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Case Report

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Role of GLP-1 receptor agonists in weight management of adolescents with Bipolar disorder and Type 1 DM.

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Abstract

Bipolar disorder is a disabling psychiatric disorder characterized by mania, hypomania, and depressive episodes. Antipsychotics are highly effective and commonly utilized agents in the management of this disease. One of the most common and distressing side effects of antipsychotics is weight gain. Challenges in treatment arise when patients have a comorbid disease like diabetes mellitus. We present a case of a 15-year-old boy with bipolar disorder and insulin-dependent Type 1 Diabetes Mellitus (T1DM). In our case, concomitant use of antipsychotics for bipolar disorder and insulin therapy poses a risk for weight gain. Weight gain in adolescents is not only associated with metabolic complications but also with substantial psychosocial distress. This case highlights the necessity of agents that regulate weight in adolescents with multiple comorbidities. Usage of glucagon-like peptide-1 receptor agonists (GLP-1RAs) facilitates euglycemia and weight loss. Although there are several studies demonstrating the GLP-1RA effect on antipsychotic-induced weight gain or on T1DM insulin-related weight gain, there are no comprehensive studies on GLP-1RA usage in adolescents with comorbidities. Our report also underscores the need for further research into GLP-1RA effects in adolescents with several comorbid disorders.

Keywords

Bipolar disorder, Type 1 Diabetes Mellitus, GLP-1RAs, euglycemia and weight loss.

Introduction

Bipolar disorder (BD) and other conditions on the bipolar disease spectrum are chronic affective disorders characterized by weeks-long cycles of significant mood lability (Grande et al., 2016). Over one percent of the world population experiences BD, with a 2.4 percent prevalence rate among every nationality, ethnic group, and socioeconomic status. (Grande et al., 2016). The average time between onset of BD and appropriate diagnosis is 5-10 years, which can be further delayed if a patient presents with a depressive episode rather than (hypo)mania (Grande et al., 2016).

Mood swings in BD generally relate to functional and cognitive impairment, consequently leading to a reduction in quality of life (Martinez-Aran et al., 2007). Even effects of mania in the brain have been shown ventricular dilation, brain tissue density reduction (Coffman & Nasrallah, 1985). Medical conditions concurrent with BD emerge earlier in life and contribute to the rising mortality rate and obesity is highly comorbid with BD (Grande et al., 2016; Doane et al., 2023).

Despite obesity having a multifactorial etiology, pharmacological side effects from antipsychotics, antidepressants, and mood stabilizers are strong contributors to weight gain (Doane et al., 2023). This is challenging for individuals managing BD and their weight simultaneously, even more so if an individual has a weight-promoting disease or receives medical treatment [e.g., insulin for diabetes mellitus (DM)] (Doane et al., 2023).

DM is a chronic metabolic disorder marked by hyperglycemia that arises from impairments of insulin secretion, insulin action, or both, it often presents with classic symptoms, polyuria, polydipsia, and weight loss; approximately 30% of pediatric patients present with diabetic ketoacidosis (DiMeglio et al., 2018). It is usually classified into type 1 and type 2, among other less frequent groups (Schuster & Duvuuri, 2002). Specifically type 1 DM (T1DM) is a polygenic disease: while prevalence highly depends on geographical location, the overall global lifetime prevalence is 1 in 250 people and continues to increase (Redondo, 2001). Although T1DM tends to be a juvenile diagnosis, adult-onset T1DM can be seen (DiMeglio et al., 2018).

Although several insulin therapy modalities and delivery options have been developed, only around 20% of patients achieve adequate glycemic control (Peter et al., 2016; Foster et al., 2019). Because of poor glycemic control and adverse effects of insulin therapy, new non-insulin therapies have gained attention.

The prevalence of obesity among patients with T1DM has outpaced the general population in recent years, remarking the need for new interventions such as glucagon-like peptide-1 receptor agonists (GLP-1RA) (Maffeis et al., 2018). GLP-1RAs have demonstrated effectiveness in T1DM and obesity by HbA1c reduction, leading to significant weight loss (Resnick et al., 2025). However, these medications are not currently included in any guidelines for managing T1DM (Resnick et al., 2025).

Here, we present the case of a 15-year-old male with T1DM (insulin-dependent), also diagnosed with BD, whose metabolic and psychiatric conditions were challenging to control, generating a complex clinical situation.

Case Presentation

We present a fifteen-year-old patient with a two-year history of insulin-dependent T1DM. His family history included bipolar disorder, generalized anxiety disorder, depression, and obesity.

Upon his diagnosis of T1DM, the patient reported he was socially withdrawn, exhibited reactive mood, school refusal and was defiant towards school teachers and peers. Cognitive behavioral therapy, escitalopram 10 mg QD, and an insulin pump were initiated for managing his anxiety, depression, and T1DM, respectively. However, he was noncompliant with his regimen and reported his symptoms were unresponsive to medications. The patient constantly complained of restlessness, stomach ache, difficulty falling asleep, and impulsivity related to methylphenidate (which the patient had tolerated prior to his diagnosis of T1DM and mood disorder).

His mood disorder was initially thought to be depressive; it was reclassified to oppositional defiant disorder to account for significant mood fluctuations, social withdrawal, aggression, and pervasive oppositional defiant behavior. Escitalopram was discontinued to attempt fluoxetine 40 mg QD, but the patient became progressively more aggressive, easily distracted, and defiant of parents, teachers, and peers. While he did not have any frank mania related symptoms, his persisting irritable and agitated mood and sleep disturbances with sporadic periods of high energy, impulsivity, excessive spending and bragging behaviors were highly suggestive of bipolar disorder. Due to weight concerns and glucose dysregulation, topiramate 25 mg QD and lamotrigine 100 mg QD were prescribed, but response was minimal. The patient was prescribed aripiprazole 10 mg QD with sporadic compliance. The family requested long acting injections of aripiprazole. Patients received long-acting formulation of Aripiprazole 400 mg along with lithium 300 mg daily.

Within two weeks, his parents reported significant improvement in the patient's mood, sleep routine, and concentration. Aggressiveness and restlessness were also better controlled.

As for the patient's T1DM, adherence to his diet restrictions and indications were irregular, generally correlated with his levels of anxiety and quality of sleep. The patient's body mass index was reported to be twenty nine; the patient was described by his parents as a picky eater, with a preference for fast food, snacks, and meat. Since initiating aripiprazole, the patient showed a marked increase in appetite, gained around ten pounds within the first month of treatment, and recorded average blood sugar levels ten mg/dl higher than prior. His glycated hemoglobin (HbA1c). was found to be 9.1 mg/dl one at that time. The dose of aripiprazole was decreased to three hundred mg every month to contribute to the management of his T1DM. His dietary control was stricter henceforth, and lifestyle changes with a follow-up with endocrinology were strongly recommended. The patient was still advised to

monitor any side effects related to his psychiatric medications and continue his treatment regimen. We are consulting the endocrinology team to consider the role of GLP-1 in management of his TIDM considering that Aripiprazole is a long term treatment plan for management of his adolescent Bipolar disorder.

Discussion

BD follows a course of remissions and exacerbations, and functional/cognitive impairment could be seen even in the remission phase (Grande et al., 2016). Post-mortem studies also showed dendritic spine loss in patients with BD (Grande et al., 2016). Because of these impairments, bipolar disorder is known as a highly disabling condition, especially considering the effects on working-age young adults (Vieta et al., 2018). Every exacerbation in the disease course creates a predisposition to the next one, and BD can even transform to a malignant version with rapid cycling, environment-sensitive episodes, and resistance to drug therapies; therefore, early interventions have a key role in preventing progression (Post et al., 1992).

The management of bipolar disorder therapy in adolescents is crucial because up to 60 percent of patients present clinically before 21 years of age (Birmaher, 2013). Although the diagnostic criteria are the same for adolescents and adults, diagnosis in adolescence is considerably more challenging (Grande et al., 2016). This difficulty arises from cognitive emotional immaturity, which may limit symptom expression and present atypically, such as mixed or rapid-cycling episodes (Grande et al., 2016). Studies have reported that 30 to 40 percent of MDD patients have underdiagnosed hypomanic or manic symptoms (Birmaher, 2013).

Mood stabilizers and antipsychotics are the first-line treatments in acute management of BD. (Yıldız et al., 2015) Several reviews suggest that antipsychotics are more effective than mood stabilisers for the management of mania, creating better and faster responses (Yıldız et al., 2015; Cipriani et al., 2011). In terms of specific agents, risperidone and olanzapine had the best efficacy, but aripiprazole, asenapine, and quetiapine have the lowest rates for discontinuation of the drug (Yıldız et al., 2015). For long term management of BD, pharmacological and psychological treatments are combined to achieve optimum treatment; medication intervention typically involves the use of mood stabilizer and antipsychotics (Yıldız et al., 2015).

Weight gain is the primary side effect of antipsychotics, followed by extrapyramidal effects and sedation (Lieberman et al., 2005). For instance, 31 percent of patients on olanzapine therapy gain more than seven percent of their initial body weight within 18 months (Lieberman et al., 2005). Even when patients discontinue medication, weight gain induced by these drugs often persists and is one of the most distressing side effects (Doane et al., 2023). A comprehensive meta-analysis indicated that the prevalence of metabolic syndrome in psychiatric patients is 32.6 percent-1.58 times higher than the general population (Vancampfort et al., 2015). Patients receiving antipsychotic treatment present an increased risk of metabolic syndrome, and the presence of any metabolic disorder is associated with poorer outcomes and treatment response in psychiatric conditions (Vancampfort et al., 2015). In this case, there is another contributor to weight gain: insulin therapy for T1DM (Maahs et al., 2010). The management of this condition is challenging due to the increased insulin resistance in puberty, vulnerability to anxiety and depression, and social stigma among others (Bombaci et al., 2024).

Although the etiology of this multifactorial disease is not fully understood, an autoimmune destruction of pancreatic beta cells triggered by a viral agent related to an HLA Class I overexpression is the generally accepted explanation (DiMeglio et al., 2018) . Insulin is the mainstay of therapy, and regimens mimic physiological insulin release (DiMeglio et al., 2018). While pramlintide is the only non-insulin medication approved for T1DM, there are other agents including metformin, glucagon-like

peptide-1 receptor agonists (GLP-1RA), dipeptidyl peptidase-4 inhibitors, and sodium-glucose co-transporter-2 inhibitors are in use off label, however fewer than 5% patients utilize these therapies (Lyons et al., 2017).

The most common prescribed off-label drug for people with T1DM is metformin to overcome insulin resistance however its efficacy remains unproven in patients younger than 18, overweight or obese and have T1DM (Libman et al., 2015). On the other hand, the prescriptions of GLP-1RA in these patients have increased consistently over the years particularly for obesity; prescription rates rose significantly from 0.3 % in 2010 to 6.6% in recent years (Li et al., 2024). Glucagon-like peptide-1 (GLP-1), also known as incretin, is normally produced in the gastrointestinal tract and has a crucial role in metabolic homeostasis, euglycemia and normolipidemia (Liu, 2024). It exerts its effects by activating downstream signaling across various tissues and organs including the satiety centers to regulate food intake, pancreatic β cells to regulate insulin secretion and adipocytes to increase the production of adiponectin (Liu, 2024).

Although GLP-1RAs are not on any guideline for T1DM, comprehensive studies demonstrate its effectiveness in patients who also present obesity (Resnick et al., 2025). These drugs not only help to reduce weight but also help to regulate HbA1c (Resnick et al., 2025). Furthermore, users or GLP-1RAs have shown consistent significant weight loss, consequently reducing cardiometabolic risk factors (Resnick et al., 2025).

Achieving metabolic and glycemic control is essential to prevent acute and chronic complications (Schuster & Duvuuri, 2002). However, only 20% of people achieve proper glycemic control (Peter et al., 2016; Foster et al., 2019). This problem is even more relevant in psychiatric patients, particularly in those with bipolar disorder since response, adherence, and adverse effects are challenging to manage (Kowatch et al., 2005). GLP-1RAs have also shown effectiveness in obese antipsychotic-treated patients by body mass index reduction, waistline reduction as well as HbA1C (Patoulias et al., 2023).

Two possibly beneficial uses for GLP-1RAs in the treatment regimens of obesity and T1DM are present in this patient.

Understanding the intrinsic limitation of this study and the more-than-probable beneficial outcomes of this intervention, it is strongly suggested that further clinical trials be conducted to determine the effectiveness and safety in similar cases.

Conclusion

Bipolar disorder is a disabling disorder in numerous aspects. In adolescents with BD, management can be significantly more challenging than in adults due to medication induced-side effects. Antipsychotics are one of the primary treatments for BD, but a primary side effect is weight gain.

T1DM can lead to even more serious complications, especially within this population. While insulin is the mainstay treatment for patients with T1DM, it naturally promotes weight gain just as antipsychotics do. Weight management becomes much more challenging when balancing two disorders simultaneously, as seen in our case.

Literature has promoted the effectiveness of GLP-1RA for patients with T1DM and for patients who have antipsychotic induced weight gain. GLP-1RA can have a role in future psychiatric clinical interventions to prevent antipsychotic induced weight gain.

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