Treating an Adolescent with Long QT Syndrome for Bipolar Disorder: A Case Presentation

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ABSTRACT - Objectives: Long QT syndrome (LQTS) is described as the development of sudden syncope attacks or death as a result of ventricular tachycardia (VT) episodes that might be observed as elongated QT interval in electrocardiography (ECG). Implantable Cardioverter Defibrillator (ICD) is recommended as first-line treatment for the condition in guidelines. We aimed to present an adolescent recently diagnosed with Bipolar Disorder (BD) who had LQTS that was treated with ICD, discussing her follow up and treatment along with relevant literature. Methods: Psychiatric assessment of the case that applied to our child psychiatry unit due to manic symptoms were carried out using Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) criteria. Symptom severity was monitored via Young Mania Rating Scale scores (YMRSS). Results: The case met criteria for Bipolar Disorder Type I (BD-I). She had improvement in her mood symptoms with treatment regimen as risperidone 3 mg/day, valproate 1000 mg/day and lorazepam 1 mg/day after her 2–week follow up as well as no reported ICD activity, reflecting fine cardiac functions and rhythm. Conclusions: LQTS is a serious health issue for children and adolescents diagnosed with BD. This condition should be kept in mind especially in cases where familial risk factors are present and precautions need to be maintained upon required assessments. These cases need to be closely monitored due to risk factors related to both BD and LQTS, in a multidisciplinary fashion, involving both psychiatry and cardiology divisions. Psychopharmacology Bulletin. 2017;47(1):33–39.

INTRODUCTION

Long QT Syndrome (LQTS) is described as the development of sudden syncope or death as a result of ventricular tachycardia (VT) episodes observed as elongation of the QT interval in electrocardiography (ECG). This condition due to functional impairment of ion channels within the cardiac muscle might emerge congenitally or acquired later in life.1–4

In the congenital form of LQTS, mutation of genes that regulate ionic gradient, particularly potassium and sodium, within ion channels in cardiac muscle cells occur. As a result of these alterations, time of repolarization of the cardiac muscle...
cell increases, in turn reflecting as elongated QT in ECG. Patients are particularly vulnerable to life-threatening ventricular arrhythmia especially when they are exposed to exercise or emotional conditions where sympathetic activity increases.²,³,⁵,⁶

Standard corrected QT intervals (QTc) for adults (with Bazett correction) recommended by Committee for patented medication products are as follows:

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<tr>
<td><strong>FEMALE (MILISEC)</strong></td>
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<tr>
<td>Normal</td>
<td>&lt; 450</td>
<td>&lt; 430</td>
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<tr>
<td>Borderline</td>
<td>451–470</td>
<td>431–450</td>
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<tr>
<td>Elongated</td>
<td>&gt; 470</td>
<td>&gt; 450</td>
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(Abovementioned values are valid within circumstances where no other medical disorder or medication use is present).⁷

Risk factors defined for QT elongation are identified as; female gender, LQTS history within the family, electrolyte imbalance, cardiovascular disorders (bradycardia, low ejection fraction, dilated cardiomyopathy), simultaneous use of a drug that might inhibit the metabolism of another drug that causes QT elongation (antihistaminic, antiarrythmic, decongestan, diuretic, antibiotic and psychotropic medications), renal or hepatic illnesses, diabetes or hypotiroidism, excess weight loss, malnutrition, obesity, intracranial disorders such as subarachnoid or cerebral hemorrhage, over and sudden emotional stress, emotional stress together with sudden or chronic exercise activity in adolescents around 15 years old and adults over 40 years, clinical hypoxia and exposure to high levels of arsenic.⁸–¹³

Fifty percent of untreated LQTS cases have been reported to face sudden death within 10 years.¹⁴,¹⁵

Literature suggests treatment with Implantable Cardioverter Defibrillator (ICD) in case combined treatment with beta-blockers and left cardiac sympatetic denervation and/or pacing fail to prevent synecopes due to VT. Moreover, ICD is identified as the first-line treatment option for patients with cardiac arrest that gain back their normal rhythm upon cardiopulmonary ressuscitation in American Cardiac Association guidelines.¹⁶

ICD is less commonly practiced in childhood. Rate of ICD application in children make up less than 1% of all ICD practice.¹⁷

While case reports of adults with the condition might be observed in the literature, scarce reports are found regarding children and adolescents with the condition.

We, hereby aim to present an adolescent with Bipolar Disorder (BD) who was diagnosed with LQTS during her routine examinations and...
had undergone an ICD procedure, while discussing her follow up and treatment processes along with relevant literature.

**CASE**

The case was a 17-year old adolescent with normal intellectual functioning. She applied to our unit due to manic symptoms such as risky behavior involving running away from home to visit her boyfriend that lived in another city, over self confidence and increase in energy, emotional lability, talking more than usual as well as fastened associations, oppositional and defiant behavior. Her first episode was described as a manic episode following depression when she was 15 years old; 3 manic and 3 depressive episodes were identified from her first clinical picture so far.

When her medical history was detailed, it was learned that she was a thalassemia carrier, her parents were first-degree relatives, one of her siblings had also LQTS and another had died due to unknown reasons when he was 3 months. She had already transferred to another school due to her psychiatric condition and was not attending school at all at the time of her application.

As her brother of 4 years younger had been diagnosed with LQTS during routine physical examination prior to sports course, whole family was screened for the condition, yielding positive for her. ICD was applied to both her and her brother in July 2015.

It was learned that she had been diagnosed with BD few months prior to being diagnosed with LQTS in another city, however there were disruptions in the adjustment to the disorder as well as regular monitoring due to her manic symptoms during her episodes and the family’s difficulties in managing the overall process. At the time of application, she was still manic and was not using the recommended treatment combination involving Valproate and Propranolol. Her initial Young Mania Rating Scale Score (YMRSS) was 26. Routine blood tests, ecocardiography (ECO), awake and sleep electroencephalography (EEG) results were normal. QTc was calculated as 550 milisec via ECG.

We planned to start the case on Valproate and increasing it to therapeutic doses. However, due to disruptions in maintaining a regular follow up and parental psychoeducation and coping skills techniques provided limited adherence to medical treatment, the case was transfered to the inpatient unit. During her inpatient follow up of 2 weeks with a medication regimen as Risperidone 3 mg/day, Valproate 1000 mg/day and Lorazepam 1 mg/day, the case was discharged with partial remission to continue her follow up in the outpatient unit, without any cardiac complaints.
It was determined that her ICD had never become active during her follow up with the abovementioned medication regimen. Upon discharge, the case had not applied to her control sessions in the outpatient unit for some time; however had visited the unit irregularly, 3 times within a span of 12 months. She was euthymic in her first two visits while had a YMRSS as 22 in her last visit. Prior to this, she was described as having a brief depressive phase. We planned to start her on Valproate once again; however due to the family’s nonadherence to monitor blood levels of the drug regularly, though they were informed about the importance, her treatment was readjusted as risperidone 1 mg/day with a plan to gradually increase the dose.

**DISCUSSION**

BD cases need to be carefully monitored for accompanying LQTS since both elevated emotional reactivity and risk-taking behavior during manic episodes might cause an increase in sympatheitic activity as well as possible problems in cardiac rhythm that might be caused by psychotropic drugs used.

Use of psychotropic medications carry the risk of QT elongation. In the meantime, BD is a psychiatric condition that requires long-term and regular use of psychotropic medication while involving emotional lability and behavioral problems that might create an incline in sympatheitic activity during its natural course which also needs to be managed properly with concomittant cardiac conditions.

Regarding medium and long term outcomes, ICD is identified as a safe practice during childhood. Similar indications outlined in adults apply to children, in the context of ICD application.18,19

Associated risk factors in our case were being female, positive family history for LQTS, presence of a comorbid disorder such as BD that might cause sudden and excess emotional stress and the requirement to use psychotropic medication for clinical improvement. During her inpatient follow up phase due to abovementioned risk factors and treatment rejection during her outpatient follow up, it was seen that she was partially remitted for BD within a short time of 2 weeks without any occurring cardiac problems.

ICD application was immediately carried out upon diagnosis in our case. ICD application in our case might have protected her from developing highly-possible rhythm problems due to psychotropic medication we had used for treating BD. The fact that she had not used recommended medication for BD prior to ICD implantation might have created the impression of a decline in cardiac-associated health risks while increasing morbidity associated with BD.
For this case’s treatment, we chose to use a combined treatment regimen of Valproate as the mood stabilizer and an atypical antipsychotic as risperidone which is described as less likely to cause an elongation of QTc interval in the literature. As valproate was clinically effective even in lower doses for our case, there was no need to increase the dose of risperidone or to add another psychotropic medication to the regimen, which might have provided better cardiac outcomes, though we believe that the application of ICD was the most important factor in not encountering a rhythm problem in this case.

Medication list that might cause QT elongation that was published by Credible Meds and updated in May 15, 2016 includes Lithium as a potentially risky agent among mood stabilizers, while no such information regarding Valproate is present. Even though risperidone is identified as a possible risky agent and carries a warning that it might cause an increase in the QT interval, as our case was non-adherent to the recommended medication and unable to provide regular blood level tests for valproate, her treatment was continued with risperidone. When relevant literature was reviewed, one sudden death related to risperidone was identified, while cause of death for this reported case was not due to LQTS. To our knowledge, no death due to LQTS related to Lithium or Valproate was identified as well.

It is recommended to use the lowest possible doses of antidepressant and antipsychotic medications that are clinically effective and to screen the patients with ECG in the beginning and within regular intervals when cases of LQTS need to be started on high-risk agents and especially at the onset of combination treatment. Among psychotropic medication, antidepressants and antipsychotics have been related to QT elongation.

Among typical antipsychotics, phenothiazine group has been particularly associated with elongated QT, in turn, causing guidelines to include ECG monitoring during delirium treatment with IV haloperidol. No sudden death case associated with frequently used atypical antipsychotics olanzapine and quetiapine have been reported in literature. Reports that clozapine causes serious cardiac problems are more common. Ziprasidone is reported to have more effect on QT elongation compared to haloperidol, risperidone, olanzapine or quetiapine; while less compared to sertindole and tioridazine.

Regarding relevant literature, scarce reports are present in the literature involving children or adolescents that had an ICD application due to LQTS, while no case with comorbid BD has been identified so far, to best of our knowledge.

Monitoring inappropriate shocks upon ICD application is of great importance, as well. Irregular psychiatric and cardiological follow-up taken together.
up and inability of the family to manage the process prevented us to monitor her in relation to inappropriate shock or any other rhythm problem that might have caused ICD activation, leaving our case at high risk, for both conditions.

We believe professionals working in this field need to be attentive to LQTS which is an important health problem among children and adolescents diagnosed with BD; particularly in cases with familial history of the condition, taking necessary precautions with recommended examination and tests.

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CONFLICTS OF INTEREST

None.

REFERENCES


