CASE REPORT

Case Report: Long QT syndrome in the setting of post COVID depression [version 1; peer review: awaiting peer review]

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Abstract
Long QT syndrome is a genetically inherited heart disease caused by mutations in genes coding for the ion channels expressed in the heart cells. Like any other hereditary pathology Long QT Syndrome manifestations often start at a young age. We report the case of a 65-year-old woman who presented a syncope after taking antidepressants, revealing a congenital long QT syndrome. The onset of cardiovascular symptoms in elderly subjects with such an unrecognized entity is very rare and is most often due to transient biological disturbances or to the use of certain drugs, which prolong the QT interval.

Keywords
Long QT syndrome, COVID-19, depression, antidepressants, syncope

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Any reports and responses or comments on the article can be found at the end of the article.

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Introduction
The Coronavirus Disease (COVID-19) Pandemic has caused over five million deaths at the time of this publication worldwide. In addition to the direct pathological impact of the virus and its social and economic repercussions, there has been a significant increase in the incidence of depressive and anxiety disorders, especially with lockdown and sanitary curfew taking effect in different countries. Simultaneously, there has been a rise in the prescription of different classes of anti-depressants with numerous side effects often forgotten, sometimes neglected, that may have serious cardiovascular consequences. For instance, these medications may be an occasion to reveal rare latent hereditary conditions, such as long QT syndrome (LQTS). It is a genetically transmitted cardiac condition due to mutations in cardiac ion channels genes, usually revealed by syncope, palpitations, seizures, and sudden cardiac death, in patients with structurally normal heart, with different degrees of QT prolongation and repolarization abnormalities on the surface EKG. Clinical manifestations usually begin in young age with recurrent cardiovascular events.

Aim
We aim through this case report to raise the awareness of practitioners on the importance of pretreatment screening of possible signs and symptoms of latent LQTS as well as EKG abnormalities, even in the elderly, in addition to the importance of continuous surveillance under certain types of treatment that could prolong the QT interval.

Case report
A 65 year old woman with a personal past medical history of diabetes mellitus, arterial hypertension and dyslipidemia, and with family history of sudden unexplained death, was admitted in Cardiology department with repetitive syncope following the use of Escitalopram, a selective serotonin reuptake inhibitor (SSRI) prescribed for a major depressive disorder, developed in the middle of the first sanitary lockdown announced in the country during the first vague of COVID-19, a few weeks after getting infected with mild symptoms. No chest pain was reported, nor palpitations, nor dyspnea. An EKG was not performed prior to the prescription of this treatment.

Clinical examination was normal. EKG findings revealed multiple torsades de pointe with a long QT Interval of 480 ms and negative T waves in inferior and anterior leads. No biological abnormalities were found particularly no electrolyte disorders and normal troponin levels. Trans-thoracic echocardiography showed a preserved ejection fraction with mild mitral regurgitation. Coronary angiography was normal. The initial diagnosis was acquired Long QT syndrome following exposure to Escitalopram and the patient was discharged.

Eight months later, she was readmitted with the same symptoms. EKG findings revealed the same abnormalities with long QT interval of 490 ms. All first investigations were normal. No iatrogenic factor was found. Cardiac magnetic resonance imaging was performed in search of signs of arrhythmogenic dysplasia of the right ventricle, showing only one minor criterion: regional right ventricle dyskinesia with an ejection fraction of 43%. Congenital Long QT syndrome was thus suspected, and the patient was put under Nadolol 80 mg per day with regression of symptoms. She also received a list of contraindicated drugs.

Figure 1. 12 leads EKG after magnesium sulfate administration.
Eight months later, the patient, still under Nadolol, was readmitted with recurrence of syncope and upper abdominal pain following emotional stress (death of her sister), where multiple torsades de pointe were recorded in the EKG realized in the Emergency department, treated with 2 g intravenous magnesium sulfate followed by continuous intravenous infusion of 6 g/24 h.

After the tachycardia was stopped, EKG revealed multiple multiform premature ventricular contractions, sometimes in form of non-sustained ventricular tachycardia, with long QT interval of 638 ms (Figure 1). Biological tests were normal and no iatrogenic factor was found. The patient was admitted in our cardiology department for Dual chamber implantable Cardioverter Defibrillator (ICD) implantation.

**Discussion**

Anxiety, memory or concentration difficulties, and depressed mood, have increasingly been reported since the outbreak of The virus Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) - the causative pathogen of the coronavirus disease 2019 (COVID-19) - in Wuhan city, Hubei Province, China on December 8, 2019. These symptoms have long been attributed to the isolation conditions with lockdown and sanitary curfew being more and more indicated, as well as the increase in hospitalization especially among relatives and the fear of death. However, since many systemic effects of the virus are progressively being discovered and understood each day, scientists have been conducting various studies in search for a molecular mechanism that may explain the relationship between COVID-19 and the development of depressive conditions. Current findings suggest that the production of high concentrations of pro-inflammatory mediators may alter the permeability of the Blood-brain barrier, activating Toll-like receptors of the microglia and astrocytes, exacerbating neuro-inflammation and altering the homeostasis of the central nervous system, which causes cognitive and mood changes.

Treatments of depression aim to increase the concentration of certain central neuromodulators incriminated in its emergence, mainly serotonin, noradrenaline, and dopamine. Simultaneously, as the arrhythmogenicity of certain Psychotropic medications, especially neuroleptics, continue to raise concern with more restrictive pretreatment screening recommended with time, studies are continuously examining rates of sudden death among various antidepressants with varying conclusions. For instance, in August 2011, the Food and drug administration (FDA) issued a Drug Safety Communication to health care professionals and the public warning them of QT prolongation with citalopram use. However, no other guidelines or reviews that state this adverse effect among SSRIs other than citalopram have been issued yet and the risks associated with paroxetine, fluvoxamine, fluoxetine, and sertraline are only limited to case reports. Whereas the FDA alert regarding citalopram specifies that the risk of QT prolongation does not apply to Escitalopram; the S-isomer of citalopram; regardless the dose administrated, the British Medicines and Healthcare Products Regulatory Agency (MHRA), the Arizona Center for Education and Research on Therapeutics (ArizonaCERT), as well as the product package insert itself, approve of the risk of this side effect with Escitalopram, despite controversial studies on the matter.

Concerning tricyclic antidepressants, the impact on QT interval is well documented. Charlotte van Noord et al. study the impact of psychotropic drugs on QT interval among more than 8000 patients as part of the Rotterdam study, a prospective cohort study ongoing since 1990 in the city of Rotterdam in the Netherlands, found a statistically significant QTc prolongation with maprotiline, amitriptyline, nortriptyline, and imipramine. However, this statistical significance was found when calculating the QTc using the Bazett and Fridericia formula, and appears to be lost when adjusting the QT interval to the heart rate.

Long QT syndromes represent a large variety of conditions with similar manifestations, EKG findings and consequences. They may be due to several acquired causes like electrolyte disturbances and certain drugs/medications, or hereditary, due to mutations in cardiac ion channels genes, mainly K+ channels, sometimes sodium channels, resulting in abnormal myocardial repolarization with prolongation of the action potential. Congenital LQTS affects approximately 1:2500 individuals of the general population, with symptoms varying from syncope, palpitations, seizures, to sudden cardiac death, representing a major cause of sudden unexplained death accounting for 20–25% of the cases. Therapeutic measures have considerably changed the course of the condition, and include mainly Lifestyle modifications, beta-blockers and implantable cardioverter defibrillator (ICD) implantation.

β-Adrenergic blocking agents, specifically propranolol and nadolol, represent the first-choice therapy in symptomatic or asymptomatic LQTS patients. They have shown excellent results in preventing stress-triggered arrhythmias, reducing the risk by 80% or more, all types of LQTS included, but have low to no effect on sleep-triggered cardiac events. ICD implantation is an important treatment, indicated for patients suffering from LQTS who survived a cardiac arrest, patients who remain symptomatic despite a well-conducted treatment using beta-blockers, or for whom they are contra-indicated.
In all cases, precautions including avoiding competitive and exertional sports, exposure to loud noises, the use of medicines that prolong the QT interval and treatment of electrolyte abnormalities that may occur during diarrhea, vomiting or some diets, should be done as much as possible regardless to the symptoms or the type of LQTS.

**Conclusion**

Patients undergoing antidepressant treatment should be screened for long QT syndrome regardless to their age, based on family history, search for neglected or forgotten cardiac events and EKG characteristics. Furthermore, even with an initial normal QT interval, Surveillance should remain active during treatment to detect QT prolongation that may be the only expression of the disease. This raises the problem on the modalities of treatment of depressive patients suffering from LQTS and should benefit of standardized guidelines.

**Consent**

We confirm that we have obtained written consent to use data from the patient included in this study.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**References**

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