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Research Paper

Risperidone Induced Neuroleptic Malignant Syndrome: a Case Report and Discussion

Pharmacology

KEYWORDS : atypical antipsychotics, neuroleptic malignant syndrome (NMS), risperidone

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ABSTRACT

Objective: Neuroleptic malignant syndrome (NMS) is an emergent, rare but a life threatening effect of the antipsychotic or neuroleptic medication. The syndrome is characterized by motor, behavioural, autonomic and laboratory abnormalities. Thus evaluating the side effects is necessary while prescribing such medications.

Method: A case of a sixteen year old boy who was brought to the casualty with complaints of fever, stiffness in the neck and altered sensorium and history of intake of antipsychotic medication risperidone five days earlier.

Results: Clinical examination revealed classical features of NMS and investigation confirmed the diagnosis. The patient was adequately treated with bromocriptine and dantrolene and discharged from the hospital

Conclusion: Our case suggests that clinicians need to be aware that NMS can be caused by risperidone despite the markedly lower incidence of extra-pyramidal side effects. Therefore a proper medical history, proper follow up and investigations are necessary while prescribing such drugs.

BACKGROUND

Neuroleptic Malignant Syndrome (NMS) is an idiosyncratic adverse effect of the antipsychotic medication and appears due to almost all typical antipsychotics (neuroleptics).[1] However numerous cases of apparent NMS related to atypical neuroleptics have also been reported.[2] It is independent of the dosage and the duration of therapy.[3] The main clinical findings are hyperthermia, altered mental state, hemodynamic deregulation, autonomic instability, elevated serum creatinine kinase levels, and muscle rigidity.[4] In recent years numerous cases of NMS have been reported with Risperidone, a benzisoxazole–derivative with high serotonin ($5\text{-}HT_2$) receptor blockade and dose related D_2 receptor blockade. Intensive care therapy is required due to life threatening consequences. The approach to management is withdrawal of the causative agent and supportive care .The incidence of NMS varies between 0.02-3% of patients on neuroleptic therapy.[5]

CASE REPORT

A sixteen year old boy presented in the casualty with complaints of high grade fever, disorientation and stiffness of neck and history of intake of risperidone five days earlier. It was prescribed by a local physician to whom he had presented with diffuse non-radiating dull headache. The boy was a known case of migraine with a familial tendency. The patient was relieved of symptoms next day.

Three days after that there was an onset of high grade fever with chills and rigors associated with palpitations, altered sensorium with fecal and urinary incontinence. This was followed by **s**udden deterioration of his condition in the next five days in which developed hyperthermia, altered sensorium, no adequate control over the bowels and bladder and neck rigidity. Thus infectious cause was ruled out before investigating to confirm the diagnosis of NMS as adverse drug reaction to risperidone.

CLINICAL FINDINGS

Upon admission to the hospital the clinical examination of the boy revealed that he was hyperthermic (103ºF), tachycardic (pulse rate, 140 beats per minute), hypotensive (Blood pressure 100/70 mm of Hg) and tachypneic (Respiratory rate: 28 breaths / minute). Glasgow Coma scale showed that the patient was disoriented. Eye movements were conjugate and pupils were equal and reactive to light. On neurological examination muscle rigidity was present (lead pipe) with autonomic instability. Deep tendon reflexes were brisk and symmetrical jaw jerk was normal. The remainder of the physical examination was normal

LABORATORY FINDINGS

- HAEMATOLOGICAL INVESTIGATION REVEALED **MARKED LEUCOCYTOSIS (TLC 14,700, N75, L18, MO2, E01**)
- **CPKMB – 7860**
- URINE CULTURE & SENSITIVITY SHOWED NO GROWTH.
- ANTIBODIES FOR SALMONELLA WERE DETECTED NEGATIVE
- BLOOD UREA –110
- SERUM CREATININE –1.2
- NA^+-147
- K^+ -3.4
- ABSOLUTE BLOOD GAS ANALYSIS WAS NORMAL
- THERE WAS PRESENCE **MYOGLOBULIN IN URINE**
- FASTING BLOOD SUGAR WAS –108MG/DL

MANAGEMENT

Patient was prescribed plenty of fluids for hydration. He was started on Injection gramocef 1.2 gm b.d. Injection midas was also started. He was given bromocripine 2.5mg and dantrolene 100 mg b.d. for one week. Slowly his symptoms began to improve. Along with he was also prescribed torsemide

DISCUSSION

NMS is a potentially life threatening complication of narcoleptics therapy with a mortality rate of 11.6%.[6] Cases have been reported in all the age groups but men with younger age are more predisposed. Factors that increase the risk of developing NMS are high doses of neuroleptic drugs, parenteral administration, depot preparations, parallel treatment with lithium or other psychotropic drugs, alcohol abuse, addiction and other acute diseases.[7] Yacoub et al designed an NMS rating scale to aid recognition and quantify the severity and clinical course of NMS once a diagnosis has been established.[8] The most important laboratory parameter is high CPK (> 1000 IU/L).[9] Leukocytosis is a consistent finding, and there are mild elevations in LDH and transaminases, electrolyte imbalance and myoglobinemia with the possibility of myoglobinuric acute renal failure. In differential diagnosis, a physician should think of neurological diseases such as infections of the central nervous system, epilepsy or acute intracranial process, acute intoxication, heat stroke and tetanus. Diagnosis is clinically made. Treatment consists of neuroleptic therapy discontinuation and further supportive therapy. Benzodiazepines have been recommended for managing agitation and reversing catatonic symptoms of NMS.[10] Of the specific measures, dantrolene, bromocriptine and amantadine can be used. Clinical studies on the use of these drugs have not been implemented, and recommendations are based on the cases described in the literature.[11] In most cases applied therapy leads to

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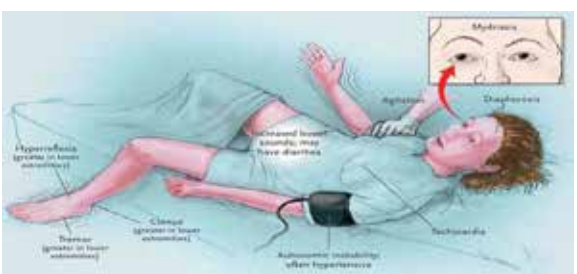
a regression of the disease within 14 days of the onset of symptoms. Re-initiation of neuroleptic therapy is not contraindicated in recovered patients, but great caution is necessary

Table 1: SALIENT FEATURES OF FRANCIS-YACOUB NMS RATING SCALE

[Not scored] Proper Pharmacological Setting	Catatonia	Dehydration	Serum iron level
Extrapyramidal features: rigidity of extremities	Body temperature	Incontinence	Myoglobinemia/ myoglobinuria
Extrapyramidal features: pharyngeal/ swallowing	Systolic blood pressure		Acid base balance
Extrapyramidal features: pharyngeal/speech	Pulse	Serum CPK	
Extrapyramidal features: tremors at rest	Diaphoresis	WBC	
Consciousness/ mental status change	Respiration	Serum transaminase, ASY	Total score

IMAGE DEPICTING THE CLINICAL FEATURES OF NMS



CONCLUSION

Clinicians need to be aware that NMS can occur with risperidone despite markedly lower incidence of extrapyramidal symptoms .Therefore caution must be exercised while prescribing atypical agents and high index of NMS should be maintained. In our case a positive clinical outcome resulted by using supportive therapeutic measures (fluid and electrolyte replacement, antipyretics, support for cardiac respirator and renal functions) and early initiation of the pharmacotherapy consisting of bromocriptine and dantrolene. Due to relatively rare incidence of the disease and insufficient literature (lack of clinical studies and the lack of clear treatment guidelines), we should emphasize the necessity for early diagnosis to prevent further complications and the importance of placing timely doubt in high-risk patients. Regarding the possibility of regression and the need for further treatment of the underlying disease, to reduce the risk of relapse we emphasize the need to follow the general recommendations summarized in Table 2

Table 2: GENERALIZED GUIDELINES ON RESTARTING NEUROLEPTIC THERAPY

Wait at least 2 weeks before resuming therapy, longer if any clinical residua exist
Use lower rather than higher potency agents
Start with low doses and titrate upward slowly
Avoid concomitant antipsychotics if NMS has occurred
Avoid dehydration and carefully monitor for symptoms of NMS

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