Case Report

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A Rare Case of Complicated Neuroleptic Malignant Syndrome with Rhabdomyolysis and Acute Kidney Injury

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Abstract

A 38 years old female, a known case of MDP/Schizophrenia, was brought to ED with 5 days h/o high fever, tightness of whole body, altered mental status, reduced urine output, inability to eat and speak, following an intake of an atypical antipsychotic Amisulpiride 100mg over period of 2-3 days prior to symptoms. With the history, physical examination and investigations, a diagnosis of neuroleptic malignant syndrome (NMS) with rhabdomyolysis and acute kidney injury (AKI) was made and supportive treatment started with hydration, dopamine agonism, anticholinergic drugs and urine alkalinization. She started improving after 1 week of aggressive treatment and was discharged in stable condition after 3 weeks.

Keywords: Neuroleptic Malignant Syndrome; Manic Depressive Psychosis; MDP; Schizophrenia; Muscle Rigidity; Rhabdomyolysis; Acute Kidney Injury; Kidney Failure; Amisulpiride; Antipsychotic; Neuroleptic; Idiosyncratic; Dopamine; Dopaminergic; Prolonged QTc; Urine Alkalinization; Creatinine Phosphor Kinase; CPK.

Introduction

Neuroleptic Malignant Syndrome is a life-threatening idiosyncratic reaction to neuroleptic antipsychotic drugs [2] like typical antipsychotics such as chlorpromazine, haloperidol and atypical antipsychotics such as olanzapine, risperidone, aripiprazole, amisulpiride.

The reported incidence of NMS is around 0.02-3.0% in patients taking antipsychotic medications [4].

This is characterized by high fever, altered mental status, muscle rigidity, autonomic instability which typically occurs shortly after starting of neuroleptic drugs or alteration of these medications.

There is more risk with typical antipsychotics than with atypical antipsychotics.

This can also develop when dopaminergic drugs like levodopa is abruptly reduced or stopped [3].

Drugs with anti-dopaminergic activity like metoclopromide can also induce NMS.

In short, NMS occurs with reduced dopaminergic activity, either from withdrawal of dopaminergic drugs or from blockade of dopaminergic receptors.

Neuroleptic drugs or antipsychotic drugs are commonly used for schizophrenia and Manic Depressive Psychosis (MDP).

Dopamine, a neurotransmitter responsible for mood cycling, is found to be high during manic episode of MDP and psychosis.

The neuroleptic drugs act by blocking dopaminergic D2 receptors in hypothalamus, nigrostriatal pathways, spinal cord.

If the D2 receptor antagonism is in excess, as compared to dopamine activity, NMS can develop.

Hypothalamic D2 receptor antagonism results in elevated temperature set point which leads to hyperthermia and alteration of heat-discipating mechanisms like sweating, cutaneous vasodilatation [8].

Nigrostriatal D2 receptor blockade results in muscular rigidity.

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Spinal cord D2 receptor antagonism leads to muscle rigidity and tremors via extrapyramidal pathways.

The usual onset of symptoms of NMS is after 4-14 days, majority of cases occur within 10 days after initiation of the neuroleptic drugs. However NMS may occur even after months of the therapy.

Once symptoms start, they progress very rapidly and reaches its peak as early as 3-4 days [1].

In severe cases, NMS can be complicated by rhabdomyolysis, hyperkalemia, kidney failure and seizures [2] after which prognosis becomes very poor.

No single test is confirmatory for NMS.

This is diagnosed clinically which requires high degree of suspicion.

Treatment is mainly supportive and to prevent complications like rhabdomyolysis and renal failure.

Once complications develop, there is higher risks of mortality.

That is why it is of utmost importance to diagnose it early before the complications develop.

Case Study

A 38 years old female who was a known case of schizophrenia and MDP presented to ED with high fever, tightness of whole body, altered mental status, reduced urine output, inability to eat and speak since 5 days with progressively worsening symptoms.

Her attendants gave a h/o new drug intake called Amisulpiride since 2-3 days for her MDP.

She did not have cough, vomiting, altered bowel movement, abdominal pain, seizures, LOC.

She did not have h/o any other drug intake.

Physical examination, revealed she was drowsy and occasionally responding to verbal commands with vacant stare.

She was immediately taken to monitored bed and vitals taken.

Her pulse rate was 132/min, regular; her BP was 100/60 mmHg and was tachypneic with RR 30/min and her body temperature was 103 degree F.

Her oxygen saturation was 80% at room air and random blood sugar was 220 mg/dl.

She was started on oxygen @10LPM via facemask afterwhich saturation improved to 96%.

Her ECG showed sinus tachycardia with prolonged QTc.

Her neurological examination revealed that she was stuperous, very occasionally responding to verbal commands, increased muscle tone, brisk DTR, occasionally responding to painful stimulus and B/L plantars flexors.

Her respiratory, cardiovascular and per abdominal systemic examinations were within normal limits.

Arterial blood gas analysis showed pH = 7.40, PO2 = 56mmHg, PCO2 = 27.5 mmHg, Lactate = 2.8mmol/L, Na = 162mmol/L, K = 3.5mmol/L, Ca = 0.97.

Chest X-ray showed right lower lobe consolidation.

She was given IV paracetamol 1gm, IV normal saline 2L, IV Rabeprazole 20mg, IV Ondansetron 8mg.

Foley's catheter was inserted for urine output monitoring and urine was found to be very dark in colour and her urine dipstick showed blood +++, protein ++, specific gravity 1.030.

In view of above findings, IV fluids were started with Dextrose 10% 500ml +Sodabicarb 8.4% 200ml @ 150ml/hr to alkalinize the urine.

Ryle's tube was inserted and oral medications were given through RT. She was also started on Bomocriptine 5mg IV stat and 2.5mg PO TDS and Trihexyphenidyl 2mg PO TDS.

She was also started on antibiotics Tazact 1.125gm (piperacillin+tazobactum) in view of her pneumonia and later clarithromycin.

Neurology, Psychiatry, Pulmonology and Nephrology consultations were requested and the patient was shifted to ICU after 3 hrs of aggressive management in the ER.

Course in the Hospital and Outcome

The diagnosis of complicated Neuroleptic Malignant Syndrome with rhabdomyolysis and acute kidney injury was made.

As per Hynes and Vickar [4] scoring system, she could be classified severe NMS.

With aggressive treatment with IV fluids, urine alkalinization, paracetamol and trihexyphenidyl, bromocriptine to restore the dopaminergic tone and other supportive treatment, patient started improving after 24 hrs though gradually.

Her MRI brain plain showed no significant abdnormality.

Her blood reports showed very high CPK levels of 11099 U/L, urea = 92, creatinine = 2.47, mildly raised liver enzymes.

Her kidney functions improved gradually and she started responding to verbal commands after 7-10 days.

Her body temperature and muscle rigidity improved gradually after 24-48 hrs of treatment.

Her CPK levels reduced from 11099 to 6700 to 3790 to 1345 to 941 to 279 over a period of 1 week since admission.

She was started on high protein diet parenterally and on active and passive physiotherapy.

Her sensorium started improving gradually after 10 days of admission.

Subsequently she was shifted to ward after 10 days of ICU stay and was discharged in stable condition after 2 weeks of hospitalization with advice to take Tab Amantadine 100mg BDX1 week, Tab Trihexyphenidyl 2mg OD X 3 days, Tab Valproate 200mg BD, Tab Cefixime 200mg BDX5 days.

She was followed up after 1 week of discharge and was found to be stable with normal mentation.

Discussion and Therapeutic Considerations

This case report illustrates 38 yrs old female with complicated NMS induced by Amisulpiride, an atypical antipsychotic medication.

As discussed above, NMS is more common with traditional antipsychoitics and much less common with newer atypical antipsychotics like Amisulpiride.

Amisulpiride [5] acts by reducing signaling via dopamine D2 receptors by blocking the pre-synaptic D2 receptors. These presynaptic receptors regulate the release of dopamine into the synapse; so by blocking them, amisulpiride increases the dopamine concentration in the synapse. The increased dopamine in the synapse then acts on D1 receptors to control the depressive symptoms and the negative symptoms of schizophrenia.

However in some patients, reduced dopamine activity can lead to NMS as seen in our patient.

The mainstay of treatment is to stop the offending drug.

Bromocriptine [6] is a potent agonist at D2 receptors which counteracts the action of antipsychotic Amisulpiride.

When Bromocriptine and other supportive measures were started in our patient, she showed good and gradual improvement.

Trihexyphenidyl [7] is a synthetic antispasmodic which exerts direct inhibitory effect on parasympathetic nervous system and also exert relaxing effect on smooth muscles.

It was already late when she presented to our ED as she already had developed complications like rhabdomyolysis and kidney failure.

However with aggressive treatment, she improved and was discharged in a stable condition.

Diagnosis requires a high degree of suspicion with proper history and examination and correlating with laboratory parameters.

Conclusion

NMS when sets in, progresses very rapidly and reaches its peak in 2-3 days. Complications can develop within 1 week if not treated aggressively.

It is therefore very important to diagnose it early and reverse the disease process and to prevent its complications.

Although the usual onset of NMS is between 4-14 days but it can occur within 2-3 days of the initiation of neuroleptic medications as seen in our case.

Moreover small doses of neuroleptics can also cause NMS as in our case who ingested only around 100mg of amisulpiride over 2-3 days period.

Inspite of lower risk with atypical antipsychotics, life-threatening NMS can still develop and therefore patient education is of utmost importance to those who are taking antipsychotic medications. Emergency physicians and General physicians where the patient usually presents, must be made aware of signs and symptoms and the management of NMS.

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