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Juvenile onset acquired myasthenia gravis in a Shih-tzu dog

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Abstract : A 7-month-old female Shih-tzu dog was presented with intermittent trembling, dyspnea, generalized muscle weakness, and unconsciousness after exercise. No remarkable findings were shown in the complete blood counts and the radiographic examination. On serum biochemical profiles, alkaline phosphatase and creatine phosphokinase were mildly elevated. Based on history takings, physical examination, and neurological findings, presumptive diagnosis was made as a myasthenia gravis (MG). Clinical signs of this patient were dramatically improved after administration of neostigmine. The result of acetylcholine receptor antibody test in serum was 0.89 nmol/L and the histopathology of muscle were normal. Clinical sign of the patient evaluated in this study is stabilized with long-term administration of pyridostigmine at this time. This case report here describes clinical and clinicopathological findings of a juvenile onset acquired MG in a Shih-tzu dog.

Key words : acetylcholine receptor antibody, Acquired myasthenia gravis, dog

Myasthenia gravis (MG) is a disorder characterized by inefficient neuromuscular transmission secondary to a reduction in acetylcholine receptors on the postsynaptic muscle membrane [3]. Two forms of the disease are recognized in dogs and cats: congenital and acquired. Acquired MG is a well-characterized, immune-mediated disease in which autoantibodies are produced against nicotinic acetylcholine (Ach) receptors of skeletal muscle neuromuscular junctions. The immune response against Ach receptors results in failure of neuromuscular transmission. The resultant impairment of neuromuscular transmission is manifested clinically as muscle weakness [2, 3, 14, 15, 17]. Historically, clinical signs of MG were described as generalized skeletal muscle weakness that worsens with exercise and improves with rest. In contrast to absence of antibodies to acetylcholine receptors in congenital MG, diagnosis of acquired MG is made based on increased acetylcholine receptor antibodies titer [3, 6].

Clinical signs may vary from focal disease involving extraocular, pharyngeal, laryngeal, or esophageal muscles to generalized muscle weakness, stiff gait, or peracute collapse [15]. The generalized form of MG is classically described as appendicular skeletal muscle weakness precipitated and exacerbated by exercise and relieved by rest. Additional signs may include lameness, shortening of stride, drooping of facial features, difficulty in fully closing the mouth, collapse, regurgitation, drooling, ventroflexion of the neck, dysphonia, and tremors. The focal form is characterized by esophageal dilation and regurgitation, but appendicular muscles are normal. Muscle tremors and decrementing or absent palpebral reflexes may be present as a feature of the muscle weakness.

The purpose of this report is to describe the clinical, serologic, and biochemical manifestations of juvenile onset MG in a Shih-tzu dog.

A 7-month-old intact female Shih-tzu dog of 3.3 kg body weight was presented to the Veterinary Medical Teaching Hospital of Konkuk University due to trembling, generalized muscle weakness, and unconsciousness after exercise. On history taking, the dog was tired easily and the owner observed abnormal clinical sign since the dog was 3 months old. However, acute muscle

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weakness and unconsciousness of the patient were improved with rest and worsened after severe exercise. Physical examination revealed mild muscular shivering, nystagmus, unconsciousness, and arrhythmia. On neurological examination, palpebral reflexes of both eyes were absent.

Results of complete blood count (CBC) profiles were within reference range. Serum chemistry profiles showed increased alkaline phosphatase (330 U/L; reference range, 0 to 142 U/L) and creatine phosphokinase (516 U/L; reference range, 10 to 199 U/L). Thoracic radiography and urinalysis exhibited no remarkable findings. Based on history takings, physical examination, and neurological findings, neuromuscular dysfunction, MG was strongly suspected. Diagnosis was made with administration of neostigmine methylsulfate (0.04 mg/kg, IM; Kwang myung pharma, South Korea). Following administration of neostigmine, clinical signs were dramatically improved and the patient was stabilized after therapy. However, Clinical signs were relapsed 5 hours after the withdrawal of neostigmine administration. And we measured the concentration of acetylcholine receptor antibody in serum and also performed muscle biopsy of pelvic limbs (Comparative Neuromuscular laboratory, University of California, San Diego, LaJolla, CA 92093-0612, USA) to differentiate acquired from congenital MG.

Result of acetylcholine receptor antibody test in serum was increased (0.89 nmol/L, reference rage; 0~ 0.6 nmol/L) [9]. These findings were consistent with those typical in acquired MG. And results of muscle biopsy were no remarkable findings. Therefore we diagnosed this case as generalized form of juvenile onset acquired MG. We ruled out hypothyroidism based on TSH stimulation test and basal T4 concentration.

After pyridostigmine bromide (1 mg/kg, PO, BID; Myung moon pharma, South Korea) administration, clinical signs were disappeared. Long-term management with pyridostigmine bromide is successful for 2 years and muscle weakness is occasionally observed when the patient hardly exercise.

Canine MG was first reported in 1961 by Ormrod [12], and since that time many cases have been reported [2, 6, 8, 10, 11, 13, 15]. MG in adult dog is generally acquired, whereas in young dogs it is generally a congenital disease. However, a juvenile case of acquired MG (onset at 8 weeks of age) has been reported [6, 8, 11]. Although severe problem in this case was not noted until the dog was 7 months old, weakness and trembling after exercise have been observed by the owners since the dog was 3 months old.

An acetylcholine receptor antibody concentration of greater than 0.30 nmol/L is diagnostic for acquired MG in cats, while greater than 0.6 nmol/L is diagnostic in dogs [5, 6, 8, 10, 11, 14, 17]. Result of acetylcholine receptor antibody concentration in our case was 0.89 nmol/L and muscle biopsy of pelvic limbs were normal.

Generalized muscle weakness and unconsciousness in our case were characteristics of MG in that it was worsened by exercise and was relived by rest and by administration of anticholinesterase agents. In radiographic findings, thymoma or thymic cysts or megaesophagus were not detected in this case. In one study [16] of 152 dogs with idiopathic megaesophagus, 40 dogs (26%) had serum antibody titers to acetylcholine receptors consistent with a diagnosis of acquired MG. In human beings and dogs, thymic neoplasia has been associated with MG [7, 16, 17]. In human beings with MG, the highest incidence of thymoma is seen in patients with acute fulminating MG. Respiratory failure, presumably caused by aspiration pneumonia and loss of strength in muscles involved in respiration, is a consistent complication of acute fulminating MG in dogs and a common cause of death.

The prognosis for recovery from MG in dogs is good if severe aspiration pneumonia or pharyngeal weakness is not present. In one study [2], more than half of the myasthenic dogs died or were euthanized due to severe aspiration pneumonia within one year of diagnosis. In contrast to those described above, this patient did not show any respiratory distress, such as secondary aspiration pneumonia at this time. However, aspiration pneumonia could also be occurred in this patient at any time. Thus, in order to maximize the chance of a favorable outcome in canine MG patients, aggressive prevention and/or treatment of aspiration pneumonia is essential and crucial [6, 17].

References

1. **Dewey CW, Bailey CS, Shelton GD, Kass P H, Cardinet GH.** Clinical forms of acquired myasthenia gravis in dogs: 25 cases (1988-1995). J Vet Intern Med 1997, **11**, 50-57.
2. **Dewey CW, Coates JR, Ducote JM, Meeks JC, Fradkin JM.** Azathioprine therapy for acquired

myasthenia gravis in five dogs. J Am Anim Hosp Assoc 1999, **35**, 396-402.

3. **Ettinger SJ, Feldman EC.** Peripheral nerve disorders. In: Ettinger SJ, Feldman EC (eds.). Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat. 5th ed. pp. 675-676, Saunders, Philadelphia, 2000.
4. **Flagstad A, Trojaborg W, Gammeltoft S.** Congenital myasthenic syndrome in the dog breed Gammel Dansk, Honsehund: clinical, electrophysiological, pharmacological and immunological comparison with acquired myasthenia gravis. Acta Vet Scand 1989, **30**, 89-102.
5. **Indrieri RJ, Creighton SR, Lambert EH, Lennon VA.** Myasthenia gravis in two cats. J Am Vet Med Assoc 1983, **182**, 57-60.
6. **King LG, Vite CH.** Acute fulminating myasthenia gravis in five dogs. J Am Vet Med Assoc 1998, **212**, 830-834.
7. **Klebanow ER.** Thymoma and acquired myasthenia gravis in the dog: a case report and review of 13 additional cases. J Am Anim Hosp Assoc 1992, **28**, 63-69.
8. **Lipsitz D, Berry JL, Shelton GD.** Inherited predisposition to myasthenia gravis in Newfoundlands. J Am Vet Med Assoc 1999, **215**, 956-958, 946.
9. **Lorenz MD, DeLahunta A, Alstrom DH.** Neostigmine responsive weakness in the dog, similar to myasthenia gravis. J Am Vet Med Assoc 1972, **161**, 795-800.
10. **Miller LM, Hegreberg GA, Prieur DJ, Hamilton MJ.** Inheritance of congenital myasthenia gravis in smooth fox terrier dogs. J Hered 1984, **75**, 163-166.
11. **Miller LM, Lennon VA, Lambert EH, Reed SM, Hegreberg GA, Miller JB, Ott RL.** Congenital myasthenia gravis in 13 smooth fox terriers. J Am Vet Med Assoc 1983, **182**, 694-697.
12. **Ormrod AN.** Myasthenia gravis in a cocker spaniel. Vet Rec 1961, **73**, 489-490.
13. **Palmer AC.** Myasthenia gravis. Vet Clin North Am Small Anim Pract 1980, **10**, 213-221.
14. **Pendens J.** Junctionopathies: Disorders of the neuromuscular junction. In: Dewey CW (ed.). A Practical Guide to Canine and Feline Neurology. 1st ed. pp. 467-488, Iowa State Press, Ames, 2003.
15. **Shelton GD, Schule A, Kass PH.** Risk factors for acquired myasthenia gravis in dogs: 1,154 cases (1991-1995). J Am Vet Med Assoc 1997, **211**, 1428-1431.
16. **Shelton GD, Willard MD, Cardinet GH 3rd, Lindstrom J.** Acquired myasthenia gravis. Selective involvement of esophageal, pharyngeal, and facial muscles. J Vet Intern Med 1990, **4**, 281-284.
17. **Uchida K, Awamura Y, Nakamura T, Yamaguchi R, Tateyamas.** Thymoma and multiple thymic cysts in a dog with acquired myasthenia gravis. J Vet Med Sci 2002, **64**, 637-640.