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Olanzapine Treatment of Clozapine-Induced NMS

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INTRODUCTION

The treatment of patients who must stop clozapine because of severe side effects is a serious clinical problem. Patients receive clozapine only after failure of typical neuroleptics and after that there are limited options if clozapine must be stopped. We recently reported two cases of clozapine-induced agranulocytosis who were treated successfully with olanzapine with no recurrence of hematological side effects (Lokshin *et al*., 1998). We now report a case of clozapine-induced NMS, itself a rare phenomenon (Amore *et al*., 1997; Tsai *et al*., 1995; Goates and Escobar 1992; Reddig *et al*., 1993; Nopoulos *et al*., 1990; Miller *et al*., 1991), treated in follow-up with olanzapine.

CASE REPORT

A 34 year old man has suffered for 5 years from paranoid schizophrenia with constant and resistant bizarre delusional thinking and prominent unpleasant auditory hallucinations, sometimes with suicidal imperative content. He was treated with clozapine, 300 mg daily, because conventional neuroleptics had caused severe EPS. During 5 years of clozapine treatment, physical and neurological examinations were normal, and there were no EPS. Repeated laboratory tests, including WBC, CPK, and hepatic transaminases were within the normal range. Suddenly, the patient developed shivering and a tremor and was hospitalized in the general hospital. He became confused, diaphoretic, tachycardic, and his muscles were rigid. His temperature was 38°C; blood pressure 120/80. Laboratory tests showed elevated CPK level 1589 IU/l, without leukocytosis. Chest x-ray and plasma electrolytes were normal.

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Clozapine was stopped and the patient was treated with bromocriptine, dantrolene and fluids. Within the week the patient's condition improved, his consciousness level and vital signs gradually returning to normal. Two days later his mental condition deteriorated; he felt tension, heard imperative voices, and his behaviour was very bizarre. The patient was psychiatrically hospitalized and a trial of olanzapine, 10 mg per day, was started. His condition improved within a week; he calmed down, auditory hallucinations decreased, his behaviour became organized. He has continued to receive olanzapine 10 mg daily with no signs of rigidity or fever. CPK level and hepatic transaminases are normal.

DISCUSSION

This case supports the concept that olanzapine, although structurally and pharmacologically similar to clozapine, can be an effective substitute for clozapine if severe side effects develop. The subject was taking clozapine because of EPS with conventional neuroleptics, and olanzapine is known to produce few side effects. If the patient had been taking clozapine because of resistance to therapeutic effects of conventional neuroleptics, it is an open question as to whether olanzapine can effectively substitute. It is also possible that the patient will develop NMS with olanzapine in the future, since NMS with clozapine developed after 5 years.

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