week. The noted episodes consisted mainly of air licking and lip smacking. The owner called back again a week later and reported that there was only one minor incident that week when a fly became trapped in the car and the dog started to chase it. After she removed the fly, the owner was able to verbally control the dog and successfully instructed him to lie down to interrupt one episode of fly snapping and air licking. This was something she had not been able to do before. At that point the owner also reported that the dog was doing better overall, was full of energy, and even the joint issues seemed to be better. During the fourth week of treatment, the owner reported a mild regression, having witnessed four episodes during the last week. These episodes were all minor and did not last longer than 2 min. The owner was not able to interrupt the dog during one of these episodes and reported that she witnessed more star gazing and air licking than in the preceding weeks. The owner asked if she could increase the dose of Huperzine A to 50 μg three times a day. We agreed that this would be the best course of action for her, so that dosing change was made. The owner checked in again 1 week after the dose increase (fifth week of treatment). Once more she reported improvement; there had only been one or two episodes of air licking and lip smacking that entire week. The owner thought these incidents might have been triggered by a fly in the house. Overall the owner was very pleased with the improvement.

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