# Olanzapine induced Diabetic ketoacidosis and neuroleptic malignant syndrome

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## Introduction

Neuroleptic malignant syndrome (NMS) is an uncommon life threatening adverse reaction with the use of atypical antipsychotics like olanzapine. In addition, Olanzapine therapy is associated with increased incidence of diabetes. Here we describe a rare occurrence of Diabetes Keto Acidosis (DKA) and NMS in a young male treated with Olanzapine.

## Case report

An 18 year old male with bipolar affective disorder (BPAD) who has been on Olanzapine and Carbamezapine for the last two years presented with shortness of breath for one day duration. He developed diabetes mellitus six months after commencement of Olanzapine therapy and was started on Metformin. Patient has experienced throat discomfort, loss of appetite and oral ulcers three days prior to the admission and has not taken any medication during that period.

After careful history, examination and investigations cardiac, respiratory and renal causes were excluded for the presentation. Patient was diagnosed to have diabetic ketoacidosis on admission with a random capillary blood sugar of high index, with positive urinary ketone bodies and high anion gap metabolic acidosis on Arterial Blood Gas analysis. (pH -7.15, $pCO_2$ – 14 mmHg, $PO_2$ – 122 mmHg, Na – 139 mmol/ dl, K – 3.7 mmol/dl, $HCO_3$- 4.9, BE -24). At the same time he had altered level of consciousness with high fever spikes, exaggerated tendon reflexes and generalized rigidity. He was diagnosed to have NMS. Creatinine Phospho Kinase was 2195 u/L.

DKA was managed according to the standard guidelines and he was started on oral Bromocriptene 2.5mg tds and later it was increased up to 5mg tds as patient had high AST (283U/L) and ALT (502U/L). Despite Bromocriptene therapy his CPK levels was elevated to 3810 U/L. Then patient was started on Intravenous Dantrolene (1mg/kg/day) considering the benefits over risk of possible hepatotoxicity. His CPK levels and AST/ALT levels dropped dramatically after initiation of Dantrolene therapy (293U/L, 38U/L, 37U/L respectively). Dantrolene was stopped after 7 days considering the cost, and patient developed a recurrence of NMS and Dantrolene therapy was recommenced and continued for 10 days and gradually tailed off by reducing 10% of maintenance dose daily. Patient recovered completely and discharged on 25th day from admission without Olanzapine.

## Discussion

A case of NMS may present with various signs and symptoms. It is mainly seen with typical antipsychotic medication use. However, this case illustrates that NMS can also occur due to treatment with atypical antipsychotic medications (like Olanzapine) (1,2,3). NMS is more common in affective illness, young male and mental retardation which are also risk factors present in this case. A rapid loading of antipsychotics is considered to be the causal factor in the development of NMS by causing a sudden and massive down-regulation of dopaminergic transmission. But NMS also appears as an idiosyncratic reaction with atypical antipsychotics without dose adjustment and after long term therapy with the same dose (4) as seen in our patient. There was improvement after stopping the medication and treatment with Dantrolene.

In our patient liver enzymes were possibly elevated due to the disease activity of NMS. Although Dantrolene can cause hepatotoxicity, it can be started in life threatening situations considering benefits over risks. In our patient Dantrolene reduced liver enzymes by improving disease activity of NMS.

## Conclusion

NMS can occur with atypical antipsychotics like Olanzapine especially in the presence of risk factors. NMS remains a dangerous condition and early diagnosis and proper treatment will save lives. Possible treatment modalities are withdrawal of the offending agent, hydration and pharmacotherapy with bromocriptene/dantrolene or amantadine.

## References

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