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Case Report

Typical Neuroleptic Malignant Syndrome Presented in Patient on Maintenance Quetiapine

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ABSTRACT

Neuroleptic malignant syndrome is an acute, life-threatening medical complication caused by antipsychotics. It is commonly seen with typical antipsychotics and very rare with atypicals. Cases have been reported with quetiapine also, but this case is of special interest because it occurred in patient who was stable on maintenance quetiapine 200 mg/day for last 5 years.

Key words: Antipsychotics, neuroleptic malignant syndrome, quetiapine

INTRODUCTION

In 1960, Delay et al. described the “syndrome akinetic hypertonique” as a life-threatening complication of neuroleptic drugs.[1] Neuroleptic malignant syndrome (NMS) is an acute, potentially fatal, idiosyncratic reaction to neuroleptic medications. It can occur anytime during the course of antipsychotic treatment. The motor and behavioral symptoms include muscular rigidity, dystonia, akinesia, mutism, obtundation and agitation. The autonomic symptoms include high fever, sweating and increased pulse and blood pressure. Laboratory findings include an increased white blood cell count and increased levels of creatine phosphokinase (CPK), liver enzymes, plasma myoglobin and myoglobinuria, occasionally associated with the renal failure.[2]

The prevalence of the syndrome is estimated to be 0.02-2.4% of patients exposed to dopamine receptor antagonists. The mortality rate is 10-20%.[2]

NMS is usually seen with typical antipsychotics and relatively less commonly with atypical. Cases have been reported with risperidone, clozapine, olanzapine, ziprasidone and quetiapine.

We present a case report of NMS in a middle age male patient with schizoaffective disorder well-maintained on quetiapine 200 mg/day and divalproex 500 mg/day for last 5 years. The patient was hospitalized in Intensive Care Unit at Tertiary Care Hospital at Bhavnagar (Gujarat) during October 2011.

CASE REPORT

A 46-year-old male patient was brought to Emergency Department of Tertiary Care Centre at Bhavnagar, with, generalized stiffness, fever, generalized tremulousness mutism, perspiration, inability to swallow, intermittent tongue protrusion, sialorrhea, restlessness and insomnia for the last 3 days. Patient was seen by emergency team and was hospitalized in critical care unit. He was diagnosed with schizoaffective disorder of 11 year...
duration. He was under regular treatment of quetiapine 200 mg/day, divalproex sodium 500 mg/day and lorazepam 4 mg in two divided doses/day since 2006, confirmed by relatives and clinical case records. There was no past history suggestive of similar symptoms, medical disorder or substance use. The paternal uncle was having symptoms of self-talking, abusive, poor self-hygiene, roaming on roads who died at the age of 50 years.

On examination, patient was confused, not oriented to time and place. His temperature was 102°F, blood pressure 150/90 mm of Hg, heart rate 104/min, respiratory rate 20/min. He had generalized tremors, cogwheel rigidity in all extremities and orofacial dystonias. The pupils were normal size and reactive to light. Planters were flexor both sides. He was agitated and was pulling intravenous (IV) lines.

Clinically, NMS was suspected. Other differential diagnoses such as meningitis, encephalitis, substance/overdose or withdrawal, metabolic disturbances, seizure, heat stroke were ruled out. Serotonin syndrome was ruled out because of presence of severe rigidity, absence of hyperreflexia, clonus, diarrhea, in coordination and no use of serotonergic reuptake inhibitors. Lethal catatonia was ruled out because patient did not have initial psychotic symptoms. Blood and urine and cerebrospinal fluid (CSF) samples were sent for examination and culture. A head computed tomography scan, chest X-ray and urine analysis and CSF analysis were unremarkable. The physical and laboratory parameters are shown in Table 1.

Patient was admitted in intensive care unit and nasogastric tube and urine catheter was inserted. Quetiapine and divalproex were discontinued. Patient was given 6000 ml/day including dextrose and saline for hydration. Cold water sponging was done regularly to control hyperthermia. Bromocriptine 10 mg in four divided doses through nasogastric tube and intramuscular lorazepam 8 mg/day in two divided doses was started. There was hypernatremia (151 mEq/L) on day 1, which was corrected with successful fluid resuscitation. Vitals, electrocardiogram and urine output were monitored daily. As shown in Table 1 clinical condition improved on day 3 and patient was able to take oral fluids. The patient was clinically stable and was ambulatory on day 5. There was reemergence of psychotic symptoms such as delusion of jealousy, auditory hallucinations, increased talkativeness and psychomotor activity on the 10th day. Clozapine 25 mg in divided was started with divalproex 500 mg/day. Dose was increased and patient was discharged on the 22nd day with 150 mg/day of clozapine and divalprox 1000 mg/day. Patient significantly improved on discharge and was advised for regular follow-up. Patient well-maintained with the same treatment on follow-up.

DISCUSSION

The most striking feature in our case is the timing of onset of the symptoms of NMS after starting antipsychotic drug. Shalev and Munitz found the average time to onset of symptoms in 65 cases of NMS was 4.8 days. Caroff et al. reported onset of NMS within 24 h after initiation of antipsychotic drugs in about 16% of cases, within a week in 66% of cases and within 30 days in virtually all cases.

Gortney et al. reported two cases of 2 month duration and one case of 5 month duration. Quetiapine dose ranges from 50 mg to 200 mg daily and two cases with doses of 800 mg and 1000 mg. Our patient was on 200 mg/day and had no change of dose for last 5 years.

### Table 1: The physical and laboratory parameters

| Parameter                  | Day 1               | Day 2               | Day 3               | Day 4               | Day 5               |
|----------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| Temperature (°F)           | 102                 | 100                 | 99.8                | 99.2                | 98.4                |
| Heart rate                 | 104                 | 108                 | 98                  | 96                  | 82                  |
| Blood pressure (mm Hg)     | 150/90              | 134/80              | 130/80              | 120/70              | 116/80              |
| Tremor*                   | +++                 | +++                 | ++                  | ++                  | +                   |
| Rigidity*                  | +++                 | ++                  | ++                  | +                   | ±                   |
| Dystonia                   | Present             | Absent              | Absent              | Absent              | Absent              |
| WBC count (c/mm³)          | 9000                | 8600                | 8900                | 6800                | 5000                |
| Serum CPK total (IU/L)     | 846                 | –                   | –                   | –                   | 381                 |
| SGPT (IU/L)                | 18.0                | –                   | –                   | –                   | 42                  |
| SGOT (IU/L)                | 48.0                | –                   | –                   | –                   | 76                  |
| Blood urea (mg/dL)         | 65                  | 63                  | –                   | 23                  | 24                  |
| S. Creatinine (mg/dL)      | 1.00                | 0.8                 | –                   | 0.6                 | 1.0                 |
| Treatment                 | IV fluids, bromocriptine through nasogastric tube, IM lorazepam | IV fluids, bromocriptine through nasogastric tube, IM lorazepam | Oral fluids, bromocriptine, lorazepam | Oral fluids, bromocriptine, lorazepam | Oral fluids, bromocriptine, lorazepam |

*+++ – severe; ++ – moderate; + – mild; ± – equivocal; CPK – Creatine phosphokinase; SGPT – Serum glutamate pyruvate transaminase; SGOT – Serum glutamate oxalate transaminase; WBC – White blood cell; S. Creatinine – Serum creatinine; IV – Intravenous; IM – Intramuscular
Most of the NMS cases have occurred within few days of initiation and increasing dose of quetiapine. There is no unique method of dosing (i.e., high vs. low dose, rapid increase, drug withdrawal) that would more likely herald NMS associated with a neuroleptic drug.[3]

The usual presentation consists of four primary features including Hyperthermia, extreme generalized rigidity, autonomic instability and altered mental status.[6] In our patient, the all these presenting features were seen. The patient met all criteria described in DSM IV TR[7] and those described by Caroff et al.[4] This is typical NMS presentation, which is less common reported with atypical antipsychotic induced NMS. NMS can occur in patients given atypical antipsychotics and resembles “classical” NMS.[6] The recovery is faster in our patient as compare with other typical antipsychotic induced NMS as patient showed improvement on the 3rd day of treatment.

Risk factors in our patient were dehydration, hypernatremia (sodium 151 mEq/L), male gender and affective disorder. Other risk factors described in the literature[6] including infection, concurrent presence of dementia, use of other neuroactive medications, higher relative doses and parenteral administration of neuroleptics, prior history of NMS, medical or neurologic illness and a recent history of substance abuse or dependence were absent in our patient.

Though laboratory investigations have a key role in identifying NMS, total white blood cell count was normal in our patient. CPK level in this patient was four fold higher (Normal value is 51-294 IU/L in adult male). This finding supports the dictum: “Treat the patient and not the test.” Severe rhabdomyolysis and oliguric renal failure was not observed in our patient. On applying naranjo adverse drug reaction probability scale[9] the score of seven suggests probable casual association.

CONCLUSION

Atypical antipsychotic quetiapine may cause life-threatening NMS. Quetiapine induced NMS may have a variable clinical and laboratory presentation. NMS may present quiet late in maintenance treatment phase with quetiapine.

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