

<Case Report>

Acquired myasthenia gravis in a domestic shorthair cat with cranial mediastinal mass

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Abstract : A 7-year-old castrated male domestic short-hair cat presented with anorexia, constipation, depression, and voice alteration. Physical and neurological examinations revealed hyperthermia (40.5°C), ventroflexion of the neck, reduced responses to external stimuli, generalized muscle weakness, and exercise intolerance. Thoracic radiographs revealed the presence of a cranial mediastinal mass. The history, clinical signs, and other examination results were compatible with acquired myasthenia gravis (MG). Acetylcholine receptor (AChR) antibody titers were determined to confirm MG and the serum AChR antibody concentration was 1.24 nmol/L (reference interval, < 0.3 nmol/L). This is the first diagnosis of acquired MG in a cat in Korea.

Keywords : acetylcholine receptor antibody titer, myasthenia gravis, thymoma

Myasthenia gravis (MG), a disease of the neuromuscular synapses, occurs due to a reduced number or function of acetylcholine receptors on the postsynaptic muscle membrane [3]. This disease can be either congenital or acquired, and it has been reported in both dogs and cats, but the condition is rarer in the cat [7].

Abyssinians and the related Somali cats are the breeds most predisposed to acquired feline MG [7]. Clinical signs, such as regurgitation, changes in vocalization, constipation, weakness, and ventroflexion of the neck, have been described [1]. Mediastinal masses are commonly observed with acquired MG in cats [2]. For the diagnosis of acquired MG, serum acetylcholine receptor (AChR) antibody detection has been the most trustworthy diagnostic test (serum AChR antibody titers over 0.3 nmol/L are diagnostic for acquired MG) [2]. Clinical signs of MG are alleviated by treatment with anticholinesterase drugs that prolong the action of acetylcholine at the neuromuscular junction [5]. The use of corticosteroids and immunosuppressive drugs is also indicated, but these should be used with care [5].

To our knowledge, this is the first reported case of acquired MG secondary to a thoracic mass in our country. Diagnosis of acquired MG was made by an AChR antibody titer test; however, the thoracic mass was not examined further.

A 7-year-old castrated male Korean short hair cat (5.52 kg body weight) presented with pyrexia, anorexia, constipation, depression, generalized muscle weakness, vomiting, and alterations in voice. The cat had been showing clinical signs,

such as ventroflexion of the neck, limbs stiffness, dyspnea, and dysphagia, for the past 6 months. The patient received the oral administration with prednisolone (PDS; 1 mg/kg, q12h) over a period of 7 weeks by the referring veterinarian. The treatment improved the clinical signs; however, the other symptoms (intermittent pyrexia, anorexia, constipation, depression, generalized muscle weakness, vomiting, and alteration in voice) persisted for several months.

A physical examination revealed hyperthermia (40.5°C), panting, and reduced responses to external stimuli. Thorax auscultation demonstrated the presence of harsh lung sounds. Generalized weakness was present in all four limbs, but no ataxia was observed. Hematological and biochemical examinations revealed leukocytosis ($28.05 \times 10^3/\mu\text{L}$; reference, $6-17 \times 10^3/\mu\text{L}$), thrombocytopenia ($67 \times 10^3/\mu\text{L}$; reference, $200-500 \times 10^3/\mu\text{L}$), and increased aspartate aminotransferase (AST; 63 U/L; reference, 0-48 U/L) and creatinine kinase (CK; 344 U/L; reference, 10-200 U/L) levels (Table 1). Thoracic radiographs confirmed a cranial mediastinal soft tissue density mass (Fig. 1). No other abnormality was observed in the imaging examinations.

The presence of the cranial mediastinal soft tissue density mass and the hematological and biochemical examination results led to a diagnosis of a tumor of the mediastinum and paraneoplastic syndrome. The history, clinical signs, and other examination results were compatible with acquired MG, and the soft tissue density mass was suspected to be a thymoma or mediastinal lymphosarcoma. The titer of the acetylcholine

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Table 1. The values for the complete blood count and serum chemistry in a cat with myasthenia gravis

Parameters	Value	Reference range
WBC ($10^3/\mu\text{L}$)	28.05	2.8–17.0
RBC ($10^6/\mu\text{L}$)	8.42	6.5–12.2
PCV (%)	38.3	30.3–52.3
HB (g/dL)	12.5	9.8–16.2
PLT ($10^3/\mu\text{L}$)	67	151–600
ALT (U/L)	19	12–130
AST (U/L)	63	0–48
ALP (U/L)	21	14–111
BUN (mg/dL)	15	16–36
Creatinine (mg/dL)	1.6	0.8–2.4
Total protein (g/dL)	6.7	5.7–8.9
Albumin (g/dL)	3.0	0–3.14
Creatinine kinase (U/L)	344	0–314
AChR antibody titer (nmol/L)	1.24	< 0.3

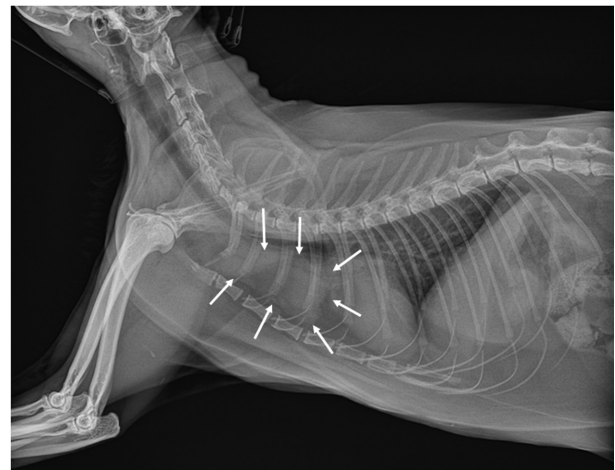
WBC, white blood cell; RBC, red blood cell; PCV, packed cell volume; Hb, hemoglobin; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; AChR titer, acetylcholine receptor antibody titer.

receptor (AChR) antibody was determined to confirm MG. Serum AChR concentration was 1.24 nmol/L (reference interval, < 0.3 nmol/L; IDEXX Laboratories, USA).

Further diagnostic tests and surgical intervention were suggested, but were declined by the owner. The cat was started on medical management with pyridostigmine bromide (0.5 mg/kg, q12h, per orally [PO]; Hana Pharm, Korea). Clinical signs were improved after the pyridostigmine bromide treatment; however, after a 3-month treatment, the cat was presented with dyspnea, tachypnea, and syncope. The owner declined further diagnostic testing. For adjunctive immunomodulatory treatment, PDS (2 mg/kg, q24h, PO) was added to the therapy and the cat's clinical status improved mildly. However, the owner had discontinued treatments and the patient died 4 months after treatment.

Acquired MG is an immune-mediated disease characterized by the development of antibodies against the postsynaptic nicotinic acetylcholine receptor in the neuromuscular junction [8]. Neoplastic and autoimmune diseases are commonly found in association with acquired MG, but a variety of other diseases can also be related to acquired MG [6]. MG has been classified as three types: focal, generalized, and fulminant [1]. Focal MG results in clinical signs of regional muscle dysfunction; generalized MG results in generalized weakness, with or without signs of focal MG; and acute fulminant MG results in a severe onset of generalized weakness that progresses to severe respiratory arrest due to intercostal and diaphragmatic muscle weakness [4].

The patient in the present study showed clinical signs consistent with generalized MG, including a soft mass on the

**Fig. 1.** Right lateral thoracic radiograph of a cat with generalized muscle weakness. A large cranial mediastinal mass was revealed at the time of presentation (arrows).

cranial mediastinum and characteristics of generalized weakness and respiratory compromise. Historically, the cat responded positively to an immunosuppressive drug (PDS 1 mg/kg, q12h, PO) and discontinuation of the immunosuppressive drug resulted in recurrence of the clinical signs. The differential diagnoses for this cat included an immune-mediated neuromuscular disease, such as MG, polymyositis, or polyneuropathies. A neurologic examination of this cat showed generalized weakness, however muscle reflexes were normal and there was no marked muscle atrophy. Although, electrodiagnostic tests and muscle biopsy were not performed for further evaluation, the observations with the cranial mediastinal mass suggested possibility of MG. A presumptive diagnosis of MG was reached and AChR antibody titer test was performed. While awaiting AChR antibody test results, a positive response to the pyridostigmine bromide treatment strengthened the tentative diagnosis of MG in this cat.

Acquired MG associated with a cranial mediastinal mass was relatively common in cats. According to the previous retrospective studies, 25.7% (27 of the 105 cats) and 52% (69 of the 133 cats) cats with MG had cranial mediastinal mass [2, 7]. The most common tumor types located in the mediastinal region are thymoma and lymphoma [12]. Thymic lymphoma occurs in young patients, whereas thymoma is encountered more frequently in older patients [12]. The paraneoplastic effects of thymomas include the conditions of MG, polymyositis, myocarditis, and dermatitis [13]. The present patient's superficial lymph nodes were not affected. This patient's age and its normal superficial lymph node size therefore indicated a greater possibility for thymoma than for lymphoma. The MG was followed by the development of paraneoplastic effects. The connection between thymic disease and MG may reflect a generalized immune dysfunction or the induction of antibodies against thymic cells that are antigenically analogous to cells expressing the acetylcholine

receptor of the neuromuscular junction [11].

A variety of clinical signs are presented in MG, depending on the areas of the body affected [12]. Megaesophagus, regurgitation, and aspiration pneumonia are reportedly less common in cats than in dogs because of the presence of more smooth muscle in the feline esophagus when compared with the skeletal muscle found in the canine esophagus [7]. In the present case, the cat also showed clinical signs, including constipation, generalized muscle weakness, vomiting, and alterations in voice.

Anticholinesterase is considered the first line treatment of MG, and other treatment options used to treat MG include immunosuppressive drugs, intravenous immunoglobulin, plasma pheresis, and therapeutic vaccines [5]. Recently, anti-CD20 antibody and rituximab show clinical benefit in severely affected, drug-resistant human patient with MG [10]. The cat reported here responded well to anticholinesterase and immunosuppressive therapy, but the patient suddenly died 4 months after the first appearance of the clinical signs. The cause of death was assumed to be respiratory failure, either due to the obstruction of the airway or from the pulmonary metastasis of the tumor.

A variety of different methods have been described for the treatment of thymomas, including surgery, radiation therapy, and chemotherapy. A recent retrospective study indicated that the median survival time of cats with thymoma treated by surgery alone was 790 days to 1825 days [5]. The 1- and 3-year survival rates were 89% and 74% for cats [5]. Almost all cases of myasthenic cats with cranial mediastinal mass need medical therapy to control clinical sign of MG after thymectomy [2, 9, 13]. A combination of surgery for the cranial mediastinal mass and anticholinesterase therapy can improve the prognosis in cats.

In conclusion, the cat in the present study was diagnosed with acquired MG secondary to a cranial mediastinal mass that was suspected to be a thymoma. Early in the treatment, the cat responded well to anticholinesterase drugs, but three months later the cat's condition was rapidly exacerbated by the development of respiratory distress.

References

1. **Ducote JM, Dewey CW, Coates JR.** Clinical forms of acquired myasthenia gravis in cats. *Compend Contin Edu Pract Vet* 1999, **21**, 440-448.
2. **Hague DW, Humphries HD, Mitchell MA, Shelton GD.** Risk factors and outcomes in cats with acquired myasthenia gravis (2001-2012). *J Vet Intern Med* 2015, **29**, 1307-1312.
3. **Lindstrom JM.** Acetylcholine receptors and myasthenia. *Muscle Nerve* 2000, **23**, 453-477.
4. **Meeking SA, Prittie J, Barton L.** Myasthenia gravis associated with thymic neoplasia in a cat. *J Vet Emerg Crit Care* 2008, **18**, 177-183.
5. **Penderis J, Martin-Vaquero P.** Junctionopathies: disorders of the neuromuscular junction. In: Dewey CW, da Costa RC (eds). *Practical Guide to Canine and Feline Neurology*. 3rd ed. pp. 521-557, John Wiley & Sons, Ames, 2015.
6. **Shelton GD.** Acquired myasthenia gravis: what we have learned from experimental and spontaneous animal models. *Vet Immunol Immunopathol* 1999, **69**, 239-249.
7. **Shelton GD.** Myasthenia gravis and disorders of neuromuscular transmission. *Vet Clin North Am Small Anim Pract* 2002, **32**, 189-206.
8. **Shelton GD, Ho M, Kass PH.** Risk factors for acquired myasthenia gravis in cats: 105 cases (1986-1998). *J Am Vet Med Assoc* 2000, **216**, 55-57.
9. **Shilo Y, Pypendop BH, Barter LS, Epstein SE.** Thymoma removal in a cat with acquired myasthenia gravis: a case report and literature review of anesthetic techniques. *Vet Anaesthe Analg* 2011, **38**, 603-613.
10. **Sieb JP.** Myasthenia gravis: an update for the clinician. *Clin Exp Immunol* 2014, **175**, 408-418.
11. **Vincent A.** Unravelling the pathogenesis of myasthenia gravis. *Nat Rev Immunol* 2002, **2**, 797-804.
12. **Withrow SJ, Vail DM, Page RL.** *Withrow and MacEwen's Small Animal Clinical Oncology*. 5th ed. pp. 688-691, Elsevier, St. Louis, 2013.
13. **Zitz JC, Birchard SJ, Couto GC, Samii VF, Weisbrode SE, Young GS.** Results of excision of thymoma in cats and dogs: 20 cases (1984-2005). *J Am Vet Med Assoc* 2008, **232**, 1186-1192.