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# A RARE CASE OF NEUROLEPTIC MALIGNANT SYNDROME WITH LITHIUM ENCEPHALOPATHY

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**ABSTRACT**

A rare case presentation of 50 year old male patient with neuroleptic malignant syndrome(NMS) & lithium encephalopathy simultaneously .Antipsychotics like trifluoperazine are used in mania but it can cause neuroleptic malignant syndrome. lithium is used in treatment of bipolar mood disorders extensively but it can cause CNS toxicity and consequent encephalopathy and renal failure.NMS is an idiosyncratic reaction to antipsychotics.The underlying pathopysioloic mechanism can be explained by marked and sudden reduction in central dopaminergic activity resulting fromD2 dopaminergic receptor blockade within nigrostriatal,hypothalamic,limbic/cortical pathways on the basis of clinical features of NMS.Lithium has narrow therapeutic index(0.5 to 1.2 meq/l).Overdose symtoms are regularly seen at concentration above 1.5 meq/L.The identified risk factors for lithium toxicity includes age>50 years,subnormal endogenous creatinine clearance and thyroid dysfunction.

## 1. CASE REPORT

A case of 50 year old male patient of bipolar mood disorder since 20 years and seizure disorder since 2 months presented to emergency department of civil hospital, Ahmedabad with acute onset of diarrhea, rigidity and fever since two days followed by convulsion one day back. Patient was on antipsychotics trifluoparazine, and phenytoin, carbamazepine since two month and he was taking Lithium SR (450) 1-1-1 since 15 years for bipolar mood disorder. No nausea,vomiting,focal neurological deficit and pedal edema. No significant personal history and family history .On admission patient had Tachycardia (94/min), normal blood pressure(130/80mm of hg) ,Tachypnea(RR-24)and elevated body temperature(101F). On CNS examination patient was unconscious and responds to deep pain stimuli (DPS) without any focal neurological deficit.On motor system examination rigidity was present throughout the movement of limbs and neck rigidity was also present.Superficial reflexes were present. Deep tendon reflexes were normal with extensor plantar response. On examination RS and CVS were normal.So our differential diagnosis were metabolic encephalopathy, meningoencephalitis, neuroleptic malignant syndrome(NMS),heat stroke. Investigations were done in the forms of -Hb-11.20gm/dl.WBC-14200/ cmm .PLATELETS-313000/ cmm .ESR-53 after 1hour.SGPT-827.30 IU/L (0-45 IU/L) ,S.Billirubin-0.68 mg/dl (0.2-1.2 mg/dl) S.Direct Billirubin0.40.S.Na-133.60(135-145 meq/L) ,S.K-3.30 meq/L (3.5-5.1 meq/L). S.TSH-2.3600Uiu/ml(0.4-4uIU/ml).In ABGA-PH 7.27,HCO3-9.3 O2 Saturation 96.7.

**S.Creat-**5.92 mg/dl ↑ (0.6-1.4mg/dl) .
**S.Urea-**215.6 mg/dl ↑ (10-45 mg/dl) .
**CPK TOTAL-**2900.70IU/L ↑ (25-200IU/L) .
**S.LITHIUM-**2.30mmol/L↑(0.5-1.2mmol/L ) .

URINARY MYOGLOBIN->1000 ng/ml (Normal value <25 ng/ml) CSF R/M was normal and ADA was also normal.

MRI BRAIN PLAN WITH CONTRAST(P+C) Study was also normal.

Patient was shifted to ICU(Intensive Care Unit) and put on a ventilator in a view of life threatening medical emergency for intensive monitoring of vitals including body temperature, blood pressure, respiration and urine output.Patient was initially treated by iv fluids and higher antibiotics.Acidosis was treated by bicarbonate infusion initially . All antipsychotics and lithium were withheld, Hemodialysis was initiated in a view of rhabdomyolysis as well as lithium induced renal failure. Hemodialysis was done for 6 times,meanwhile laboratory parameters were monitored as per need.S.creatinine was reduced from initial value of 5.92 mg/dl to 5.41mg/dl, 3.88mg/dl, 2.30mg/dl, 1.32mg/dl subsequently.S.urea was reduced from initial value of -215.6 mg/dl to 123.8mg/dl, 88.90mg/dl, 56mg/dl, 32mg/dl subsequently.CPK TOTAL was reduced from initial value of 2900.70IU/L to 294 IU/L, 140IU/L subsequently.S.lithium was reduced from initial value of-2.30mmol/L to 1.80 mmol/L, 1.20mmol/L, 0.80mmol/L subsequently. Patient improved gradually and became conscious. Antiseizure medication carbamazepine was continued to prevent convulsion. Antipyretics and cold sponging were used to control body temperature .Ventilatory support was removed on 15 th day of admission and patient was shifted to ward.

## 2. DISCUSSION

Bipolar disorder is characterized by unpredictable swing on mood from mania to depression. Lithium carbonate is the main stay of treatment bipolar disorder although sodium valproate and carbamazepine can be used. as well as number of second generation antipsychotics (aripiprazole, olanzatine, quetiapine…) are also used.

Nueroleptic malignant syndrome is an idiosyncratic reaction to antipsychotics characterized by triad of elevated body temperature, altered mental status, acute onset of muscles rigidity. It is associated with autonomic dysfunction hyperthermia, tachycardia, labile blood pressure,. Renal failure and mark -ed elevated creatinine kinase level occurred by rhabdomyolysis. Symptoms evolve within days or weeks after starting first generation antipsychotics treatment which are potent dopamine D2 blocking agents. Treatment involves immediate cessation of offending agent and mainly supportive. Patient need to be taken to intensive care setting for monitoring , control of body temperature, electrolyte replacement.

In a treatment of mania lithium is started initially as 300 mg BID / TID and the target is to achieve normal therapeutic range blood level of lithium is between 0.8 to 1.2 meq/l. A sustained blood level of Lithium 0.8 meq/l is important for optimal prophylaxis but overdose symptom are regularly seen at concentration above 1.5 meq/l. In acute intoxication symptom progress to muscle twitching, delirium, coma, convulsion. Dialysis, Osmotics diuretics and bicarbonate infusion is given to promote lithium excretion.

A case report was published by Brian D.Berman et al and it was found that NMS is a neurologic emergency.Patient was managed by the same as we did. First step is to cessation of offending neuroleptic agent, initiation of supportive medical therapy. Aggressive hydration is often required,especially if highly elevated CPK level threatens to damage the kidneys. Recurrence of NMS do occur so most patients who require anti psychotics ,it should be safely reintroduced with proper precautions including very slow titration and careful monitoring after a waiting period of about 2 weeks.Another case report regarding lithium encephalopathy was published byD Smith and P Keane et al and It was found that Haemodialysis is the cornerstone in treatment for lithium toxicity.Aggresive treatment (Intravenous fluids, haemodialysis) should be given when S.Lithiun exceeds 2 mmol/L.

## 3. CONCLUSION:

Lithium is the mainstay in treatment of bipolar disorder and the response rate is 70 to 80% in acute mania, but it has narrow therapeutic range (0.5 to 1.2 meq/l.) so strict monitoring is required for blood level of lithium regularly to prevent its toxicity and consequent encephalopathy. Trifluoperazine is a first generation antipsychotics, which is a potent dopamine blocking agent and so it can cause neuro leptic malignant syndrome like condition. So second generation antipsychotics (weak D2 blocking agent) is preferred. Nueroleptic malignant syndrome plus lithium toxicity is a life threatening emergency particularly with renal failure and associated with high mortality rate up to 50% . So omission of 1st generation antipsychotics should be done in treatment of bipolar disorder.

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