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Severe weight gain after 4-year treatment with aripiprazole in a young man with schizophrenia

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Summary

Schizophrenia is one of the major problems of modern psychiatry. Due to its chronic nature, it requires continuous treatment with antipsychotics. Weight gain is one of the major side-effects associated with the pharmacological treatment of schizophrenia. Aripiprazole is an atypical antipsychotic with a relatively good metabolic profile; there are very few published cases of aripiprazole-induced weight gain. We present a case of significant (50 kg) weight gain during a 4-year treatment with aripiprazole in a 21-year-old Caucasian man with a diagnosis of paranoid schizophrenia. The mechanism underlying aripiprazole-induced weight gain may be associated with its potent binding to serotonin 5-HT_{2C} receptor. This case confirms the significance of patient monitoring in antipsychotic therapy.

aripiprazole / schizophrenia / weight gain / adverse effects

Weight gain is one of the major drawbacks associated with the pharmacological treatment of schizophrenia. Of the available antipsychotics, aripiprazole is considered as having the best metabolic profile and patients taking aripiprazole have lowest weight gain. Although there are very few published cases of aripiprazole-induced weight gain, Bak et al. [1] have shown that it may be associated with clinically significant weight gain. Here we present a case of significant (50 kg) weight gain during a 4-year treatment with aripiprazole (Abilify®, Bristol-Myers Squibb). The patient gave free, informed consent for the publication of his case.

A 21-year-old Caucasian man with a diagnosis of paranoid schizophrenia (DSM-IV code 295.30, ICD-10 code F20.0) was admitted to our unit in August 2016. His psychiatric treatment started in 2012, and since then he had been hospitalized in psychiatric units two times. He was treated with aripiprazole (with doses up to 30 mg/day), with good treatment adherence. Prior to treatment his body mass was 70 kg, with a corresponding body mass index (BMI) of 24.7 kg/m^2. Before he was diagnosed with schizophrenia he had no history of endocrine or metabolic disorders. The patient was referred to our department for a modification of treatment due to weight gain that exceeded 50 kg over the 4-year period. Upon admission his body mass was 120.0 kg (BMI 37.0 kg/m^2). Physical and neurological examinations revealed no significant abnormalities. Other laboratory tests were normal: urinalysis, complete blood count, triglycerides (109.8 mg/dL), total cholesterol (145.8 mg/dL), HDL cholesterol (38.9 mg/dL), LDL cholesterol (84.9 mg/dL), fasting plasma glucose (94.9 mg/dL), alanine aminotransferase (33.0 U/L), aspartate aminotransferase (26.0 U/L), total bilirubin (1.0 mg/dL), C-reactive protein (<3.0 mg/L), creatinine (1.13 mg/dL), urea (23.6 mg/dL), thyroid-stimulating hormone (3.25 μIU/ml), prolactin (3.5 ng/mL). He was on

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aripiprazole (15 mg/day) monotherapy for his psychosis. Due to treatment-refractory hypertension (which developed over the past 4 years, secondary to obesity) he was also taking telmisartan (20 mg/day), amlodipine (2.5 mg/day) and bisoprolol (2.5 mg/day). He did not smoke and did not drink alcohol or took illicit drugs.

Since he reported a moderately depressed mood and lack of energy, with no psychotic symptoms for more than 6 months, we decided to reduce the dose of aripiprazole. One week after aripiprazole dose had been reduced, he developed anxiety due to increased psychotic symptoms (delusions of reference, auditory hallucinations). Therefore, amisulpride was introduced, with doses up to 600 mg/day (aripiprazole was continued at 7.5 mg/day). He also received nutritional counseling to prevent further body weight gain. During hospitalization we observed no significant changes in his body mass. In our department we regularly monitor body composition in patients treated with antipsychotics using dual-energy X-ray absorptiometry and a Lunar iDXA scanner (GE Healthcare, USA). Table 1 shows the results of the patient's body composition analysis on day 1 and day 45. Gradually, his condition significantly improved and in week 12 he was discharged from the hospital in a stable condition. As well as further psychiatric care, regular monitoring of body weight, abdominal circumference, blood pressure, blood lipids and glucose was recommended.

Table 1. Changes in body composition

	Day 1	Day 45	Change (day 45 – day 1)
Body weight (kg)	120.0	117.5	–2.5
Body mass index (kg/m^2)	37.0	36.3	0.7
Fat mass (%)	43.7	42.2	–1.5
Fat mass (kg)	52.4	50.6	–1.8
Lean mass (%)	52.2	52.8	0.6
Lean mass (kg)	62.7	62.0	–0.7
Visceral fat mass (g)	1696	1692	–4
Visceral fat volume (cm^3)	1798	1794	–4

The mechanism underlying aripiprazole-induced weight gain may be associated with its potent binding to serotonin 5-HT$_{2C}$ receptor, which is important for appetite and weight control [2]. While there are very few reports describing weight gain on aripiprazole treatment [3,4], this is the first observed case of such severe weight gain during treatment with this antipsychotic. In our case, after applying the Naranjo adverse drug reaction probability scale [5], a score of 3 (of maximum 13) for aripiprazole was found, indicating a possible adverse drug reaction to the drug. Apart from aripiprazole itself, other potential causes of weight gain should be considered. We have excluded hypothyroidism, diabetes, steroid treatment and the Cushing's syndrome. The patient confirmed reduced physical activity and increased appetite (with high consumption of sweet snacks).

This case highlights the importance of monitoring the metabolic parameters in patients taking antipsychotics. The most commonly used protocol for this purpose is that developed in November 2003 by the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity [6].

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