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Clonidine for ADHD with Comorbid Oppositional Defiant Disorder in a Patient with Congenital Long QT Syndrome

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Abstract

Background: Oppositional defiant disorder (ODD) and attention-deficit/hyperactivity disorder (ADHD) co-occur in roughly half of children with ADHD. Pharmacological management for both disorders typically involves stimulants or antipsychotics. However, in patients with congenital Long QT syndrome (LQTS), the use of stimulants might present an additional clinical risk for ventricular arrhythmias. Alternatives must be sought as the impact of these untreated psychiatric conditions can be significantly limiting to these patients.

Case Presentation: A 14-year-old male with ODD and comorbid ADHD was started on risperidone 0.25 mg daily for severe behavioral dysregulation following incidents of serious aggression towards an infant sibling. Electrocardiography demonstrated marked QT prolongation (QTc = 508 ms) and subsequently confirmed a diagnosis of congenital LQTS with a maternal family history over 3 generations. Risperidone was discontinued and nadolol 20 mg daily was initiated by a pediatric cardiologist. After a second psychiatric opinion for persistent ADHD, oppositionality, aggression, and suicide risk, he was started on clonidine, a possible alternative to avoind the use of stimulants or antipsychotics. At the one-month follow-up, parents reported a lessening of impulsivity, physical aggression, and improved emotional self-regulation. He is continuing with psychological and cardiac monitoring.

Discussion: This case demonstrated a different approach to treating patients with congenital LQTS and neurodevelopmental disorders when first-line pharmacotherapies present a risk to the patient. Clonidine offered clinical benefits without the risk of arrhythmia that comes with stimulants or antipsychotics. Given the lack of studies done on this population, more controlled studies are needed to study the effects of clonidine on patients with congenital LQTS and ODD with comorbid ADHD.

Conclusion: Clonidine may be a promising alternative for treating ADHD and ODD in patients with congenital Long QT syndrome, although further research is needed to confirm its safety and effectiveness.

Keywords: Clonidine, Attention-Deficit/Hyperactivity Disorder, Oppositional Defiant Disorder, COngenital Long QT Syndrome

Introduction

Oppositional Defiant Disorder (ODD), a common childhood disruptive behavioral disorder, is characterized by frequent and persisting patterns of irritability, defiant behavior, and vindictiveness (American Psychiatric Association [APA], 2013). Prevalence rates for ODD average around 3.3% (APA, 2013). This disorder usually presents between ages 2 and 8, rarely in later adolescence, and occurs more often in males than females at a ratio of 1.59:1 (APA, 2013). Attention-deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder affecting both adults and children with

symptoms such as inattention, hyperactivity, and impulsivity (APA, 2013). Stimulants are the main therapy for ADHD and are associated with adrenergic side effects (Zhang *et al*., 2015) [8]. ADHD is one of the most common comorbid conditions with ODD, occurring together in about half of children with a combined presentation of ADHD (APA, 2013). The high rates of co-occurrence between ADHD and ODD reflect possible shared risk factors between both disorders (APA, 2013).

While the first-line treatment for ODD is behavioral and psychosocial interventions, antipsychotic medications such as risperidone are used off-label to address the symptoms of ODD. However, the use of antipsychotic medications carries an elevated risk in patients with congenital Long-QT syndrome (LQTS) (Zhang *et al*., 2015) [8]. LQTS is a hereditary channelopathy characterized by increased or prolonged QT interval (QTc) when at rest, and increased likelihood of ventricular arrhythmias, syncope, aborted cardiac arrest, and sudden cardiac death (Zhang *et al*., 2015) [8]. Since LQTS is a risk factor for drug-induced QTc prolongation, the use of antipsychotics in these patients carries a theoretical risk for arrhythmic events, thereby complicating the pharmacological management of patients with ODD (Chohan *et al*., 2015) [2].

Clonidine, an alpha-2 adrenergic agonist, is a possible alternative to antipsychotics in the treatment of ODD (Patel & Saadabadi, 2025; Pringsheim *et al*., 2015) [6, 7]. Evidence from trials and reviews has indicated that clonidine has been used in treating ODD (Pringsheim *et al*., 2015) [7]. Since clonidine has a safer cardiac risk profile than antipsychotics, clonidine may represent a safer pharmacological option for managing ODD with comorbid ADHD in patients with congenital LQTS.

Case Presentation

A 14-year-old male with a history of ODD and ADHD was referred for a secondary psychiatric evaluation after being diagnosed with congenital LQTS, which limited the pharmacological options for his behavioral symptom management.

He is the youngest out of five children. In early childhood at home and at school, he exhibited signs of hyperactivity, irritability, impulsivity, emotional dysregulation, oppositional behaviors, and aggression toward family members, specifically his mother. After almost 4 years of outpatient psychotherapy and behavioral interventions such as parenting therapy, his symptoms failed to improve. During this period, his aggression escalated, culminating in an incident in which he slammed his infant sister to the ground, thereby prompting further psychiatric interventions.

His first psychiatrist began treatment with risperidone (0.25 mg daily) for severe behavioral dysregulation. After approximately a month of treatment, the patient experienced an adverse event while playing soccer, including symptoms of sudden dizziness and loss of consciousness without any preceding prodrome. Cardiological evaluation, including electrocardiography, showed severe QT interval prolongation (QTc = 508 ms). Further testing confirmed a diagnosis of congenital long QT syndrome 1 subtype. Medical history obtained from his parents revealed a family history of LQTS in the mother, maternal grandfather, and maternal great-grandmother, consistent with an inherited arrhythmia syndrome, so corresponding genetic testing was performed (not provided by the parents), and confirmed the diagnosis. Risperidone was immediately discontinued due to concerns of potential additional QTc prolongation, and the patient was started on nadolol (20 mg daily) by the pediatric cardiologist for the next month. Additionally, he was commenced on sertraline (60 mg daily).

The patient was referred for a second psychiatric opinion due to persisting symptoms of ADHD, impulsivity, aggression, and ODD. The patient and parents reported significant academic difficulty with poor concentration, impaired task initiation, procrastination, organizational deficits, and school avoidance and skipping. Behavioral symptoms related to aggression resurfaced and caused incidents such as physical violence towards his mother, temper outbursts, and sensory sensitivities. He revealed in an interview that he felt stressed and anxious at school due to having social anxiety, poor peer relationships, and being bullied because of his height. The patient denied having any manic symptoms, psychosis, or obsessive-compulsive symptoms.

Considering the patient's congenital LQTS and the associated risk of ventricular arrhythmias with QT-prolonging psychotropic medications, both stimulant and antipsychotic treatments were considered clinically risky. After discussing treatment options and their respective cardiac safety profiles, clonidine (0.1 mg daily) was initiated and progressively titrated to 0.4 mg daily within 1 month, to target ODD and ADHD symptoms, with no adverse effects noted.

Clinical improvement was noted as early as one month during follow-up. His parents reported that he had ceased physical aggression towards his mother, decreased his impulsive behaviors, and improved self-regulation of emotions. Follow-up care with child psychiatry, a therapist, and pediatric cardiology was continued to monitor psychiatric progress and cardiac safety, no new Qt segment prolongation was reported for 12 weeks after the initiation of the new treatment.

Discussion

The management of ODD and comorbid ADHD in a patient with congenital LQTS showcases a conflict between psychopharmacology and possible cardiac risk to the patient. First-line psychiatric drugs used for disruptive behavior in ODD are often psychostimulants or second-generation antipsychotics such as risperidone (Pringsheim *et al*., 2015) [7]. It has been documented that risperidone or other antipsychotic medications pose a threat to patients with LQTS by prolonging the QT interval (Chohan *et al*., 2015) [2]. A systematic review and meta-analysis conducted by Pringsheim *et al*. (2015) [7] concluded that psychostimulants are effective in treating oppositional behavior, conduct problems, and aggression in youths with ADHD. However, psychostimulants also raise heart rate and shorten diastole (Zhang *et al*., 2015) [8]. This effect poses a danger for patients with LQTS as arrhythmias such as torsades de pointes can occur (Zhang *et al*., 2015) [8]. Psychotropic medications such as antipsychotics have been known to lead to QT interval prolongation in different degrees due to the medications' effect on potassium channels in the heart, leading to QTc elongation of >500msec (Chohan *et al*., 2015) [2]. In this patient, the risk of arrhythmia was expressed as the patient experienced an adverse fainting event while being undiagnosed with LQTS and on antipsychotics.

Considering this, the use of clonidine in treating patients with LQTS is one way of treating symptoms of disruptive behavior, aggression, and irritability while keeping arrhythmia risk low. In a meta-analysis of 11 double-blind trials, clonidine was shown to exert a moderate effect on ADHD symptoms and also moderately reduced impulsivity and aggression (Connor *et al*., 1999) [4]. Connor *et al*. (2000) [3] reported that clonidine monotherapy improved oppositional and conduct disorder symptoms in a similar population.

However, clonidine is not necessarily the most effective non-stimulant medication to reduce a patient's oppositional behavior. Pringsheim *et al*. (2015) [7] rated clonidine's ability to reduce oppositional behavioral symptoms as small. Moreover, clonidine isn't without cardiovascular risk. Studies have shown that clonidine lowers heart rate and blood pressure, and carries the risk of rebound hypertension on abrupt withdrawal (Patel & Saadabadi, 2025) [6]. Kofoed *et al*. (1999) [5] found no systematic effect of clonidine on QTc interval across 42 children in the study. Although some symptoms of ODD and ADHD persisted, the patient's initial response to clonidine suggests that clonidine is a safer pharmacologic option in the presence of congenital LQTS.

While interpreting these results, it is also important to note that the patient was on sertraline as well as clonidine. Sertraline, an antidepressant from the Selective serotonin reuptake inhibitors (SSRIs) family, is mainly prescribed for emotional distress and anxiety symptoms and has only a minimal to no effect on oppositional behavior or QTc interval prolongation (Beach *et al*., 2013) [1]. While SSRIs are not the common treatment for core symptoms of ADHD or ODD, improvements in this patient's anxiety, mood, and emotional regulation may have also indirectly led to an improvement in symptoms of ODD. Therefore, although sertraline was prescribed, the initiation of clonidine to improve impulsivity and aggression is most likely the reason behind clinical improvement in symptoms of ODD and ADHD in this patient.

Limitations

There are several limitations inherent to this case report. First, findings from this report cannot be generalized to a broader population of patients with ODD, ADHD, and congenital LQTS. Any causal inference regarding the efficacy of clonidine cannot be established due to the absence of a control group. Secondly, improvement in symptoms, such as aggression and physical violence, was assessed through parental report rather than through standardized rating scales, which introduces subjectivity and recall bias into the outcome. Third, the patient was also on sertraline while on the effects of clonidine. However, there is a lack of empirical evidence or studies on the effects of sertraline and QT interval prolongation (Beach *et al*., 2013) [1]. Fourth, the follow-up period reported was only after twelve weeks, which limits conclusions regarding the durability of the clinical response and long-term cardiac safety of clonidine. Lastly, there may be reporting bias due to lack of literature surrounding the use of alpha-2 agonists in this specific clinical context, and either favorable or unfavorable outcomes may be more likely to have been published.

Consent Statement

Written informed consent was obtained from the patient's legal guardian for publication of this case report.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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The authors have no external source or funding to disclose.

Conclusion

This case highlights the clinical challenge of managing ODD and comorbid ADHD in a pediatric patient with congenital LQTS for which conventional pharmacological treatment options (stimulants and antipsychotics) carry clinical risks for QT-related arrhythmia. The use of clonidine in patients with ODD and ADHD has been associated with reductions in aggression, impulsivity, and behavioral dysregulation without the adverse cardiac risks or effects associated with stimulants or antipsychotics. Given the limited evidence in the literature for the use of clonidine and the possibility of a confounding effect related to the use of sertraline along with clonidine in this case, more controlled studies are needed to establish the efficacy of clonidine in patients with LQTS.

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