Title
Animal behavior case of the month. Noise phobia, cognitive dysfunction, separation anxiety, attention-seeking behavior, and medical causes.

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Animal Behavior Case of the Month

**Statement of the Problem**

A Labrador Retriever mix was evaluated because of panic attacks in response to loud noises, including noises made by a household African grey parrot (*Psittacus erithacus*) mimicking the sound of a smoke detector.

**Signalment**

The patient was a healthy 40-kg (88-lb) 9-year-old castrated male Labrador Retriever mix.

**History**

The dog had been acquired by the owner from a friend 1 year prior to the initial evaluation. A male African grey parrot also lived in the house. The owner ran a pet-sitting business, and the dog interacted regularly with other dogs of various ages and breeds. According to the previous owner, when the dog had been a puppy, children cornered it and terrorized it with fireworks, causing it to become fearful of fireworks. Ever since the current owner had acquired the dog, it would, whenever it heard noises such as fireworks or the sound of the bird mimicking a smoke detector, perk its ears up and move toward the noise with head lowered and tail either up or down. After several days, the dog would run to and destructively chew the front or back door. When it had access to a dog door, it would run outside, chew through the fence, and escape. After escaping, the dog would usually sit by the owner’s car but would sometimes wander away. During the previous Fourth of July, its body shook and the dog chewed through the carpet, chewed the door, and chewed a glass doorknob. Acepromazine (unknown dosage) was prescribed that night, and although sedation was started, the dog became aggressive toward unfamiliar dogs, and use of the drug was discontinued, ending the aggression. At the time of the initial evaluation, the dog was not receiving any medications, either orally or topically, and was being fed a well-balanced diet.

**Physical Examination Findings**

In the examination room, the dog paced with its ears back for 15 minutes and then lay down. When fireworks noises were played on a stereo, the dog looked at the stereo with its ears up and began to pant. Later, it responded to the beep of a pager by standing with its ears back, panting, walking toward the door, and pacing. The owner called the dog, and although it turned toward her, the dog continued to pace and did not respond to commands. On physical examination, the dog had a body condition score of 6 on a scale from 1 to 9. All canine teeth and the maxillary fourth premolar teeth bilaterally were fractured. All other physical and neurologic examination findings were unremarkable.

**Diagnosis**

Diagnostic evaluations that were considered for the dog’s panic reaction to noises included noise phobia, cognitive dysfunction, separation anxiety, attention-seeking behavior, and medical causes. Noise phobia was diagnosed on the basis of the dog’s history of anxious behavior, destructiveness, and self-trauma during loud noises and observation during playback of sounds on the stereo. Cognitive dysfunction was ruled out given the lack of other clinical signs and the fact that the behavior had been occurring from a young age. Separation anxiety was considered owing to the fact that it is commonly seen in conjunction with noise phobia but ruled out because the dog was not destructive and did not escape from the house when home alone. The dog’s behavior was not consistent with attention seeking as a primary
etiology owing to the severity of somatic responses and body postures consistent with anxiety. Other medical and neurologic causes were considered less likely given the unremarkable findings on physical examination, but a CBC, serum biochemistry panel, and urinalysis would be a first step to rule out underlying medical conditions. A higher index of suspicion for neurologic disease would have prompted further diagnostic testing, such as MRI, to evaluate for underlying intracranial disease. Additionally, multiple fractured teeth were diagnosed in the dog.

**Treatment**

The owner was instructed to avoid the dog’s noise triggers to prevent continued fearful reactions and to facilitate controlled reintroduction of the noises. This included putting up a room-dividing screen to block the bird’s cage, use of cotton balls as ear plugs, and playing music to cover up unavoidable noises. Use of the cotton balls was to be discontinued if they caused any distress to the dog or became lodged in its ears. A command-response-reward program that would create structure and predictability for the dog and teach it to look to the owner in difficult situations was advocated. The owner taught the dog an eye contact command to help the dog focus on her, with the expectation that this command would then be used with future systematic desensitization and counterconditioning programs; low-calorie palatable treats were used as a reward to prevent weight gain. Desensitization and counterconditioning and pheromones have been shown to improve behaviors associated with fear of noises; however, pheromones were previously unsuccessful in reducing the dog’s anxiety. Systematic desensitization is defined as a decrease in an undesired response that is induced by gradual exposure to a stimulus that elicits the response. Counterconditioning is defined as a decrease in an undesired response that is induced by gradual exposure to a stimulus.[12] The dog was fitted with a head collar for better control during desensitization and counterconditioning. The owner was instructed to follow up with a veterinary dentist to address the dog’s fractured teeth.

**Follow-up**

At the 5-week recheck examination, the dog was becoming increasingly nervous around the bird. The dog would look behind a screen put in front of the bird cage and back away from its food in the morning while a sheet was still on the bird’s cage; however, it was less anxious overall, which the owner attributed to the bird making less noise. The dog reliably learned the eye contact command and wore its head collar comfortably. The owner was instructed to implement desensitization and counterconditioning by playing smoke detector and fireworks noises downloaded from a website at a low volume so that the dog was calm when she gave it commands, and she rewarded it with special treats for responding.

Blood and urine samples were obtained for analysis. Results were unremarkable except for isosthenuria, mild leukopenia, and mild hypocalcemia. Isosthenuria in a single urine sample could be caused by drinking a large amount of water just before the sample is obtained; therefore, the first step in evaluation would be to recheck the specific gravity in the dog’s first urine sample of the day. Causes of persistent isosthenuria include early renal insufficiency, hyperadrenocorticism, and psychogenic polydipsia. Diabetics mellitus, hypoadrenocorticism, hepatic failure, hypercalcemia, and hypokalemia were eliminated as differential diagnoses on the basis of clinicopathologic test results. Results of a CBC were normal except for mild leukopenia characterized by mild lymphopenia, attributable to stress. Serum biochemistry findings were unremarkable, except for mild hypocalcemia, and a recommendation was made to recheck serum total calcium concentration and evaluate serum ionized calcium concentration. Differential diagnoses for the hypocalcemia included a spurious result and early renal insufficiency, considering the isosthenuria. Primary hypoparathyroidism and intestinal malabsorption were considered less likely owing to the dog’s lack of other signs. It was recommended that the owner follow up with the referring veterinarian to monitor and evaluate the dog’s hypocalcemia and isosthenuria.

Long-term administration of an antianxiety medication such as a selective serotonin reuptake inhibitor was strongly recommended; the owner initially declined but, 8 weeks after the initial evaluation, reconsidered. Selective serotonin reuptake inhibitors work by inhibiting the reuptake of serotonin, resulting in an increase in serotonergic neurotransmission.[18,19] With prolonged use, there is a downregulation of serotonin receptors. Selective serotonin reuptake inhibitors can be used in cases of specific anxieties and have fewer adverse effects than tricyclic antidepressants.[18,19] Although the owner reported aggression while the dog was receiving clorazepate, another benzodiazepine with a shorter duration of action, alprazolam (0.05 to 0.075 mg/kg [0.023 to 0.034 mg/lb], PO, as needed, up to 3 times daily), was prescribed for acute relief of anxiety associated with unavoidable loud noises while behavior modification was instituted. The anxiety relief benzodiazepines provide can result in loss of inhibition, leading to aggression, but the risk was likely lower with alprazolam, given that alprazolam has a shorter duration of action than clorazepate and was to be used only on an as-needed basis, instead of a daily basis. Benzodiazepines have a rapid onset of action and work by facilitating γ-aminobutyric acid, an inhibitory neurotransmitter, in the CNS. Behaviors associated with thunderstorm phobia have been shown to decrease significantly with administration of alprazolam and clomipramine (a tricyclic antidepressant) and behavior modification.[21] The risk of adverse effects, including aggression and sedation, and extralabel use were discussed. Hepatic and renal parameters were assessed prior to use, and the unknown etiology of the dog’s isosthenuria was considered, prompting use of a conservative initial dosage of alprazolam, which is excreted through the kidneys.

Eight weeks after the initial evaluation, the dog was prescribed a selective serotonin reuptake inhibitor, fluoxe-
etine (0.75 mg/kg, PO, q 24 h). Again, a conservative initial dose was chosen because fluoxetine is excreted through the kidneys. Ten weeks after the initial evaluation (2 weeks after the start of fluoxetine administration), the owner reported sedation. The immediate actions of selective serotonin reuptake inhibitors lead to immediate adverse effects, and desensitization of the receptors correlates with tolerance and reduced adverse effects.19 Lowering the dosage was discussed, but the owner decided to continue administration at the same dosage to determine whether the sedation would lessen. Thirteen weeks after the initial evaluation (5 weeks after the start of fluoxetine administration), the dog ran to the door when the neighbors set off fireworks, but did not try to escape. The dog would go to the door in response to the bird’s vocalizations, but the owner could call and easily redirect it by giving the dog a command and rewarding it with a treat.

Seventeen weeks after the initial evaluation, the dog continued to improve, and when it heard fireworks, it looked at the owner before she even gave the dog a command. At that time, the owner reported that the dog started to lunge and bare its teeth at familiar dogs in close proximity. The owner was advised to avoid this situation. Lowering the dosage was discussed, but the owner decided to continue use at the same dosage to determine whether the aggression would subside.

Twenty-two weeks after the initial evaluation (14 weeks after the start of fluoxetine administration), the dog started charging and barking at unfamiliar people. The dog was weaned off of fluoxetine over a month, and the dog’s aggression toward familiar dogs and unfamiliar people had stopped. When fluoxetine was administered at a dosage of 0.25 mg/kg (0.11 mg/lb), PO, once daily, the dog’s aggression toward familiar dogs and unfamiliar people had stopped. When fluoxetine was administered at a dosage of 0.25 mg/kg (0.11 mg/lb), PO, once daily, the dog’s sedation was resolved. The dog’s sedation seemed to be dose dependent, and the optimal dosage for the dog was only a fraction of the reported optimal dosage.18 It is possible that the low effective dosage of fluoxetine in this dog, along with the persistent adverse effects at the published dosage, was the result of impaired renal function altering medication excretion.18 After 4.5 months of treatment with fluoxetine, the dog was completely weaned off, but its anxiety to the bird returned.

Seven months after the initial evaluation, the dog was again prescribed fluoxetine (0.25 mg/kg, PO, q 24 h). This low dosage helped with the dog’s noise phobia yet left it alert and without signs of aggression. Switching to another selective serotonin reuptake inhibitor or a tricyclic antidepressant was considered because a different medication could potentially further reduce anxiety without causing undesirable adverse effects; however, owing to the unavoidable nature of the noise stimuli and the risk of increased aggression, which the owner could not tolerate because of her pet-sitting business, fluoxetine was chosen, considering that it was known to previously have been effective at a lower dosage without causing an increase in aggressive behavior. The owner continued desensitization and counterconditioning. Eight months after the initial evaluation, the dog would either bring the owner a ball when the bird vocalized or calmly go outside until the bird was quiet, with no signs of anxiety. The owner had never given alprazolam to the dog. Despite repeated recommendations, the owner had not followed up with treatment of the fractured teeth or further investigation into the causes of the hypocalcemia and isosthenuria.

References