

Olanzapine Induced Fever: A Case Report

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ABSTRACT

Antipsychotics have been reported to be associated with neuroleptic malignant syndrome, which is a life-threatening complication, with fever being one of the main symptoms. We are reporting a case of olanzapine induced isolated fever in a patient with paranoid schizophrenia, with other causes being ruled out with the fever subsiding only after the withdrawal of olanzapine.

Keywords: Olanzapine, Antipsychotics, Fever, Neuroleptic malignant syndrome.

INTRODUCTION

Olanzapine, an atypical antipsychotic, with varying affinities for dopamine (D_{1-4}), serotonin ($5-HT_{1-3, 6, 7}$), muscarinic (M_{1-5}), histamine (H_1) and adrenergic (α_1) receptors, is used in the management of schizophrenia and bipolar disorders.¹

Common adverse effects of olanzapine include somnolence; increased appetite and weight gain; hyperprolactinemia; dizziness; fatigue; elevated plasma glucose, triglyceride and liver enzymes; eosinophilia; oedema; orthostatic hypotension; constipation and dry mouth.

Neuroleptic malignant syndrome (NMS) is known to be associated with usage of typical antipsychotics. Atypical antipsychotics such as clozapine and olanzapine causing NMS have also been infrequently reported.² Isolated fever with olanzapine is rarely reported. This is a case report of a probable case of olanzapine induced fever.

CASE

A 43-year-old man was admitted to Kempegowda Institute of Medical Sciences and Research Center, Bangalore, for symptoms of schizophrenia. He was initially started on risperidone 2 mg (0-0-1) which was increased to 4 mg (0-0-1), following which he developed extrapyramidal symptoms such as stuttering. Risperidone was tapered off and was replaced by olanzapine 15 mg (0-0-1) and clonazepam 0.5 mg (1-1-1). There was good clinical improvement in his symptoms and he was discharged home with the same treatment plan. Two weeks following discharge, he returned with complaints of fever, headache and body ache for which paracetamol 650 mg (1-0-1) was prescribed on an outpatient basis. The fever did not subside even after 5 days of paracetamol and he was subsequently readmitted for evaluation of fever.

CLINICAL COURSE

The patient was started empirically on IV ceftriaxone 250 mg and sulbactam 125 mg (1-0-1), artesunate 120 mg IV stat followed by 120mg after 6 hours, oral pantoprazole 40 mg (1-0-0) and oral paracetamol 650 mg (1-1-1). Olanzapine and clonazepam were, however, continued in his psychiatric management. Fever was continuous and did not subside even after 3 days of treatment with the above regimen and axillary body temperature remained elevated between 99°F to 102°F (Figure-1).

Based on the results of laboratory tests (Table-1) and poor therapeutic response to the above drug regimen, olanzapine-induced fever was suspected and the medication was stopped. With the stoppage of olanzapine, the body temperature gradually returned to normal over the next 3 days. Olanzapine was replaced by amisulpride 200 mg (0-0-1) and the patient was discharged on the 6th day of admission with complete remission of his fever.

DISCUSSION

Fever may be associated with drugs due administration-related reactions, pharmacological action of the drug, idiosyncratic or hypersensitivity reactions or due to their effects on thermoregulation. NMS was ruled out as the patient did not exhibit any features associated with autonomic instability, muscle rigidity, cognitive changes. Fever due to administration-related reactions or due to idiosyncrasy / hypersensitivity was also ruled out.³ Antipsychotics are known to impair hypothalamic thermoregulatory mechanisms which can result in either hypothermia or hyperthermia. Atypical antipsychotics such as clozapine, olanzapine, aripiprazole, ziprasidone and

quetiapine are associated with NMS and fever is one of its cardinal symptoms.⁴

Development of fever by olanzapine is probably due to blockage of dopaminergic and serotonergic receptors and also activation of the immune system and increased production of interleukins like IL-1 and TNF- α are known to act on the thermoregulatory center and elevate the 'set-point' to a higher level.⁵

The temporal relationship of olanzapine therapy with the onset and resolution of fever, negative laboratory findings and poor clinical response to pharmacological intervention are supportive of a causal relationship. This adverse drug reaction (ADR) was determined to be "probable" on assessment with both WHO-UMC and Naranjo causality assessment criteria (score 5). Severity assessment through the adapted Hartwig severity assessment scale revealed this ADR to be and "moderate" in severity (level 4) (Table-2).

CONCLUSION

Olanzapine is frequently used in the management of schizophrenia and other bipolar disorders. Although olanzapine is known to have minimal adverse effects and is known to cause NMS, health care practitioners must be aware of the medication such as olanzapine causing isolated fever in patients.

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Table 1. Laboratory investigation

Investigations	Results
Hematological examination	Hb-11.9g%, TC-5670 cells/mm ³
Serum electrolytes	Na ⁺ , K ⁺ & Cl ⁻ were within normal limits
LFTs	Total bilirubin, SGOT, SGPT, Alkaline phosphatase, albumin, total protein were within normal limit.
RFTs	Blood urea and serum creatinine were within normal limit
Screening for other causes of fever	Serum HBsAg was negative VDRL was negative HIV was non reactive Leptospirosis Ab was non reactive MP QBC – was negative
USG of abdomen	Fatty hepatomegaly

LFT-liver function test, RFT-renal function test, USG – ultrasound, VDRL- venereal disease research laboratory, HIV- human immunodeficiency virus, MP QBC- malarial parasite quantitative buffy coat

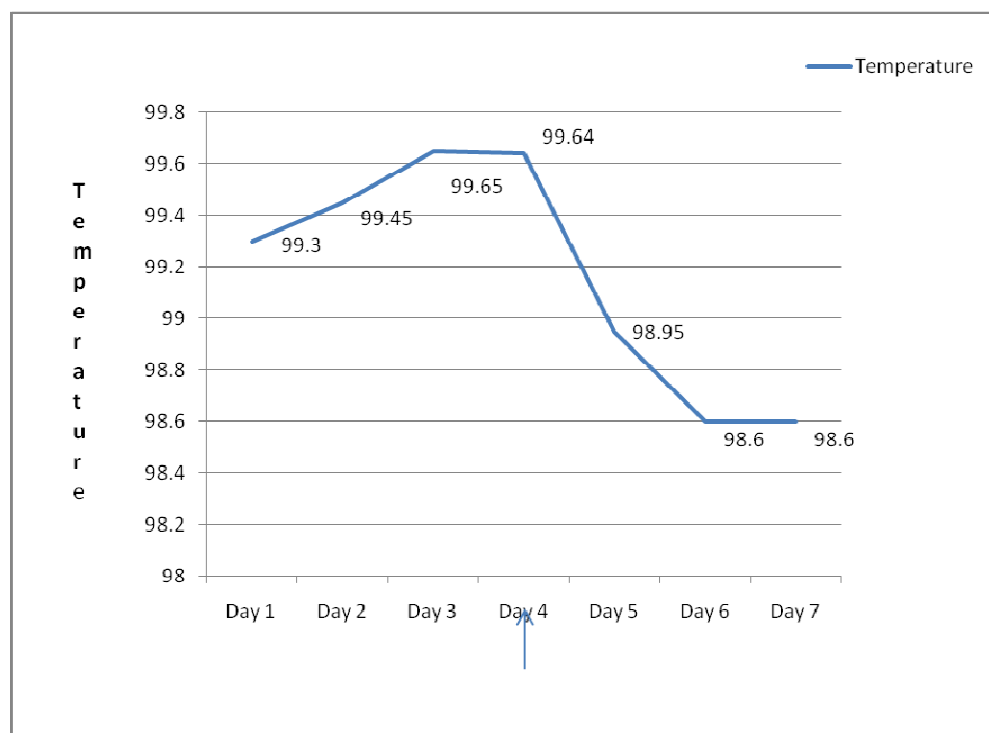


Figure 1. Changes in body temperature during course of therapy

Olanzapine stopped → Day 4