Neuroleptic malignant syndrome due to risperidone misdiagnosed as status epilepticus

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Abstract

Neuroleptic malignant syndrome (NMS) is a rare but potentially fatal disease characterized by fever, muscle rigidity, delirium and autonomic instability. Here we report a child, with NMS due to the risperidone misdiagnosed as status epilepticus. Nine year old boy, who had been under high dose risperidone treatment for 8 weeks, admitted to the emergency room because of the contractions (evaluated as status epilepticus) persisting for 7 hours. Since there was neuroleptic treatment in the past medical history and, unconsciousness, muscular rigidity, diaphoresis, hypertermia and, hypotension in physical examination, leucocytosis and elevated creatininphosphokinase levels in laboratory tests, the patient was evaluated as NMS and discharged without any complications. We reported this case to point out that; NMS may be misdiagnosed as status epilepticus in children when EEG monitoring is unavailable. When a child admitted to the emergency room because of suspicious convulsion neuroleptic drug use must surely be asked.

Introduction

Neuroleptic malignant syndrome (NMS) is a rare but potentially fatal disease characterized by fever, muscular rigidity, delirium and autonomic instability.¹ Yearly prevalence of the disease in patients under neuroleptic treatment ranges between 0.02% and 2.4%. Mortality rate of the patients without specific treatment is approximately 21%.^{2,3} Mortality rate may be higher in patients with misdiagnosis like our patient. The classic presentation of this syndrome has been most commonly associated with the typical neuroleptic drugs such as haloperidol.²

Risperidone is a new atypical neuroleptic agent. 5-HT_{2A} antagonism partially protects against D₂ antagonist-induced-neurologic side effects and, may improve negative symptoms and cognitive functioning via modulation of mesocortical DA activity. In addition, blockade

of adrenoceptors may further increase prefrontal cortical activity and could enhance antipsychotic efficacy by modulations of mesolimbic DA activity. Unlike other atypical agents, risperidone does not differ from conventional agents in its dissociation contrast for D₂ receptor; this feature perhaps accounts for the risk of EPS (extrapyramidal side effects) at high doses.⁴ However in large multicentre studies it was shown that risperidone had similar side effects like other typical neuroleptic agents.⁵ As far as we know the number of cases due to risperidone treatment in the literature is limited and most of the reported cases are adults. In most of these cases risperidone induces NMS after two weeks of treatment.⁶

Here we report a child with NMS due to risperidone treatment who was misdiagnosed as status epilepticus. The patient reported here met DSM-IV criteria for NMS.¹

Case Report

Nine years old boy was admitted to the emergency department because of the convulsions persisting for seven hours. He had attention deficit hyperactivity disorder and he had been under risperidone (2×2 mg/day) treatment orally for 8 weeks because of moderate mental retardation and psychological disorder. Risperidone dose was four times more than usually recommended pediatric dosage. Additionally the patient had been suffering vomiting, tremor and fever for two weeks.

Physical examination in the emergency room revealed a body temperature of 39°C, a respiratory rate of 10 breaths/min, and, a pulse rate of 158 beats/min. Blood pressure was too low that it couldn't be measured initially. The patient's general appearance was lethargic. There was muscular rigidity, tremor and, diaphoresis. He was dehydrated. Heart sounds were rhythmic and tachycardic. His respiration was weak and respiratory sounds were normal. Bilateral pupil reflexes were positive. Deep tendon reflexes were brisk and bilateral Babinski reflexes were positive. There were no meningeal irritation signs.

Initial laboratory analysis revealed a white blood cell count of 21580 cells/mm³, with 2% band neutrophils, 62% neutrophils, 30% lymphocytes, 6% monocytes. Serum electrolytes were in normal ranges included a sodium level of 136 mEq/L; potassium, 5.4 mEq/L; chloride 105 mEq/L and, calcium 8.2 mEq/L. The blood glucose was 316 mg/dl. Initial venous blood gases showed a pH of 7.04; carbon dioxide tension 95 mmHg; bicarbonate 26 mEq/L and, base excess, -5.8 mmol/L. The serum creatinine phosphokinase (CPK) level was 1658 U/L. Blood, urine and stool cultures were negative. Urinalysis, chest radiograph, cranial CT and

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EEG were unremarkable.

Although the tremors accompany muscular rigidity were mimicking convulsions and the patient was admitted with status epilepticus diagnosis, the patient was not diagnosed as status epilepticus because there were neuroleptic treatment in his medical history, muscular rigidity, diaphoresis, hypertermia and hypotension in physical examination, leucocytosis and elevated CPK levels in laboratory tests. By the help of the sign and symptoms above, the patient was diagnosed as NMS by pediatric critical care intensivist, pediatric neurologist and pediatric psychiatrist. NMS diagnosis was confirmed with EEG and risperidone treatment was ceased.

In the emergency department the patient was intubated because of respiratory failure. Then he was admitted to the pediatric intensive care unit and mechanically ventilated. Intravenous diazepam infusion (0.3 mg/kg hour) and carbidopa/levodopa were given for NMS treatment. In the first day of the admission to the intensive care unit the patient had hyperthermia resistant to the antipyretic treatment and his blood pressure was unstable. Central venous catheter was placed and hemodynamic parameters of the patient were regulated in normal ranges. In the second day of the admission to the intensive care unit the patient was extubated. All the clinical and laboratory signs and symptoms of the patient improved except elevated creatinin phosphokinase levels which turned back to normal values on the fifth day of the admission. Then he was discharged from the hospital without complications.

Discussion

Here we report a patient with NMS who was misdiagnosed as status epilepticus before admission to our hospital. Our patient was diagnosed as NMS due to presence of mentioned criteria of NMS.¹ Mortality rate of NMS in the patients without specific treatment is approximately 21%.^{2,3} Mortality rate may be higher in patients with misdiagnosis. NMS signs and symptoms may be difficult to differentiate from status epilepticus by inexperienced physicians when EEG monitoring is unavailable. As mentioned before, our patient was diagnosed as status epilepticus before he was admitted to our hospital and he had been tried to be treated as status epilepticus at the beginning.

The clinical signs and symptoms of our patient emerged in the second week of the risperidone treatment. As it was pointed out before NMS may occur in anytime during neuroleptic treatment.⁶

First step of the NMS treatment is to cease antipsychotic drugs. After we diagnosed NMS we discontinued the risperidone treatment. Cooler blankets and antipyretics for hyperthermia and supportive treatment including fluid electrolyte therapy must be supplied. In medical treatment in order to reduce muscular rigidity dopamine agonists are used. Similarly we used dopamine agonists for our patient. Additionally dantrolene may be used alone or

with dopamine.

Previously it was thought that NMS was only associated with the use of classical neuroleptics. However there are some NMS cases due to atypical neuroleptics in the literature.⁷ As far as we know in the literature only two NMS cases due to risperidone treatment were reported in children.^{8,9} We think that atypical neuroleptics will be extensively used in children in the future and the clinicians especially the pediatricians must be familiar to NMS and its differential diagnosis.

We report this case in order to underline that neuroleptic malignant syndrome may be misdiagnosed as status epilepticus in children when EEG monitoring is unavailable. When a child is admitted to the emergency department because of unconsciousness muscular rigidity, diaphoresis, hypertermia and hypotension; neuroleptic drug use must surely be asked. Furthermore this is the third neuroleptic malignant syndrome case due to risperidone treatment in children. Early diagnosis and proper treatment of NMS may decrease the mortality rates significantly.

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