**INTRODUCTION**

Neuroleptic malignant syndrome (NMS) is an uncommon clinical picture related with antipsychotic use; however, it is one that cannot be predicted and may be lethal.¹ Its typical symptoms and signs may be seen as fever, muscular rigidity, altered consciousness (confusion, stupor, coma), disorders pertaining to the autonomous nervous system (hypertension, tachycardia, tachypnea, sweating, urinary incontinence), and deterioration in various blood values [decrease in serum electrolytes, increase in creatinine phosphokinase (CPK), leukocytosis].² Patients usually encounter a dopamine antagonist within 72 hours of symptoms onset. Common rigidity which usually does not respond to antiparkinson drugs, is an important feature of this disorder. Electroencephalography (EEG) demonstrates a general slowdown, whereas cerebrospinal fluid (CSF) examinations and neuroimaging studies are usually ordinary.³

The incidence rate of NMS ranges between 0.01–0.02%.⁴ Symptoms begin hours-days after starting the drug. It develops within 30 days at the latest in nearly all cases. The average recovery period is 7–10 days in the aftermath of medication discontinuation.⁵ It was reported that the mortality rate was about 10–20% when NMS was not identified.⁶,⁷ Parenteral administration, rapid dose adjustments and higher total drug doses have increased the possibility of this syndrome’s occurrence; however, NMS usually emerges in the therapeutic dose range of antipsychotics.⁸ NMS is more frequently seen with typical antipsychotics as compared with atypical antipsychotics.¹,⁹ Treatment usually consists of discontinuation of the causative agent and supportive treatment under intensive care conditions, supplying intensive hydration therapy and treatment with dantrolene or bromocriptine.¹⁰

**CASE**

The patient discussed herein was tracked in the psychiatric service for diagnostic purposes; this was a short-term case of NMS that developed in the aftermath of multiple antipsychotic use in a patient who had no prior history of antipsychotic treatment in which no rigidity was observed.

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A Neuroleptic Malignant Syndrome Without Rigidity

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Neuroleptic malignant syndrome (NMS) is an uncommon but potentially lethal idiosyncratic reaction which may emerge in the aftermath of the treatments with neuroleptics demonstrating itself with the symptoms of altered consciousness, high fever, impaired autonomic functions, and muscle rigidity. Although various risk factors have been identified for NMS, its etiology is not completely known. The mortality and morbidity related with NMS could be reduced by early diagnosis, interruption of the neuroleptics used within a short period and aggressive treatment. Our case is different from general NMS cases due to lack of rigidity. A NMS case which developed within a short time in the aftermath of multiple antipsychotic use and wherein no rigidity was observed shall be discussed in this case report.

Key Words Neuroleptic malignant syndrome, Muscular rigidity, Antipsychotic agents.
loss of appetite, behavior change, suspicion, thought about being harmed by others, and forgetfulness which had continued for about two months. The patient was admitted to our service for diagnosis and treatment.

On the day of admission to hospital, in his first psychiatric examination his consciousness was clear, the place-time-person orientation was full, but his self-care was poor. He had euthymic mood and his affection was limited. A memory pathology was not considered. His attention was observed as normal. No perceptual pathology was observed. His intelligence seemed normal. He had a circumstantial, sometimes tangential process of thinking. He had delusions of persecution in his thought content. No suicidal thoughts were observed. He was assessed as to have no insight, and a distorted ability to judge and evaluate reality.

No pathology was detected in routine examinations that were requested on the day of admission. The patient was immediately started on quetiapine 200 mg/day because of his active psychotic symptoms. The patient had confusion during his first night of hospitalization, he was agitated and said that he wanted to go home and attempted to jump out of the window. Upon which, the patient was restrained and a zuclopenthixol 50 mg/mL intramuscular (IM) injection was administered to provide sedation for that night. The patient could not be sedated, and thus was given chlorpromazine 75 mg IM, haloperidol 15 mg IM, and clonazepam 2 mg tablets, respectively, at one-hour intervals for 3 hours.

The treatment was reevaluated on the second day of admission, and was arranged as olanzapine 20 mg/day, and a 10-mg haloperidol IM injection was applied due to his agitation. The patient's temperature was 39°C in the morning of the 3rd day. Recurrent oral fever measurements were also detected above 39°C. His systolic blood pressure varied; the systolic blood pressure ranged from 80 to 160 mm Hg. Although he was inclined to sleep, he responded to verbal stimulants. His extrapyramidal symptoms were evaluated using the Extrapyramidal Symptom Rating Scale and no rigidity was detected. According to this scale, his rigidity subscale score was 0. Increases in his biochemical parameters were detected in laboratory investigations. In the follow-up, the patient's aspartate aminotransferase (AST) and creatinine phosphokinase (CPK) were high at 993 U/L and 38247 U/L, respectively, and his white blood cells (WBC) were 12.6 K/μL, normal prothrombin time was INR: 1.22 IU, and his activated partial thromboplastin time (aPTT) was 36.5 sec. Infectious Diseases and Neurology departments were consulted. Cranial computerized tomography (CT), magnetic resonance imaging (MRI), and EEG were within normal limits. Encephalitis, meningitis, and possible neurologic and infectious diseases were excluded.

NMS was diagnosed upon observing altered consciousness (confusion, somnolence), elevation of fever, sweating, blood pressure variability, CPK and AST elevation, and leukocytosis in his examination.

Follow-up of the patient began in the intensive care unit

| Time period               | Medication and dosage                                                                                           | Symptoms                                                                                     |
|---------------------------|----------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| First day of admission    | 18:00–Quetiapine 200 mg tab                                                                                   | Consciousness was clear                                                                      |
|                           | 23:00–Chlorpromazine 50 mg IM                                                                                 | Full place-time-person orientation                                                           |
|                           | 00:00–Haloperidol 10 mg IM+Chlorpromazine 25 mg IM                                                            | Circumstantial, sometimes tangential thinking                                                |
|                           | 01:00–Clonazepam 2 mg tab+Haloperidol 5 mg IM                                                                 | Delusions of persecution                                                                      |
|                           |                                                                                                                | Normal biochemical parameters                                                                |
| Second day of admission   | 13:00–Olanzapine 20 mg tab                                                                                     | Confusion                                                                                     |
|                           | 20:00–Haloperidol 10 mg IM                                                                                    | Agitation                                                                                     |
| Third day of admission    | Antipsychotic medication stopped                                                                              | Circumstantial, sometimes tangential thinking                                                |
|                           | 09:00–Paracetamol 10 mg/mL 100 mL IV+1000 cc isotonic solution IV                                              | Delusions of persecution                                                                      |
|                           | 13:00–Paracetamol 10 mg/mL 100 mL IV                                                                           | Temperature 39°C. Recurrent measurements were all above 39°C                                 |
|                           | 18:00–Paracetamol 10 mg/mL 100 mL IV+500 cc dextrose 5% IV                                                    | Systolic blood pressure ranged from 80 to 160 mm Hg                                          |
|                           | 20:00–Transferred to the intensive care unit                                                                  | Inclination to sleep, he responded to verbal stimulants                                       |
| 4–12th days               | Intensive hydration therapy daily                                                                               | AST: 993 U/L and CPK: 38247 U/L, WBC: 12.6 K/μL, INR: 1.22 IU and APTT: 36.5 sec          |
|                           |                                                                                                                | Cranial CT, MRI, and EEG within normal limits                                                |
|                           |                                                                                                                | Fever, blood pressure, and biochemical parameters (AST, CPK and WBC levels) were at normal levels|
|                           |                                                                                                                | Volatility of consciousness remained                                                        |

**Table 1. The patient’s medication, dose, and symptoms as time progressed**

IM: intramuscular, IV: intravenous, AST: aspartate aminotransferase, CPK: creatinine phosphokinase, WBC: white blood cells, INR: international normalized ratio, APTT: activated partial thromboplastin time, CT: computerized tomography, MRI: magnetic resonance imaging, EEG: electroencephalography
A Neuroleptic Malignant Syndrome Without Rigidity (ICU). The patient’s fever subsided after 8 days of intensive hydration in the ICU and his blood values returned to normal limits. His medication, doses, and symptoms as time progressed are presented in Table 1.

DISCUSSION

According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-IV-TR), NMS is diagnosed upon the existence of two or more of the following findings: fever and muscular rigidity (major findings), sweating, tachycardia, altered or generally elevated arterial tension, elevated white blood cell count, altered consciousness, tremor, urinary-fecal incontinence, and elevated CPK (minor findings).\(^{11}\) Regarding NMS, which is reported under the heading of “drug-induced motion disorders and other...
er side effects of medicines” in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), although it is stated that the symptoms mentioned in DSM-IV-TR have been observed, a diagnosis criterion classification has not been made such as that in DSM-IV-TR.\(^5\)

Patient diagnosed as having NMS according to the DSM-5 and Nierenberg diagnostic criteria, cannot be diagnosed as having NMS according to DSM-IV.\(^3,12\) The arrangement made in DSM-5 for NMS has also been useful from the aspect of helping patients to be diagnosed and treated more easily. DSM-IV-TR, DSM-5, and the Nierenberg diagnostic criteria are presented in Table 2.

The absence of rigidity in spite of high fever and elevated CPK values is a different situation from typical NMS. Although rigidity is a major criterion, patients with NMS who had no rigidity have been described in the literature.\(^13\) It is very difficult to diagnose NMS in patients with no elevation of temperature or muscular rigidity.\(^14\) From this point of view, it is thought that such a case is important in terms of its contribution to the literature.

It was reported that in approximately 10–40% of NMS cases caused by atypical antipsychotics, fever and rigidity were lighter or only one could be found.\(^15\) In the absence of such major symptoms, diagnosis may be delayed due to the inadvertent assessment of deterioration of primary psychotic disorder, extrapyramidal effects of drugs, or delirium associated with neurologic, infectious or other causes.\(^16\) Even if there is no rigidity in line with such cases, it should be emphasized that NMS must be suspected in the presence of other symptoms.

The risk factors for NMS are specified as the initiation of drugs that reduce levels of dopamine, dose increases in such drugs, the use of medications in depot form, multiple drug use, dehydration of the patient, past NMS experience, brain injury or mental retardation in the patient.\(^17\) It was reported that there was limited information on persistent sequelae levels in the aftermath of NMS, the rate of which is between 3.3–10%.\(^18\) Death is often caused by respiratory problems, cardiac arrest or kidney failure, which developing along with muscle destruction. The most important approach to reduce mortality is to promptly diagnose NMS and monitor patients under intensive care settings.\(^19\)

Regarding treatment, first, the drugs being used should be discontinued, the patient’s fever should be lowered, and the provision of hydration is recommended. In addition, initiation of dantrolene, bromocriptine, and benzodiazepine accelerates clinical improvement.\(^1,20\)

Our patient was followed up under intensive care setting and through rigorous hydration therapy without the need for additional medical treatment. The AST, CPK, WBC levels, and fever, which were initially high, returned to normal. However, the volatility of consciousness has continued, although this is rare. NMS is a condition that needs immediate identification and urgent treatment. The mortality rate is very high when not diagnosed or treatment is delayed. Therefore, it should be remembered that NMS may develop in all patients using antipsychotics, it should be diagnosed early, and treatment should be started rapidly.

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