<Case Report>

Focal form of acquired myasthenia gravis with megaesophagus in a Yorkshire terrier dog

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Abstract: A 12-year-old, castrated male Yorkshire terrier dog presented with frequent regurgitations that had begun 45 days earlier and become more progressive. Radiographs revealed an air-trap region behind the cranial esophageal sphincter muscle in the esophagus and esophagographies with barium contrast showed mild esophageal dilation with decreased motility. Esophageal motility increased within 5 min of neostigmine methylsulfate administration and acetylcholine receptor antibodies titer increased to beyond the normal range. Based on these findings, acquired myasthenia gravis with focal form was diagnosed, making this the first such case diagnosed by an acetylcholine receptor antibody test in Korea.

Keywords: acetylcholine receptor antibody titer, dog, focal form, megaesophagus, myasthenia gravis

Myasthenia gravis (MG) is a common neuromuscular disease in the veterinary field that has various clinical signs related with skeletal muscle weakness due to a deficiency or functional disorder of acetylcholine (Ach) receptor at neuromuscular junctions [16]. According to the previous report [16], there are two types of MG in dogs. The first is congenital MG that presents mutations in genes coding for the Ach receptor. The other is acquired MG that is caused by circulating autoantibodies against the Ach receptor.

Acquired MG shows several forms of clinical signs such as focal form, generalized one or acute fulminating one. Focal signs include regurgitation, dysphagia, voice change or multiple cranial nerve disorders without generalized muscle weakness. Generalized MG is associated with general weakness. Acute fulminating form shows rapid onset of megaesophagus, severe muscle weakness and respiratory failure [2, 16, 17].

Until recently, generalized and acute fulminating forms of acquired MG have been reported in Korea [5, 6, 9, 10]. However this is the first report of acquired MG with focal form diagnosed by Ach receptor antibody test and managed well with an acetylcholinesterase inhibitor treatment.

A 12-year-old, castrated male, Yorkshire terrier dog had been presented with frequent and progressive regurgitations, which were started 45 days ago. Although the patient showed good appetite and did not have other remarkable signs in physical examinations, regurgitations appeared right after drinking water and feeding. Complete blood counts also showed no remarkable findings. A serum biochemical examinations confirmed decreased creatinine (0.4 mg/dL; reference, 0.5 to 1.3 mg/dL), elevated alanine transaminase (133 U/L; reference, 19 to 70 U/L), elevated gamma-glutamyl transpeptidase (20 mg/dL; reference, 0 to 6 mg/dL), and elevated amylase (839 U/L; reference, 185 to 700 U/L). In plain radiographic examination, air-trap region was observed behind cranial esophageal sphincter muscle in esophagus (Fig. 1). Esophagographies with barium contrast showed mild esophageal dilation with decreased motility (Fig. 2). The contrast agent in esophagus remained for 30 min. However, within 5 minutes after the injection of neostigmine methylsulfate (0.05 mg/kg IM; DAI HAN PHARM, Korea), increased esophageal motility was shown on additional esophagographies (Fig. 3). In addition, Ach receptor antibodies titer which were determined by immunoprecipitation radioimmunoassay abnormally increased (2.57 nmol/L; reference, 0.0 to 0.6 nmol/L; ANTECH Diagnostics, USA). Based on clinical signs, neostigmine response and Ach receptor antibodies titer, acquired MG with focal form was diagnosed.

Serologic examinations were performed to rule out other disorders associated with megaesophagus. Hypothyroidism was excluded based on T4, free T4, and endogenous TSH concentration test. Autoimmune conditions involving the thyroid gland also were ruled out as thyroglobulin autoantibodies test was negative. Other autoimmune disorder such as

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systemic lupus erythematosus was excluded by testing antinuclear antibodies titer.

Treating with pyridostigmine bromide (1 mg/kg PO, BID; Myungmoon Pharm, Korea) was chosen for improving esophageal muscle motility as an anticholinesterase agent. The client was educated that the dog should be fed in an upright position and kept in such position for 15 min after feeding. The number of regurgitations markedly decreased after medication and change of feeding procedure. The dog did not show other clinical signs and was discharged from the hospital.

MG is a common neuromuscular disease of dogs by a either a depletion or a functional problem of the postsynaptic nicotinic Ach receptors as in congenital forms or an immune-mediated attack against Ach receptors of skeletal muscle resulting in acquired forms [11, 17].

Megaesophagus concurrent with regurgitations and aspiration pneumonia is common in dogs with acquired MG resulting from the large proportion of skeletal muscle in the canine esophagus [2, 17]. Common clinical signs of acquired MG are classified by focal form, generalized form and acute fulminating form.

Additionally, paraneoplastic forms of MG have been reported with cholangiocellular carcinomas and CNS lymphomas as well as thymomas [8, 12].

The definitive diagnosis for immune-mediated MG is the detection of serum autoantibodies against native Ach receptor by immunoprecipitation radioimmunoassay [15]. False-positive tests are greatly rare [17]. The Ach receptor antibody concentration is commonly lowest in cases with focal forms and highest in cases with acute fulminating forms [1]. The assumptive diagnosis method for acquired MG is an intravenous administration of the edrophonium chloride (0.1−0.2 mg/kg), a short-acting anticholinesterase drug [15]. A neostigmine methylsulfate injection (40 μg/kg administered intramuscularly or 20 μg/kg administered intravenously) would be alternative to the edrophonium chloride injection [15]. Temporary improvement in muscle movement is a positive response [2, 16]. However, such improvement in muscle strength may also been found in other myopathic or neuropathic disorders, and negative responses does not eliminate a diagnosis of MG [16].

Single-fiber electromyography may be used for assumptive diagnosis of MG by detecting delayed or failed neuromuscular transmission. This method is sensitive but has low

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**Fig 1.** Plain radiographs in this case show air-trap region behind cranial esophageal sphincter muscle in esophagus. (A) Lateral thoracic radiograph. (B) Lateral esophageal radiograph.

**Fig 2.** Barium contrast radiographs after 5 min in this case show dilated esophagus and decreased esophageal motility. (A) Lateral thoracic radiograph. (B) Ventrodorsal thoracic radiograph.
sensitivity because other disorders of the nerve, muscle, and neuromuscular junction show positive findings [4, 13].

Acquired MG may be associated with other concurrent disorders. The conditions include hypothyroidism, hypoadrenocorticism, thrombocytopenia, or hemolytic anemia [3, 14]. Thoracic radiographs should be performed to find esophageal dilatation and cranial mediastinal masses [16].

Until recently, there are many options to treat acquired MG. The goal is to improve muscle strength and minimize the adverse effects of medications. For mild disease, anticholinesterase agents and changing feeding procedure may be sufficient. Pyridostigmine bromide and neostigmine bromide are commonly used as anticholinesterase drugs. Pyridostigmine is preferred because it has longer duration of action and fewer side effect than neostigmine bromide does [7]. Sometimes, for more severe conditions, rapid use of immunosuppressants may be required [7].

As the previous reported case of focal MG [18], the dog was a 10-month-old, castrated male, American cocker spaniel with megaesophagus, aspiration pneumonia, but no appendicular muscle weakness. After confirming diagnosis of focal MG by acetylcholine receptor antibody titer test, treatment with upright feeding position and anticholinesterase drugs was initiated. First, a neostigmine methylsulfate was administered (0.04 mg/kg SC, QID; Sabex, Canada). However the dog showed clinical signs such as diarrhea, muscle fasciculations, and hypersalivation after the second dose. For that reason, the dosage was decreased (0.01 mg/kg SC, QID; Sabex). The dog was clinically improved and regurgitation disappeared. After 3 days of medication with the neostigmine, a pyridostigmine bromide (0.76 mg/kg PO, QID; Mestinon; Icn Canada, Canada) was administered instead. The dog was discharged from the hospital and no clinical signs in home with that medication.

The dog in this case showed only regurgitations associated with megaesophagus and the result of Ach receptor antibody concentration was positive, which is consistent with focal form of MG. The dog was resolved by managing only with pyridostigmine bromide medication and education of feeding practice.

Focal form of acquired MG shows usually low Ach receptor antibody titer, although the relationship between the titer and the severity of disease has not been identified [1]. It is necessary to compare with the titer and the clinical severity in more MG cases in the future. Also, additional long-term monitoring of Ach receptor antibody titer is required in this case.

In conclusion, this case firstly describes acquired MG with focal form diagnosed by Ach receptor antibody test in our country.

References


