Canine Narcolepsy
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Introduction
Narcolepsy is a disorder of the central nervous system that is characterized by sudden, recurring attacks of sleep. Although narcolepsy was first described in the human medical literature over ninety years ago, the first case of canine narcolepsy was recognized in 1973. It currently has been reported in several breeds of dogs, in cats, and in horses. It is a well defined neurological condition in human beings, affecting as many as five to ten people out of every 10,000. The major symptoms of the disease in man are excessive daytime sleepiness, cataplexy and, less often, sleep paralysis and hypnogogic hallucinations.

Soon after Knecht et al first reported canine narcolepsy in 1973, Stanford University acquired several dogs affected with the disease as models for the human disorder. Since then narcolepsy has been diagnosed in several mixed and pure breeds of dogs.

Development of Narcolepsy
Features common to both human and canine narcolepsy are the development of sleepiness and cataplectic attacks early in life. Cataplexy in the dog manifests itself as postural collapse, areflexia, and partial to complete muscle atony with a sparing of the respiratory and ocular muscles. These symptoms generally appear prior to six months of age in the canine (over 75% showed symptoms by 6 months in a study conducted by Foutz et al). No correlation between the age of onset of cataplexy and the severity of the disorder has been noted. Thus narcolepsy may develop abruptly and undergo little change for the rest of the patients life. It is interesting to note that in man the symptoms of narcolepsy begin between 10–20 years of age in three out of four of the cases.

Heritability
Narcolepsy is thought to be an inherited trait, since the incidence of the disease in related individuals is 200 times that of the normal population. In dogs, studies have been carried out in a Stanford University colony by mating narcoleptic Doberman Pinschers. Thus far, four litters have yielded 22 puppies, all of whom developed cataplexy. However, the breeding of two narcoleptic beagles has produced seven pups, all unaffected. The debate continues as to whether the disease is a polygenic or a single dominant gene with low penetrance. Narcolepsy is definitely hereditary in some breeds, however it may also be derived from developmental accidents or other nongenetic factors.

Symptoms of Narcolepsy
Sleepiness: Excessive somnolence is a primary complaint among human narcoleptic patients. These sleep attacks are sudden, reversible, and last about 10 to 15 minutes. Generally they occur while the patient is performing in a boring situation. However, these “sleep attacks” may occur under a variety of situations, including driving, dancing, or even swimming.

In most cases, somnolence does not significantly affect the dog’s behavior. Therefore this is usually not a primary complaint or presenting symptom by the owner. The most common and most obvious clinical sign in the dog is cataplexy.

Cataplexy: Cataplexy presents as an acute attack of flaccid paralysis. These attacks are frequently precipitated by the excitement of such things as the presentation of food, another dog, sexual activity, or sudden ap-
pearance of their masters. Young puppies seem more susceptible to attacks during periods of playful activity. Cataplectic attacks may last from a few seconds to several minutes. The dog will collapse in any position and its eyes are open, alert, and following any movement in the room. These attacks are reversible by an external stimulus such as petting or calling the animal's name.

Sleep paralysis is reported in man to be an inability to move or cry out and is often associated with hypnogogic hallucinations (i.e. a frightening or threatening dream). Neither of these occurrences has been documented in the canine.

Normal Sleep Patterns in the Canine

It is believed that sleep in dogs, cats and in humans occurs in three stages: nonrapid eye movement (NREM), light slow-wave sleep (LSWS), NREM deep slow-wave sleep (DSWS), and rapid eye movement (REM) sleep. Each of these stages can be characterized by the presence or absence of dreaming, muscle tone, and alternations in the electroencephalogram (EEG). NREM sleep is identified by the absence of REM, a high voltage, slow activity EEG pattern, the presence of muscle tone, and little or no dreaming. REM sleep is characterized by REM's, low voltage, fast activity EEG pattern, an absence of muscle tone, and dreaming. It is generally accepted that normal sleep patterns consist of a period of NREM, LSWS, NREM, DSWS, and REM sleep. In man, sleep periods change from NREM to REM sleep every 80 to 120 minutes.

Abnormal Sleep Patterns in the Narcoleptic Canine

The dog afflicted with this disease demonstrates altered normal sleep patterns. These variations may manifest themselves as excessive daytime sleepiness, disturbed night time sleep, and abnormal REM sleep. It is important to note that the time spent sleeping does not differ from normal but the duration and distribution of sleep phases are altered. Pathological REM sleep is observed clinically in the dog by a sudden onset of sleep from an alert state. The REM sleep in the canine is characterized by closed eyelids, fascicular twitches of the distal musculature, weak vocalization, immobility, and a low voltage, fast activity EEG pattern. The usual period of NREM sleep is absent or at least greatly reduced in time.

Etiology

The exact etiology of the narcoleptic syndrome has never been determined. Many possible causes for narcolepsy have been proposed in the human literature. Between 1920 and 1960, psychoanalysis developed many theories emphasizing a psychogenic etiology. Their theories proposed that feelings such as sexual impulses, guilt feelings, hatred, etc. were so unacceptable to the patient that the narcoleptic sleep and cataplectic attacks served as defense mechanisms for the repression of such feelings.

Current investigations suggest the origins for the disease may be in the area of the reticular activating system. It is known that REM sleep is initiated and regulated by areas of the pontine reticular formation. Certain areas here also initiate the muscle inhibition and areflexia of REM sleep. NREM sleep is thought to result from the inhibition of the reticular activating system. Some authorities propose there is either an increased REM discharge or a loss of the REM inhibition. Recent theories suggest narcolepsy is a neurotransmitter problem. Current biochemical analysis of cerebral spinal fluid in narcoleptic dogs suggest reduced concentrations of serotonin and dopamine and a decreased turnover of norepinephrine. This suggests there are low levels of neurotransmitters in the brain of narcoleptics. Treatment of narcolepsy is aimed at increasing the concentration of these neurotransmitters.

Diagnosis

The diagnosis of narcolepsy and cataplexy is based primarily on the basis of history, clinical signs, age of onset, and the exclusion of other more common diseases. Foutz described a food-elicited cataplexy test to confirm the diagnosis of cataplexy in affected dogs. Ten one ml pieces of food are placed in a row approximately 30 cm apart. The time required to eat the food and the number of attacks that occur is an index of severity. Phystostigmine salicylate (Antilirium), an anticholinesterase, given intravenously at doses ranging from .05 to 0.1 mg per kg greatly increases the probability of a spontaneous attack within 5 to 15 minutes after its injection.

An important differential that should be
made is epilepsy. During cataplexy, no urinary or fecal incontinence or excessive salivation are seen. No tonic rigidity of the musculature occurs with cataplexy either. It should be noted that the nonepileptic will not show improvement in response to anticonvulsants or barbiturates.

Another important differential is myasthenia gravis. Myasthenia can be ruled out if the condition fails to improve with peripheral acting anticholinesterases such as neostigmine.

Hypokalemia may result in similar symptoms, however, the blood chemistry in narcoleptic dogs is within the normal range. Differentials in human medicine also include hypoglycemia and suspect hypothyroidism.9

Treatment

Amphetamines, tricyclic antidepressants and MAO inhibitors are the primary drugs used in the treatment of the narcoleptic humans. These drugs work by blocking the re-uptake of CNS neurotransmitters, thereby allowing their concentrations to increase at the synaptic clefts, or by stopping excess or normal enzymatic breakdown of neurotransmitters.

In narcoleptic humans, treatment is aimed at control of excessive sleep and control of cataplexy. Central nervous system stimulants have been used in man to treat excessive daytime sleepiness while tricyclic antidepressants have been used to treat cataplexy.5

Controlling somnolence in dogs may not be a high clinical priority since it usually fails to significantly affect the animal’s behavior. Current drug therapy in the canine is aimed at control of the cataplectic attacks. The general stimulant methylenidate hydrochloride (0.25 mg per kg) has marked anti-cataplectic properties. It acts by suppressing both REM and NREM sleep.3 The tricyclic antidepressant imipramine (Trofanil, 0.4 to 0.8 mg per kg) is used more commonly for controlling cataplexy. It blocks the uptake of serotonin and norepinephrine and suppresses only REM sleep.

Another possibility for treatment that is currently being investigated in dogs is the use of monamine oxidase inhibitors. Their use in man has been discontinued due to complications such as hypertension, edema, impotence and severe cardiovascular side effects when the diet contained tyramine.8,9

The clinician should not hope to completely block cataplexy but should attempt to achieve an acceptable reduction in frequency and duration. It must be stressed that the disease is not in itself life-threatening and that it will not significantly get worse with time. The owner should avoid exposing the animal to situations that elicit unusual excitement and to places where attacks may be dangerous (e.g. busy streets).2

REFERENCES