

Neuroleptic Malignant Syndrome During the use of Extended Release Quetiapine: A Case Report

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ÖZET:

Uzatılmış salınımlı ketiapin kullanımında nöroleptik malign sendrom: Olgu sunumu

Nöroleptik malign sendrom (NMS), antipsikotiklerin kullanımı sırasında nadir görülen, potansiyel olarak yaşamı tehdit eden bir durumdur. NMS, dopaminerjik reseptörlerde blokaj gelişmesi ve santral nörotransmitterlerde dengesizlik oluşumu ile karakterize bir sendromdur. Bu sendromda hipertermi, kas rijiditesi, tremor, otonomik disfonksiyon, serum kreatin fosfokinazda yükselme, lökositoz ve bilinç değişiklikleri görülebilir. Bu yazıda, 5 yıldır atipik psikotik bozukluk tanısıyla takip edilen 50 yaşındaki kadın hastada uzatılmış salınımlı ketiapin kullanımı sırasında ortaya çıkan NMS olgusu sunulmuştur.

Anahtar sözcükler: Nöroleptik malign sendrom, ketiapin

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ABSTRACT:

Neuroleptic malignant syndrome during the use of extended release quetiapine: a case report

Neuroleptic malignant syndrome (NMS), is a potentially life-threatening condition which is rarely seen during antipsychotic use. Neuroleptic malignant syndrome is characterized by the imbalance of central neurotransmitters, in which a dopaminergic block is developed. Hyperthermia, muscular rigidity, tremor, autonomic dysfunction, an increase in serum creatine phosphokinase levels, leukocytosis, and altered mental status can be seen in this syndrome. In this study, we present a 50 year old woman with NMS that occurred during the use of extended release quetiapine, who had been diagnosed with atypical psychotic disorder for 5 years.

Key words: Neuroleptic malignant syndrome, quetiapine

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INTRODUCTION

Neuroleptic malignant syndrome (NMS) is rarely seen during use of antipsychotics, but it has a vital importance. Its prevalence is between 0.01 and 3%. When NMS is untreated, its mortality risk is 10% (1,2). Although the etiology of Neuroleptic Malignant Syndrome is not known, it is considered to be idiosyncratic and it has been observed that it develops after use of antipsychotics in many patients. It is thought that a dopaminergic block which is characterized by an imbalance of central neurotransmitters resulting in the development of NMS (2,3). NMS is generally seen in young adult males. Its clinical signs are

characterized by changes in mental state, motor abnormalities (bradykinesia and muscle rigidity), autonomic dysfunction (tension instability, diaphoresis and tachycardia), and hyperthermia (4,5). Laboratory findings such as elevated creatine phosphokinase (CPK), leukocytosis and raised liver enzymes are also found (6). The risk of NMS increases in patients who are dehydrated, have low oral intake, have developed NMS previously, are on high dose or parenteral antipsychotics, have had their antipsychotic dose increased quickly, have a low serum iron level, are agitated, have a high temperature, and are using lithium or anticholinergic or antidepressant drugs (2,5,7,8).

While NMS is generally seen with use of typical antipsychotics, there have been cases reported with atypical antipsychotic use. In the literature, NMS cases have been reported during the use of quetiapine (9,10). Our aim in this case is to emphasize NMS development during use of extended release form of quetiapine.

CASE

A 48-year old female patient was seen in emergency room with complaints of high fever, perspiration, and speech problems, and was hospitalized in the intensive care unit with a pre-diagnosis of meningoencephalitis. In the findings on physical examination were: fever: 40.7°C, pulse: 110/min, BP: 168/95 mm/Hg, mild neck stiffness and common muscle rigidity in four extremities, especially the upper extremities. The first laboratory findings in the intensive care unit were: leukocytes: 6900/mm³, erythrocyte sedimentation rate: 10 mm/hour, CRP: 13 mg/dl, CPK: 2000 IU/L, CK-MB: 72 U/L, SGOT: 261 U/L, SGPT: 156 U/L, urea: 36 mg/dL, creatine: 0.93 mg/dL, Na: 148 mEq /L, K: 2.61 mEq/L, Cl: 115 mmol/L. Laboratory findings performed three days later were: CPK: 2420 IU/L, leukocytes: 12,400/mm³, BP: 180/120mm/Hg, pulse: 105/min, fever: 38°C. A lumbar puncture was planned while the patient was hospitalized but it could not be performed because the patient could not be properly positioned due to muscle rigidity. In keeping with the meningoencephalitis provisional diagnosis, empiric ceftriaxone 2x2 gm intravenous (IV) was initiated. Cranial computer tomography (CCT) and contrast cranial magnetic resonant imaging (MRI) examinations showed no findings related to meningoencephalitis. Abdominal ultrasonography and an EKG were carried out to investigate the etiology of the fever, no pathology was found. As no improvement was seen in the clinical and laboratory findings in spite of IV antibiotic therapy and the patient had a psychiatric diagnosis and treatment history, a psychiatry consultation was requested. It was revealed that the patient had been undergoing psychiatric ambulatory treatment for five years due to a diagnosis of atypical psychotic disorder, had used extended release quetiapine 50 mg/day for approximately one month, and had not used any other drug for the previous three months. It was determined that the patient had used olanzapine and risperidone in her previous psychiatric treatments. From

the history obtained from the patient and her relatives, it was determined that the patient had showed no sensitivity to any drug and had not suffered any adverse effects due to use of antipsychotics in the past. On psychiatric examination of the patient, she was conscious, cooperative, fully oriented to place, time and people, indifferently self-respected and she appeared to be her age. Her psychomotor activity decreased, associations were proper and purposeful, and no pathology was described in her thinking content and perception. On physical examination, the patient showed 4+ rigidity in her upper and lower extremities. When the history of the patient, her physical examination findings and laboratory studies were evaluated, it was believed that the patient had NMS due to muscle rigidity, fever, and hypertension, leukocytosis, higher CPK, CPK-MB and liver enzymes, and so the antibiotic treatment was stopped.

For the treatment of the NMS, antipsychotics were discontinued as a first step, fever was decreased with antipyretics, and supportive treatment was given including monitoring fluid and electrolytes and correcting if needed. Bromocriptine 50 mg/day and low dose diazepam were prescribed for muscle rigidity. The patient had recovered completely by 10th day of treatment.

DISCUSSION AND CONCLUSION

Although there are many diagnostic criteria for NMS in the literature, the most commonly used one is the definition used in the DSM-IV (11). According to the DSM-IV-TR, in order to diagnose NMS, there should be muscle rigidity and fever together (criterion A); diaphoresis, dysphagia, tremor, incontinence, alteration in consciousness, mutism, tachycardia, high or labile blood pressure, leukocytosis and at least two laboratory findings showing muscle damage (criterion B). When the clinical and laboratory findings of the patient were evaluated, hyperthermia and lead pipe rigidity were detected according to DSM-IV-TR diagnostic criteria A. From diagnostic criteria B, diaphoresis, hypertension, tachycardia, leukocytosis and increased CPK were detected.

The patient had been treated with low dose extended release quetiapine, an atypical antipsychotic for four weeks before the clinical signs of NMS appeared, and the patient had used only this drug regularly. It was believed that the use of quetiapine was effective in treating the patient's

psychiatric symptoms. When the risk factors related to NMS were evaluated, no distinctive risk factor was seen in the patient; her oral intake was good before the onset of NMS, she was not dehydrated, and she was using the low dose oral atypical antipsychotic as a single drug (2,5,7,8).

Furthermore, as the diagnosis met the clinical NMS criteria, malignant hyperthermia was not considered, since no anesthesia had been given prior to development of catatonia. In terms of hyperthermia, a differential diagnosis was made with infectious diseases such as meningitis, viral encephalitis, and tetanus. Moreover, differential diagnoses were made to exclude an intracranial mass, central anticholinergic syndrome, intoxication, drug-related hyperthermia, severe dystonia, hyperthyroidism, Parkinson disease, and streptococcal pharyngitis (1,12).

Acute medical complications that may be seen in NMS are acute renal failure, respiratory insufficiency, pneumomediastinum, disseminated intravascular coagulation, sepsis, epileptic seizures, heart attack, arrhythmia, and death (12). Deaths generally result from arrhythmia, renal and respiratory failure or cardiovascular shock (13). Effective triggers for mortality are myoglobinuria and renal failure (12).

In the treatment of NMS, it is necessary to stop the trigger agent, to provide intravenous supportive treatment, to maintain an open airway, to provide necessary

ventilation, to cool the patient and to ensure electrolyte balances (13,14). Electrolyte levels, urea output and renal functions should be monitored carefully. Cold blankets, ice bags, dantrolene and diazepam should be available during acute treatment (12). It is suggested not to use anticholinergic drugs that may cause diaphoresis but to use bromocriptine and other D2 receptor agonists and also dantrolene in drug treatment. In analytical studies related to treatment, bromocriptine and amantadine used together with dantrolene and ECT treatment are found to be the most useful (13,14).

Although NMS usually occurs during the use of typical antipsychotic drugs, cases have been reported with the use of atypical antipsychotic drugs (6,9). In the literature, 12 cases have been noted in which NMS developed during the use of quetiapine. Eight of these cases showed atypical and 4 cases showed typical NMS clinical symptoms. In these cases, the fact that NMS developed during use of a low dose of quetiapine was explained by the idiosyncratic nature of the syndrome (10,11). We could not find any NMS case developed during treatment with extended release quetiapine in the literature.

Our case is the first case in which NMS developed during use of extended release quetiapine. Clinicians should be aware that rarely fatal NMS may develop during use of extended release quetiapine.

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