A Case of Acquired Myasthenia Gravis in German Shepherd Dog

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Abstract: A three-year old intact female German shepherd dog weighing 32 kg was presented with the history of regurgitation and vomiting. Physical examination revealed a thin body condition, hoarse voice, hypersecretion, and pelvic limb weakness. In radiograph, megaesophagus was identified. The neostigmine challenge test was positive. The titer of acetylcholine receptor (AChR) antibody was 1.58 nmol/L (reference range, <0.6 nmol). Therefore, the dog was diagnosed to be suffering with chronic generalized form of acquired myasthenia gravis and followed by treatment with pyridostigmine bromide, 1 mg/kg, q12 hrs. Treatment improved the pelvic limb weakness, however intermittent regurgitation and vomiting persisted. This resulted in aspiration pneumonia for which antibiotics were administered. However, the dog was euthanized due to poor management and owner's request.

Key words: Myasthenia gravis, acetylcholine receptor antibody, pyridostigmine bromide, dog.

Introduction

Myasthenia gravis (MG) is a neuromuscular disorder resulting either from a deficiency or a functional disorder of the nicotinic acetylcholine receptor (AChR) leading to congenital MG (CMG) or an autoimmune attack against AChRs resulting in depletion of receptors in acquired MG (AMG). AMG is the most completely characterized autoimmune disease affecting the neuromuscular system. Unlike most other autoimmune diseases, the inciting autoantigen is known. Therefore, the specific and sensitive diagnostic tests are available and the specific therapeutic measures can be undertaken. As a result of autoantibody-mediated destruction of nicotinic AChRs at the neuromuscular junction, there is a clinically apparent muscular weakness and excessive fatigability that may affect ocular, facial, oropharyngeal, esophageal, or limb muscles.

An increased risk for AMG has been identified in Akitas, various Terriers, German short-haired pointers, and Chihuahuas. In contrast Rottweilers, Doberman pinschers, Dalmatians, and Jack Russell Terriers have low relative risk as compared to mixed breed dogs. Despite these statistics, German shepherd and Labrador/Golden retriever are the breed most commonly diagnosed with this disease.

MG involves a spectrum of clinical signs that vary in both distribution and severity of muscle involvement. Three major categories have been identified in dogs; focal, chronic generalized, and acute fulminant generalized. The focal form has a clinical sign which includes regurgitation, dysphagia, voice change, or multiple cranial nerve abnormalities without generalized muscle weakness. The chronic generalized form

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Case Report

A three-year old intact female German shepherd dog weighing 32 kg was presented to the Joen Animal Hospital with the history of frequent regurgitation and vomiting. The dog was regularly vaccinated, received deworming agents and monthly heartworm preventatives. The owner reported vomiting and regurgitation of undigested food a few minutes after eating, a change in the voice, and progressive pelvic limb weakness 2 days prior to presentation. Mild dyspnea was observed after light exercise on the day before presentation. Physical examination revealed a thin body condition, hoarse voice, hypersecretion, and pelvic limb weakness (Fig 1).

Body temperature, heart rate and respiration rate were in a normal range. On thoracic auscultation, mild respiratory crackle was detected. The dog was ambulatory, but obviously weak and reluctant to bear weight on the hind limbs. Complete blood counts and blood chemistry panel showed mild neutrophilia and eosinophilia. Thoracic radiograph revealed megaesophagus, but lung pattern was not remarkable (Fig 2).

The anticholinesterase challenge test was performed. Neostigmine methylsulfate (0.02 mg/kg; Daehan Pharm, Korea) was injected intravenously. The pelvic stiffness disappeared within 1 minute after injection of neostigmine methylsulfate with rapid improvement in limb strength. The dog showed normal gait and walked for about 4 minutes. However, pelvic stiffness relapsed after 5 minutes suggesting a possibility
A Case of Acquired Myasthenia Gravis in German Shepherd Dog

For a definitive diagnosis, serum sample was collected and sent to Comparative Neuromuscular Laboratory, School of Medicine, University of California San Diego for determination of acetylcholine receptor antibody titer by immunoprecipitation radioimmunoassay with $^{125}$I-alpha-bungarotoxin for detection of AChR antibodies. The titer of acetylcholine receptor antibody was 1.58 nmol/L (reference range, <0.6 nmol/L), which confirmed canine AMG (chronic generalized form).

The dog was treated with pyridostigmine bromide (Pyrinol®, Myungmoon Pharm, Korea), a long-acting anticholinesterase, 1 mg/kg every 12 hrs. The dog was fed in an upright position and held in an elevated position for 5-10 minutes after feeding to prevent the aspiration pneumonia.

On follow up, the clinical signs, especially pelvic limb weakness improved but intermittent regurgitation, vomiting and cough persisted. On radiograph, mixed lung pattern induced by aspiration pneumonia was found (Fig 3). The dog was treated with parenteral fluid therapy, cefazolin 22 mg/kg intravenously and/or amoxicillin 20 mg/kg orally every 8 to 12 hrs for short period. Although neostigmine therapy was performed, megaesophagus did not returned normal status.

The dog was severely emaciated over the two months in spite of treatment and the clinical signs including weight loss and dehydration were progressing. The owner requested euthanasia. The dog was euthanized on 56th days after the first observation of clinical sings.

Discussion

This case may be the first case report of canine acquired myasthenia gravis (AMG) diagnosed by history, physical examination, radiography, anticholinesterase challenge test and acetylcholine receptor antibody titer in Korea. Myasthenia gravis (MG) involves a spectrum of clinical signs that vary in both distribution and severity of muscle involvement and is
classified as focal, chronic generalized, and acute fulminant generalized form\(^1\). The focal form occurs in approximately 36% of recognized cases and consists of variable degrees of facial, pharyngeal, laryngeal, and esophageal dysfunction\(^2\). The two generalized forms are distinguished primarily by the rate with which clinical signs develop. Twenty-five percent of dogs with generalized neuromuscular weakness have acute, fulminate clinical signs that result in nonambulatory tetraparesis and severe dyspnea within 72 hrs, whereas in 39% cases exhibit a more chronic onset and gradual progression of clinical signs\(^3\).

Clinical signs may be focal in nature and limited to regurgitation (as a result of esophageal dilatation), dysphagia (as a result of pharyngeal dysfunction), voice change (as a result of laryngeal paralysis), or multiple cranial nerve abnormalities in the absence of generalized muscle weakness. In a recent study, 43% dogs with a confirmed MG did not have clinically detectable limb muscle weakness. Generalized weakness was present in the remaining 57% cases, with 13% having generalized weakness without any esophageal or pharyngeal dysfunction\(^4\). Fulminant associated with sudden onset of esophageal dilatation, rapid progression to quadriplegia, respiratory failure, and high mortality, myasthenic crisis, and the highest percentage of thymomas\(^5\).

In our case, chronic generalized form with esophageal dilatation was diagnosed. On radiograph, cranial mediastinal mass as seen in thymoma was not observed. Thoracic magnetic resonance image (MRI) or computed tomography (CT) or examination of antibody against RyR was not performed.

In practice, the cases of megaesophagus with regurgitation may be frequently encountered, but additive test for diagnosis of MG are not performed routinely because no laboratory in Korea has a facility to measure acetylcholine receptor (AChR) antibody titer for dogs.

It appears that the cognition and the devoted and constant efforts for the management of dogs with MG are most important for relatively good prognosis and prevention of complication such as aspiration pneumonia, dehydration and nutrient deficiency as shown in this case. Although, nutritional support may reduce morbidity and improve immune status, there is a delay in identification of megaesophagus, inadequate nutrition and poor hydration may occur for several days, which may worsen the clinical status of the animal\(^6\).

Aspiration pneumonia was treated with cefazolin and amoxicillin because aminoglycosides and ampicillin have possible detrimental effects on neuromuscular transmission. Also several drugs including antitussive agents, phenothiazines, methoxyflurane, and magnesium may reduce the efficiency of neuromuscular transmission and worsen clinical signs in myasthenic animals\(^1\). Therefore, the caution in the choice of antibiotics and other drug was needed.

In this case, unfortunately, the cause of AMG was not identified. Further studies about the causes of AMG and the relationship of concurrent diseases are required.

**Conclusions**

For the diagnosis of immune-mediated MG the demonstration of serum autoantibodies against muscle AChRs by immunoprecipitation radioimmunoassay should be performed and this assay is specific and sensitive. Also, it is important that not only definitive diagnosis of MG but also adequate therapy especially good management is undertaken in order to treat acquired myasthenia gravis.

**References**

개에서 발생한 후천성 중증근육무력증 일례

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요약: 체중 32 kg의 3년령 암컷 독일제퍼드가 식이억류와 구토로 내원하였다. 신체검사에서 체중감소, 음성변화, 유연 및 후구유약이 관찰되었다. 방사선검사에서 기대식도가 관찰되었다. Neostigmine challenge test는 유성되었으며 acetylcholine receptor에 대한 항체기준 1.58 nmol/L로 양성이었다. 따라서 후천성 중증 근육무력증의 유무성으로 진단 하였다. Pyridostigmine bromide 1 mg/kg을 1일 2회 두어하여 치료하여 후각의 욕약 증상은 원적으로 개선되었고, 정상 보행을 보였다. 치료과정 중 이상성 폐렴이 발생하였고, 항생제 치료를 실시하였으나 관리의 어려움과 경제적 문제로 인한 보호자의 요구로 안내가 되었다.

주요어: 중증근육무력증, acetylcholine receptor antibody, pyridostigmine bromide, 개.