

# Clozapine Withdrawal Catatonia or Lethal Catatonia in a Schizoaffective patient with a family history of Parkinsons Disease

Catatonia has been documented since 1874 and may be attributable to many causes.<sup>1</sup> It has been observed even prior to the advent of antipsychotics in association with extreme psychosis and was termed lethal catatonia.<sup>2</sup> Sometimes catatonia has occurred on abrupt cessation of drugs especially clozapine.<sup>3</sup> Clozapine has dual actions in a psychotic patient with Parkinson's Disease (PD) in that it both treats psychosis as well reduces tremors of PD.<sup>4</sup> Abrupt discontinuation of clozapine generally causes a recurrence of tremors. The following case report illustrates a patient, whose parents both suffered from PD but who himself manifested no evidence of the disease.

Mr. D .M, a middle aged Asian gentleman diagnosed with Schizoaffective disorder for five years, was fairly well maintained on Clozapine 200mg daily. He lived in Europe, but decided to return to Malaysia for two months to visit family. He was well on arrival but became paranoid and fearful following his return. He developed generalized, prominent tremors of both upper limbs. He deteriorated and eventually became unresponsive to call and was hospitalised. The family was unsure whether the patient had taken his medication regularly as he lived alone and was unsupervised. Though both his parents suffered from PD our patient had never manifested any symptoms.

Examination revealed a febrile patient with temperature of 39.8°C. Autonomic instability, with fluctuating blood pressure in the range of 120-160mmHg systolic, 70-90mmHg diastolic as well as tachycardia up to 130 bpm was present. He was febrile for the first 11 days of admission despite commencement of antibiotics at day 2. He suffered from generalized rigidity as well as cog wheel rigidity and appeared expressionless. He was mute and did not obey commands. No other neurological deficit was noted. His Glasgow Coma Scale (GCS) was 4/15 (Eye 2, Motor 1, Verbal 1).

Blood investigation revealed an increased creatinine kinase (CK) level of 1889 U/L (n= 35-230 U/L) that increased to

3711 U/L after 15 days in hospital. He had a raised white cell count of 13,400 cells/mm<sup>3</sup> on admission. Computerized Tomography showed generalized cerebral atrophy and Electro Encephalogram (EEG) findings the day after admission showed frequent frontal discharges in the frontal cortex. Thus a diagnosis of neuroleptic malignant syndrome (NMS) was made. Lumbar puncture was non contributory. He was treated in the intensive care unit. He was ventilated from the 6th to the 10th day of his admission due to further deterioration of his condition.

Bromocriptine was commenced the day after admission at a dose of 2.5 mg daily, increased to 5 mg three times daily by day 3 and continued for 33 days. An anticholinergic was administered for the first 18 days and oral diazepam for first 6 days post admission. IV Ceftriaxone 2 g daily from day 2 to 12 followed by IV Tazocin (a combination of piperacillin, and tazobactam) 4.5mg QID for another 10 days was given as treatment for aspiration pneumonia. He improved by day 12. Mental state examination revealed florid persecutory delusions, auditory and visual hallucination, but on history he reported that he had indeed run out of Clozapine one week prior to admission into our ward. Aripiprazole was commenced at 5mg daily on day 20 and titrated to a dose of 20 mg by day 47 after which he was discharged well.

A few issues are pertinent in this case. Firstly, in retrospect we feel that the patient had become psychotic due to Clozapine discontinuation, leading to a catatonic state, as evidenced by immobility, stiffness, mutism, rigidity, and stupor. Clozapine withdrawal catatonia is an uncommon presentation following abrupt cessation of Clozapine. It is postulated to be due to cholinergic rebound and serotonergic hyperactivity.<sup>5</sup> The catatonia resolves within one week of reinstatement of clozapine or another atypical antipsychotic.<sup>6</sup> Another fact in favor of clozapine withdrawal catatonia is the presence of elevated CK levels. Literature shows that clozapine withdrawal catatonia often has elevated CK levels.<sup>7</sup> Other possible complications of sudden cessation of clozapine include motor dyskinesias.<sup>8</sup> The re-emergence of tremors may have been due to the removal of the therapeutic effect that clozapine has been shown to have on Parkinsons patients with tremor. Our patient may have had

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subclinical PD. Secondly, NMS may have been a possible diagnosis as the CK level was high, but the patient did not have a history of recent increase in neuroleptics nor was he on anti Parkinsons medication, the sudden withdrawal of which may cause NMS like syndromes.<sup>9</sup>

Clinical differentiation between neuroleptic malignant syndrome (NMS) and clozapine withdrawal catatonia is important in management, especially if patients live alone and an accurate history is unavailable.

Thirdly, lethal catatonia was a possibility as the patient's catatonia occurred without neuroleptics. He was also being given bromocriptine when he presumably did not need it. Whilst no conclusive diagnosis was made the presentation emphasizes avoidance of sudden cessation of clozapine and to keep in mind the presence of comorbid conditions especially those affecting the extra pyramidal areas.

Clinicians, patients and caregivers should be aware of a catatonia as a possible clozapine withdrawal syndrome. Clozapine must always be tapered over a few weeks.<sup>10</sup> Genetic predisposition towards movement disorders such as PD should be considered when managing patients. Clinical and laboratory differentiation between the various causes of catatonia requires further study, and would be especially useful where a history is unavailable.

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## References

1. Rajagopa SI. Catatonia. *Adv In Psychiatric Treatment* 2007; 13 : 51-59.
2. E Castillo, RT Rubin and E Holsboer-Trachsler. *Clinical Differentiation between lethal catatonia and Neuroleptic Malignant Syndrome. Am J Psychiatry* .1989; 146(3):324-328.
3. Wadekar M, Syed S. Clozapine withdrawal catatonia. *Psychosomatics* 2010; 51(4):355-355.
4. Orr G, Munitz H, Hermesh H. Low-dose clozapine for the treatment of Parkinson's disease in a patient with schizophrenia. *Clin Neuropharmacol* 2001; 24(2):117-9.
5. Yeh, Andrew Wei-Chiang, Lee J W Y, Cheng Tsun-Chi, Wen Jung-Kwang, Chen Wei-Hsi. Clozapine Withdrawal Catatonia Associated With Cholinergic and Serotonergic Rebound Hyperactivity: A Case Report. *Clin Neuropharmacol* 2004; 27(5) : 216-218.
6. Lee JWY, Robertson S. Clozapine withdrawal catatonia and neuroleptic malignant syndrome: a case report. *Ann Clin Psychiatry*. 1997; 9: 165-169.
7. Fink M. Lethal Catatonia, Neuroleptic Malignant Syndrome, and Catatonia: A spectrum Of Disorders. Reply. *Journal Of Clin Psychopharmacology* 1997; 17(3): 237.
8. Ahmed S, Chengappa KN, Naidu VR, et al: Clozapine withdrawal-emergent dystonias and dyskinesias: a case series. *J Clin Psychiatry* 1998; 59: 472-477.
9. Theresa A Zesiewicz, Sujatha Borra, Robert A Hauser. Clozapine Withdrawal Symptoms in a Parkinson's disease patient. *J Of Mov Disord*.2002; 17 (6) :1365-1367.
10. Metzler, Herbert Y. Clozapine Withdrawal: Serotonergic or Dopaminergic Mechanisms? *Arch Of Gen Psychiatry* 1997 ; 54(8): 760-763.