CASE REPORT

MYASTHENIA GRAVIS IN A TOY POODLE DOG: A CASE REPORT

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Original Submission:
25 January 2024
Revised Submission:
28 February 2024
Accepted:
15 March 2024

How to cite this article: Ljubez A, Čamo D, Mutevelić T. 2024. Myasthenia gravis in a toy poodle dog: A case report. Veterinaria, 73(1), 72-76.

ABSTRACT

Myasthenia gravis (MG) is an immune-mediated, neuromuscular disorder primarily characterized by muscle weakness and excessive fatigue. Three forms of myasthenia gravis have been described in dogs: focal, generalized, and acute fulminating form. A six-year-old, male toy poodle presented with weakness, intermittent paresis, voice change, and inability to jump or climb the stairs for seven days. Clinical examination revealed ataxia, muscle weakness, and ambulatory tetraparesis. Forelimb hopping revealed poor follow-through, and wheelbarrow was abnormal. The withdrawal reflex was reduced. Complete blood count showed thrombocytopenia, a slight increase in mean platelet volume (MPV), and decreased level of plateletcrit (PCT). Biochemistry analysis was unremarkable. An acetylcholine receptor (AChR) antibody test was performed due to the suspicion of myasthenia gravis. The test detected circulating antibodies to the acetylcholine receptor and positive results confirmed the suspected diagnosis. Acetylcholinesterase (AChE) inhibitors are usually the first line of therapy. Pyridostigmine bromide is the most commonly used AChE inhibitor, and it was the drug of choice in this case (2,5 mg/kg PO q 12h). The dose of pyridostigmine bromide was reduced by 50% after nine months, and the therapy was discontinued after one year due to the test results in the reference values, and the absence of clinical signs.

Key words: Dog, muscle, myasthenia gravis, pyridostigmine bromide, tetraparesis

INTRODUCTION

Myasthenia gravis (MG) is a neuromuscular disorder primarily characterized by muscle weakness and excessive fatigue due to abnormal transmission of the message between the nerves and the muscles (Shelton, 2002). Previous classification has included both - acquired and congenital MG. However, in recent years, the term myasthenia gravis solely refers to an acquired autoimmune disease with autoantibodies against the neuromuscular junction of skeletal muscle, while the term "congenital myasthenic syndromes"

doi.org/10.51607/22331360.2024.73.1.72

has replaced the term "congenital myasthenia gravis" (Shelton, 2016). There are three forms of myasthenia gravis in dogs: focal, generalized and acute fulminating form (Penderis and Martin-Vaquero, 2016). Clinical signs and findings vary from patient to patient, but often include: focal or generalised muscle weakness (appendicular, facial, pharyngeal and/or laryngeal), regurgitation, dyspnea and aspiration pneumonia in dogs with megaesophagus, voice changes, neurologic deficits (Dewey et al., 1997). The main test to diagnose myasthenia gravis is AChR antibodies test, which detects AChR autoantibody concentration using radioimmunoassay (Mignan et al., 2020). Treatment begins with anticholinesterase drugs and, if muscle strength has not returned to normal, immunosuppressive treatment should be initiated (Platt and Shelton, 2014). Here, we report the first recorded case of myasthenia gravis in a dog from Bosnia and Herzegovina.

Case description

A six-year-old, male toy poodle presented with weakness and intermittent paresis, initially in the hind limbs and then evolving to the forelimbs for seven days. The owner also reported that voice change has been noticed, as well as the inability to jump or climb the stairs. The history, physical examination and neurological evaluation were followed by spine radiography and blood sampling from the cephalic vein into an IDEXX EDTA KE/1.3 microtube and an L-heparin LH/1.3 microtube for hematology and biochemistry blood tests. Hematological blood analysis was performed using a ProCyte® Hematology Analyzer, (Idexx Laboratories Inc., REF: 98-70000-01), and blood biochemistry using a Catalyst One® Chemistry Analyzer, (Idexx Laboratories Inc., REF: 89-92525-00). Potential differential diagnoses included metabolic disorders, lesion in the C6-T2 spinal cord segment, myasthenia gravis, or acute polyradiculoneuritis. Due to the suspicion of myasthenia gravis, an AChR antibody test (indirect fluorescent antibody test (IFAT) method) was performed in an accredited Laboklin laboratory. IFA test is useful for the diagnosis of autoimmune diseases, including myasthenia gravis. In this test, cells grown in culture and fixed to a glass slide are permeable to antibody. These cells are exposed to serum from a patient suspected of AChR antibodies and then to a fluorescent antibody. After an incubation and wash, the cells can be examined for fluorescence by fluorescence microscopy. Visible fluorescence demonstrates the presence of AChR antibodies in the patient's serum (Im et al., 2019).

At clinical examination, the patient was responsive. According to WSAVA recommendations (2013), the body condition score was 5/9. Its body temperature, and heart and respiratory rates were within reference ranges. The peripheral lymph nodes were unremarkable. The neurological evaluation confirmed ataxia, muscle weakness, and ambulatory tetraparesis. Forelimb hopping revealed poor follow-through and wheelbarrow was abnormal. The withdrawal reflex of all limbs was reduced. The blood analysis revealed thrombocytopenia (PLT 50 K/µl, normal range 148-484 K/µl), a slight increase in MPV (13,4 Fl, normal range 8,7-13,2 fL), and decreased level of PCT (0,07%, normal range 0,14-0,46%). The rest of the parameters for cell blood count were in the normal range. Biochemistry analysis (Chem 17 CLIP) was unremarkable, and no abnormalities were found in electrolytes (Lyte 4 CLIP). Spine radiography did not show any changes or damages. Oral cobalamin (BOSNALIJEK a 1000 mcg – 1 tablet twice a day) and propentofylline (Canergy a 100mg – ¼ tablet twice a day) therapy was prescribed before the diagnosis of MG was confirmed. The AChR antibody test detected circulating antibodies to the acetylcholine receptor, and positive results confirmed the diagnosis of myasthenia gravis (cell line TE671: 800, reference values < 400; cell homogenate: 600, reference values < 300). Time elapsed from the onset of clinical signs until confirmation of diagnosis is four weeks. At the control examination, before the start of the therapy with pyridostigmine bromide (Mestinon a 60 mg – 2,5 mg/kg PO q 12h), a significant improvement was observed. The patient could climb the stairs although muscle

weakness and hind limb ambulatory paresis were still noticeable. Daily oral treatment with pyridostigmine bromide further improved the condition. After nine months, the clinical signs of the disease have completely disappeared. The AChR antibody test was repeated, and the AChR antibody titre was not elevated any more (cell line TE671: <50; cell homogenate: <50). The dose of pyridostigmine bromide was reduced by 50%, and the test has been repeated again after three months (cell line TE671: <50; cell homogenate: <50). Due to the results in the reference values and the absence of clinical signs, Mestinon therapy was discontinued two months ago (Table 1). The dog has been in follow-up for two months, and there has not been recurrence of the clinical signs during this period.

Table 1 Acetylcholinreceptor-antibodies test results and pyridostigmine dosage

PARAMETER	1ST TEST (December, 2022)	2ND TEST (September, 2023)	3RD TEST (December, 2023)	REFERENCE VALUES (circulating antibodies to the Acetylcholinreceptor)
Cell line TE671	800.00	<50	<50	< 400
Cell homogenate	600.00	<50	<50	<300
Pyridostigmine dosage	2.5 mg/kg q 12h	1.25 mg/kg q 12h	Discontinued	

DISCUSSION AND CONCLUSION

Myasthenia gravis is an immune-mediated, neuromuscular disorder with autoantibodies against neuromuscular junction of sceletal muscle, which results in impaired neuromuscular transmission. As a result of autoantibody mediated destruction, this disease is manifested clinically as muscular weakness (Shelton, 2016; Dewey et al, 1997). Three forms of myasthenia gravis have been described in dogs: focal, generalized, and acute fulminating (Dewey et al., 1997). Focal myasthenia gravis includes 26% to 43% of all cases, and the only clinical signs of this form are regurgitation, megaoesophagus, and/or dysphagia (Platt and Shelton, 2014). Generalized form includes dogs with appendicular muscle weakness, as was found in this case, and it includes 57% to 64% cases of myasthenia gravis. This form is characterized by different degrees of muscular weakness, and 90% of dogs with generalized form have megaesophagus (Khorzan et al., 2011). In this case, megaesophagus was excluded due to the absence of clinical signs in the form of dysphagia and regurgitation, as well as due to the radiographs. Acute fulminating form presents severe and rapidly progressing form of myasthenia gravis which is associated with a rapid onset of paralysis and megaesophagus (Penderis and Martin-Vaquero, 2016; Platt and Shelton, 2014). German Shepherd Dogs, Golden Retrievers, Labrador Retrievers, Akitas, terrier group, Scottish Terriers, German Shorthaired Pointers, and Chihuahuas appear to be predisposed to acquired myasthenia gravis (Platt and Shelton, 2014; Shelton et al., 1997). The Poodle is not considered to be predisposed, but there is a recorded case report of myasthenia gravis in this breed (Richardson, 2011). In dogs, just like in humans and cats, a bimodal age of onset has been presented. It usually occurs in young dogs between 4 months and 4 years, and in older dogs between 9 and 13 years of age, but in this case, the dog was 6 years old. Myasthenia gravis should be considered

in every animal with megaesophagus, dysphagia, and/or muscular weakness. A complete blood count and biochemistry panel should be performed to rule out other causes of generalized weakness (Khorzad et al., 2011). Muscle damage may lead to an increased value of the muscle enzyme creatine kinase (CK) (Penderis and Martin-Vaquero, 2016). The "gold standard" for the diagnosis is positive testing by measurement of AChR autoantibody concentration using radioimmunoassay (Khorzad et al., 2011). The treatment is based on response and severity of the disease, but AChE inhibitors are usually the first line of therapy. The mechanism of action of these drugs is to inhibit hydrolysis of acetylcholine at the neuromuscular junction, which prolongs the action of acetylcholine (Khorzad et al., 2011). Pyridostigmine bromide is the most commonly used AChE inhibitor. It is given at a dose of 0,5-3,0 mg/kg q8-12h (Platt and Shelton, 2014). If muscle strength has not been returned to normal, immunosupresive therapy should be considered (0,5 mg/kg orally q24h) (Platt and Shelton, 2014). In this case, the initial dose was 2,5 mg/kg. Given that the response to the therapy was adequate, and given that the chances of remaining in remission are greater in dogs that only received AChE inhibitors (Khorzad et al., 2011), corticosteroids were not used.

CONFLICT OF INTEREST

The authors declared that there is no conflict of interest.

CONTRIBUTIONS

Concept – ALJ, DČ, TM; Supervision – DČ; Data Collection and/or Processing – ALJ, DČ; Analysis and/or Interpretation – ALJ, DČ, TM; Literature Search – ALJ; Writing Manuscript – ALJ, DČ, TM; Critical Review – DČ.

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MIASTENIJA GRAVIS KOD TOY PUDLE: PRIKAZ SLUČAJA

SAŽETAK

Miastenija gravis predstavlja autoimuno neuromišićno oboljenje karakterizirano prvenstveno mišićnom slabošću i izraženim zamaranjem. Opisana su tri oblika miastenije gravis pasa: fokalni, generalizirani i akutni fulminantni oblik. Šest godina star mužjak toy pudle doveden je sa znakovima slabosti, intermitentne pareze, promjene glasa, te nemogućnosti skakanja i penjanja uz stepenice, izraženih tokom posljednjih sedam dana. Kliničkim pregledom utvrđena je ataksija, mišićna slabost i ambulatorna tetrapareza. Proba poskakivanja prednjih ekstremiteta je bila oslabljena, proba kolica odsutna. Refleks povlačenja bio je oslabljen. Hematološkom analizom krvi utvrđena je trombocitopenija, blago povišene vrijednosti srednjeg volumena trombocita i snižena vrijednost trombokrita. Biohemijskim panelom nisu utvrđene abnormalnosti. Zbog sumnje na miasteniju gravis rađen je test za dokazivanje antitijela na acetilholinske receptore. Testom su detektovana cirkulirajuća antitijela na acetilholinske receptore, a pozitivnim rezultatom testa dijagnoza je potvrđena. Kada je u pitanju terapija, inhibitori acetilholinesteraze su prvi izbor, a najčešće korišteni je piridostigmin bromid koji je i u ovom slučaju propisan u dozi od 2,5 mg/kg na svakih 12h. Nakon devet mjeseci doza piridostigmin bromida snižena je za 50%, a terapija je prekinuta nakon godinu dana zahvaljujući rezultatima testova u referentnim vrijednostima, uz odsustvo kliničkih znakova.

Ključne riječi: Miastenija gravis, mišić, pas, piridostigmin bromid, tetrapareza