

Letter to Editor

Clozapine-induced atypical neuroleptic malignant syndrome

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Sir,

Neuroleptic Malignant Syndrome (NMS) is a potential fatal adverse reaction to antipsychotic drugs. Almost all typical neuroleptics have been reported to cause NMS.^[1] Some have hypothesized that atypical neuroleptics would not cause NMS since there is no intense dopaminergic blockade.^[2] However, numerous cases of NMS related to atypical neuroleptics have been reported and most of these are associated with muscular rigidity and tremors only.^[2] We encountered a case which underwent fatal course.

A 31-year old male presented in the emergency department with two days history of fever which was high grade, and altered mental status. He had a significant past history of psychiatric disorder for which he was taking clonazepam and sodium valproate tablets per oral. Seven days prior to presentation, patient developed increased irritability and psychotic episodes and he was started on tablet clozapine. On clinical examination, he was unresponsive, with a core temperature of 41.38^oC. His pulse rate was 112 beats/minute, blood pressure was 90/60mmHg, respiratory rate was 28 cycles/minute and crepitations were heard over all lung fields. There was no rigidity. Imaging studies showed normal MRI of brain and sterile blood and CSF cultures. In addition, there was leukocytosis (17.2 x 10⁹/l), raised titer of creatine phospho-kinase (CPK) (16000U/L) which confirmed NMS. Clozapine was stopped and patient was

treated in the intensive care unit (ICU) with dantrolene injection (2mg/Kg), supportive treatment and antibiotics for possible chest infection. Patient passed on two days after despite aggressive management.

Although NMS occurs less commonly with the atypical antipsychotics, its incidence is increasing with more prescriptions of these drugs.^[3] It seems that there have been many atypical cases similar to our case that might have been missed due to mild presentations. Our case supports the observation by Trollor *et al.* who reported Australian Adverse Drug Reaction Advisory Committee (ADRAC) database-based study which showed relative absence of rigidity in clozapine-induced NMS.^[3]

In conclusion, we strongly recommend the need for further studies regarding proper definition of NMS criteria in order to prevent the under diagnosis of the disorder, especially following the high rate of prescribing atypical anti-psychotics. Further studies on pharmacogenetic mechanisms underlying these idiosyncratic reactions are urgently needed.

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