

Myasthenia Gravis in a Dog

Hasan BATMAZ, Fikriye SÜZER, Engin KENNERMAN, Zeki YILMAZ
Uludağ University, Faculty of Veterinary Medicine, Department of Internal Medicine, Bursa-TURKEY

Received: 28.02.1997

Abstract: A seven-month-old male collie was brought to our clinic with complaints of exhaustion and fatigue for the past month, inability to stand on its hind legs, loss of voice and anorexia for the past week. In clinical examination, increase in heart frequency, difficulty in lifting the head, tetraparesis, regurgitation and urinary incontinence were observed. MG was suspected and 0.05 mg/kg i.m. neostigmine methylsulfate was given for clinical diagnosis. A positive response was seen within 30 minutes of drug application. The same drug was administered 3 hours later and the same positive clinical findings were observed. The disease was diagnosed as MG. The serum AChR antibody concentration was determined to be 0.03 nmol/l. Pyridostigmine bromide was used for four weeks and prednisolone was used for two weeks. The patient was able to walk normally after 15 days and had a good appetite. The dog was sent back home in good health six weeks later and the disease did not relapse for more than two years.

Key Words: Myasthenia gravis, dog.

Bir Köpekte Myasthenia Gravis

Özet: Yedi aylık, erkek Collie köpek son bir ayda kas zayıflığı belirtileri, son bir hafta içinde arka ayakları üzerinde duramama, sesin kaybolması ve iştahsızlık şikayetleri ile kliniğimize getirildi. Yapılan klinik muayanesinde, kalp frekansında artış, başını güçlükle kaldırdığı, ayağa kalkamadığı, regürjitasyon ve idrarını tutamadığı gözlemlendi. MG'dan şüphelenildi ve klinik tanı için 0.05 mg/kg neostigmine methysulfate'in i.m. yolla verildi. Bu ilacın verilmesinden 30 dak. içinde klinik yanıt alındı. Üç saat sonra aynı ilaç tekrar edildi, aynı klinik bulgular gözlemlendi. Hastalık MG olarak değerlendirildi. Serum AChR antikor konsantrasyonu 0.03 nmol/l olarak saptandı. Pyridostigmine bromid dört hafta ve prednisolone iki hafta kullanıldı. Hasta 15 gün sonra normal olarak yürüdü ve iyi bir iştaha sahip oldu. Köpek altı hafta sonra sağlıklı olarak evine gönderildi. Bu hastalık iki yılı aşkın sürede nüks etmedi.

Anahtar Sözcükler: Myasthenia gravis, köpek.

Introduction

Myasthenia Gravis (MG) is a neuromuscular disease characterized by muscle weakness and fatigue (1, 2). MG occurs in both acquired and congenital forms (3). It has been reported that although acquired MG in dogs is seen to begin in animals from eight weeks to eleven years of age, it is usually observed between the ages of one and eight years (3, 4). The clinical symptoms of congenital MG have been reported to arise in 6-8 week-old puppies (3).

The cause of MG is the reduction in the number of functional acetylcholine receptors in the postsynaptic membrane of the neuromuscular junctions (1, 5). Acquired MG is characterized by the presence of autoantibodies against acetylcholine receptors (1, 2). Although the cause of autoantibodies is not exactly known, it has been suggested that the thymus may play a role (1, 2). Thymoma has been observed in some cases (6, 7, 8); however, autoimmunity signs have been reported to be absent in congenital MG (1, 3).

MG is a disorder which appears with exercise and is characterized by fatigue in skeletal muscles (4, 5). Most patients show clinical such signs as dysphagia, salivation and megasophagus along with regurgitation. It has been reported that, as a result of clinical symptoms, aspiration pneumonia can occur (3). According to some authors (3, 4) the definitive diagnosis for MG can be made by its reply to cholinesterase drugs, electrodiagnostics and the presence of antiAChR antibodies in the sera of the patients. Treatments for MG in dogs have been reported to be mainly cholinesterases and immunosuppressive drugs (1, 4).

Case Report

A seven-month-old male Collie weighing 15 kg was brought to our clinic with complaints of exhaustion and fatigue for the past month and inability to stand on its back legs, loss of voice and anorexia for the past week. The following parameters were recorded in the first physical examination: heart frequency 104-108/minute,

respiration frequency 28-32/minute, temperature 38.2°C, total leukocyte count 7300/mm³, hematocrit value 38%, creatin phosphokinase 166 U/L and aspartate aminotransferase 13.3 U/L.

The dog was hospitalized. Over two days the following symptoms were observed: inability to stand (tetraparesis), difficulty in lifting the head, increase in heart frequency, regurgitation and urinary incontinence (Figure 1). Clinical findings were evaluated and, on the assumption that the disease might be MG, neostigmine methylsulfate (Prostigmine amp., Roche) was given at a dose of 0.05 mg/kg IM, and a positive clinical reply occurred within 30 minutes. Three hours later, the drug was readministered (0.85 mg) and the same findings were obtained (Figure 2). The disease was diagnosed as MG. Following drug use, heart frequency decreased and defecation was observed; however, cholinergic crisis findings such as salivation, vomiting and diarrhea did not occur. Although megaesophagus was suspected in thoracic radiographs, no signs of thymoma or aspiration pneumonia were observed. The following day, neostigmine was administered in respective doses of 0.85 mg, 1mg, 1mg and IM. On the third day, as there was no longer any risk of regurgitation, oral administration of pyridostigmine bromide (Mestinon dr., Roche) with the effect of long-term anticholinesterase was begun. It was administered 2 mg/kg twice daily for two weeks, and gradually decreased to 10 mg (0.64 mg/kg) over the next two weeks. Two days after pyridostigmine bromide treatment was started, prednisolone was administered twice daily at a dosage of

2 mg/kg IM and, over a period of weeks, was decreased to 1.5 mg/kg once a day. After this, prednisolone treatment was discontinued.

It was observed that within two days the dog was able to stand on its forelegs. Between the second and fifth day the dog could drag its hindlegs and was able to consume a liquid diet. On the fifth day, the dog was able to control its urination and defecation, and between the seventh and fourteenth days could walk with support and stand up on its own to defecate. The dog barked for the first time on the ninth day. On the fifteenth day it walked normally and its appetite returned. Two weeks after the pyridostigmine treatment was discontinued, the dog was examined in our clinic. Although treatment had stopped, the dog began running. No relapse of the disease was observed as much as two years after the patient was returned to its owners (Figure 3).

Serum anti-AChR antibody concentrations were determined at Comp. Neuromuscular Lab, CA, USA. Serum AChR concentration was 0.03 nmol/l before treatment and 0.0 nmol/l after treatment.

Discussion

Although the most common findings of MG are reported to be walking disorders following exercise (1, 4), such symptoms are also seen in peripheral neuropathy and polymyositis. In these diseases, the walking abnormalities are continuous, and there is atrophy in the muscles, and other findings associated with MG are not



Figure 1. Appearance of the dog with myasthenia gravis before neostigmine methylsulfate administration.



Figure 2. Appearance of the dog with myasthenia gravis after neostigmine methylsulfate administration.



Figure 3. Nine months after the treatment, appearance of the dog.

present (9). In this case, as well as swaying of the backside after walking, symptoms such as loss of voice, regurgitation, total inability to stand up and difficulty in lifting the head were observed.

Although the serum AChR antibody concentration recorded before the treatment was normal, serum AChR antibody concentration after treatment was found to have decreased. However, this serum AChR concentration was in agreement with those recorded in MG patients by other researchers (7). According to some investigators (4, 10), AChR antibodies can be determined in 80 to

90% of canine and human patients with acquired MG; however, no complete correlation has been determined between a single antibody concentration and the severity of disease (4). Additionally, suggested explanations of seronegativity include the following: low titre of high affinity antibody with all available antibody bound to receptors, inability of the standard radioimmunoassay to detect antibodies bound to the α -bungarotoxin site, antibody present to end-plate determinants other than the acetylcholine receptor, technical factors affecting test sensitivity and antigenic differences in acetylcholine

receptors (10). Receptor antibodies in humans with thymoma and MG are always positive and are inclined to have higher concentrations than MG patients without thymoma (4). Thymoma was not revealed in this dog.

MG requires long-term combination therapy (11). Cholinesterase inhibitor drugs are the principal agents used in the management of canine MG (4). Anticholinesterase drugs inhibit enzymatic hydrolysis of ACh at the neuromuscular junction, prolonging the interaction of ACh released at the nerve terminus with the remaining AChRs, thereby increasing the effective concentration and duration of the effect of ACh in the synaptic cleft (1). Although some investigators (7, 11) have reported using anticholinesterases for a period between 6 weeks and 6 years, in this case pyridostigmine bromid was used for only a month.

Corticosteroids have been reported to be widely used in the treatment of acquired MG (2, 3, 4). The primary beneficial effect of corticosteroids in this disease is related to suppression of initiating aberrant immune response against acetylcholine receptors (1, 4). It has been reported that corticosteroids have also been reported to be successful on their own in the treatment of acquired MG (12). On the other hand, although myasthenic crisis and signs of MG during treatment can quickly be cured by the use of corticosteroids and cholinesterases (2), it has been reported that corticosteroids cannot be recommended in all case (1).

In this case, successful results were achieved by a combined treatment trial. Six weeks after being given both groups of drugs, the dog returned to its home in good health. The dog was observed for a further two years and relapse of the illness was seen.

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