Case Report

Unusual Weight Loss in a Schizophrenic Patient Following Treatment With Aripiprazole: A Case Report

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ABSTRACT

Background: The main problem with second-generation antipsychotic (SGAs) drugs is weight gain. It was shown that aripiprazole can induce mild weight loss in some patients.

Case Report: In this study, we present a 32-year-old man with schizophrenia who, before initiating aripiprazole, had been treated with clozapine (standard oral tablets) at a daily dosage of 300 mg. During 9 years of clozapine therapy, the patient experienced substantial weight gain, totaling 51 kg, which increased his weight to 145 kg. Concurrently, he displayed limited interest in social interactions, remained primarily confined to his home watching television, and was unemployed. At the time of hospitalization, clozapine treatment was discontinued, and aripiprazole was introduced with the patient weighing 145 kg. Over the subsequent 60 days of aripiprazole treatment, the patient demonstrated a significant weight loss of 28 kg, a reduction that was both remarkable and clinically significant.

Conclusion: Switching from clozapine to aripiprazole led to significant weight loss in a patient with schizophrenia, highlighting aripiprazole's potential in managing antipsychotic-induced weight gain.

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Introduction

Second-generation antipsychotics (SGAs) commonly used to treat schizophrenia include clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole. Robust evidence suggests a strong association between SGAs and metabolic disorders such as hyperglycemia, hyperlipidemia, and weight gain [1]. Over the past 40 years, the prevalence of obesity (defined as a body mass index [BMI] >30) has significantly increased worldwide. A 2016 study reported that the global prevalence of obesity among adults was 13% [2].

Obesity is a well-established risk factor for diabetes mellitus, hypertension, and various other physiological dysfunctions. In individuals with severe psychiatric disorders, the impact of obesity and metabolic disorders appears to be even more pronounced, contributing to worse health outcomes. Contributing factors include limited access to appropriate healthcare, unhealthy lifestyle choices, and additional side effects associated with antipsychotic medications [3].

The primary mechanism underlying obesity associated with SGAs involves activation of ghrelin receptor growth hormone secretagogue receptor type 1a signaling and antagonism of serotonin receptor 2c (5-HT2cR) [4]. Weight gain plays a pivotal role in the development of metabolic disorders induced by SGAs. Studies indicate that clozapine and olanzapine are associated with significant weight gain. At the same time, quetiapine and risperidone lead to moderate weight gain, and aripiprazole and ziprasidone have a relatively lower risk of weight gain [5].

In cases where SGA treatment leads to weight gain, it is recommended to switch the patient to a medication with a lower risk of inducing weight gain [6]. This decision should be taken by clinical criteria outlined in guidelines such as the American Psychiatric Association (APA) practice guidelines or the Canadian Schizophrenia Guidelines, which emphasize monitoring weight changes, assessing metabolic risks, and evaluating the patient's overall psychiatric stability before making changes to their treatment regimen [7]. Clozapine raises significant concerns regarding its side effects, especially its potential to induce weight gain and exacerbate metabolic disorders. Among SGAs, clozapine is associated with the highest likelihood of weight gain, often resulting in poor tolerance and treatment discontinuation after a short duration [8].

Aripiprazole, a quinolinone-derived SGA, has a unique pharmacological profile. It acts as a partial agonist at dopamine D2 and serotonin 5-HT1A receptors while exhibiting antagonistic activity at serotonin 5-HT2A receptors [9].

Studies revealed that aripiprazole is unlikely to cause weight gain compared to clozapine [8] and olanzapine [10]. The most common side effects of aripiprazole include increased appetite, nausea, dyspepsia, headache, akathisia, and drowsiness. Aripiprazole has fewer side effects than other antipsychotics, such as sedation, QT prolongation, and prolactin elevations [11].

In this article, we report a patient with schizophrenia who had significant weight loss when clozapine switched to aripiprazole. According to our knowledge, there are limited reports regarding weight loss following aripiprazole administration. A study published in 2014 showed that carrying of the ADRA2A rs1800544 GG genotype and the MTHFR rs1801131 C allele are linked with BMI decrease after switching antipsychotics to aripiprazole and ziprasidone [12]. Another case report published in 2019 showed that a 26-year-old male with schizophrenia gained weight while on high-dose antipsychotic therapy. After switching to olanzapine and aripiprazole, he lost nearly 37 pounds in four months without significant changes in diet or activity [13]. Therefore, our study is essential as it highlights a rare but significant clinical observation of weight loss in a patient with schizophrenia after switching from clozapine to aripiprazole, contributing to the limited literature on aripiprazole's metabolic effects.

Case Presentation

A 32-year-old male patient with schizophrenia diagnosed according to description diagnostic and statistical manual of mental disorders, 4th edition (DSM-IV-TR) and diagnostic and statistical manual of mental illnesses fifth edition (DSM-5) criteria was under treatment for 15 years. His schizophrenia was characterized by persistent positive symptoms, such as auditory hallucinations, delusions, and disordered thinking, along with negative symptoms, including social withdrawal and reduced emotional expression. The patient had no significant medical comorbidities or past surgery beyond his psychiatric illness. He had no family history of major psychiatric disorders.

Initially, the patient received flupentixol 20 mg weekly alongside risperidone 6 mg daily. After five years of inadequate response, clozapine therapy was initiated. The

patient was started on oral clozapine tablets at 300 mg per day. Over the subsequent 9 years, his weight progressively increased from 94 to 145 kg, a total gain of 51 kg. During this period, the patient's schizophrenia symptoms were partially controlled, with occasional exacerbations. He exhibited limited social engagement, was unemployed, and spent most of his time at home watching television. Attempts to discontinue clozapine resulted in exacerbation of symptoms and recurrent hospitalizations.

During a recent hospitalization, clozapine was reintroduced at low doses but was subsequently discontinued due to the severity of the patient's obesity, as recommended by the attending psychiatrist. Switching from clozapine to aripiprazole was abruptly and under medical supervision to minimize withdrawal symptoms, rebound psychosis, or adverse effects. Aripiprazole was started at 10 mg once daily on the first day (the patient's weight was 145 kg) and increased to 15 mg on days 2-7, and the patient tolerated it well. At the time of initiation of aripiprazole, serum lipid levels were within normal ranges (triglyceride [TG]: 85 mg/dL, cholesterol [Chol]: 159 mg/dL, high-density lipoprotein [HDL]: 42 mg/dL, and low-density lipoprotein [LDL]: 100 mg/dL). The aripiprazole dose was gradually titrated to 30 mg daily (on day 8), and the patient also continued flupentixol at 20 mg weekly.

The patient remained on this regimen for 60 days, during which time his schizophrenia symptoms showed relative improvement. He adhered to a calorie-controlled diet, and his physical activity level remained consistent with previous periods. After 60 days, the patient's weight had significantly decreased to 117 kg, a loss of 28 kg. Serum lipid levels remained within the normal range with no significant changes (TG: 100 mg/dL, Chol: 144 mg/dL, HDL: 40 mg/dL, and LDL: 84 mg/dL).

The patient was on aripiprazole but re-hospitalized three weeks later due to symptom recurrence. Upon readmission, his weight had further decreased to 110 kg, while his lipid profile had remained relatively stable (TG: 114 mg/dL, total Chol: 147 mg/dL, HDL: 37 mg/dL, and LDL: 88 mg/dL).

Discussion

Before initiating aripiprazole, the patient was on clozapine (standard oral tablets) at a daily dosage of 300 mg. Over 9 years, the patient experienced significant weight gain, totaling 51 kg, with his weight increasing to 145 kg. During this time, he showed limited interest in social interactions, remained at home most of the time watching television, and was unemployed. At the time of hospitalization, clozapine was discontinued, and aripiprazole was initiated, with the patient's weight at 145 kg. Over the subsequent 60 days of treatment with aripiprazole, the patient experienced a remarkable weight loss of 28 kg, which represented a substantial and clinically significant reduction.

In other similar studies, weight loss has been reported, but none of them reported the weight loss that we reported; in the survey of schizophrenic patients with weight gain of ≥2.5 kg while taking clozapine for ≥3 months, after 16 weeks of combinations therapy with 5–15 mg/d of aripiprazole 2.15 kg weight loss reported [14]. Similar to this study, weight loss in an 8-week study with aripiprazole-augmented clozapine treatment was 2.8 kg (mean change) [15]. Another study showed weight change within 3 months in the aripiprazole treatment (-2.0 kg; -2.30% from baseline) [16]. Switching to aripiprazole resulted in larger reductions in weight (difference, 2.9 kg) [17]. The results of a meta-analysis focused on switching to aripiprazole indicated that mean weight reduction was 2.55±1.5 kgs [18].

Although weight loss during treatment with aripiprazole has been reported in most studies, some studies have shown other results. In an investigation in which schizophrenic patients treated with aripiprazole lauroxil (AL), a long-acting injectable antipsychotic, after one year, 88 patients (18%) gained ≥7% body weight, and 59 (12%) lost ≥7% body weight. The mean weight change was 0.8±5.9 kg [19]. In a recent study of patients with mood disorder and schizophrenia, they were split into those who received aripiprazole as a monotherapy and those who were given aripiprazole as part of a combination therapy. The mean weight gain percentage after 180 days was 3.40% in patients on aripiprazole monotherapy [20]. Extreme weight loss in our patient may have been due to the patient's high initial weight. Unlike previous studies, our patient's Chol and TG levels remained normal and did not change significantly by switching the medication. Aripiprazole-augmented clozapine treatment was associated with a significant decrease in total Chol, LDL, and non-HDL Chol [15]. In another study, a switch to aripiprazole showed significantly decreased mean non-HDL cholesterol and TG levels and increased HDL levels [17].

This case highlights the potential of aripiprazole as an effective strategy for managing antipsychotic-induced weight gain, particularly in patients with severe obesity. Compared with previous studies that reported modest

weight loss (2–3 kg), our patient experienced a significant weight loss of 28 kg in just 60 days, suggesting that individuals with high baseline weight may benefit more from switching to aripiprazole. Furthermore, unlike some studies reporting changes in lipid profiles, our patient's cholesterol and triglyceride levels remained stable, suggesting that metabolic effects may vary across individuals. These findings suggest that clinicians should consider aripiprazole as a viable alternative for patients struggling with excessive weight gain on clozapine, potentially improving physical health and psychiatric outcomes.

Conclusion

This case highlights the potential for significant weight reduction following a transition from clozapine to aripiprazole in a patient with schizophrenia who experienced substantial weight gain during prolonged clozapine therapy. The observed 28 kg weight loss over 60 days underscores the importance of considering aripiprazole as an alternative antipsychotic agent in patients where metabolic side effects, such as severe weight gain, are a concern. Further studies are warranted to explore the mechanisms and long-term outcomes of switching antipsychotic regimens to mitigate metabolic complications in similar cases.

Ethical Considerations

Compliance with ethical guidelines

Written informed consent was obtained from the patient who contributed in the current case report. The present study was conducted in compliance with the declaration of Helsinki.

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Authors' contributions

Interviewing the patient: Amir Asadi and Javad Setareh; Writing: All authors.

Conflict of interest

The authors declared no conflict of interest.

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