Long QT Syndrome in Young Athletes

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Long QT syndrome is a disease associated with a high risk of sudden cardiac (arrhythmic) death. The frequency of sudden cardiac death is approximately 1: 100,000 young athletes, while autopsies often do not detect changes, which indicates a primary arrhythmogenic death. The article describes two clinical cases of young athletes with prolongation of the QT interval. The possible causes of the long QT syndrome and the difficulties of diagnosing this syndrome in children and adolescents involved in sports are discussed. Regardless of the reasons leading to the prolongation of the QT interval, there is a risk of arrhythmic events. Timely diagnosis of long QT syndrome is the way to the primary prevention of sudden cardiac death in young athletes.

Keywords: sports; young athletes; congenital long QT syndrome; secondary causes of QT interval prolongation; sudden cardiac death.

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Синдром удлиненного интервала QT у юных спортсменов

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Синдром удлиненного интервала QT — заболевание, ассоциированное с высоким риском внезапной сердечной (аритмической) смерти. Частота внезапной сердечной смерти составляет примерно 1 : 100 000 юных спортсменов, при этом на вскрытии зачастую не обнаруживают изменений, что указывает на первично аритмогенную смерть. В статье приводится описание двух клинических случаев юных спортсменов с удлинением интервала QT. Обсуждаются возможные причины синдрома удлиненного интервала QT, трудности диагностики данного синдрома у детей и подростков, занимающихся спортом. Независимо от причин, приводящих к удлинению интервала QT, существует риск развития аритмических событий. Своевременная диагностика синдрома удлиненного интервала QT — путь к первичной профилактике внезапной сердечной смерти у юных спортсменов.

Ключевые слова: спорт; юные спортсмены; врожденный синдром удлиненного интервала QT; вторичные причины удлинения интервала QT; внезапная сердечная смерть.

Sudden cardiac death (SCD) is a tragic event, particularly for athletes who undergo routine medical examinations and are considered healthy. The incidence of SCD is approximately 1:100,000 in young athletes, with autopsy often showing no abnormalities indicating primary arrhythmogenic death [1]. The causes of SCD can be acquired or genetic. Acquired causes include myocarditis and coronary artery disease, and genetic causes include genetically determined structural heart diseases and channelopathies [2]. An example of channelopathies is the hereditary (congenital) long QT syndrome (LQTS). The prevalence of congenital LQTS is estimated at 1:2000 [3], and for its diagnostics, the criteria developed by Schwartz in 1985 [4] and supplemented by him in 2011 [5, 6] are currently used. Over the past 25 years, 17 genes have been associated with LQTS; however, a recent analysis based on a gene- and disease-specific approach developed by the Clinical Genome Resource classified several of these genes as limited or controversial. This analysis selected seven genes with definitive or conclusive evidence of a causal relationship [7]. All of these remaining genes, i.e., KCNQ1, KCNH2, SCN5A, CALM1, CALM2, CALM3, and TRDN, encode ion channels involved in cardiac repolarization, their modulating subunits, or proteins that regulate or modulate ion channel function [7]. The LQTS genotype can be identified in 75% of sick people with a clear phenotype, and this is important because it determines the approach to their treatment [8]. In addition to congenital LQTS, various causes (conditions) lead to secondary prolongation of the QT interval. One of them is an electrolyte imbalance, such as hypokalemia, hypocalcemia, and hypomagnesemia, which can occur under the influence of many triggers, for example, with long-term intake of diuretics, especially loop diuretics (furosemide).

CLINICAL CASES

Young female athlete A, aged 16 years, was referred for a consultation with a cardiologist because of identified changes in the electrocardiogram (ECG). The history revealed that the patient has been doing rhythmic gymnastics since the age of 3.5 years. At the time of the consultation, the duration of training was 3.5 h a day 5–6 times a week, and she was a sub-master athlete. She coped with exertions, and syncope conditions were not registered. She underwent a planned thorough medical examination (TME). During the regular TME, pathological changes in the ECG, such as prolongation of the QT interval, were detected. In the analysis of the family history, cases of SCD and syncope conditions did not occur in the next of kin. The QT interval duration in the parents was normal.

On examination, the condition was satisfactory. Her height, weight, and body mass index were 163 cm, 42 kg, and 15.8 kg/m², respectively. The skin color was normal. Breath sounds were heard in all lung fields, there were no rales, and the respiratory rate was 20 per min. Visually, the region of the heart was not abnormal. Percussion borders of relative cardiac dullness were within the age norm. The heart sounds were clear, and her heart rate (HR) was 64 per minute and regular in a lying position. Her blood pressure and oxygen saturation were 100/60 mm Hg and 99%, respectively. The abdomen was soft and nontender on palpation. The liver was not enlarged. There was no peripheral edema. The pulse on the femoral arteries was determined on both sides. Bowel and bladder habits were normal.

On a surface 12-channel ECG (computer electrocardiograph CARDI, Medical Computer Systems, Moscow, Zelenograd, Russia), with a recording speed of 50 mm/s (Fig. 1), moderate sinus bradycardia was recorded with an HR of 54–57 beats/min, QT interval (V5) of 460 ms, and corrected QT (QTc) interval of 438–451 ms.

When taking an ECG in an upright position (Fig. 2) in the presence of an increase in sinus rhythm up to 82 beats/min, the duration of the QT interval (V5) was 540 ms and QTc was 635 ms (pronounced prolongation of the QT interval).

Given the QT interval prolongation, Holter ECG monitoring (ECG HM) was performed using the Poly-Spectrum-SM system, Neurosoft, Ivanovo, Russia.

During ECG HM, a prolongation of the QT interval up to 680 ms was registered (Fig. 3).

The QT interval prolongation persisted regardless of the HR, namely, 680 ms in sinus rhythm with an HR of 53 beats/min, 580 ms with an HR of 85 beats/min (Fig. 4), and with a norm according to ECG HM findings up to 480 ms [9].

Fig. 1. 12-lead electrocardiogram in young athlete A., 16 years old
According to the automatic analysis of QT (the norms are presented according to the National Russian recommendations for the use of the HM technique in clinical practice), an elongation of this interval was also revealed, where the average QT interval was 471 (normal 342–401) ms, QTc by Bazett was 500 (normal 396–447) ms, and QTc by Fridericia was 490 (normal 384–421) ms.

Rare (total 354, extrasystole density 0.4%) single ventricular extrasystoles and episodes (3) of trigeminy (Fig. 5) were registered.

Transthoracic echocardiography (EPIQ 5 Ultrasound Device, Philips, Netherlands) showed normal biventricular systolic function. The valvular apparatus had no pathological abnormalities, and the transvalvular flow was normal. No enlargement/hypertrophy of the heart chambers was detected. To rule out possible secondary causes of QT interval prolongation in a young athlete, the level of electrolytes in the blood serum was determined. The analysis revealed hypokalemia (potassium 2.2 mmol/L; normal, 3.6–5.6 mmol/L). During a conversation with the patient, it was established that she had been taking furosemide without control for 1.5 years to reduce weight. After drug correction of the potassium level, the QT interval was normalized according to the results of ECG (Fig. 6) and ECG HM, ventricular extrasystoles were not recorded.

Bicycle ergometry (Corival Lode, Netherlands) at all stages of the load, with 4 min of recovery, did not reveal an elongation of the QT interval.

During the follow-up period (catamnesis 2 years), the athlete fulfilled the standard of mastery of sports in rhythmic gymnastics, and her blood level of potassium and the duration of the QT interval remained within the normal range.

Young female athlete E, aged 10 years, was examined due to acute respiratory disease at the Children’s Scientific and Clinical Center for Infectious Diseases of the Federal Medical and Biological Agency. The prolongation of the QT interval was revealed by ECG with a recording speed of 50 mm/s. ECG (Fig. 7) recorded sinus arrhythmia, episodes of bradycardia (HR 63–86 bpm), QT (V5) of 420 ms, and QTc of 429–506 ms (increase in QTc interval with an increase in HR). The two-humped T wave morphology and notched T wave were revealed in leads V4–V6, which is characteristic for long QT syndrome.
During ECG HM (Cardioline System, Italy), the QT interval was prolonged up to 540 ms (recording channel 3) at a minimum HR of 46 beats/min (Fig. 8) at a rate of up to 480 ms. Serum electrolytes were normal. Transthoracic echocardiography revealed no pathological changes.

The anamnesis revealed that the patient has been doing rhythmic gymnastics since the age of 4, with training 5–6 times a week for 3 h. No pathological changes in the ECG were detected during the scheduled TME. She had no episodes of loss of consciousness. As regards heredity, the girl’s mother had two episodes of loss of consciousness (at the age of 33 and 35 years). The first attack was related to stress, and the other had no apparent cause. The attacks were accompanied by convulsions and involuntary urination. Regarding fainting, the patient was examined in one of the clinics in St. Petersburg and consulted by a neurologist, and a diagnosis of autonomic dysfunction syndrome was made. The ECG of the mother (Fig. 9) revealed sinus rhythm with an HR of 70–80 beats/min and a significant prolongation of the QT interval, where the QT (V5) at an HR of 76 beats/min was 500 ms and QTc was 562 ms. The T morphology was also characteristic of the molecular genetic variant 2 of the hereditary LQTS.

Based on the generally accepted diagnostic criteria proposed by Schwartz [4, 6], patient E was diagnosed with hereditary LQTS, familial variant (inheritance on the mother’s side), and molecular genetic variant 2. Whole-genome DNA sequencing was performed at the EVOGEN Medical Genetic Laboratory (Moscow), which revealed a previously undescribed variant p. Met554ValfsTer100 (leading to the formation of a premature stop codon) in the heterozygous state in exon 7 of 15 exons of the KCNH2 gene responsible for the development of the molecular genetic variant 2 of LQTS (LQT2).

Atenolol was recommended at a daily dose of 1 mg/kg. Training at the sports school has been discontinued.
DISCUSSION

LQTS is a disease associated with a high risk of SCD due to the development of torsade de pointes polymorphic ventricular tachycardia [11]. Regardless of the causes of LQTS (such as hypokalemia due to long-term intake of furosemide in clinical case 1 and a mutation in the KCNH2 gene in clinical case 2, which caused the development of LQT2), patients with LQTS are at risk of life-threatening arrhythmic events. In a study conducted in the USA, LQTS causes SCD in 2% of athletes [2], and 0.4% of Olympic athletes may experience ventricular tachyarrhythmias associated with this syndrome [12]. Before diagnosing young athletes with congenital LQTS, acquired causes of QT prolongation must be ruled out. The most common causes include medications that prolong QT, metabolic changes, and electrolyte disorders. One of the routine methods to detect changes typical for LQTS is a standard 12-lead ECG. The interpretation of the ECG in athletes includes an estimate of the length of the QTc, calculated using the Bazett equation. However, difficulties may be encountered in assessing the QT interval in young athletes. Approximately 25%–35% of patients with a genetically confirmed hereditary LQTS may have normal QT interval on the ECG at rest [2]. Determining the duration of the QT interval associated with sinus bradycardia characteristic of athletes is even more difficult, especially when identifying the prolongation of the QT interval associated with an increase in HR (an example of a 10-year-old rhythmic gymnast diagnosed with LQT2). Moreover, when registering severe sinus arrhythmia on the ECG, the response of the QT interval to a change in the HR is not instantaneous and complete adaptation takes 1–3 min [13]. Problems can also arise when making a differential diagnosis between the U wave and the two-humped T wave, characteristic of LQT2, on the body-surface ECG.

Until now, there are conflicting opinions on the admission of athletes with a diagnosed congenital LQTS to training and competitions. The 2005 ESC guidelines for participation in sports competitions are the most restrictive [14]. They state that congenital LQTS is a contraindication for any sports, even in the absence of documented serious cardiac arrhythmias. The 2015 European Society of Cardiology guidelines for the treatment of ventricular arrhythmia and the prevention of SCD recommended avoiding intensive swimming, particularly in the case of LQT1; however, no other sports have been mentioned [15]. More recently, the 2018 American eligibility and disqualification guidelines for athletes with channelopathies (including LQTS), who take part in competitions, are less restrictive [16]. According to these guidelines, athletes with symptomatic LQTS (except for competitive swimming with LQT1) may be eligible to compete after the initiation of treatment and appropriate precautions, as long as they have been symptom-free during treatment for at least 3 months and these athletes and their family members received information about potential risks.

In the Russian national recommendations on the admission of athletes with abnormalities in the cardiovascular system to training and competitions, for athletes with a history of an episode of cardiac arrest or syncope conditions, presumably associated with LQTS, regardless of the QTc interval or genotype, all sports are contraindicated, except for class IA [17].

Thus, these cases clearly demonstrate the existing difficulties in diagnosing LQTS in young athletes and the need for a comprehensive analysis of possible causes of LQTS, which, in some cases, will help preserve the possibility of continued involvement in the chosen sport and reduce the risk of SCD in other cases. To detect QT prolongation in young athletes, further studies including stress tests and molecular genetic testing are needed to search for gene mutations responsible for the development of this syndrome.

REFERENCES

Список литературы


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**ИНФОРМАЦИЯ ОБ АВТОРАХ**

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