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Original Article

High creatinine kinase levels in Olanzepine induced neuroleptic malignant syndrome: A case report

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ABSTRACT

Neuroleptic malignant syndrome is an uncommon complication of antipsychotic drugs. Along with the signs and symptoms like psychosis, muscular rigidity, fever and altered mental status, the biochemical parameters especially elevated creatinine kinase levels play an important role in establishing the diagnosis of the syndrome. Here we report a case involving an eighteen-year-old boy with newly diagnosed bipolar mood disorder who presented with neuroleptic malignant syndrome after Olanzepine was started. With nonspecific psychiatric clinical symptoms and deteriorating condition, the diagnosis was becoming doubtful. Diagnosis was confirmed by severely elevated Creatinine kinase activity along with other biochemical parameters, thus ascertaining the role of clinical laboratories in medicine.

1. Introduction

Neuroleptics were first reported to have caused a syndrome of severe illness - neuroleptic malignant syndrome (NMS) by Delay and colleagues [1] in 1960. It is a rare, idiosyncratic reaction to a neuroleptic medication, characterized by fever, muscular rigidity, movement disorders, altered mental status and can be fatal.

Abnormal laboratory tests include leukocytosis, elevated CK and liver enzymes. Presence of fever, muscular rigidity and elevated CK are considered the major diagnostic criteria, while tachycardia, tachypnea, hypertension, diaphoresis, altered sensorium, and leukocytosis are minor criteria for definitive diagnosis [2]. The presence of all three major or two major and four minor manifestations indicate a high probability of NMS [2].

2. Case report

An eighteen-year-old boy, suffering from psychotic illness with abusive and violent behavior, was brought to tertiary care hospital with complaints of altered mental status for past 20 days. He was on Olanzepine 15 mg/day before admission to hospital. He showed increased psychomotor activity, increased self esteem and delusion of grandeur. He had no history of fever, pain, at the time of admission. He was diagnosed to be suffering from Bipolar Mood Disorder. After hospitalization to control his psychotic condition high potency Olanzepine 15mg was continued in divided doses. After two days of admission ie 22 days after intake of Olanzepine, the patient became abruptly somnolent with body temperature reaching 39.7 º C and severe muscle rigidity in both upper and lower extremities. He showed fluctuation of blood pressure and pulse. Laboratory data revealed elevation of white blood cells to 13500 K/L, creatine phosphokinase to 6537 U/L (normal <174 U/L) with normal CKMB, and mild elevation of serum alanine and aspartate aminotransferase (SGOT was 165 U/L, SGPT 28 U/L) and LDH was 1452 U/L. Slight increases in blood urea, and serum creatinine were seen. Thyroid function tests were normal. Mental state remained altered.

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A presumptive diagnosis of neuroleptic malignant syndrome was made. Olanzapine was immediately discontinued and supportive care was initiated. He was treated with Benzhexol 4 mg and lorazepam 4-6 mg /day was given in divided doses as needed for behavioral agitation along with a fixed 0.5 mg intravenous push twice daily. Tablet phenargen 50 mg was also added. Fever and muscular rigidity resolved in 24 hours. There was definite improvement in his condition after 2 days. Fever had begun to decrease. Serum CPK and LDH concentrations started falling after the third day. Major symptoms disappeared 5 days after the neuroleptic drug was n stopped and the patient was discharged from the hospital.

3.Discussion

In present case, the main drug responsible for development of NMS was Olanzepine. NMS was precipitated because of dehydration. Diagnosis was confirmed by laboratory tests like elevated CK total, LDH and lecocytosis. The frequency of NMS ranges from 0.07% to 2.2% among patients receiving neuroleptic medications and mortality is 10%–30% [3]. NMS is a hypodopaminergic state of the brain. It has now been reported to occur with all drugs that affect the central dopaminergic system (including dopamine agonists and levodopa). It can be precipitated by all antipsychotic drugs, although potent neuroleptics (eg, haloperidol, fluphenazine) are more frequently associated with NMS [4]. Other agents that can cause NMS by blocking central dopamine pathways are: prochlorperazine, promethazine, clozapine, and risperidone, metoclopramide , amoxapine, and lithium [5]. Neuroleptic malignant syndrome has been reported most frequently in patients taking haloperidol and chlorpromazine. The treatment of NMS includes discontinuation of contributing drugs and supportive therapy, but specific treatment with dantrolene, bromocriptine, nondepolarizing neuromuscular paralysis and benzodiazepines, among other such agents, has been reported only anecdotally.

Both physiologic and environmental factors have been suggested to predispose patients to the development of neuroleptic malignant syndrome, dehydration[6] and hot and humid conditions, agitation, and exhaustion being most common . Also some evidence exists that iron deficiency is a risk factor in a number of movement disorders besides neuroleptic malignant syndrome, such as akathisia and nocturnal myoclonus [7].

Pathophysiology : Neuroleptics cause dopamine receptor blockade at the striatum and hypothalamus, which account for motor manifestations and impaired heat dissipating mechanisms. The most widely accepted mechanism by which antipsychotics cause neuroleptic malignant syndrome is that of dopamine D2 receptor antagonism. Central D2 receptor blockade in the hypothalamus, nigrostriatal pathways, and spinal cord leads to increased muscle rigidity and tremor via extrapyramidal pathways. Hypothalamic D2 receptor blockade results in an elevated temperature set point and impairment of heat-dissipating mechanisms. Peripherally, antipsychotics lead to increased calcium release from the sarcoplasmic reticulum, resulting in increased contractility, which can contribute to hyperthermia, rigidity, and muscle cell breakdown. Dopamine plays a major role in the hypothalamic regulation of temperature. Dehydration with the concomitant use of neuroleptics has been implicated as a risk factor for the syndrome, because the decreased blood volume induces peripheral vasoconstriction and impairs heat dissipation. Role of CK in diagnosing NMS has been very imporatnt. It has been seen that clinical manifestations of NMS with more severe rigidity lead to more profound creatine kinase (CK) elevation. In NMS, CK is typically more than 1000 IU/L and can be as high as 100,000 IU/L [3,8,9]. In absence of rigidity, CK levels might not increase, particularly early in the onset of the syndrome. Mild to moderate elevation of CK, is not specific for NMS and is often seen in patients with acute and chronic psychosis due to intramuscular injections and physical restraints, and sometimes without specific explanation [8]. CK levels greater than 1000 IU/L, however, have been suggested to be more specific for NMS, and the degree of CK elevation correlates with disease severity and prognosis [10].

NMS can often be prevented by ensuring that patients receiving neuroleptics are well hydrated. Treatment of NMS includes dantrolene sodium and Bromocriptine (in refractory cases - electroconvulsive therapy), in addition to withdrawal of offending drug. Alternatives include levodopa-carbidopa, amantadine, anticholinergic agents, and calcium channel blockers.

In the present case the offending drug i.e. Olanzepine was stopped immediately as soon as NMS was suspected clinically. Patient was treated with anticholinergic Bezhexol along with supportive treatment such as fever reduction, hydration and maintenance of nutrition. CK, LDH levels reduced dramatically over a few days and patient was discharged.

4.Conclusion

Here we intend to support the fact that although CK elevation is not a diagnostic laboratory test for NMS but elevated CK levels during psychosis do predicts future NMS risk. CK elevation helps support the diagosis of NMS if correlated with other symptoms.

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