The Pharma Innovation Journal 2021; SP-10(12): 1835-1838

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2021; SP-10(12): 1835-1838

www.thepharmajournal.com
Received: 11-10-2021
Accepted: 15-11-2021

Enbavelan PA
Assistant Professor, Department of Veterinary Clinical Medicine, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Tamil Nadu, India

Venkatesakumar E
Assistant Professor and Head, Department of Veterinary Clinical Medicine, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tamil Nadu, India

Jeyaraja K
Professor, Department of Veterinary Clinical Medicine, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Tamil Nadu, India

Ramprabhu R
Professor and Head, Veterinary Clinical Complex, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tamil Nadu, India

Corresponding Author
Venkatesakumar E
Assistant Professor and Head, Department of Veterinary Clinical Medicine, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tamil Nadu, India

Diagnosis and clinical management of generalized myasthenia gravis in a dog

Enbavelan PA, Venkatesakumar E, Jeyaraja K and Ramprabhu R

Abstract
A two years old male Labrador retriever weighing 45.4 kg was brought to Teaching Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli with complaints of exhaustion and fatigue for the past one month and inability to stand on its hind legs, loss of voice, vomiting immediately after taking food. Clinical examination showed depressed animal, congested and moist mucous membrane, fever (40.4 °C), tachypnoea (46/min), lateral recumbency, change in the voice, ptyalism and pelvic limb weakness. Haemato-biochemical evaluation revealed leucocytosis and neutrophilia, elevated alkaline phosphatase enzyme. Lateral thoracic radiograph showed megaesophagus. Myasthenia gravis was suspected and treated with fluids, antibiotics, nervine tonics for five days immunosuppressor and pyridostigmine for fifteen days. The animal was able to stand and walk, eat by its own after treatment.

Keywords: myasthenia gravis, megaoesophagus, Labrador retriever, pyridostigmine

Introduction
Myasthenia Gravis (MG) is a disorder of neuromuscular transmission in which autoantibodies against nicotinic acetylcholine receptors (AChRs) at the neuromuscular junction results in reduction of AChRs and muscle weakness and fatigue (Shelton, 2002) [1]. The auto antibodies destroy AChR and diminish muscle response to Acetyl choline (Ach) released into synaptic cleft. MG occurs in both acquired and congenital forms. Hopkins (1992) [2] reported that acquired MG in dogs was seen from eight weeks to eleven years of age. There are three types of the clinical syndrome of MG, Type I is focal MG (FMG) with muscle weakness restricted to specific groups of ocular, pharyngeal, oesophageal, laryngeal, or facial muscles, Type II is generalized MG with exercise induced appendicular muscle weakness and megaesophagus and Type III is acute fulminating MG that involves a rapid onset of appendicular muscle weakness, dyspnoea, and collapse (Moffet, 2007) [3]. The tendency for canine MG to develop megaesophagus and aspiration pneumonia was present in 85% of canine cases of MG, due to the striated musculature in the canine oesophagus (Shelton, 2002) [1]. Aspiration pneumonia is the main reason for death and euthanasia in acquiring MG dogs with megaesophagus (Dewey *et al*. 1999) [4]. The diagnosis of MG is based on demonstration of serum autoantibodies to muscle AChRs and distinguishing MG from other causes of canine megaesophagus (Webb *et al*., 1997) [5].

Materials and Methods
A two years old male Labrador Retriever weighing about 45.4 kg was presented to Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli with complaints of exhaustion and fatigue for the past one month and inability to stand on its hind legs, loss of voice, and anorexia. The detailed clinical examination and neurological examinations like cranial nerve evaluation, spinal reflexes and test for postural reactions were carried out as per standard protocol. Five millilitre of blood was collected and 2 ml added into vacutainer with EDTA for haematology and 3 ml into vacutainer with clot activator for serum biochemistry. Plain and contrast radiography of thoracic part of oesophagus and other parts of gastrointestinal tract were done. Electrocardiography, echocardiography and abdominal ultrasonography were performed. The animal was treated with fluids, antibiotics, metoclopramide, nervine tonics, azathioprine, pyridostigmine.

Results and Discussion
A two years old male Labrador Retriever weighing 45.4 kg was presented with complaints of exhaustion and fatigue for the past one month and inability to stand on its hind legs, loss of

voice, vomiting immediately after taking food. Vaccination and deworming were done as per schedule. Clinical examination showed depressed animal, congested and moist mucous membrane, fever (40.4 °C), tachypnoea (46/min), lateral recumbency, change in the voice, ptyalism and pelvic limb weakness (Fig 1). Thoracic auscultation revealed mild respiratory crackle over lung field. Abdomen was moderately distended and tense during palpation. Cranial nerve reflexes pertaining to head and neck were normal (Table 1). Spinal reflexes of fore limbs were normal and hindlimbs showed sluggish patellar and absence of gastrocnemius muscle reflexes (Table 2). Haemato-biochemical evaluation revealed leucocytosis and neutrophilia which might be because of mild respiratory tract inflammation and elevated alkaline phosphatase enzyme might be due to cholestasis subsequent to anorexia. All other haemato-biochemical parameters were within the normal range (Table 3). No changes in haemoto-biochemical parameters, evidence of inflammation in aspiration pneumonia were observed in dogs with MG. The screening tests for metabolic causes of neuromuscular weakness like hypocalcemia, hypothyroidism and hyperadrenocorticism might be done to differentiate from MG (Shelton, 2010) [6]. Contrast radiograph revealed barium stasis in thoracic part of oesophagus indicating megaoesophagus (Fig 2). Generalized MG associated with megaesophagus in the majority of cases. It was reported that in many cases of acquired megaesophagus was irreversible in nature, leading poor prognosis (Gaynor *et al*., 1997; Mears and Denovo 1999) [7,8]. By contrast, Shelton *et al*. (1990) [9] reported clinical improvement in 48 percent of dogs with megaesophagus due to the focal form and generalized form of MG and concluded that early diagnosis and institution of appropriate therapy were important for successful management of MG in dogs. Electrocardiography revealed sinus rhythm. Echocardiography and abdominal ultrasound scanning showed normal study. Abdominal ultrasound might be useful to rule out paraneoplastic causes of acquired MG in aged dogs (Krotje *et al*., 1990) [10]. Based on the history, clinical signs and radiographic findings, the condition was diagnosed as generalised myasthenia gravis. The animal was treated with Inj. Ringers lactate @ 10 ml/kg bwt bid iv, Inj. Dextrose Normal Saline @ 10 ml/kg bwt bid iv, Inj. Ceftriaxone @ 20 mg/kg bwt bid iv, Inj. Metoclopramide @ 0.4 mg/kg bwt iv and Renerve plus (containing B1, B2, B12) 2 ml iv for five days along with the oral administration of Tab. Azathioprine @ 1mg / kg bwt SID and Tab. Pyridostigmine bromide 2 mg/kg bwt BID for 15 days. The elevated feeding with semisolid food was advised. The post treatment radiography revealed normal thoracic part of oesophagus (Fig 3). The animal was taking food and walking normally (Fig 4). The acquired MG was usually a temporary state and might be resolved in months of supportive care (Silverstein and Hopper, 2009) [11]. Generalized MG was the most common neuromuscular disease that could be diagnosed and treated in dogs (Shelton, 2002) [1]. The gold standard for the diagnosis of MG was a demonstration of an increased AChRs antibody titre (Wray and Sparkes 2006) [12]. The sensitivity of this test was more than 90% and false positive had not been documented (Moffet, 2007) [3] but the result of this test was time consuming. Administration of short acting anticholinesterase drug Edrophonium could be used to assess the improvement in muscle strength, gait and ability to swallow in MG cases (Ducote and Dewey, 2001) [13]. The fulminating MG with megaoesophagus could be treated symptomatically after excluding the other diseases causing megaesophagus like botulism, polymyositis, dysautonomia, foreign bodies in oesophagus. Anticholinesterase drugs administration was the cornerstone of therapy for acquired MG in dogs (Shelton 2002) [1] and the mechanism of action was by prolonging the action of acetylcholine at the neuromuscular junction and enhancing neuromuscular transmission. Although pyridostigmine bromide @ 2 mg/kg orally was reported for the treatment of generalized MG with improvement muscle strength within days of the therapy (Batmaz *et al*., 1998) [14], but it has side effect by increasing the frequency of the vomiting. The dosage and schedule of administration must be tailored to the animal's needs. Immunosuppressive drugs like cyclosporine, mycophenalate moftil and azathioprine were used frequently with acquired MG to reduce the levels of circulating autoantibodies by targeting adaptive immune response (Dewey *et al*., 1999) [4]. The most important complication of MG with megaoesophagus was aspiration pneumonia that might lead to death or euthanasia in most cases. The dogs with megaoesophagus were managed with small, frequent feeding in the upright position and were monitored closely for signs of aspiration pneumonia (Atiba *et al*., 2014) [15]. In the present case, the elevated bowel feeding further helped to prevent the aspiration pneumonia, the complication of megaoesophagus.

Table 1: Cranial nerve examination

Cranial Nerve Examination	Result
Pupillary light reflex	Normal
Palpebral reflex	Normal
Corneal reflex	Normal
Menace reflex	Normal
Position of eyeball	Normal
Nystagmus	Absent
Strabismus	Absent
Tongue retraction	Normal
Jaw tone	Normal
Gag reflex	Normal
Nasal mucosal stimuli	Normal

Table 2: Examination of Spinal Reflex

Fore Limb		
Reflex examination	**Left**	**Right**
Extensor carpi radialis	Normal	Normal
Withdrawl reflex	Normal	Normal
Deep pain reflex	Normal	Normal
Hind Limb		
Patellar	Sluggish	Sluggish
Gastrocnemius	Absent	Absent
Withdrawl reflex	Normal	Normal
Deep pain reflex	Normal	Normal

Table 3: Haemato-biochemical examination

Haemotological examination	
Hb	16 g/dl
PCV	40.4%
RBC	6.78 x10^6/ cmm
WBC	44,500 /cmm
Platelets	1,80,000/cmm
Neutrophil	**86**
Lymphocyte	11
Monocyte	1
Eosinophill	2
Peripheral Blood smear	Negative for blood parasites
Serum Biochemical examination	
BUN	21.2 mg/dL
Creatinine	1.3 mg/dL
Total protein	6.89 g/dL
Albumin	2.8 g/dL
ALT	80 IU/dL
ALP	560 IU/dL
Calcium	9.9 mg/dL
Potassium	6.5 mmol/dL
Sodium	141.5 mmol/dL
Chloride	110.8 mmol/dL

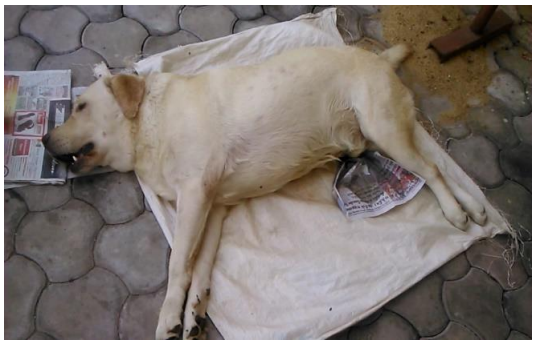

Fig 1: Labrador Retriever dog with MG -Lateral recumbency

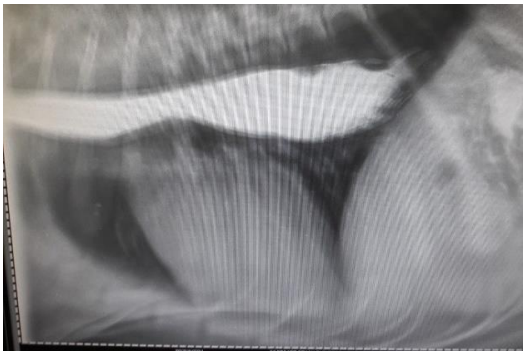

Fig 2: Contrast radiography of thoracic part of oesophagus with barium stasis – Megaoesophagus

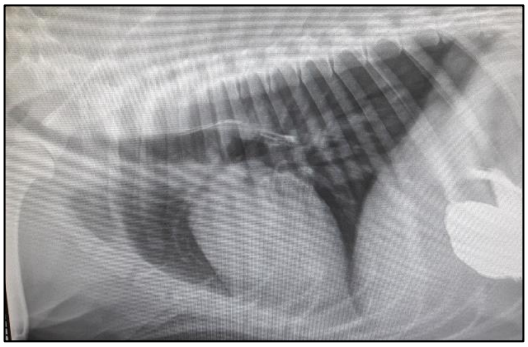

Fig 3: Post treatment radiography - normal thoracic part of oesophagus.

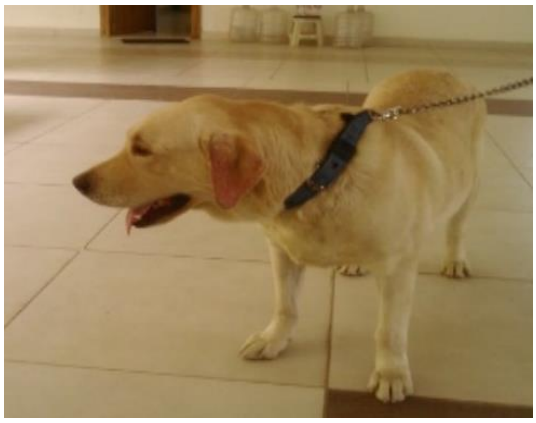

Fig 4: Recovered dog - able to walk normally

Conclusion

A Labrador Retriever dog with generalised myasthenia gravis with megaoesophagus was diagnosed clinically and treated with pyridostigmine and azathioprine successfully. Megaoesophagus is one of the clinical signs of myasthenia gravis in dogs which may also be present in several other conditions that could be differentially diagnosed before starting the treatment for Myasthenia gravis.

Reference

1. Shelton GD. Myasthenia gravis and disorders of neuromuscular transmission. Veterinary Clinics of North America - Small Animal Practice. 2002;32:189 2002.
2. AL Hopkins AL. Canine myasthenia gravis. Journal of Small Animal Practice. 1992;33:477.
3. Moffet AC, Metastatic thymoma and acquired generalized myasthenia gravis in a Beagle. Canadian Veterinary Journal. 2007;48:91-93.
4. Dewey CW, Coates JR, Ducote JM, Meeks JC, Fradkin JM. Azathioprine therapy for acquired myasthenia gravis in five dogs. Journal of American Animal Hospital Association. 1999;35:396.
5. Webb AA, Taylor SM, McPhee L. Focal myasthenia gravis in a dog. Canadian Veterinary Journal. 1997;38:493-495.
6. Shelton GD. Routine and specialised laboratory testing for the diagnosis of neuromuscular diseases in dogs. Veterinary Clinical Pathology. 2010;39:278.
7. Gaynor AR, Shofer FS, Washabau RJ. Risk factors for acquired megaoesophagus in dogs. Journal of the American Animal Hospital Association. 1997;211:1406-1412.
8. Mears EA, Denovo RC. Canine megaesophagus. In: Kirk's Current Veterinary Therapy XIII. Ed J. D. Bonagura, W.B. Saunders, Philadelphia, PA, USA. 1999, 602-607.
9. Shelton GD, Willard MD, Cardinet GH, Lindstorm J. Acquired myasthenia gravis: selective involvement of esophageal, pharyngeal, and facial muscles. Journal of Veterinary Internal Medicine. 1990;4:281.
10. Krotje LJ, Fix AS, Potthoff AD. Acquired myasthenia gravis and cholangiocellular carcinoma in a dog. Journal American Veterinary Medical Association. 1990;197:488.
11. Silverstein DC, Hopper K. Small Animal Critical Care Medicine, Saunders Elsevier, St. Louis, Missouri, 2009, 433-434.
12. Wray JD, Sparkes AH. Use of radiographic

measurements in distinguishing myasthenia gravis from other causes of canine megaesophagus. Journal of Small Animal Practice. 2006;47:256-263.
13. Ducote JM, Dewey CW. Acquired myasthenia gravis and other disorders of the neuromuscular junction. August JR: Consultations in feline internal medicine. 4th Ed WB Saunders Philadelphia. 2001, 374-380.
14. Batmaz H, Suzer F, Kennerman E, Yilmaz Z. Myasthenia Gravis in a Dog. Turkish Journal of Veterinary and Animal Sciences. 1998;22:427-430.
15. Atiba A, Yoshida C, Nakashima N, Ueno H, Uzuka Y. Focal Myasthenia Gravis in Two Dogs. Journal of Advanced Veterinary Research. 2014;4(3):145-148.