Case Report

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Author Affiliation:
[1-2]Senior Resident, Department of Internal Medicine, [3]Postgraduate Student, [4-6]Intern, Department of General Medicine, School of Medical Science and Research, Sharda University, Greater Noida, Uttar Pradesh 201310, India.

Coressponding Author:
Ankush Sharma, Senior Resident, Department of Internal Medicine, School of Medical Science and Research, Sharda University, Greater Noida, Uttar Pradesh 201310, India.

E-mail: drankushsharma2014@gmail.com

Clozapine-Induced Diabetic Ketoacidosis: A Case Report

Syed Mohsin Ishaq[1], Ankush Sharma[2], Vinay Gupta[3], Fleming Mathew[4], Mawra[5], Seher Kirmani[6]

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Abstract

Atypical antipsychotics are of great benefit to patients suffering from psychiatric disorders, such as bipolar disorder and schizophrenia. Yet they have a wide array of adverse effects including metabolic disturbances. One such rare but potentially fatal complication is Diabetic ketoacidosis, associated with the use of Clozapine, an atypical antipsychotic.

The objective of this article is to report a case of a 35-year-old male with underlying schizophrenia on clozapine 200mg BD who presented in the emergency with complaints of abdominal discomfort, sweating, vomiting and palpitations. The patient was managed as a case of diabetic ketoacidosis(DKA). Thorough investigations ruled out other possible causes. This study outlines the importance of being vigilant while managing a case with psychiatric disorder being treated with clozapine as the drug can lead to new-onset diabetes and diabetic ketoacidosis. Patients on clozapine must be regularly monitored especially during the early course of treatment to avoid the onset of such fatal adverse effects.

Keywords: Diabetic Ketoacidosis; Clozapine-Induced.

Introduction

Clozapine is an antipsychotic drug used for the management of schizophrenia. Due to its sideeffects, it is reserved for patients unresponsive to, or intolerant of the conventional antipsychotic drugs.[1] Clozapine is used for people with schizophrenia who have had an inadequate response to at least two standard neuroleptics. It has an unusual neuropharmacological profile, with a low affinity for dopamine D2 receptors (unlike other antipsychotic drugs), but a high affinity for D4 and 5-HT2 receptors.[2] It has good efficacy and causes fewer extrapyramidal side-effects than the conventional neuroleptics. About 30% of patients respond after 6 weeks, 49% by 6 months and 61% by a year. However, its side-effects prevent it being used as a first-line treatment. The major complication is agranulocytosis which occurs in 0.8% of treated patients.[3]

Case report

In our case, a 35 year old male with underlying schizophrenia on clozapine 200mg BD, was admitted with complaints of abdominal discomfort, easy fatigability, sweating, vomiting and palpitations.

Patient denied any history of fever, loose

motions, cough , headache, burning micturation or chest pain suggestive of infection.

There was no family history of hypertension or diabetes. But there's a history of intake of atypical antipsychotic- clozapine which was initially started on 100mg BD and later on changed to 200mg BD from previous 6 months. On examination, Pulse -150 beats/min, Respiratory rate- 24 minute, BP: 150/90 mmhg, SpO2: 96% .

Systemic examination was within normal limits.

Blood glucose done which was 350 mg/dL.

Further Investigations revealed: Hb- 15 gm/dL, TLC: 11.72/cumm, DLC: P-62 L-23, Platelets: 351, Blood Urea : 20mg/dL, Creatinine: 0.5 mg/dL. LFT was within normal limits, Urine examination was with in normal limits, ECG revealed Sinus tachycardia, USG abdomen Grade 1 fatty liver and Chest X-Ray was Normal. Blood and urine cultures were taken were sterile. ABG showed metabolic acidosis with pH of 7.18, Bicarb of 12 and lactate of 1. Urine examination revealed presence of sugar with +ve ketones in urine.(Table 1)

Patient was managed as a case of diabetic keto-acidosis and was administered IV fluids, insulin infusion, potassium infusion till acidosis was resolved and ketones came out to be negative in the urine & patient improved clinically.

Table 1: Systemic examination.

Bloodglucose (mg/dl)	360	350	292	280	242	185	120
Arterial pH	7.18	7.24	7.32	7.38	7.4	7.42	7.40
Serum Bicarbonate	12	18	21	23	24	25	25
Lactate	1.2	1.3	1.5	1.2	1	0.8	1
Serum potassium	4.6	4	4.3	4.9	4.7	4.8	4.7

Since infections were ruled out by investigations a diagnosis of Diabetic keto-acidosis precipitated by clozapine intake was made. Patient was discharged in a hemodynamically stable condition on MSI of 'insulin aspart' 10U TDS and Glargine 10U HS. Clozapine was stopped and it was substituted by aripriprazole 15mg OD and at the time of discharge, fasting Blood glucose was 96 mg/dL and Post prandial value was 156 mg/dL.

Discussion

Among atypical antipsychotics currently in use, clozapine and olanzapine are known to have the highest risk of metabolic complications.[2,3]

The risk factors for the development of DKA during clozapine treatment are unclear since clozapine treatment has been associated with DKA even in patients with no documented history of hyperglycemia, diabetes, or weight gain. However, people of African- American or African Caribbean descent have been reported to be more susceptible to this adverse effect.[2,4,7,8] The association between clozapine and DKA does not appear to be dose dependent. In the reported cases of DKA, among clozapine-treated patients, clozapine doses have ranged from 150 mg/day to 500 mg/day.[7,9,10] Reports and clinical experience suggest that in a case of clozapine-associated diabetes or DKA, discontinuation of the drug may result in resolution of the hyperglycemia and diabetes.[7,9,10]

Conclusion

Clozapine is a potent drug known to cause diabetes and DKA. The initial 3-5 months of clozapine treatment are specially high risk period for such complications.The treating physician must be aware of this rare yet lethal problem with clozapine. Patient should be screened for blood sugar and HbA1c at the start of treatment and should be followed by same biochemical investigations.

Conflict of interest: None

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