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CASE REPORT
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Polymyositis Associated with Brainstem Signs in a Dog

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ABSTRACT

***Background*:** Polymyositis is a generalized inflammatory myopathy which can lead to rhabdomyolysis. This affection may have several origins, including degenerative, metabolic, autoimmune, infectious, inflammatory, ischemic, traumatic, by drug use, induced by toxins and also of idiopathic origin. Diagnosis is made with seric dosage, electrodiagnostic tests and muscle biopsy. Lesions in the rostral oblong medulla may affect the central vestibular system, and there may be signs such as opisthotonos, nystagmus, and strabismus. The aim of this report is to describe a case of a mixed breed dog with manifestation of polymyositis associated with brainstem signs of probable idiopathic origin.

***Case*:** A 5-year-old mixed breed male dog was attended with opisthotonos episodes for 2 days, and pelvic limbs extension and thoracic limbs flexion that lasted 10 to 20 min at intervals of approximately 1 h. The animal was anorexic and had also presented one episode of emesis. Upon neurological examination, ventromedial strabismus and Horner's syndrome was observed on the right side, besides vertical nystagmus, flaccid tetraparesis and absence of proprioception in the four limbs. Biochemical analyses revealed creatine kinase (CK) increased (2,433.9 UI/L - reference: 1.5-28.4 UI/L), and urinalysis showed dark color and presence of occult blood without, however, erythrocyturia. Electrocardiogram (ECG) showed QS wave and deviation of the electrical axis. Treatment with prednisolone (1 mg/kg, BID), phenobarbital (2 mg/kg, BID), maropitant citrate (1 mg/kg in 2 doses), and crystalloid fluid therapy (50 mL/kg/day) were prescribed. On the 4th day, the dog was more active and feeding without a tube, so it recommended keep the treatment at home. On the 10th day, the animal had proprioception present on the 4 limbs and normorexia. Biochemical analyses and urinalysis showed no alterations, but normochromic normochromic anemia with thrombocytopenia and leukocytosis by neutrophilia showed in blood count exam. PCR to *Ehrlichia canis*, *Hepatozoon* sp., and *Babesia canis* resulted negative. On the 15th day, blood count, biochemical analyses and urinalysis showed no alterations. Neurological examination revealed only positional vertical nystagmus. which remained as a sequel.

***Discussion*:** Polymyositis may be accompanied by rhabdomyolysis, characterized by acute muscle necrosis, increased CK and myoglobinuria. The animal had polymyositis of acute onset, with myoglobinuria and elevated CK values, whose presentation included myalgia and muscle weakness. In humans, polymyositis is accompanied by changes in electrocardiographic tracing without clinical alterations. In dogs, the first report that showed cardiac involvement was compatible with myocarditis. The changes in ECG in the present case was attributed to failure in myocardial electrical conduction. The patient also showed signs of brainstem and central vestibular system injuries. Stress myopathy, intoxication, snakebite, infectious, and metabolic diseases were discarded leading to a clinical suspicion as idiopathic origin. Similar to a published case, the patient of this report received symptomatic and supportive treatment, being discharged from the hospital 20 days after the onset of clinical signs. Thus, polymyositis may be accompanied by signs indicative of brainstem injury. Patients with rhabdomyolysis require intense monitoring due to the high risk of developing acute renal failure. Since no causative agent was identified, symptomatic treatment combined with the prevention of possible complications were fundamental for the maintenance of the animal's life.

Keywords: myoglobinuria, rhabdomyolysis, Horner's syndrome.

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INTRODUCTION

Generalized inflammatory myopathy is commonly called polymyositis [10], which can lead to rhabdomyolysis, and is characterized by acute necrosis, myalgia, collapse, or muscle weakness, marked elevation of the enzyme creatine kinase (CK) and dark-colored urine [8]. Diagnosis is made with seric dosages, electrodiagnostic tests and muscle biopsy [2]. Polymyositis may have several origins, including degenerative, metabolic (such as hypokalemic myopathy, Cushing's myopathy, hypothyroid myopathy and stress myopathy), autoimmune or infectious, inflammatory, ischemic, traumatic, by drug use, induced by toxins and also of idiopathic origin [2,8].

The brainstem is composed of the midbrain, bridge, and oblong medulla. This last anatomical area also contains rostral, medial, caudal, and lateral vestibular nuclei, so lesions in the rostral oblong medulla may affect the central vestibular system [2]. Diseases in this site may be inflammatory/infectious, neoplastic, toxic, metabolic, vascular origin, among others [1,3,6,10].

Prognosis and treatment of brainstem injury and polymyositis vary according to the origin. In cases where rhabdomyolysis occurs, the treatment is based on aggressive fluid therapy with isotonic solutions, promotion of diuresis and symptomatic treatment of pain and acute renal failure, if present [10]. The aim of this report is to describe a case of a mixed breed dog with manifestation of polymyositis associated with brainstem signs of probable idiopathic origin.

CASE

A 5-year-old mixed bred male dog was attended at the veterinary hospital. The dog had an updated vaccination, history of opisthotonos episodes for 2 days, as well as pelvic limbs extension and thoracic limbs flexion that lasted approximately 10 to 20 min at intervals of approximately 1 h. The animal was anorexic and had also presented an episode of emesis, when a distemper test was performed, with a non-reagent result.

During physical examination, the dog presented dehydration of 6% and rectal temperature 36.8ºC, but other parameters were within the normal range. Upon neurological examination, ventromedial strabismus was observed on the right side, vertical nystagmus, flaccid tetraparesis and absence of proprioception in the 4 limbs. Blood count and biochemical analyses (albumin, alanine aminotransferase (ALT), alkaline phosphatase (FA), glucose) were performed, and hypoalbuminemia (2.7 ref.: 2.6 to 3.3 g/dL) and creatinine and CK increase were verified (Table 1). Urinalysis was also performed (collection by urethral catheter), and a dark color was verified, with the presence of occult blood without, however, erythrocyturia (Figure 1A).

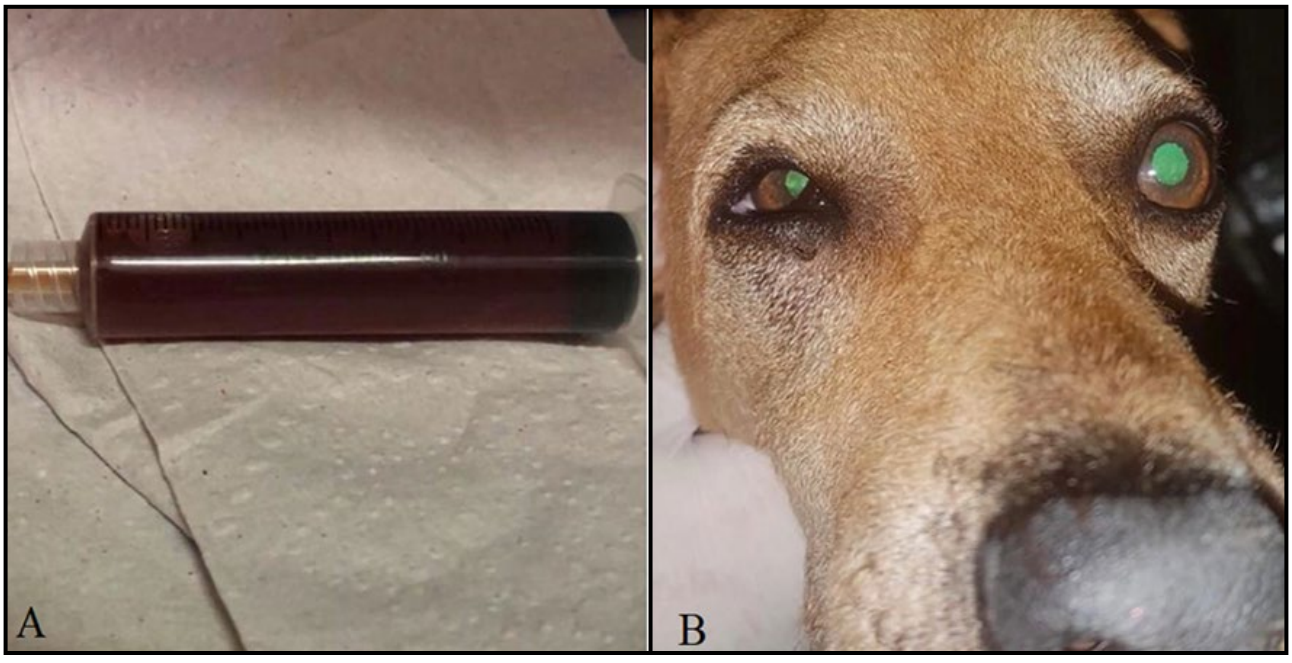

Figure 1. A- Dark coloured urine ("coke like"). B- Honer's syndrome at the right side.

Based on the findings of physical and laboratory tests, prednisolone[1] [Prediderm® - 1 mg/kg, v.o., BID, for 3 days], phenobarbital[2] [Fenocris® - 2 mg/kg, i.v. BID], maropitant citrate[3] [Cerenia® - 1 mg/kg, sc. in 2 doses] were prescribed and the dog was referred for overnight hospitalization with recommendation of crystalloid fluid[4] therapy [50 mL/kg/day, i.v.].

On the 2nd day, in addition to the neurological alterations previously observed, it was noticed Horner's syndrome on the right side (Figure 1B). The patient was catheterized for urinary output monitoring, which was 1.1 mL/kg/h, but progressed to oliguria, with 0.33 mL/kg/h (ref.: oliguria= < 1.1 mL/kg/h in fluid therapy). The reestablishment of urine output was achieved after furosemide injection[5] (1 mg/kg, sc.). Systolic blood pressure (SBP) (100 mmHg), thyroid stimulating hormone (TSH) [0.06 - ref.: 0.05 to 0.68] and free thyroxine (free T4) [0.18 - ref.: 0.7 to 3.03] were measured in order to discharge hypothesis of hypothyroidism. Hemogasometry also showed results within the normal range.

Dosages of total cholesterol (177 - mg/dL ref.: 135 to 270 mg/dL), glucose (126 mg/dL - ref.: 70 to 110 mg/dL), phosphorus (4.38 ref.: 2.6 to 6.2 mg/dL), ALT, aspartate aminotransferase (AST), enzyme creatine kinase MB (CK-MB), CK, and creatinine were also performed (Table 1).

The electrocardiogram evaluation demonstrated the presence of sinus rhythm, with heart rate of 80 bpm, despite the increase in P wave duration (0.05 s, reference: > 0.04 s) and QRS complex dysfunction, characterized by the absence of the R wave (Figure 2A) and left axis deviation (-90º to -60º, reference: +40º to +100º). In view of the suspicions of atrial overload and failure in myocardial electrical conduction with consequent alteration in ventricular contractility, chest x-ray and echocardiogram were also requested.

Chest x-ray showed no changes in cardiac silhouette. Echocardiogram presented only mild mitral valve insufficiency, without hemodynamic repercussion. Radiographic examination showed alveolar opacification near the caudal pulmonary lobes compatible with pneumonia, which was attributed to possible aspiration pneumonia, because before feeding via nasoesophageal tube, the owner was administering food by syringe. Therefore, amoxicicillin with clavulalate[6] [Agemoxi CL® - 20 mg/kg, v.o., BID], and ondansetron[2] [Nausedron® - 0.5 mg/kg, v.o. QID] was started, as well as recommended inhalation. Due to rhabdomyolysis, dipyrone[6] [Analgex V® - 25 mg/kg, v.o., QID] and tramadol hydrochloride[2] [Tramadon® - 2 mg/kg, QID] were also started. As the dog had no longer presented episodes of opisthotone, phenobarbital and prednisolone were suspended.

On the 3rd day, the urine was already normal in color and with urinary output reestablished, although urinalysis still indicated presence of occult blood without proteinuria (UP/C: 0.10 - ref.: < 0.2). The coagulation profile, ionic calcium, potassium, and sodium were within the normal range. On the 4th day, serology for toxoplasmosis, neosporis and leishmaniasis was performed with all non-reagent results, in

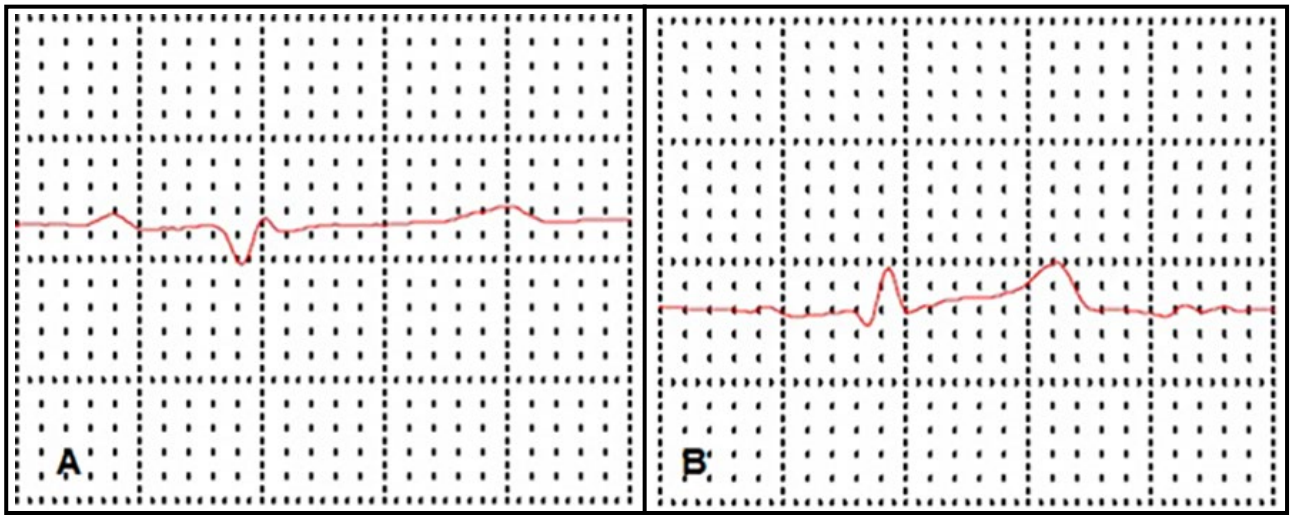

Figure 2. Electrocardiographic tracing of lead II and speed of 50 mm/s in the dog with polymyositis. Time intervals are measured in seconds (s), wave amplitudes in millivolts (mV). A- First electrocardiographic examination, showing the absence of R wave. B- After clinical improvement, electrocardiographic reassessment showed only an increase in the amplitude of the T wave.

Table 1. Results of biochemical analysis of a 5-year-old mixed breed male dog throughout the treatment period.

Exam	Day 1	Day 2	Day 4	Day 8	Day 10	Day 15	Day 17	Reference intervals
ALT	43.1	45.1	30.7	35.3	28.6	30.2	32.7	21-86 UI/L
AST	------	68.2	23.3	16.7	25.1	19.2	22	6.2-13 UI/L
CK	2,433,9	756.1	208.9	123.5	267.3	69	149.7	1.5-28.4 UI/L
CK-MB	------	545.8	268.5	56.9	------	------	------	94-262 UI/L
Creatinine	1.8	1.5	1.3	1.5	1.3	1.5	1.6	< 1.4mg/dL

addition to the reassessment of ALT, AST, CK-MB, CK and creatinine (Table 1). Although the animal was still tetraparetic, it was already more active and managed to feed without a tube, so it was released to keep the treatment at home and return later for reassessment.

On the 8th day, the animal returned, and it was already trying to stand up on the 4 feet, was active (trying to play with the other animals of the house) but was still hyporetic. Neurological examination revealed positional vertical nystagmus, absent proprioception only in the right pelvic and right thoracic limbs, in addition to decreased patellar, sciatic and flexor reflex in pelvic limbs. ALT, AST, CK-MB, CK, creatinine (Table 1) and complete blood count were repeated, evidencing thrombocytopenia (105,000 - ref.: 200,000 to 500,000 mm^3), leukocytosis (20,200 mm^3 - ref.: 6,000 to 17,000 mm^3) by neutrophilia (15,150 mm^3 - ref.: 3,000 to 11,500 mm^3), normochromic normocytic anemia (erythrocytes: 5.36 x 10^6/µL ref.: 5.5 to 8.5 x 10^6/µL; haemoglobin: 11.2 g/dL ref.: 12 to 18 g/dL; hematocrit: 34.3 % ref.: 37 to 55 %)

On the 10th day, the animal already had proprioception present on the 4 limbs and normorexia. Biochemical analyses (Table 1) and urinalysis were performed and showed no alterations, but normocytic normochromic anemia was observed, besides thrombocytopenia (167,000 mm^3 - ref.: 200,000 to 500,000 mm^3) and leukocytosis (19,200 mm^3 - ref.: 6,000 to 17,000 mm^3) by neutrophilia (12,936 mm^3 - ref.: 3,000 to 11,500 mm^3). PCR was performed for *Ehrlichia canis*, *Hepatozoon* sp. and *Babesia canis*, all resulting negative.

On the 15th day, the dog returned and was normoretic, active, physical parameters were within normal range and neurological examination revealed only positional vertical nystagmus. Blood count and urinalysis were performed and showed no alterations, in addition to the dosage of ALT, AST, CK, creatinine (Table 1). On the 17th, day the animal returned with no changes in the clinical picture. SBP (120 mmHg) was again measured, as well as complementary tests (blood count, biochemical, urinalysis), and the only remaining alteration was CK concentration (Table 1). On this day, another electrocardiogram was performed, that revealed the increase in the amplitude of the T wave (0.2 mV - ref. <0.045 mV - 25% of the R wave) and deviation of the electrical axis to the left (0º to +30º, reference: +40º to +100º) [Figure 2B]. The dog remained with positional vertical nystagmus as a sequela and after the end of treatment, which was 20 days after the beginning of the clinical signs, it no longer presented evolution of the condition.

DISCUSSION

When polymyositis occurs acutely and severely, it may be accompanied by rhabdomyolysis, characterized by acute muscle necrosis, increased CK and myoglobinuria. If the disorder is idiopathic or secondary to other diseases, the animal may present signs such as muscle edema, myalgia, weakness, or muscle collapse [5,8]. The reported animal had polymyositis of acute onset, with the presence of myoglobinuria and elevated CK values, whose clinical presentation included myalgia and muscle weakness.

In addition to polymyositis, the patient described showed signs of brainstem injury (opisthotonus and Horner's syndrome) and central vestibular system (strabismus, vertical nystagmus, and absence of proprioception). Injuries in the central vestibular system can lead to changes in behavior and changes in mental status, vertical nystagmus, strabismus, in addition to non-ambulatory tetraparesis and proprioceptive deficits [2].

Polymyositis in humans is accompanied by changes in electrocardiographic tracing in 77% of patients without clinical cardiac alterations [9]. In dogs, however, cardiac involvement in polymyositis was first

described in a case [11], and histopathological findings were compatible with myocarditis. The presence of the QS wave (characterized by the absence of the R wave) and deviation of the electrical axis were the main alterations observed in the first examination of the dog from this report, which can be attributed to failure in myocardial electrical conduction.

The improvement of the clinical picture was followed by the improvement of the electrocardiographic tracing, in which there were formation of the R wave again and less deviation of the axis, evidencing the involvement of the cardiac musculature in polymyositis.

The diagnosis of polymyositis can be made through serum CK dosage (with an increase greater than 10 times), electrodiagnostic tests, muscle biopsy, immunohistochemistry, and biochemical analyses (for the detection of inflammatory infiltrate), but samples of at least 2 different muscles are required [2,5,10]. Due to the unavailability of the electroneuromyographic examination and the lack of authorization from the owner to perform muscle biopsy, in the case described, the diagnosis was made through the seric dosage of CK and AST.

One of the main clinical alterations described was the "coke color" urine associated with the presence of oliguria and variations in creatinine levels, indicating that the animal presented a transient acute renal failure. In all conditions that lead to muscle necrosis, the release of myoglobin, an important protein of the muscular sarcoplasm, occurs, leading to myoglobinuria that can be suspected by the presence of occult blood in the urine without the presence of erythrocyturia. Myoglobinuria is what results in dark urine so-called "coke color" which commonly leads to acute renal failure [8].

Brainstem lesions may be of neoplastic, infectious, inflammatory, metabolic, or toxic origin, among others, and are also associated with brainstem infarction as a cause of signs of central vestibular system [1,2]. The most common origin of rhabdomyolysis is by effort, but there may be also degenerative, metabolic (hypokalemic, Cushing's syndrome and hypothyroidism), inflammatory, infectious, ischemic, and traumatic origin [6]. Other causes included are drugs (accidental exposure to alcohol), or exposure to toxins such as scorpion venom (which may also cause tremors, hyperthermia, vomiting, tachycardia and cardiotoxicity or neurotoxicity) [4], and snakes (which may cause neurotoxic, coagulant/anticoagulant, myotoxic, neurotoxic and nephrotoxic effects) [7,8].

In cases such as the one here described it is mandatory to adopt a diagnostic approach in order to find the causal agent. Thus, stress myopathy, infectious diseases (*Ehrlichia canis*, *Hepatozoon* sp. and *Babesia canis*, leishmaniasis, toxoplasmosis, neosporosis) and metabolic diseases (hypokalemia, hypocalcemia, and hypothyroidism) were discarded. In addition, he had no history of exposure to drugs and had no marks that indicated a snakebite or prick by venomous animal, leading to a clinical suspicion as idiopathic origin. Similar to the case described, a dog with severe acute rhabdomyolysis of idiopathic origin was discharged from the hospital after 13 days of treatment [12]. The patient from our report received symptomatic and supportive treatment with fluid therapy with crystalloid solution, analgesia, and diuretics to maintain diuresis, being discharged from the hospital 20 days after the onset of clinical signs.

Severe acute polymyositis may be accompanied by signs indicative of brainstem injury, which may lead to sequelae after resolution of the clinical picture. Those patients with rhabdomyolysis require intense monitoring due to the high risk of developing acute renal failure, which might be fatal. The identification of the cause must be an essential factor for the institution of the most appropriate treatment. However, in the described case, once there was no causative agent identified, symptomatic treatment combined with the prevention of possible complications were fundamental for the maintenance of the animal's life.

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