Neuromyotonia in a horse

Luiza Stachewski Zakia | Mariana Isa Pocci Palumbo | Raffaella Bertoni Cavalcanti Teixeira | Luiz Antônio Lima Resende | Mauro Pereira Soares | José Paes de Oliveira-Filho | Rogério Martins Amorim | Alexandre Secorun Borges

1Department of Veterinary Clinical Sciences, School of Veterinary Medicine and Animal Sciences, Sao Paulo State University (Unesp), Botucatu, Sao Paulo, Brazil
2School of Veterinary Medicine and Animal Sciences, Federal University of Mato Grosso do Sul, Campo Grande, Mato Grosso do Sul, Brazil
3School of Veterinary Medicine, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil
4Department of Neurology, Psychology and Psychiatry, School of Medicine of Botucatu, Sao Paulo State University (Unesp), Botucatu, Sao Paulo, Brazil
5Federal University of Pelotas, Pelotas, Rio Grande do Sul, Brazil

Correspondence
Alexandre Secorun Borges, Rua Prof. Doutor Walter Mauricio Correa, Unesp Campus de Botucatu 18618-681, Sao Paulo, Brazil. Email: alexandre.s.borges@unesp.br

This article describes the clinical and electromyographic findings of neuromyotonia in a 19-month-old male crossbred Quarter Horse that presented with stiffness and muscle asymmetry in the hind limbs as well as sacrococcygeal, paravertebral, and gluteal myokymia. An electromyographic study showed spontaneous continuous muscle fiber activity with high-frequency discharges, fibrillations, positive sharp waves, fasciculation potentials, and complex repetitive discharges. Histological examination of the gluteal muscle showed a mixed neurogenic and myopathic pattern. The findings are consistent with neuromyotonia.

KEYWORDS
electromyography, equine, myokymia, myopathy, stiffness

1 CASE REPORT

A 19-month-old male Thoroughbred/Quarter Horse cross was referred to the Large Animal Internal Medicine Service for evaluation of hind limb muscle asymmetry of >6 months duration.

Initial physical examination disclosed bilateral stiffness, enlargement, and continuous undulating movements (myokymia) of the sacrococcygeal, paravertebral, and gluteal muscles, and prolonged dimpling was elicited by percussion (Supporting Information Video 1). The horse walked stiffly, and muscular hypertrophy (mainly associated with the semitendinosus, semimembranosus, cervical trapezius, thoracic trapezius, brachiocephalic, cervical splenius, superficial gluteus, and gluteus femoris muscles) was present in both hind limbs. Muscle atrophy (of the gluteus medius and longissimus dorsi muscles) also was observed. Patient respiratory rate, heart rate, and rectal temperature were within normal values. No other clinically relevant findings were identified on physical examination. The horse had no signs of hyperhidrosis, or facial and testicular abnormalities. Ophthalmologic evaluation was normal.

The horse was followed for 6 months before being donated to the School of Veterinary Medicine. At the time of this report, the horse was 8 years old and still showing signs of myokymia, bilateral stiffness, and dimpling.

Eight serum biochemical profiles were performed at different times over 7 years, and creatine kinase activity was mildly increased on 7 occasions (up to 723 IU/L; reference range, 145-270 IU/L). Complete blood count, serum total protein, albumin and globulin concentrations, alkaline phosphatase, alanine transferase, and gamma-glutamyl transferase activity, as well as serum urea, creatinine, cholesterol,

Abbreviations: CRD, complex repetitive discharges; PNH, peripheral nerve hyperexcitability; HYPP, hyperkalemic periodic paralysis; VGKC, voltage-gated potassium channel.
triglyceride, sodium, potassium, calcium, magnesium, phosphorus, and chloride concentrations were within reference ranges at all sampling times.1

Plasma triiodothyronine (T3), thyroxine (T4), and blood glucose concentrations were measured on 3 different occasions (2, 2.5, and 3 years of age) to evaluate endocrine function and were within reference ranges.1 Venous blood gases and electrolyte concentrations measured using a portable clinical analyzer (i-STAT Analyzer) were within the reference range for horses.2 Serum testosterone concentration at 7 years of age was 484.7 pg/mL (reference range, 65-1600 pg/mL).3

The horse sired 5 mares when it was 5 years old; none of the foals developed similar clinical signs during a 3-year observation period. Echocardiogram, performed twice (12 months apart) with the horse in a standing position, showed no abnormalities, but when the horse was 6 years old, an echocardiogram identified pulmonary, tricuspid, and mitral insufficiency. A grade III diastolic murmur of the pulmonary valve was present at the time.

DNA was extracted from whole blood, and PCR performed for known Quarter Horse breed mutations, such as hyperkalemic periodic paralysis (HYPP), polysaccharide store myopathy type 1, and malignant hyperthermia.4,5 This horse was wild type for these mutations.

Electromyographic examination of the gluteal and paravertebral muscles was performed without sedation using standard concentric needle electrodes. Analysis time was set to 10 or 20 msec/div, sensitivity to 50 or 500 μV/div, and filter band pass to 10–10 000 Hz. All examinations were performed using a 2-channel Synergy Viasys Healthcare system. Spontaneous continuous muscle fiber activity with high-frequency discharges was observed at rest (Figure 1A) with frequent fibrillations, positive sharp waves, and fasciculation potentials also seen (Figures 1B, C, D, arrows). Frequent high-frequency complex repetitive discharges (CRD) were observed and produced a typical mechanical "pinging" sound (Figure 1E).

Neuromyotonia is a condition of muscle hyperactivity caused by peripheral nerve hyperexcitability (PNH) and is well described in humans6 and dogs.7 Isolated examples of neuromyotonic discharges have been described in horses,8,9 but we were unable to find a case with clinical signs of neuromyotonia associated with documented neuromyotonic discharges in the veterinary literature. The horse described here had the clinical, histological, and electromyographic findings consistent with neuromyotonia.

Several inherited, metabolic, toxic, and inflammatory myopathies occur in horses,5,10 and clinical, electrodiagnostic, and histological evaluations are essential for diagnosis. Myotonia is a type of myopathy characterized by prolonged muscle contraction or delayed muscle relaxation after muscle stimulation. Affected animals have gait impairment, muscle hypertrophy, stiffness, and hypertonicity. Myotonia can occur concurrently or without muscular dystrophy.10 Myotonic potentials are a common finding in these animals and represent spontaneous repetitive discharges with waxing and waning amplitudes and...
Dystrophic myotonia is a progressive disorder initially characterized by generalized myotonia with hypertrophy and hypertonicity of the larger hind limb and forelimb proximal muscles. It is associated with a dystrophic histological pattern (ie, sarcoplasmic masses, ringed fibers, moth-eaten fibers, adipose and connective tissue inflammation). A few cases have been described in horses. As the disease progresses, muscle stiffness, weakness, and atrophy develop. Prolonged percussion dimpling can be elicited, particularly in the large proximal hind limb muscles. Testicular atrophy and mild opacity of the lens also have been described. The main electromyographic finding observed in horses has been described as “dive bomber” sound, which is associated with trains of repetitive discharges that wax and wane in frequency and amplitude, suggesting true myotonia, but some authors have described CRD. The horse described here did not have true myotonia, and muscular dystrophy was not observed. Percussion dimpling and stiff gait were present, but no abnormalities of the testicles or eyes were observed. Electromyography identified typical CRD, as described previously, and neuromyotonic discharges.

Complex repetitive discharges are potentials with sudden onset and cessation. These potentials do not wax and wane like those of myotonia, and waveform shape, amplitude, and frequency may change during discharge. These CRD have been described in several different disorders, such as equine grass sickness, equine motor neuron disease, rhabdomyolysis, hypocalcemia and hypomagnesemia, HYPP, pituitary pars intermedia dysfunction, congenital centronuclear myopathy, and dystrophic myotonia. Complex repetitive discharges also have been described in normal horses.

The horse described here presented with myokymia and neuromyotonia of the gluteal muscles, which are signs consistent with PNH. Neuromyotonia and myokymia are clinical manifestations associated with peripheral nerve excitability syndrome in humans and animals. PNH is a motor neuron dysfunction with heterogeneous clinical signs, the most important clinical manifestations being muscle fasciculations, myokymia, neuromyotonia, muscle cramps, and tetany. Myokymia describes a contraction of an independent muscle or grouped muscle fibers, which induces continuous undulating or wave-like movement of the overlying skin. Myokymia is a clinical sign of neuromyotonia. Neuromyotonia is clinically characterized by a combination of muscle twitching or myokymia, persistent muscle contraction, muscle stiffness, impaired muscle relaxation, and continuous electromyographic activity. Clinical and electromyographic examinations are important to differentiate neuromyotonia and myokymia, although these clinical entities can occur simultaneously.

Electromyographic recordings in cases of neuromyotonia disclose spontaneous, continuous, irregularly occurring doublet, triplet, or multiplet single or partial motor unit discharges, firing at a high intraburst frequency (30-300 Hz). Spontaneous discharges at the highest frequencies (150-300 Hz) that occur in prolonged bursts, and which begin and end abruptly and often wane in amplitude, have been called neuromyotonic discharges. Each burst of electrical activity usually occurs irregularly, with variable interburst frequencies (from 100 milliseconds to >10 seconds). Myokymic discharges tend to occur at lower frequencies (often <60 Hz), often as doublets, triplets, or multiplets, in short semi-rhythmic bursts, followed by a few seconds of silence. The horse described here showed clinical and electromyographic signs of myokymia and neuromyotonia, and a mixed neurogenic-myopathic histological pattern also was observed.

In veterinary medicine, clinical neuromyotonia is well described in Jack Russell Terriers and, to a lesser extent, in cats. A classification system for PNH is established based on the system used in...
human medicine and recently summarized. This system included hereditary channelopathies (eg, voltage-gated potassium channel [VGKC] mutation), immune-mediated channelopathies (eg, VGKC-antibodies), paraneoplastic causes, polyneuropathies (demyelination leading to paranodal reorganization of VGKC), motor neuron disease, neurodegenerative disease, metabolic disease, and benign causes (stress or exercise).

The horse described here could not be categorized using this classification system, as it also had a myopathic pattern on histology that was uncommon in cases previously classified using this system.

Neuromyotonic discharges were described in 2 horses with problems when being ridden. Electromyographic findings suggested generalized myopathy, but the cause remained unclear. Another report described neuromyotonic discharges in 4 horses with grass sickness, but none of these reports described clinical signs of neuromyotonia. Neuromyotonic discharges and CRD have been found with very low prevalence in clinically normal horses that underwent electromyography for control studies, possibly because the muscle fibers lost contact with their nerve terminals because of necrosis of a portion of the muscle fibers. A form of PNH associated with fasciculations also was described in horses with equine motor neuron disease, but the clinical signs differed from those of the horse described here.

This horse had clinical neuromyotonia with neuromyotonic pattern on electromyography and a neurogenic and myopathic pattern in muscle biopsy specimens. We were unable to find similar previously described cases in the veterinary literature.

Based on clinical and electromyographic data suggestive of PNH and the presence of a neurogenic and myopathic pattern on histology, we conclude that this horse displayed clinical and electromyographic neuromyotonia.

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CONFLICT OF INTEREST DECLARATION
Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION
Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION
Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION
Authors declare human ethics approval was not needed for this study.

ORCID
Alexandre Secorun Borges https://orcid.org/0000-0001-6256-8089

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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