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Focal Myasthenia Gravis in Two Dogs

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Abstract

Two dogs were presented with history of regurgitation. Both dogs were diagnosed with focal myasthenia gravis (FMG). Thoracic radiography was consisted with megaesophagus. Acetylcholine receptors (AChRs) antibody titer was positive. Both dogs were treated with pyridostigmine bromide as sole treatment. One case rapidly resolved with the recovery of the esophagus, while the other case even the AChRs antibody titer was normalized after 60 days but the clinical remission was occurred after long time. This report suggested that clinical signs of FMG were resolved, but we can't predict the time required, additionally, pyridostigmine bromide might be effective for palliation of symptoms.

Keywords: AChRs antibody; Dog; Megaesophagus; Myasthenia gravis; Pyridostigmine bromide

Introduction

Myasthenia gravis (MG) is a disorder of neuromuscular transmission resulting from either a deficiency or functional disorder of the nicotinic acetylcholine receptors (AChRs) as in congenital MG or an autoimmune attack against AChRs resulting in depletion of receptors in acquiring MG, and the result is muscle weakness (Webb *et al*., 1997). There are 3 types of the clinical syndrome of MG: 1) focal MG (FMG) with muscle weakness restricted to specific groups of pharyngeal, esophageal, laryngeal, or facial muscles; 2) generalized MG with exercise induced appendicular muscle weakness and megaesophagus; 3) acute fulminating MG that involves a rapid onset of appendicular muscle weakness, dyspnea, and collapse (Moffet, 2007). In almost every aspect, acquired canine MG is remarkably similar to the analogous disease of human beings (Dewey *et al*. 1999). The tendency for canine MG to develop megaesophagus and aspiration pneumonia is present in 85% of canine cases of MG, due to the striated musculature in the canine esophagus (Shelton, 2002). Aspiration pneumonia is the main reason for death and euthanasia in acquiring MG dogs with megaesophagus (Dewey *et al*. 1999). The diagnosis of FMG is based on demonstration of serum autoantibodies to muscle AChRs and distinguishing FMG from other causes of canine megaesophagus (Webb *et al*., 1997). In the present paper, we describe FMG in two dogs with different time of recovered megaesophagus.

Case History

A 2-years-3-months-old, 9.58 kg male French bulldog (Case 1) was referred to Gifu University teaching animal hospital with 3 week history of regurgitation. On presentation the dog showed a good health condition with rectal temperature 39.4°C, the heart rats 80 times/min. Hematology and serum biochemical profile revealed no abnormalities. Thoracic radiographic examination revealed megaesophagus and for confirmation

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barium swallow had been performed (Fig. 1). Serum sample was sent to determine the anti-AChRs antibody concentration (IDEXX Laboratories, Tokyo). The differential diagnoses for the underlying diseases causing megaesophagus were performed as the following: thyroid hormones concentration, ACTH stimulation test and the anti-nuclear antibody for hypothyroidism, hypoadrenocorticism and systemic lupus erythrematousus respectively (Table 1). There was no evidence of muscle or joint pain, or other systemic diseases. From the previous data the case was suspected to be FMG. The treatment course was started with 0.5 mg/kg of the pyridostigmine bromide BID, PO. The low dose was chosen to minimize the risk of a cholinergic crisis. The owner was instructed to feed small and frequent meals from a height and to hold the dog in vertical position for 10 minutes after feeding to minimize regurgitation. On 25th day the result of AChRs autoantibodies titer was 1.04 nmol/L (reference value 0.6 nmol/L) and so the dose of pyridostigmine bromide was increased to 2 mg/kg TID (Batmaz *et al*., 1998). During the follow up the dog condition was re-evaluated by the response to treatment dose, frequency of vomiting (Fig. 2), anti-AChRs antibody titer and the degree of megaesophagus by radiographic examination. It was observed that the frequency of vomiting was increased after the dose of 2 mg/kg pyridostigmine bromide and we suspected that related to pyridostigmine side effect and so the medication was stopped on the 39th day. During that time, other adverse effects included the mild salivation and soft feces. The medication was resumed again on the 51st day with 0.5 mg/kg pyridostigmine bromide. A recheck serum anti-AChRs antibody titer was normal (< 0.6 nmol/L) on the day 60th, 135th, and 241st. On the day 345th, the fluoroscopic examination of the chest showed that the esophagus was returned to its normal condition. Eighteen months later, the dog continued to do very well, and the physical examination and biochem-

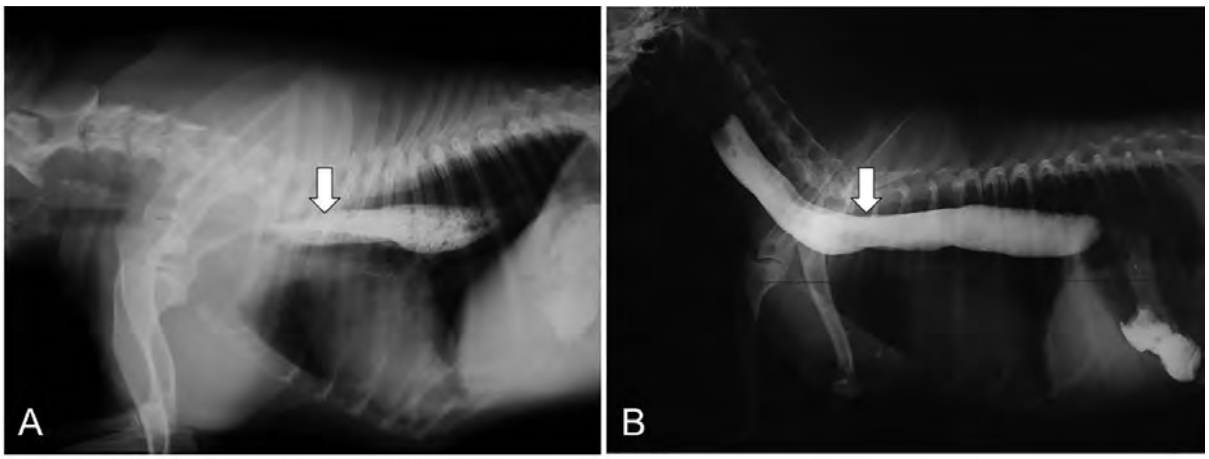

Fig. 1. Right recumbency contrast thoracic radiograph of case 1. The existence of the megaesophagus is shown.

Table 1. Screening examinations of the two dogs

Inspection item		Case 1	Case 2	Reference range
Anti-nuclear antibody		(-)	(-)	
Anti-AChRs antibody titer		1.05nmol/L	1.25nmol/L	0-0.6 nmol/L
Thyroid hormone	T4	0.54 μg/dl	1.49 μg/dl	1.1-3.6 μg/dl
	FT4	1.02 μg/dl	2.30 μg/dl	0.9-2.6 μg/dl
	TSH	0.11 ng/ml	NE	0.08-0.32 μg/dl
ACTH stimulation test	pre	0.91 μg/dl	2.89 μg/dl	1-7.8 μg/dl
	post 1-hr	2.93 μg/dl	14.95 μg/dl	1-7.8 μg/dl
	post 2-hr	3.14 μg/dl	8.31 μg/dl	1-7.8 μg/dl
Plasma lead concentration		NE	<3.0 μg/dl	<3.0 μg/dl

NE: not examined

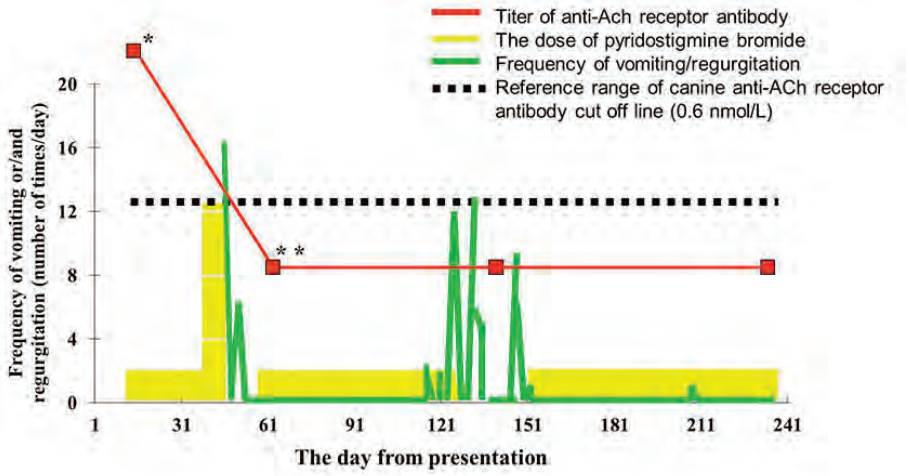

Fig. 2. Clinical and treatment course in case 1 until 241 days. The disappearance of the esophageal dilation and the recovery of the systolic function of the esophagus was recognized by the fluoroscopy on the 341st day. * Titer of anti-AChRs antibody at initial presentation (1.04 nmol/L), ** Titer of anti-AChRs antibody on the day 60th, 135th, and 241st (0.4 nmol/L).

istry panel remained normal.

A 7-years-old, 3.32 kg female Yorkshire Terrier dog (Case 2) was referred with 1-week history of regurgitation. On presentation the animal showed good heath condition. Hematology and serum biochemical profile revealed no abnormalities. Thoracic radiograph revealed megaesophagus (Figure 1). Serum examination of autoantibodies to muscle AChRs, thyroid hormones concentration, ACTH stimulation test and anti-nuclear antibody was carried out (Table 1). From the previous data the case was diagnosed as FMG. The dog was treated with pyridostigmine bromide at a dose of 0.5 mg/kg BID orally. It was observed that within three days after treatment the dog was normal without any abnormalities in the esophagus that was confirmed by radiography and fluoroscopic examination. No relapse of the disease was observed as much as 1 year after the first visit.

Discussion

Acquired MG is an immune-mediated condition in which circulating anti-AChRs antibodies are directed against AChRs in skeletal muscles, inhibiting neurotransmission and accelerating AChRs exocytosis and degradation (Wray and Sparkes, 2006). The reason that dogs with MG developed autoantibodies directed against their own AChRs is unknown (Paciello *et al*., 2003). Acquired MG is probably the most common neuromuscular disease that can be diagnosed and treated in dogs (Shelton, 2002). Several clinical forms of MG have been described (Webb *et al*., 1997). FMG in dogs has selective involvement of the esophageal skeletal muscles and it appears that a similar focal weakness affecting only the extraocular muscles occurs in human MG.

The gold standard for the diagnosis of MG is a demonstration of an increased AChRs antibody titer (Wray and Sparkes 2006). The sensitivity of this test is more than 90% and false positive have not been documented (Moffet, 2007) but the result of this test takes time so suspecting FMG with megaoesophagus when excluding the other diseases causing megaesophagus.

Similar to acquire human MG, anticholoinesterase drugs form the cornerstone of therapy for acquiring MG in dogs (Shelton 2002), acting by prolonging the action of acetylcholine at the neuromuscular junction and enhancing neuromuscular transmission. Although pyridostigmine bromide at the dose of 2 mg/kg was reported for the treatment of acquired MG with obvious gains in muscle strength within days of the therapy (Batmaz *et al*. 1998), but we found that it has side effect by increasing the frequency of the vomiting. This dose is recommended for generalized MG but not for FMG. The dosage and schedule of administration must be tailored to the animal's needs.

The most important complication of FMG with megaesophagus is aspiration pneumonia that may lead to death or euthanasia in most cases. The dogs with megaesophagus are managed with small, frequent feeding in the upright position and are monitored closely for signs of aspiration pneumonia

(Gaynor *et al*. 1997; Harvey *et al*. 1974). The present two cases had an only clinical sign of regurgitation without signs of respiratory distress.

FMG associated with megaesophagus as in the majority of cases has a variable prognosis for recovery. It was reported that many case series of acquired megaesophagus emphasized the frequently irreversible nature of the condition and poor prognosis (Harvey *et al*. 1974; Gaynor *et al*. 1997; Mears and Denovo 1999). By contrast, Shelton *et al* 1990 reported clinical improvement in 48 percent of dogs with megaesophagus due to the focal form of MG and concluded that early diagnosis of MG and institution of appropriate therapy may be important to a successful clinical outcome.

In the follow up of the case 1, despite therapy with pyridostigmine bromide and the serum AChRs antibody concentration was normalized after a short period (60 days) but the clinical remission was occurred after long time, while in case 2 the clinical remission was occurred spontaneously after only 10 days from the onset of the symptoms. Both dogs are currently not received any immunosuppressive therapy and continued to do well.

Conclusion

We concluded that dogs with megaesophagus due to acquired FMG, would be resolved spontaneously but we can't predict the time of remission of the clinical signs. In addition, pyridostigmine bromide might be helpful in reducing the frequency of regurgitation although the administered dose was determined carefully.

References

Batmaz, H., Suzer, F., Kennerman, E., Yilmaz, Z.,1998. Myasthenia Gravis in a Dog. Turkish Journal of Veterinary and Animal Sciences 22, 427-430.

Dewey, C.W., Coates, J.R., Ductoe, J.M., Meeks, J.C., Fradkin, J.M.,1999. Azathioprine therapy for Acquired myasthenia Gravis in five Dogs.Journal of the American Animal Hospital Association 35, 396-402.

Gaynor, A.R., Shofer, F.S., Washabau, R.J., 1997. Risk factors for acquired megaesophagus in dogs.Journal of the American Animal Hospital Association 211, 1406-1412.

Harvey, C.E., O'Brien, J.A., Durie, V.R., Miller, D.J., Veenema, R., 1974. Megaesophagus in the dog: a clinical survey of 79 cases. Journal of the American Animal Hospital Association 165, 443-446.

Mears, E.A., Denovo, R.C., 1999. Canine megaesophagus. In: Kirk's Current Veterinary Therapy XIII. Ed J. D. Bonagura, W.B. Saunders, Philadelphia, PA, USA. pp. 602-607.

Moffet, A.C., 2007. Metastatic thymoma and acquired generalized myasthenia gravis in a beagle. Canadian Veterinary Journal 48, 91-93.

Paciello, O., Maiolino, P., Navas, L., Papparell, S., 2003.Acquired Canine Myasthenia Gravis associated with thymoma: histological features and immunohistochemical localization of HLA type II and IgG. Veterinary Research Communications 27, 715-718.

Shelton, G.D., 2002. Myasthenia gravis and disorders of neuromuscular transmission.Veterinary Clinics of North America: Small Animal Practice 32, 189-206

Shelton, G.D., Willard, M.D., Cardinet, G.H., Lindstrom, J., 1990. Acquired myasthenia gravis.Selective involvement of esophageal, pharyngeal and facial muscles.Journal of Veterinary Internal Medicine 4, 281-284.

Webb, A.A., Taylor, S.M., McPhee, L., 1997. Focal myasthenia gravis in a dog.Canadian Veterinary Journal 38, 493-495.

Wray, J.D., Sparkes, A.H., 2006. Use of radiographic measurements in distinguishing myasthenia gravis from other causes of canine megaesophagus.Journal of Small Animal Practice 47, 256-263.