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Cardiac Changes in Horses with Atypical Myopathy

T. Verheyen, A. Decloedt, D. De Clercq, and G. van Loon

Background: Atypical myopathy (AM) is an acute, fatal rhabdomyolysis in grazing horses that mainly affects skeletal muscles. Postmortem examinations have shown that myocardial damage also occurs. Limited information is available on the effect of AM on cardiac function in affected and surviving horses.

Objectives: To describe electrocardiographic and echocardiographic changes associated with AM in the acute stage of the disease and after follow-up.

Animals: Horses (n = 12) diagnosed with AM in which cardiac ultrasound examination and ECG recording were available.

Methods: All horses underwent clinical examinations, serum biochemistry, electrocardiography, and echocardiography. Four surviving horses underwent the same examinations after 2–10 weeks.

Results: All but 1 horse had increased cardiac troponin I concentrations and 10 horses had ventricular premature depolarizations (VPDs). All horses had prolonged corrected QT (QT_{cf}) intervals on the day of admission and abnormal myocardial wall motion on echocardiography. One of the surviving horses still had VPDs and prolonged QT_{cf} at follow-up after 10 weeks.

Conclusions and Clinical Importance: The AM results in characteristic electrocardiographic and echocardiographic changes and may be associated with increased cardiac troponin I concentrations and VPDs. In survivors, abnormal cardiac function still may be found at follow-up after 10 weeks. Additional research in a larger group of horses is necessary to identify the long-term effects of AM on cardiac function.

Key words: Cardiac dysrhythmia; Cardiac ultrasound; QT interval; Rhabdomyolysis; Tissue Doppler imaging.

Atypical myopathy (AM) is a highly fatal disease occurring in grazing horses, especially during autumn and spring. The disease causes an acute degeneration of skeletal muscle, characterized clinically by weakness, stiffness, recumbency, and a mortality rate of approximately 70%.[1] The disease was first described in the United Kingdom in 1984[2,3] but now is recognized in many other European countries. Furthermore, a similar seasonal pasture myopathy has been described in the United States.[4] The etiology of the disease remains uncertain, but recent research points toward a toxin causing mitochondrial damage and multiple acyl-CoA dehydrogenase deficiency (ADD).[5–7]

Postmortem examinations indicate that AM not only causes degeneration of the skeletal muscles but also may affect the myocardium. At necropsy, diffuse or multifocal pale areas may be observed in the myocardium, as well as focal areas of hemorrhage.[1,4,8] Histopathologic changes in the myocardium are moderate to severe granular myocardial degeneration and necrosis, with lipid accumulation in the myocytes. This severe myocardial degeneration suggests that cardiac damage may be a cause for sudden death in AM-

Abbreviations:

2DST	two-dimensional speckle tracking
ADD	acyl-CoA dehydrogenase deficiency
A_m	peak radial wall motion velocity during late diastole
AM	atypical myopathy
CD	contraction duration by TDI
CD_{SC}	time to peak circumferential strain
CD_{SL}	time to peak longitudinal strain
CD_{SR}	time to peak radial strain
cf	value corrected using Fridericia's correction method
CK	creatine kinase
cTnI	cardiac troponin I
DHA	docosahexaenoic acid
E	early diastolic filling
E_m	peak radial wall motion velocity during early diastole
EAD	early after depolarization
FS	fractional shortening
IVRT	isovolumic relaxation time
IVS	interventricular septum
LVFW	left ventricular free wall
LVPEP	left ventricular pre-ejection period
LVET	left ventricular ejection time
LQTS	long QT syndrome
PSM	postsystolic motion
QT_{cf}	QT interval with Fridericia's correction method
ROI	region of interest
SC	peak circumferential strain
SD	standard deviation
SL	peak longitudinal strain
S_m	peak radial wall motion velocity during systole
SR	peak radial strain
STI	synchronicity time index
TDI	tissue Doppler imaging
t-MVO	time to mitral valve opening
VPD	ventricular premature depolarization
VT	ventricular tachycardia

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affected horses.[8] Most horses affected by AM have increased concentrations of plasma cardiac troponin I (cTnI), a specific biomarker of myocardial injury.[9,10] It is unknown to what extent the myocardium recovers in surviving horses. Previous studies have shown that tachycardia, dysrhythmias, or cardiac murmurs can be found in AM horses, but detailed information is not available.[1,10]

The aim of our study was to investigate cardiac function in horses with AM by biomarkers, electrocardiography, and echocardiography.

Material and Methods

Case Selection

Horses referred to the Department of Large Animal Internal Medicine, Ghent University (Belgium) with AM between 2009 and 2011 were included in this study. Inclusion criteria were housing on pasture, acute nonexertional rhabdomyolysis (ie, myoglobinuria, stiffness, trembling, sweating, weakness, recumbency, lethargy), rapid progression and occasionally sudden death, increased plasma creatine kinase (CK) activity, and availability of both ECG and cardiac ultrasound examination before initiation of medical treatment. Drugs given before referral (flunixin meglumine, butyl scopolamine, saline) were confirmed not to affect the QT interval. All horses underwent general examination on the day of arrival at the clinic. In nonsurvivors, the diagnosis of AM was confirmed on postmortem examination.

Study Population

The study population consisted of 12 horses (7 mares, 2 geldings, 3 stallions) of different breeds (7 warmbloods, 1 Friesian, 3 ponies, 1 Arabian) aged 3.9 ± 2.8 years (mean ± SD) with a body weight of 416 ± 103 kg. Upon arrival, heart rates ranged from 40 to 68 beats per minute, packed cell volume from 39 to 56%. Seven horses died or were euthanized within 1 to 4 days, 5 horses survived. Survivors were followed up after 2–10 weeks. At that time, they were no longer receiving any treatment.

Biochemistry

Ionized calcium, potassium, and sodium concentrations were measured[a] on lithium heparine blood samples. Magnesium and CK concentrations were determined[b] on serum. Cardiac troponin I (cTnI) concentration was determined[c] on lithium heparin plasma.

Electrocardiography

A base-apex ECG was obtained[d] at the time of echocardiographic examination in standing (n = 7) or recumbent (n = 5) position. From 20 consecutive cardiac cycles, the QT interval was measured as the time from the onset of the QRS complex to the end of the T wave, and the associated preceding RR interval was determined. Measurements from 10 healthy horses (9.6 ± 4.4 years, 509 ± 58 kg, 7 mares, 3 geldings) at rest were used as normal control values.

Echocardiography

Echocardiographic studies were performed[e] from a right and left parasternal window (n = 7), or from only 1 side in recumbent horses (n = 5). Standard 2-dimensional and M-mode images were obtained with a phased array transducer[f] at a frequency of 1.7/3.4 MHz (octave harmonics). Atrial and ventricular dimensions and fractional shortening (FS) were measured in a conventional manner.[11] On M-mode images, time to mitral valve opening (t-MVO) was measured from a short axis image at the mitral valve level as the time interval between the R wave on the ECG and mitral valve opening. Left ventricular pre-ejection period (LVPEP) was measured as the time interval between the R wave on the ECG and aortic valve opening on long axis LV outflow tract recording. Left ventricular ejection time (LVET) was measured as the time interval between aortic valve opening and closure. Isovolumic relaxation time ($IVRT_{M\text{-}mode}$) was calculated as the time from aortic valve closure to mitral valve opening.

For TDI, images were recorded from a right parasternal short axis view at the papillary muscle level. Image width was decreased to 30° and the velocity scale ranged from −32 to +32 cm/s, resulting in a frame rate of 183 frames per second. During off-line analysis,[g] a sample area was placed in the interventricular septum (IVS) and the left ventricular free wall (LVFW) with an adapted length (11–17 mm) and width (4–6 mm) depending on wall thickness. Radial peak velocities were measured during systole (S_m), early diastole (E_m), and late diastole (A_m) and the E_m/A_m ratio was calculated. Contraction duration (CD) was determined as the time from the R wave to onset of early diastolic filling (E). Isovolumic relaxation time ($IVRT_{TDI}$) was measured as the time from end S to onset E. The preceding RR interval was recorded.

For 2DST, images were recorded from a right parasternal long axis modified 4-chamber view and a right parasternal short axis view at papillary muscle level.[12] Image width was decreased to 55°, resulting in a frame rate of 41 frames per second. Off-line analysis was performed in a semiautomated fashion by the "2D Strain" application of the ultrasound software.[g] A region of interest (ROI) was drawn along the LV endocardial border in a frame at end-systole and ROI width was adjusted to wall thickness. Speckle tracking started automatically, dividing the ROI into 6 segments. Peak longitudinal (SL) strain was measured from the long axis image, circumferential (SC) and radial (SR) strain were measured from the short axis image. Contraction duration was measured as the time to peak longitudinal (CD_{SL}), circumferential (CD_{SC}), and radial (CD_{SR}) strain. The mechanical dispersion of contraction was calculated as the synchrony time index (STI), defined as the time difference between the shortest and longest contraction duration of the 6 segments per loop.[13]

All measurements were compared to those of the control group of 10 healthy horses.

Data Analysis and Statistics

The QT interval was corrected for heart rate by Fridericia's correction method ($QT_{cf}=QT/RR^{1/3}$).[14,15] Because all echocardiographic time variables are equally influenced by heart rate, the same formula was used to correct these values, as described in human medicine.[16] Data are reported as mean ± standard deviation (SD). Comparisons of means from AM horses and control horses were performed by a Student's *t*-test. Values of $P < .05$ were considered statistically significant.

Results

Twelve horses with AM were examined. Breed, sex, age, body weight, clinical status, and clinical course are shown in Table 1. Four surviving horses were followed up after a variable period of 12–72 days.

Table 1. M-mode, TDI, and 2DST echocardiographic measurements of horses with atypical myopathy compared with a healthy control group.

		Atypical Myopathy		Controls (n = 10)	
Ultrasound Mode	Variable	n	Mean ± SD	Mean ± SD	*P*
M-mode	t-MVO_{cf} (ms)	9	568 ± 38	532 ± 20	.017*
	$IVRT_{cf}$ (ms)	9	165 ± 42	90 ± 17	<.001*
	$LVPEP_{cf}$ (ms)	9	53 ± 9	78 ± 8	<.001*
	$LVET_{cf}$ (ms)	9	353 ± 38	365 ± 9	.363
	LVPEP/LVET	9	0.15 ± 0.03	0.20 ± 0.02	<.001*
	FS (%)	11	39.0 ± 3.8	36.1 ± 2.7	.056
TDI	CD_{cf} IVS (ms)	11	563 ± 30	526 ± 21	.004*
	CD_{cf} LVFW (ms)	11	554 ± 45	533 ± 25	.2
	$IVRT_{cf}$ IVS (ms)	11	224 ± 52	133 ± 26	<.001*
	$IVRT_{cf}$ LVFW (ms)	11	199 ± 57	92 ± 18	<.001*
	S_m IVS (cm/s)	11	−6.9 ± 1.4	−4.3 ± 1.1	<.001*
	S_m LVFW (cm/s)	11	7.9 ± 2.9	5.8 ± −0.8	.035
	E_m IVS (cm/s)	11	7.9 ± 2.9	13.2 ± 2.2	<.001*
	E_m LVFW (cm/s)	11	−10.8 ± 3.1	−14.4 ± 1.8	.005*
	A_m IVS (cm/s)	10	5.0 ± 3.4	3.5 ± 2.7	.305
	A_m LVFW (cm/s)	11	−10.9 ± 4.0	−7.3 ± 2.0	.019*
	E_m/A_m IVS	10	2.7 ± 2.6	7.2 ± 6.3	.071
	E_m/A_m LVFW	11	1.1 ± 0.4	2.1 ± 0.7	<.001*
2DST	SL (%)	7	−22.6 ± 1.2	−24.6 ± 1.5	.009*
	SC (%)	7	−19.5 ± 2.8	−20.0 ± 1.8	.668
	SR (%)	7	63.8 ± 7.8	62.7 ± 3.6	.700
	$CD_{SL,cf}$ (ms)	7	418 ± 32	443 ± 14	.095
	$CD_{SC,cf}$ (ms)	7	395 ± 65	426 ± 18	.265
	$CD_{SR,cf}$ (ms)	7	404 ± 75	457 ± 18	.118
	STI-$CD_{SL,cf}$ (ms)	7	102 ± 38	57 ± 29	.016*
	STI-$CD_{SC,cf}$ (ms)	7	201 ± 101	52 ± 20	.008*
	STI-$CD_{SR,cf}$ (ms)	7	80 ± 64	43 ± 23	.184

2DST, 2-dimensional speckle tracking; A, late diastolic peak velocity; CD, contraction duration; cf, Fridericia's correction method; E, early diastolic peak velocity; IVRT, isovolumic relaxation time; IVS, interventricular septum; LVET, left ventricular ejection time; LVFW, left ventricular free wall; LVPEP, left ventricular pre-ejection period; S, systolic peak velocity; SC, peak circumferential strain; SD, standard deviation; SL, peak longitudinal strain; SR, peak radial strain; STI, synchronicity time index; TDI, tissue Doppler imaging; t-MVO, time to mitral valve opening.

*Significant differences.

Biochemistry

At presentation, 10 horses had hyponatremia, 11 had hypocalcemia, and 1 had hypomagnesemia. Hyperkalemia was present in 2 horses.

The CK activity was increased in all horses (302688 ± 265670 mU/mL; range 787000–21770 mU/mL; reference range 10–146 mU/mL). Except for horse 11, all horses had cTnI concentrations exceeding the reference value of 0.10 ng/mL[17] (2.02 ± 2.7 ng/mL; range 0.12–8.95 ng/mL). In horse 5, cTnI concentration was above detection limit (>99.99 ng/mL). At follow-up 2–10 weeks later, cTnI concentrations in surviving horses had returned to normal. There was no correlation between magnitude of cTnI concentration and survival.

Electrocardiography

At presentation, 10 horses had VPDs which in 5 horses were polymorphic. Mean number of VPDs per horse was 7 ± 7 with a range of 1–17. One horse also had paroxysmal ventricular tachycardia (VT). Twenty-four hours after presentation, horse 5 developed paroxysmal VT, accompanied by a deterioration of its clinical status, necessitating euthanasia. At follow-up 2 months later one of the surviving horses (horse 6) still had VPDs at rest and during exercise.

The QT_{cf} interval was significantly longer in horses with AM ($P < .001$) compared with control horses (590 ± 40 ms; range 538–658 ms; reference value <490 ms) (Fig 1). In three of the surviving horses, the QT_{cf} interval had returned to normal at follow-up examination 8–12 days later. The QT_{cf} interval in horse 6 shortened but was still above that of the control group at follow-up 10 weeks later. The 5th surviving horse (horse 4) was lost to follow-up.

Echocardiography

M-mode and TDI measurements for AM horses and control horses are shown in Table 1. The left atrial and left ventricular dimensions were within reference values in all horses. Visual inspection of the 2-dimensional and M-mode images showed systolic wall motion abnormality in all cases. Biphasic contraction

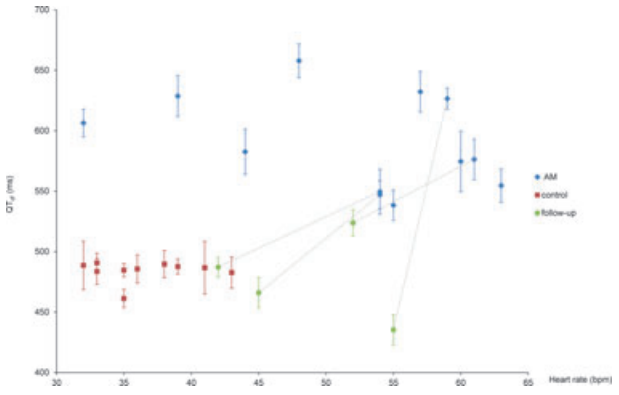

Fig 1. QT_{cf} (mean ± standard deviation) in horses with atypical myopathy compared with healthy control horses. *Y*-axis shows the corrected QT interval by Fridericia's method (QT_{cf}). *X*-axis shows heart rate. Blue symbols represent AM horses, red symbols control horses. Green symbols represent QT_{cf} at follow-up in surviving horses.

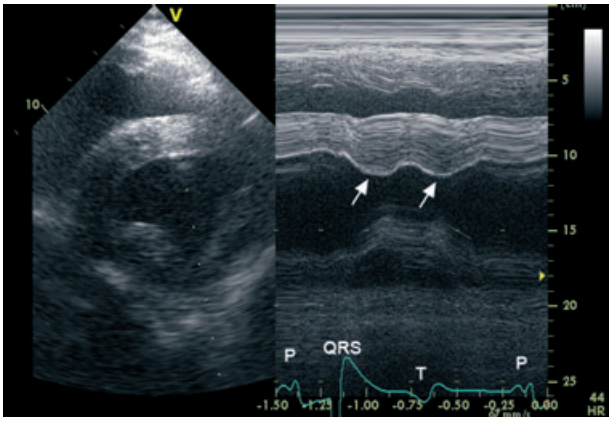

Fig 2. Short-axis 2D (left panel) and M-mode (right panel) image at papillary muscle level, showing biphasic contraction of the interventricular septum.

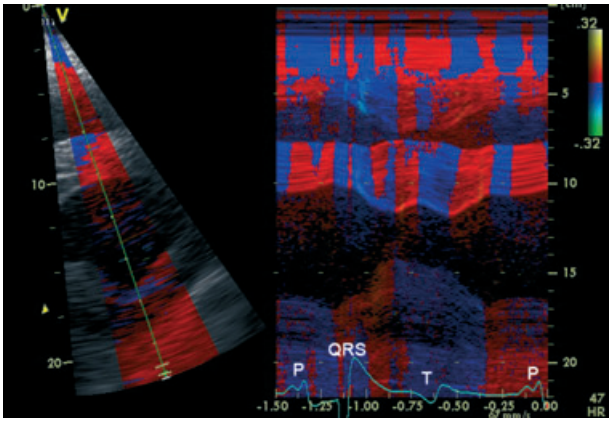

Fig 3. Short-axis 2D (left panel) and M-mode (right panel) image at papillary muscle level with tissue Doppler imaging (TDI). The biphasic wall motion in the interventricular septum is characterized by the alternation of red and blue TDI color codes, indicating wall motion velocities toward and away from the transducer, respectively.

was observed in 8 horses (Fig 2). Biphasic contraction was most obvious in the IVS, but also was present in the LVFW in 6 horses. The IVS in the remaining 4 horses had a "plateau-like" morphology during contraction. The t-MVO_{cf} and $IVRT_{cf,M\text{-}mode}$ were significantly longer in AM horses ($P = .017$ and $P < .001$, respectively), whereas $LVPEP_{cf}$ and LVPEP/LVET were significantly shorter ($P < .001$). The $LVET_{cf}$ and FS were not significantly different from control horses ($P = .363$ and $P = .056$, respectively).

Biphasic contraction was evident on TDI (Figs 3–4). In AM horses, CD_{cf} was significantly longer in IVS ($P = .004$) but not in the LVFW ($P = .2$). The $IVRT_{cf,TDI}$ was significantly longer in both the IVS and LVFW ($P < .001$). The S_m was significantly higher in both the IVS ($P < .001$) and LVFW ($P < .035$). The E_m/A_m ratio was significantly lower in the LVFW ($P < .001$) but not in the IVS ($P = .071$), whereas E_m

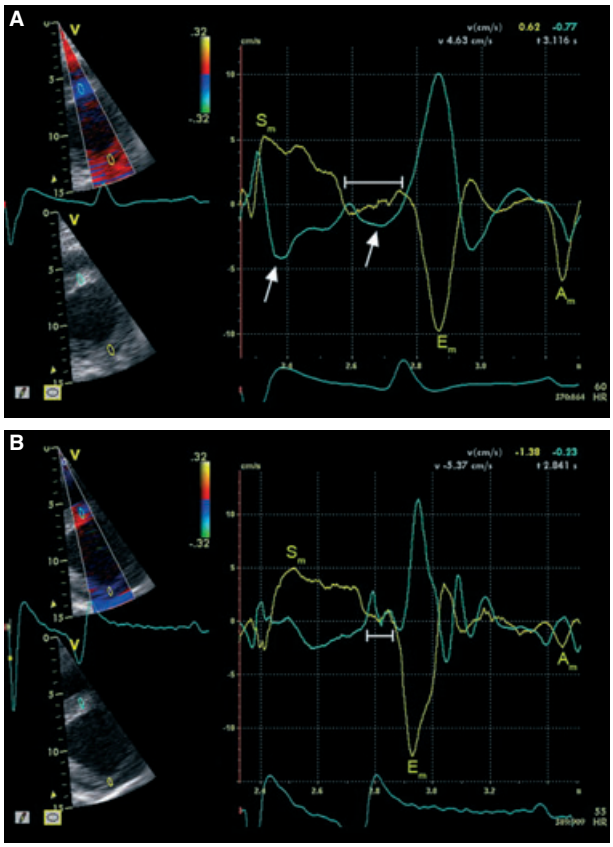

Fig 4. Wall motion velocity curve (cm/s) obtained by TDI at papillary muscle level. The ECG is displayed at the bottom. A region of interest has been placed in the left ventricular myocardium (yellow) and the interventricular septum (green). E_m represents peak radial wall motion velocity during early diastole; A_m represents peak radial wall motion velocity during late diastole. A: The biphasic contraction of the septum is seen as two separate negative velocity peaks during systole, demonstrated by white arrows. The prolonged isovolumic relaxation stime (IVRT) is shown by a white horizontal bar. B: At day 11, the biphasic contraction and prolonged IVRT are no longer present.

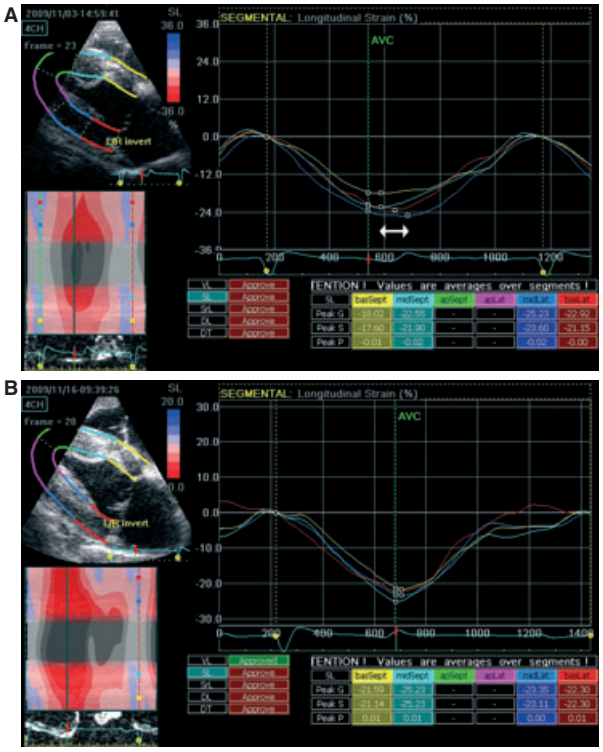

Fig 5. Longitudinal strain curve (%) obtained by 2DST from a right parasternal long axis modified 4-chamber view. The ECG is displayed at the bottom. A region of interest (ROI) has been positioned on the myocardium, which is automatically divided into 6 segments. A. Mechanical dispersion is evident as the difference between shortest and longest time to peak strain (white arrow). B. At day 14, mechanical dispersion is no longer present.

was significantly lower in both the IVS ($P < .001$) and LVFW ($P = .005$).

The prolonged contraction and biphasic wall motion also were visible in the 2DST strain curves (Fig 5). Peak SC and SR were not different from the control group, but SL was significantly lower in AM horses ($P = .009$). Although global CD_{SL}, CD_{SC}, and CD_{SR} were not prolonged, there was increased mechanical dispersion of contraction among the 6 segments per view. STI of CD_{SL} and CD_{SC} was significantly longer in AM horses, whereas the STI of CD_{SR} was not significantly different.

Discussion

Our study confirms the presence of cardiac damage in horses with AM, as previously described.[8] Ten of 12 horses had VPDs, and all but 1 horse had increased concentrations of cTnI on admission, indicating cardiac cellular injury. We did not find an association between the increase in cTnI concentrations and survival.

In addition, we found specific alterations on ECG recordings and cardiac ultrasound examination. All horses had prolonged QT_{cf} intervals in association with abnormal systolic motion of the left ventricle. The QT interval represents the time between the onset of depolarization and end of repolarization in the ventricles. Because AM horses usually have increased heart rates and because physiological QT shortening occurs at increased heart rates, QT correction is required to compare intervals regardless of heart rate.[14,15] In humans, QT interval is known to increase with age and body mass index.[18] The AM horses were younger and had lower body weight than control horses. However, all AM horses showed significantly longer QT_{cf} intervals, indicating prolonged ventricular repolarization. To our knowledge, this is the first time that long QT_{cf} interval has been reported in horses with cardiomyopathy. In human medicine, lengthening of the QT interval is well known and described as "long QT syndrome" (LQTS). Two forms of LQTS exist: inherited LQTS and acquired QT prolongation. The inherited form is caused by mutations in the genes that encode ion channel proteins, causing a maintained inward current of sodium at depolarized voltages or a decrease in delayed rectifier potassium channel currents.[19] Both defects lead to prolongation of ventricular repolarization, which translates into QT prolongation on the electrocardiogram. The acquired form mainly has been associated with exposure to a wide variety of cardiac and noncardiac drugs,[19] but also with electrolyte imbalances and toxins such as cocaine and organophosphate compounds.[20] Abnormalities in ionic currents, mainly because of blocking or inhibiting potassium channels, may cause QT prolongation in the acquired form.[19,21]

The origin of the long QT interval seen in AM horses is uncertain. Drug-induced prolongation seems unlikely because none of the horses had received treatment with a known QT-prolonging drug at the time of recording. Electrolyte imbalances may have played a role because hypokalemia and hypocalcemia are known to cause QT prolongation and dysrhythmias.[20,22,23] However, none of the horses had hypokalemia and 1 AM horse with normocalcemia also showed QT prolongation, suggesting that other mechanisms may play a role. Certain toxins also can induce QT prolongation.[20]

The etiology of AM remains unknown, but recent research points toward a myopathy of toxic origin, affecting mitochondria.[8] Studies by Westermann et al[6] and van der Kolk et al[7] showed an acquired multiple ADD in horses with AM, confirming the role of mitochondria in the pathophysiology of the disorder. Interestingly, in a recent study, Gélinas et al[24] found a link between ADD and long QT interval in mice. They also noticed a cardiac-specific reduction of docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid, in the membrane phospholipids of these mice. Results suggest that DHA could have a protective effect against QT prolongation.[25,26] In another study in ADD mice, Werdich et al[27] reported alterations in intracellular calcium homeostasis and an increased ionized calcium load in the sarcoplasmic reticulum. These changes were thought to be induced by decreased ATP

production as a consequence of ADD. This decrease in ATP hampers the β-oxidation of fatty acids and hence decreases the amount of energy available to the heart muscle cells. An increased ionized calcium load in the sarcoplasmic reticulum may increase spontaneous calcium release and lead to dysrhythmias, which was present in 10 of 12 of our AM horses. Another possible explanation for the dysrhythmias is early after depolarizations (EADs). The EADs are oscillations in membrane potential that occur when the action potential duration is increased long enough for ion channels such as L-type calcium channels to recover from inactivation and reactivate during repolarization.[19,28,29] They can trigger ectopic premature beats, but also increase electric heterogeneity and hence favor the development of reentrant ventricular tachycardias (VT) and Torsade de Pointes.[19,21] Runs of VT were present in 2 of our AM horses.

Abnormalities in ionic currents also may explain the wall motion abnormality seen on echocardiography because they can lead to prolongation of repolarization, visible on ultrasound examination as a "plateau-like" prolonged contraction. This is supported by the fact that calcium channel blockade by verapamil in LQTS patients normalized the wall motion abnormality.[30] The biphasic contraction shape that was present in 8 horses also has been recognized in human LQTS patients. This was proposed to be the mechanical equivalent of an electrical EAD.[30] However, in these horses, the biphasic contraction usually was present in each cardiac cycle, making EAD less likely. Another possibility is what is known in human medicine as postsystolic motion (PSM).[31] Although often associated with ischemia, PSM also may occur in healthy subjects. The PSM also has been described in healthy horses,[12,13] but the duration of postsystolic contraction was much longer in AM horses. In ischemic hearts, PSM can be because of a passive inward movement of affected myocardial segments caused by adjacent normal contracting segments, or it can represent a delayed active contraction after unloading of unaffected segments and hence regional wall stress decrease.[31] However, a coexisting reduction in ejection velocity is obligate, which was not present in AM horses.[32] Therefore, ischemic PSM is an unlikely explanation for the observed contraction abnormality. Based on the morphology and timing of the biphasic contraction, it is thought to be associated with aortic valve closure, causing a biphasic instead of a "plateau-like" contraction pattern in certain segments.

The TDI and 2DST measurements confirmed that the abnormal wall motion pattern was caused by delayed repolarization and thus abnormal relaxation. Similar to what has been described in human LQTS patients, the rapidity of early contraction was unaffected, as demonstrated by the shorter LVPEP and faster S_m.[33,34] The prolonged contraction duration was explained by a longer duration of the IVRT, with a normal ejection time. The impaired LV relaxation also was reflected by the diastolic myocardial velocities. The E_m was decreased and the E_m/A_m ratio was decreased, indicating diastolic dysfunction.[35,36] These findings are in agreement with findings in LQTS patients in human medicine.[37] The TDI and 2DST measurements also indicated mechanical dispersion of contraction duration. By TDI, CD was significantly longer in the IVS but not in the LVFW. By 2DST, the STI-CD for longitudinal and circumferential strain was significantly longer in AM horses. This mechanical dispersion also has been found in human LQTS patients and probably reflects electrical dispersion of repolarization.[38] The ion channels are not homogeneously distributed throughout the myocardium and thus a nonhomogeneous prolongation of action potential duration may occur. The dispersion of repolarization increases the risk of ventricular arrhythmias such as Torsades de Pointes. In the AM horses, CD was longer in the IVS compared with the LVFW. Similar results were found in human LQTS patients, and were attributed to longer action potential duration of the subendocardial Purkinje cells and midmyocardial M-cells which are located in the IVS.[37] Although FS, SR, and SC were normal, SL was significantly lower in AM horses, although still within the reference range. Because longitudinal fibers are predominantly located subendocardially, this transmural dispersion probably explains why longitudinal function was more affected both in human LQTS patients and AM horses.

Four of the surviving horses were followed up after a variable period. In all horses, cTnI concentrations returned to normal and the abnormal myocardial motion disappeared. One of the horses still showed VPDs and a QT_{cf} interval that, although shortened, remained above the reference range. There was no evidence of myocardial fibrosis on repeated echocardiographic examinations in this horse.

The number of surviving horses for follow-up was very limited, so conclusions on surviving horses must be interpreted with caution. Additional research in a larger group of horses with a longer follow-up period is necessary to evaluate the long-term consequences of AM on cardiac function and the contribution of cardiac damage to the low survival rate. The ECG recordings at the time of death might elucidate causes of sudden death associated with AM. Another limitation was the relatively low number of horses in which a full cardiac examination could be performed before initiation of treatment. However, findings were very consistent in all AM horses. Horses in the control group were not age and body weight matched to AM horses, which might be important because the QT interval is positively correlated with age and body weight.[18] However, AM horses had longer QT intervals even though they were younger and smaller.

In conclusion, AM induces myocardial damage in horses, which can lead to characteristic electrocardiographic and echocardiographic abnormalities. The exact pathophysiology remains to be elucidated, but ADD and abnormalities in ionic currents may play an important role. In 1 horse, the presence of VPDs and mildly prolonged QT_{cf} at follow-up 2 months later suggested that full recovery had not occurred.

Additional research in a larger group of horses with a longer follow-up period is necessary to evaluate the long-term consequences of AM on cardiac function and the role of dysrhythmias in the low survival rate.

Footnotes

[a] AVL 9180 Electrolyte Analyser, Roche Diagnostics, Vilvoorde, Belgium
[b] Spotchem SP-4420, Arkray Europe, Amstelveen, The Netherlands
[c] Acces Accu-TnI, Beckman Coulter Inc, Fullerton, CA
[d] Televet 100® Version 4.1.3., Kruuse, Marslev, Denmark
[e] GE Vivid 7 Pro, GE Healthcare, Horten, Norway
[f] 3S Phased Array Transducer, GE Healthcare
[g] EchoPAC Software Version 108.1.5, GE Healthcare

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