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Case Report

A case of haloperidol induced neuroleptic malignant syndrome in postpartum psychosis: a rare case report and review of literature

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ABSTRACT

Neuroleptic malignant syndrome (NMS) is a very rare and fatal complication which occurs due to use of Neuroleptic agents in the treatment of psychotic disorders. Neuroleptic drugs are assumed to be safe for both mother and foetus owing to its relative impact on untreated fulminant psychosis. NMS was observed mostly after the use of high potency first generation neuroleptic agents such as haloperidol, fluphenazine, chlorpromazine. NMS is characterised by triad of fever, muscle rigidity and altered mental status. We report a case of 26 years old G2P1L1 pregnant woman presented with abruptio placentae and intrauterine foetal demise at 35 weeks of gestation. During postpartum period, she developed NMS due to usage of haloperidol for postpartum psychosis. In this case we achieved a prompt recovery by using bromocriptine and lorazepam.

Keywords: Neuroleptic malignant syndrome, Abruptio placentae, Hyperthermia, Creatine phosphokinase

INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a lifethreatening complication which occurs as a result of antipsychotics, antiemetics like metoclopromide, promethazine, withdrawal of dopaminergics like levodopa usage. The clinical features of NMS include hyperthermia, autonomic dysfunction, altered mental status and muscle rigidity.[1] It is considered to be one of the potential dangerous obstetric emergencies in pregnancy. The mortality rate was higher in NMS affected patients mainly due to complications like rhabdomyolysis, acute respiratory distress syndrome, arrhythmias, acute kidney failure, sepsis.[2] According to Mittal et al the pathophysiology of NMS is related to antipsychotic action by dopamine receptor blockade and increased release of calcium from sarcoplasmic reticulum.[3] So, careful research analysis were required for the treatment of psychosis in the pregnant women. As per ACOG guidelines, typical antipsychotics are considered to have a safer profile than atypical antipsychotics for the treatment of psychosis in pregnant women. The extrapyramidal symptoms and NMS are more commonly seen in typical antipsychotics rather than atypical antipsychotics. The NMS in pregnancy has to be differentiated from thyrotoxicosis, catatonia, allergic reactions, extrapyramidal symptoms, encephalopathy.[4] The clinical manifestations of NMS include muscle rigidity, fever, tachycardia, labile blood pressure, akinesia, pallor, diaphoresis and altered consciousness. In NMS elevated creatine phosphokinase, leucocytosis, elevated liver enzymes can also be noted.

Our case presented as an antenatal woman with abruptio placenta and intrauterine fetal demise due to accidental fall, after delivery she developed acute psychosis followed by NMS features. We also used literature to help in the early diagnosis and prompt recovery of NMS.

CASE REPORT

A case of 26 years old gravida 2, parity 1 and live 1 (G2P1L1) with previous history of caesarean section,

gestational age of 35 weeks 4 days came to emergency department of obstetrics and gynaecology with history of accidental fall. On admission patient had complaints of abdominal pain with history of bleeding per vaginum since accidental fall. On examination, patient was afebrile, pallor noted, not dyspnoeic but mild tachypneic, no pedal oedema, CVS S1S2 heard, RS-normal vesicular breath sounds. PR-98/min, BP-140/90 mmHg. Abdominal examination revealed uterus corresponds to 36 weeks size, tensed, tender, acting, cephalic presentation, with absent fetal heart sounds and scar tenderness. Per vaginal examination revealed cervix uneffaced, OS closed, presenting part above brim, 350 gm of blood clots. Bedside ultrasound showed singleton fetal demise, posterior placenta with retroplacental clots. Patient was taken up for emergency caesarean section and intra operatively 800 grams of clots were removed after delivering fresh IUD baby. 3 units packed red blood cells, 8 units Fresh frozen plasma, 4 units cryoprecipitate were transfused. Patient was observed in obstetric ICU.

On postoperative day 3, patient had fever episodes, tachycardia and fluctuating blood pressure ranges from 150/100 mmHg-180/100 mmHg. After stabilization, Patient developed postpartum psychosis on postoperative day 10. Psychiatrist opinion was sought for complaints of aggressive behaviour, restlessness and altered mood changes. She was prescribed with antipsychotics-haloperidol (5 mg BD) and chlorpromazine (25 mg OD).

On postoperative day 20, she developed altered behaviours such as not responding to external stimuli, staying still, lack of speech, tremors, fever, rigidity, sweating. Psychiatrist review was sought and evaluated further. She had elevated levels of creatine phosphokinase (CPK) and leucocytosis confirming the diagnosis of NMS and haloperidol was stopped. MRI brain was done and found to be normal. Bromocriptine and lorazepam were started and supportive care was also given. Later, she improved symptomatically. Prompt recovery was achieved with the use of bromocriptine and she was discharged on postoperative day 34.

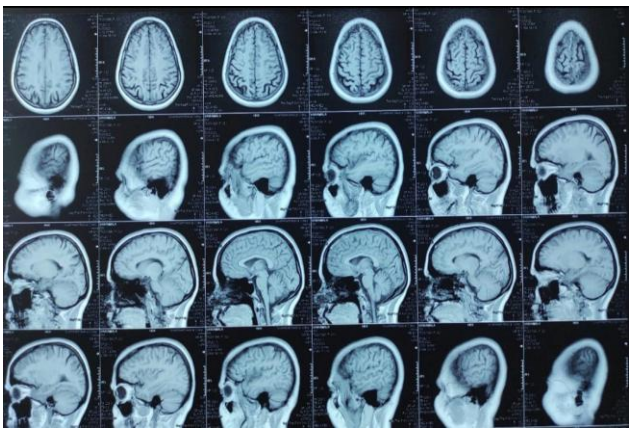

Figure 1: MRI brain imaging of the patient-normal.

DISCUSSION

The incidence of NMS ranges from 0.02 to 3% in patients using neuroleptic drugs.[5] It is a rare, potential life-threatening emergency condition in psychiatry and cause fatal complication among people using neuroleptics. The usage of neuroleptic drugs in pregnancy, efficiency, adverse effects evaluated by various studies. The details of the NMS incidence and its clinical manifestations in pregnancy are scarce in literature.

The pathogenesis of NMS includes central dopamine blockade due to usage of dopamine antagonist, withdrawal of dopamine agonist. This in turn causes hyperthermia due to dopamine depletion in hypothalamus and muscle rigidity, autonomic dysfunction due to dopamine depletion in corpus striatum and altered sensorium due to dopamine depletion in prefrontal cortex.[6] The above mechanism cannot explain all symptoms because hypothalamus thermoregulation also includes serotoninergic, noradrenergic, cholinergic pathways. Others like the toxicity effect of antipsychotic drugs on musculoskeletal fibers, genetic predisposition, reduced acetylcholine, altered GABA levels, dopamine receptor polymorphism, raised serotonin might also play role in NMS pathogenesis.[7]

Diagnosis of NMS requires presence of three major criteria and two minor criteria as per the diagnostic and statistical manual of mental disorders, 5th edition.[1] The major criteria include exposure to dopamine blockade agents, fever, muscle rigidity, diaphoresis. The minor criteria include altered sensorium, motor symptoms like tremors, dysphagia, dysarthria, dystonia, autonomic disturbances like incontinence, tachycardia, sialorrhea, mutism, leucocytosis, elevated creatine phosphokinase, exclusion of other causes like infection, substance abuse, neurological conditions.[1] Our case had fever, muscle rigidity, mutism, sweating, tremors following haloperidol intake. Investigation also revealed leucocytosis, raised creatine phosphokinase levels. Other laboratory parameters like elevated SGOT, SGPT, LDH, low calcium and magnesium levels in serum, elevated potassium, phosphate, uric acid levels, acidosis, proteinuria, myoglobinuria can also be noted.

According to Berardi et al the risk factors of NMS include acute catatonia, agitation, rapid raise of dose or recent neuroleptics intake, parenteral administration of neuroleptics, withdrawal of anti-Parkinson medication, switch from one psychiatric drug to others.[8]

Differential diagnosis of NMS as per Caroff et al includes malignant hyperthermia, malignant catatonia, serotonin syndrome, meningitis, encephalitis, hydrocephalus, seizures, drug intoxication like cocaine, amphetamine, lithium, pheochromocytoma, thyrotoxicosis, tetanus, porphyria, heat stroke.[9]

The treatment options of NMS include stoppage of causative agents and adequate supportive care. The pharmacotherapy options available as per Pileggi et al based on severity by using rigidity, catatonia, confusion, temperature, pulse rate. As per this study mild cases treated with benzodiazepine, moderate cases with bromocriptine or amantadine, severe cases with dantrolene plus above drugs.[10] Bromocriptine and amantadine act as dopamine agonists, lorazepam and diazepam are used due to muscle relaxing action and alteration of GABA action.[11] Dantrolene act as peripheral skeletal muscle relaxant by blocking ryanodine receptor and always used with bromocriptine.[12] As per Sakkas et al the supportive care includes cardiorespiratory stability, adequate hydration, prevention of deep vein thrombosis, maintaining blood pressure and fever.[11] In cases not responding to pharmacotherapy and supportive care electroconvulsive therapy can also be tried.[13] Our case was treated with bromocriptine and supportive care and stoppage of haloperidol.

Prognosis varies depending on the presence of complications like rhabdomyolysis, renal failure, sepsis, aspiration pneumonia, pulmonary embolism with mortality ranges from 5-20%. As per A Lappa et al most of the cases resolve within two weeks.[14]

CONCLUSION

The better understanding of etiology, clinical features of NMS in pregnancy is advisable so that early recognition and treatment is prompted to prevent further complications and improvise the cure rate and mortality. The typical presentation of NMS in pregnancy should be learned due to vast differential diagnosis of NMS in pregnancy and strict supportive care and careful laboratory investigations monitoring will allow early recognition and immediate treatment to ensure safety of pregnant women with psychosis.

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