

# A Case of Olanzapine-Induced Fever

By Cho-Hsiang Yang, Ying-Yeh Chen

*ABSTRACT ~ Olanzapine, a frequently used second-generation antipsychotic, has rarely been implicated as a cause of drug-induced fever in the absence of neuroleptic malignant syndrome. We describe a patient who developed isolated fever following olanzapine monotherapy, which subsided after discontinuation of olanzapine. Blockade of dopaminergic receptors and elevated cytokines concentration are possible mechanisms of fever development during treatment with olanzapine. This case calls for attention to olanzapine-induced fever in clinical practice. Psychopharmacology Bulletin. 2017;47(1):45–47.*

## INTRODUCTION

Olanzapine, a commonly used atypical antipsychotic, is similar to clozapine in its structure, side effects, and receptor binding profiles. While both can cause neuroleptic malignant syndrome (NMS), olanzapine has rarely been implicated in causing fever alone.<sup>1,2</sup> We describe a case of olanzapine-induced fever without NMS in a patient with schizophrenia.

## CASE HISTORY

A 40-year-old woman primary school teacher, with five-year history of schizophrenia and non-compliance with medication, was rotating her body purposelessly for hours before being hospitalized. For the past five years, she gradually exhibited auditory hallucination, delusion of persecution, blunted affect, inadequate verbal output, social withdrawal, poor self-care, occupational incapacity such as threatening her students. These symptoms led to a diagnosis of schizophrenia and her first hospitalization one year ago. She was not compliant with her medication and her symptoms recurred. Besides, she began to have increasingly frequent stereotypic meaningless body rotation while changing position and walking, which was not in response to delusion or hallucination. She had no pertinent past medical history, substance use, or psychiatric history in her family. Review of systems, physical examination, and laboratory studies, electroencephalography, and brain computed tomography were unrevealing. Diagnosed with schizophrenia, she was admitted for psychiatric inpatient treatment.

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We prescribed olanzapine and increased to 10 mg on the fifth day (D5). Her symptoms improved within 2 weeks of olanzapine monotherapy. However, her body temperature rose to 39°C on D17 and persisted in the range of 38.5°C–39.5°C until D51. During these weeks when she had persistent fever, there was no autonomic instability, consciousness change, muscle rigidity, involuntary movement, or signs of infection. Her physical and laboratory data, including cell counts, creatine phosphokinase, urine, blood, and sputum cultures, autoimmune antibodies, cancer antigens, cerebrospinal fluid analysis, chest films, abdominal ultrasonography, were unremarkable. Treatment with acetaminophen and antibiotics, including amoxicillin-clavulanate and ciprofloxacin, failed to improve her fever. For suspected drug-induced fever, we decreased her olanzapine to 5 mg on D47, and her fever subsided on D52. In this case, isolated fever developed during treatment with olanzapine alone, persisted for weeks, and subsided after its dose was decreased.

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Fever during antipsychotic use cautions the presence of NMS, an adverse event manifested by altered mental status, autonomic instability, muscle rigidity, high creatine phosphokinase, and leukocytosis.<sup>3</sup> The lack of major features renders NMS unlikely in this case. Without evidence of infection, autoimmune disease, malignancy, or other organic origin, olanzapine-induced fever is more likely.<sup>4</sup>

Olanzapine and clozapine may induce fever through dopaminergic antagonism which is thought to elevate the thermoregulatory set-point in the hypothalamic pre-optic area, and disinhibit serotonin activity related to heat production. Additionally, both medications possibly act as exogenous pyrogens and trigger endogenous pyrogens to stimulate central prostaglandins that induce more local cytokines and fever.<sup>2</sup> Overall, dopaminergic blockade and cytokines may account for olanzapine-associated fever.

**CONCLUSION**

In short, olanzapine may induce fever through neurotransmitter and immunological pathways. Olanzapine-induced fever may have a dose-response relationship. Its risk factors and pathophysiological consequence may need further investigation. ❀

**ACKNOWLEDGEMENTS**

The authors declare no conflict of interest.

## CONFLICTS OF INTEREST

Dr. Ying-Yeh Chen is supported by the Ministry of Science and Technology (Grant number: MOST 105-2314-B-532-004-MY3) and the Department of Health, Taipei City Government (Grant number: 10501-62-062). Dr. Cho-Hsiang Yang declares no conflict of interest.

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