H140 Lethal Masturbation of a Teenager Suffering From a Long QT Syndrome (LQTS) Type 8 With a Newly Discovered CACNA1C Gene Mutation

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After attending this presentation, attendees will be aware of one of the first described lethal cases due to a newly discovered mutation of the Calcium Voltage-Gated Channel Subunit Alpha 1 C (CACNA1C) gene causing LQTS type 8 and that masturbation could be considered as a triggering factor leading to the fatal outcome in such cases.

This presentation will impact the forensic science community by highlighting the need of cardiac genetic investigation of sudden death cases in a forensic context as it could help determine the cause and mode of death. Additionally, it could have major implications for the therapeutic strategy of the family.

Congenital LQTS affects approximately1/2500 people. It can arise from mutation(s) of one of several genes coding for the cardiac ion channels. It involves an abnormal repolarization of the heart that increases the risk of sudden death after severe polymorphic ventricular arrhythmia. Different triggering factors are often described, most of which are hyper adrenergic situations. Their identification is of great importance for clinicians in order to evaluate the best prevention strategy.

This study reports the sudden death case of an 18-year-old male, who was found dead in his bedroom on a summer day at noon, two hours after he came home from taking a school exam. An unsuccessful Cardiopulmonary Resuscitation (CPR) was performed within one hour.

At the scene, he was found with his fly unzipped, with three wet facial tissues near him that tested positive for acid phosphatase, suggesting he had just masturbated. Instruments to roll cigarettes were also found, but no cigarette butts.

Medical background was significant as the male was diagnosed with LQTS (QTc: 480ms) after a syncope at the age of ten years that occurred after swimming. Since then, he had been treated with the usual beta-blocker oral therapy (50mg/m²/day of nadolol). Family screening determined LQTS for his mother and one of his sisters.

The first cardiogenetic analysis was performed after the LQTS diagnosis: KCNQ1 and KCNH2 gene (among 15 genes currently identified) analysis was negative. The availability of the next generation DNA sequencing techniques allowed a deeper analysis of DNA on a postmortem sample and found that he was carrying one of the recently discovered mutations of the CACNA1C gene (cDNA c2573G>A, heterozygous mutation, p.Arg858His), which encodes for the Cav1.2 protein (a1 subunit of cardiac L-type calcium channel).[1] This mutation was shown to be a gain-of-function mutation, highly involved in the prolongation of the duration of the ventricular action potential.

Autopsy found no macroscopic pathological signs except for signs of CPR with epicardial petechiae and unspecific pulmonary edema and congestion. Gross anatomy of the heart and coronary arteries was normal. No sign of Timothy's syndrome was discovered.

The postmortem toxicological analysis found 24.7ng/ml of nadolol in the blood, which is consistent with a therapeutic level. No other drugs or narcotics were found at the toxicology screen, except cotinine and delta-9-tetrahydrocannabinol (0.76ng/ml) and its metabolites (THCCOOH: 2.09ng/ml, 11-OH-THC: 0.65ng/ml), suggesting occasional cannabis smoking with a last smoke within the last 12 hours.

The genetic discovery of this mutation, consistent with the context and background, led investigators to close this case by stating that is was a natural/accidental death by ventricular fibrillation triggered by probable hyper adrenergic context on an LQTS type 8 patient.

Among the possible triggering factors that could be linked to the fatal arrhythmia, masturbation seems to be the leading hypothesis as a physical and emotional exercise, even if the role of the emotional context after the school exam and of the light cannabis intoxication could not be absolutely excluded.

This case is one of the first lethal cases described involving this mutation and could be considered, for forensic purposes, as a natural/accidental form of autoerotic death.

In the medical clinical field, this case highlights that LQTS8 can be associated with a severe phenotype if we consider that sudden death can occur with "moderate" physical exercise, and is resistant to the beta-blocker therapy. This important genetic result will therefore contribute more accuracy in this family LQTS screening.

Reference(s):

1. Fukuyama M. et al. Long QT syndrome type 8: novel CACNA1C mutations causing QT prolongation and variant phenotypes. *Europace.* Dec 2014, 16 (12) 1828-1837.

Sudden Cardiac Death, Masturbation, Long QT Syndrome