International Journal of Research in Medical Sciences
Lee E et al. Int J Res Med Sci. 2025 Nov;13(11):4919-4922
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20253621

Case Report

Challenges in managing a transgender adolescent with attention-deficit/hyperactivity disorder and multiple psychiatric comorbidities: a case report

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Received: 22 August 2025
Accepted: 06 October 2025

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ABSTRACT

Transgender and gender-diverse (TGD) adolescents are individuals whose experienced gender differs from their biological sex. This group is particularly vulnerable to psychiatric disorders due to both biological factors and psychosocial stressors. Common comorbidities include attention-deficit/hyperactivity disorder (ADHD), mood, and substance use disorders. To date, numerous studies have examined the association between transgender incongruence and ADHD. However, the links with other psychiatric conditions, such as bipolar disorder, remain unclear. A 19-year-old transgender male presented with emotional instability, episodic mood swings, impulsivity, and difficulties related to gender identity. He came out to his friends as male at the age of 13. He had previously been diagnosed with depression, anxiety, and ADHD at the age of 16. The patient also experienced recurrent hypomanic episodes characterized by grandiosity and decreased need for sleep, followed by depressive phases marked by self-injurious behavior and suicidal ideation. He had a history of childhood sexual trauma perpetrated by a friend. Adopted in infancy, his relationship with his family deteriorated after he disclosed his gender identity. He was started on a mood stabilizer and an antipsychotic, with the addition of stimulants considered for later management. This case underscores the clinical challenges of managing psychiatric comorbidities in TGD adolescents, particularly the intersection of ADHD and bipolar disorder. Emerging neurobiological and psychosocial evidence suggests potential shared pathophysiological mechanisms between TGD status and psychiatric comorbidities, although definitive causal pathways remain uncertain. Comprehensive care must integrate individualized pharmacological strategies with psychosocial interventions to address the multifaceted influences.

Keywords: Transgender, Transgender and gender diverse, Gender dysphoria, Attention deficit/hyperactivity disorder, Bipolar disorder, Multiple comorbidities

INTRODUCTION

Since the early 20th century, debates on sex and gender have gained prominence, fostering the growth of related research and social activism. Despite ongoing controversy, TGD is generally defined as individuals whose gender identity or expression does not correspond with their biological sex or culturally prescribed norms.[1] In recent classifications, terms such as "gender identity disorder" and "transsexualism" have been replaced by "gender dysphoria" (GD) in the DSM-5 and "gender incongruence" in the ICD-11.[1,13]

Current diagnostic systems emphasize the psychological distress associated with gender incongruence, rather than classifying gender identity itself as pathological. Several studies reported on the prevalence of TGD groups, estimating it at approximately 0.03-0.05% of the general population.[6]

Despite these advances, TGD adolescents remain vulnerable to mental health problems.[3] Higher rates of mood instability, non-suicidal self-injury (NSSI), suicidal attempt, anxiety, and substance use have been consistently reported compared with cisgender controls.[4,9] ADHD is also more common, and substance use disorders and autism spectrum disorder (ASD) have been frequently reported.[5] Based on epidemiological findings, possible biological and neurodevelopmental mechanisms have been proposed.[16-18] However, this points to overlapping mechanisms, not a proven causal link.

Here, we present the case of a 19-year-old transgender male with an unusual constellation of psychiatric comorbidities, including bipolar disorder and ADHD. Unlike previously reported cases, this combination of disorders highlights the need for a more comprehensive and multifaceted therapeutic approach, emphasizing the clinical complexity in managing such complex presentations.

CASE REPORT

A 19-year-old bisexual biological female, currently transitioning to male, presented to the clinic with complaints of unstable mood, intermittent grandiosity, impulsivity, and distress related to disrupted gender identity.

The patient reported a long-standing sense of emptiness and fear of rejection, which contributed to difficulties maintaining long-term friendships. At age 16, the patient was diagnosed with depression, anxiety disorder, and ADHD. He engaged in two separate courses of outpatient therapy, both of which were prematurely discontinued. Subsequently, the patient experienced recurrent episodes of elevated mood with grandiosity, decreased need for sleep, typically followed by depressive episodes. During depressive periods, the patient engaged in serious self-harming behaviors, including cutting. He experienced persistent suicidal ideation, though no suicide attempts were reported. The patient used cannabis approximately twice weekly and consumed alcohol occasionally. Before the current visit, the patient was taking bupropion SR 200 mg and atomoxetine 10 mg. Previous pharmacological trials with fluoxetine and aripiprazole had been reported as ineffective.

The patient was adopted at 15 months of age, and although the relationship with his parents was initially stable, it deteriorated following his coming out. He achieved developmental milestones appropriately, although difficulties with reading and writing were noted. Throughout childhood, the patient demonstrated restlessness, hyperactivity, and frequent procrastination with poor time management. The patient also reported a history of sexual trauma involving his friend from four to 14 years of age. At age 13, the patient first disclosed a male gender identity to peers and is currently receiving testosterone therapy.

The treatment regimen was initiated with lamotrigine, titrated gradually from 25 mg to 100 mg daily. Two weeks later, cariprazine was introduced at 1.5 mg every three days and subsequently increased to 1.5 mg daily. Atomoxetine was discontinued to stabilize the mood first, and bupropion was reduced to 100 mg daily. Following these adjustments, the patient reported substantial improvement in depressive and anxiety symptoms.

The patient is currently maintained on lamotrigine 100 mg daily, cariprazine 1.5 mg daily, and bupropion 100 mg daily, with a treatment plan to consider the addition of a stimulant. In addition to pharmacological treatment, the patient initiated weekly dialectical behavior therapy (DBT) as well as affirmative, trauma-informed psychotherapy.

DISCUSSION

The definition of TGD

The concept of TGD individuals has evolved through a difficult and often contentious process, with its definition shaped by political and social debates. Prevailing psychological accounts have characterized transgender status primarily in terms of a discrepancy between sex and gender.[10] The classification of individuals as transgender or cisgender is based on whether sex and gender are seen as congruent or incongruent.[12] However, some scholars argued that defining transgender merely as a state of sex-gender incongruence is problematic because it falsely assumes a culturally independent true-gender, whereas both bodily and psychosocial experiences are co-constructed through regulatory norms.[11]

Accordingly, the term 'transgender' was reframed to reflect an experience molded by societal and regulatory forces acting on both bodily and psychological aspects.[11]

The changed concept of GD

Transgender is no longer regarded as a pathological disorder, and terms such as 'gender identity disorder' and 'Transsexualism' are no longer in use.[1,13] Instead, the psychological distress that may arise from gender incongruence, often exacerbated by social stigma and discrimination, is conceptualized as 'GD,' with the diagnostic focus placed on the associated distress rather than the identity itself.[1] GD is defined in the DSM-5-TR as a marked incongruence between an individual's experienced or expressed gender and their assigned gender, persisting for at least six months and accompanied by specific behavioral or cognitive manifestations.[1] In ICD-11, GD is replaced by gender incongruence, defined as a marked and persistent incongruence between an individual's experienced gender and assigned sex, classified under conditions related to sexual health.[13]

Psychiatric symptoms in TGD population

Individuals with gender incongruence have more chances to be isolated by their social groups, leading to economic, physical, and emotional issues.[7] Numerous studies have highlighted the increased risk of psychiatric problems in transgender children/adolescents than their cisgender controls.[3] ADHD, eating related disorders, ASD, and substance abuse are reported in patients with gender issues.[5] Findings differ across studies, but comorbidity with ADHD has been reported most consistently. Additionally, Ansari et al showed that 28.2% of the cohort with comorbid mood disorders and GD have reported.[9] Teresa et al systemically reviewed the prevalence of suicide related symptoms in transgender youth: 28.2% for non-suicidal self-injury, 28% for suicidal ideation, and 14.8% for suicidal attempts were found in transgender youth.[4]

The association of TGD adolescents with ADHD

Based on the DSM-5, ADHD presents as an enduring pattern in which difficulties with sustaining attention, controlling impulses, and regulating activity levels significantly disrupt an individual's daily functioning and developmental progress.[1] Becerra-Culqui et al reported that TGD children (ages 3-9) had a 2.4-5.6 times higher prevalence of ADHD compared to matched cisgender peers. Among adolescents (ages 10-17), the prevalence was 4.7-12.6 times higher.[16] These findings highlight a substantially increased risk of ADHD in TGD youth relative to their cisgender counterparts.

The biological mechanisms underlying the higher prevalence of ADHD in transgender individuals are not fully understood, but they may be explained by differences in neural network flexibility and hormone receptor sensitivity.[16-18] Neuroimaging studies suggest that TGD shows differences in large-scale brain networks, particularly the default mode and executive control networks, which are also central to ADHD pathophysiology.[16] In addition, genetic and hormonal studies indicate that polymorphisms in testosterone and estrogen receptors and the effects of hormone exposure during development may influence neural structures related to attention and self-regulation.[17,18] These findings support the hypothesis that altered neurodevelopmental trajectories in brain connectivity and hormone-related modulation may partly explain the higher prevalence of ADHD observed in transgender populations, although direct causal mechanisms remain unconfirmed.

Beyond biological pathways, overlapping psychosocial factors have likewise been identified in some studies. Burcu et al. conducted a cross-sectional study of 20 children and adolescents with GD compared with 40 sex-matched controls. They found that parental divorce/separation, parental psychiatric disorders, and lower income were significantly more common in the GD group, while developmental and educational levels did not differ between groups.[19] Although it remains unclear whether environmental differences directly account for the psychological difficulties observed in the transgender children and adolescents, this study highlights the need for a more detailed examination of the influence of the social factors.

TGD adolescents with bipolar disorder

Bipolar disorder is characterized by recurrent episodes of mania or hypomania and depression, marked by significant disturbances in mood, vegetative function, and activity.[1] While numerous studies have examined suicidality and trauma in the context of gender incongruence, only a limited number have addressed its association with bipolar disorder. Within TGD populations, approximately 28% are reported to experience mood-related difficulties; however, the lack of specification regarding precise diagnostic categories limits the available information.[9]

Evidence clarifying the biological underpinnings of co-occurrence between gender diversity and bipolar disorder is currently lacking. Meanwhile, converging evidence indicates that transgender cohorts and bipolar disorder share disruptions in the fronto-limbic circuits, implicated by connectivity studies in TGD groups and meta-analytic functional MRI work in bipolar disorder.[17,20] According to Rahele et al individuals with bipolar disorder show consistent changes in the fronto-limbic circuitry during tasks involving emotion and cognition, which may point to a link with TGD.[20]

Recent studies have shown that gender-affirming hormone therapy influences monoamine oxidase A (MAO-A) levels, gray matter density, and microstructure, suggesting a potential relation between such neurobiological changes and cognitive function in transgender individuals.[21]

This finding is considered to support previous reports of AR and ESR1 variants in TGD populations, which indicate differences in the sex hormone receptor sensitivity.[18]

As previously noted, TGD adolescents are often exposed to psychosocial adversity, including unstable familial and social environments. Stephen et al reported that TGD adolescents experience higher rates of parental rejection compared with their cisgender peers.[14] These findings parallel observations in bipolar disorder.

However, studies specifically examining psychosocial factors underlying the association between TGD and bipolar disorder remain limited, underscoring the need for further research.

Complexity in treating psychiatric comorbidities in TGD adolescents

When addressing comorbid conditions, clinicians must recognize that treatment complexity arises not only from the primary diagnoses but also from genetic and environmental vulnerabilities, maladaptive behaviors, and social stressors.[7] Each of these domains requires a distinct therapeutic approach, and their interplay can significantly hinder both treatment planning and recovery.[8]

When treatment targeting one symptom has the potential to exacerbate other symptoms or complicate diagnostic clarification, clinicians must exercise heightened caution in selecting the therapeutic approach. As in the present case, it is essential to prioritize the core symptoms of greatest clinical relevance and adopt a multifaceted approach to management.

CONCLUSION

This case highlights the diagnostic and therapeutic challenges faced by TGD adolescents with multiple psychiatric comorbidities. There is a co-occurrence of bipolar disorder, ADHD, anxiety, substance abuse, and trauma illustrates the complex interplay of biological, psychological, and social factors in this population. While neurobiological studies suggest shared disruptions in neural circuits and possible influences of hormone receptor sensitivity, psychosocial stressors such as stigma, family conflict, and trauma further complicate clinical management.

Accurate diagnosis and effective treatment are particularly difficult when multiple symptoms overlap, and therapeutic interventions targeting one domain may risk exacerbating others. This underscores the importance of individualized, multimodal approaches that integrate pharmacological management with psychosocial and trauma-informed care. Further research is needed to clarify the mechanisms linking gender diversity with psychiatric comorbidities and to develop tailored strategies that address the unique vulnerabilities of TGD adolescents.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Lee E, Mathew NM, Narravula R, Dua S, Phagava T, Gultekin IE, et al. Challenges in managing a transgender adolescent with attention-deficit/hyperactivity disorder and multiple psychiatric comorbidities: a case report. Int J Res Med Sci 2025;13:4818-22.