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Optimising Treatment of Disruptive Mood Dysregulation Disorder in a Patient with Autism

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Abstract
Disruptive Mood Dysregulation Disorder is defined by chronic irritability and recurrent, severe temper outbursts, while Autism Spectrum Disorder, a neurodevelopmental condition marked by social-communication deficits and restricted behaviours, frequently presents with overlapping irritability and aggression. Although risperidone and aripiprazole are FDA-approved for irritability in autism, treatment guidelines for Disruptive Mood Dysregulation Disorder remain limited, especially in refractory cases. We present the case of a 15-year-old male with autism, generalized anxiety disorder, and attention-deficit hyperactivity disorder, who was diagnosed with comorbid disruptive mood dysregulation disorder after escalating aggression and mood dysregulation. At the time of presentation, he was taking fluoxetine, clonidine, and hydroxyzine, with prior trials of risperidone and aripiprazole discontinued due to lack of efficacy. Valproate and methylphenidate were initiated and later optimized, with further adjustments in clonidine, hydroxyzine, and oral paliperidone, but symptoms persisted. In April 2025, he was transitioned to paliperidone palmitate injections given monthly. Over three months, he demonstrated mood stabilization, reduced irritability, and a significant decline in anger outbursts. This case illustrates the therapeutic challenges in managing Disruptive Mood Dysregulation Disorder in the context of autism and suggests that long-acting injectable antipsychotics may be beneficial in treatment-resistant cases, particularly where adherence and sustained control are priorities. While evidence for their use in pediatric populations remains scarce, this case highlights the potential role of paliperidone palmitate in refractory mood dysregulation and underscores the urgent need for evidence-based guidelines to better inform clinical management of Disruptive Mood Dysregulation Disorder.

Keywords: Disruptive Mood Dysregulation Disorder, Autism Spectrum Disorder, Paliperidone Palmitate, Long-acting Injectable

Introduction
Disruptive Mood Dysregulation Disorder (DMDD) is characterized by a disturbance in mood (severe irritability) and disruptive behaviour (recurrent temper outbursts that are out of proportion to the stressor) [1].
Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication skills and a pattern of restricted or repetitive interests and behaviours [2]. While irritability and temper outbursts are core symptoms of DMDD, they are also common in ASD [3]. Currently, only two atypical antipsychotics, risperidone and aripiprazole, are approved by the US FDA for treatment of significant irritability associated with ASD [4].
This is a case of an adolescent with ASD, who presented with features of DMDD and had failed previous trials of antipsychotic medications but responded well to a long-acting injectable antipsychotic.

Case Report
A 15-year-old male with a psychiatric history of ASD, Generalized Anxiety Disorder (GAD), and Attention-deficit Hyperactivity Disorder (ADHD), presented to the outpatient clinic in November 2024, with complaints of increasing aggressive behaviour as per the mother. On complete assessment, his IQ assessment was in the normal range, and he was diagnosed with DMDD. At the time of presentation, he was taking Fluoxetine 20 mg, Clonidine 0.1 mg, and Hydroxyzine 50 mg. He had previously been trialled on adequate doses and durations of Aripiprazole and Risperidone, both of which were discontinued due to a lack of efficacy. At

the clinic, Valproate 500 mg was initiated for mood stabilization, and Methylphenidate 18 mg was added to manage ADHD, while continuing his existing medications.

Due to persistent anger outbursts, Valproate was increased to 750 mg, and Paliperidone 6 mg was initiated in January 2025. In March 2025, Clonidine was increased to 0.2 mg and Hydroxyzine to 100 mg to manage mood better. Despite these adjustments, emotional and anger outbursts continued, and the patient was transitioned to Invega Sustenna (paliperidone palmitate) 156 mg IM injections, administered monthly in April, May, and June 2025. Following the initiation of Invega Sustenna, the patient showed significant clinical improvement. His mood stabilized, irritability decreased, and the frequency of outbursts diminished notably.

Discussion

ASD and DMDD are both complex neurodevelopmental and psychiatric conditions that can significantly impair a child's emotional regulation and social functioning. Globally, the prevalence of ASD is estimated to be 1 in 100 [5], with recent U.S. data indicating a higher rate of 1 in 31 among 8-year-old children (32.2 per 1,000) [6]. In contrast, a 2017 study estimated the prevalence of elevated DMDD symptoms during primary school age to be 0.79% [7]. However, while 9.2% of school-aged children in the general population were reported to have DMDD-like symptoms, this figure rose to 42.9% among children with autism, highlighting a significant overlap between the two [8].

The DMDD diagnosis was introduced in the DSM-5 in 2013 to reduce the overdiagnosis of pediatric bipolar disorder in children who exhibit chronic irritability and temper outbursts. Notably, more than a decade later, no standardized treatment guidelines exist for DMDD. Literature suggests that in cases with comorbid ADHD, stimulant optimization should be considered the first line of intervention [9]. For treatment-refractory cases, augmentation with a second-generation antipsychotic, such as risperidone or aripiprazole, or a mood stabilizer like valproic acid may be warranted [10].

In this case, the patient did not respond to risperidone, aripiprazole, or valproic acid. It was the addition of paliperidone palmitate, a long-acting injectable antipsychotic, that led to sustained improvement in emotional regulation. While the use of long-acting injectables in pediatric populations is less commonly reported, this case supports their potential role in addressing treatment-resistant mood dysregulation, particularly in the context of limited oral medication efficacy. Given the limited number of studies and lack of standardized treatment protocols for DMDD, there is a pressing need to develop evidence-based clinical guidelines to better support practitioners in the management of this condition.

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