H10 A Fatality Due to Type I Long QT Syndrome (LQTS) Associated With Electrolyte Abnormalities and Therapeutic Levels of Citalopram

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The goal of this presentation is to review the relationship between Type I LQTS, dysrhythmia, and risk factors in teenagers.

This presentation will impact the forensic science community by presenting a case report of a lethal arrhythmia in Type I LQTS associated with blood levels of citalopram in the therapeutic range.

The acquired or inherited condition known as LQTS, defined by prolongation of the QT interval (the time interval from the start of cardiac ventricular depolarization to the completion of repolarization >480msec), is due to interference with normal myocardial repolarization.[1] It may cause ventricular fibrillation, Torsades des Pointe (TdP), palpitations, syncope, seizures, and sudden death. Presentation occurs at any age but childhood or early adulthood is typical. Inherited LQTS is due to 13 genetic mutations in ionic channel genes (channelopathies), most of which are dominantly inherited. Three genes make up the majority of cases (Types 1, 2, and 3). Type 1 is caused by mutations in the voltage gated potassium channel gene KCNQ1 and is associated with arrhythmias during exercise or emotional stress. The heart usually appears grossly and microscopically normal in younger patients. Diagnosis depends on the clinical history, electrocardiogram changes, laboratory results, and a review of the patient's medication list. Known risk factors for TdP in these patients are: hypokalemia, hypomagnesemia, hypocalcemia, female gender, age over 60 years, and medications that block the potassium channel function.[2,3] One such drug is the serotonin selective reuptake inhibitor citalopram; however, the blood levels needed to produce this side effect are debated.[4-7] Of note, the Food and Drug Administration recently published a warning about citalopram used in higher doses.8

This study describes an 18-year-old female who collapsed and was found to be in ventricular fibrillation by paramedics. Just prior to collapsing, she was emotionally upset due to an argument with her boyfriend. After resuscitation, she converted to a sinus rhythm but developed prolonged seizures and expired from anoxic encephalopathy five days later. An admission electrocardiogram showed a corrected QT interval (Bazett's formula) of 648msec and serum chemistries revealed hypokalemia (2.9mEq/L) and hypocalcemia (7.6mg/dL, corrected). The reason for her electrolyte abnormalities was not identified. She had been taking 20-30mg of citalopram per day for depression; there was no history of hearing loss or sudden cardiac death in the family. The autopsy was unremarkable and her heart appeared structurally normal (337 grams). A postmortem blood sample submitted to GeneDx for genetic testing revealed a disease-causing missense mutation in the C-terminal end of the KCNQ1 (R594Q) gene, a cause of Type 1 LQTS.[9,10] This R594Q variant occurs within the assembly portion of the KCNQ1 protein. An admission blood sample analyzed by National Medical Services Laboratories had a citalopram level of 120ng/mL. Reported premortem therapeutic levels are in the 40-100ng/mL range. Reported incidental postmortem ranges for this drug vary but are slightly higher: 400ng/mL, 90-760ng/mL, a median of 300ng/mL, 90-1,300ng/ml.[11-15] Lethal levels for this drug are usually much higher.[16] The cause of death was attributed to a cardiac arrhythmia associated with the LQTS and electrolyte abnormalities. The contribution made by citalopram toward the initial dysrhythmia remains speculative but given the FDA warning about citalopram and TdP at higher doses, it is difficult to dismiss its role entirely as some would suggest.[7,17,18] The case raises the question: Should clinicians screen for LQTS with an electrocardiogram before starting females on citalopram?

In summary, this was a case of inheritable LQTS in a teenager with risk factors for the development of ventricular dysrhythmias, including hypokalemia, emotional stress, and female gender. She was also on a medication previously associated with development of TdP, although typically at higher doses than prescribed. What contribution it made is uncertain. This report adds to the literature on citalopram blood levels in cases associated with the inheritable LQTS.

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Arrhythmia, Long QT Syndrome, Citalopram