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Case Report

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A successful management with electroconvulsive therapy of neuroleptic malignant syndrome due to amisulpride

Ali Karayağmurlu[1], Elif Karayağmurlu[2], Mehmet Fatih Üstündağ[3], Ece Yazla[4]

ABSTRACT

Neuroleptic malignant syndrome is a severe complication that mainly occurs based on neuroleptic drug treatment and characterized with some autonomic symptoms, altered mental state, hyperthermia and muscle rigidity. Amisulpride is a unique atypical antipsychotic that selectively blocks D2 and D3 receptors presynaptically in the frontal cortex and atypical antipsychotics are rarely caused neuroleptic malignant syndrome (NMS).This study examine a 20-years old male with the diagnosis of acute psychotic disorder occurred amisulpride-induced NMS and successfully treated with Electroconvulsive Therapy (ECT). We decided to present that case because of the fact that there is only limited number of amisulpride-induced NMS cases reported in the literature.

Keywords: amisulpride, atypical antipsychotics, neuroleptic malignant syndrome, electroconvulsive therapy

INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a life-threatining complication of antipsychotic medication characterized by some autonomic symptoms, altered mental state, hyperthermia, and muscle rigidity (1, 2). Incidence of NMS varies from 0.02% to 3% in patients using antipsychotic medication. Although the pathogenesis of NMS is not clear yet, the blockage of the dopaminergic receptors in the nigrostriatal pathway is considered to be responsible (3). Because of that reason, typical antipsychotics are thought to cause NMS more often than the atypical drugs. However, recent studies showed that atypical antipsychotics can also cause NMS (4, 5). Amisulpride, a substituted benzamide derivative, is an atypical antipsychotic that preferentially binds to D2/D3 receptors in limbic rather than striatal structures (6). NMS is a clinical picture, arising after antipsychotic use. Therefore, antipsychotic use should be discontinued. Although, ECT is known as a safe and effective procedure in NMS, the procedure is used less frequently in youngers than in adults(7).The underlying cause of the less use of ECT in young people was that concern regarding to adverse effect of ECT, like prolonged seizure(8). This study describes a 20-years old male who was diagnosed to acute psychotic disorder, occurred NMS due to amisulpride and successfully treated with ECT.

CASE

A 20-years old single male patient (A.U.) living with his family was brought to our outpatients clinic by his relatives with the complaints of quick temper and a decline in self-care. According to the information obtained from the relatives, the patient is normally self-contained and has an introvert personality. The complaints of quick temper, increased motor activity, expressionlessly speaking, social isolation and decline in self-care was present for the last 15 days. The medical records of the patient revealed no history of previous psychiatric disorder, psychotropic drug use or substance abuse. The Clinical Global Impression Scale (CGIS) and Positive and Negative Syndrome Scale (PANSS) were used during the

[1] *Department of Child and Adolescent Psychiatry, Gaziantep Child State Hospital, Gaziantep, Turkey*
[2] *Department of Psychiatry, Gaziantep University, Faculty of Medicine, Gaziantep, Turkey*
[3] *Erenköy Training and Research Hospital for Psychiatric and Neurological Diseases, Department of Psychiatry, İstanbul, Turkey*
[4] *Department of Psychiatry, Hitit University, Faculty of Medicine, Çorum, Turkey*

Correspondence: *Ali Karayağmurlu*
Department of Child and Adolescent Psychiatry,
Gaziantep Child State Hospital, Gaziantep, Turkey.
Phone: +90 342 3600888, Mobile: +90 5055646757
Fax: +90 342 2352425

E-mail: dralikarayagmurlu@gmail.com

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interview, which gave a score of 6 (severe) and 105, respectively (9, 10). In the mental status examination revealed the patient to be conscious, full orientated and dysphoric and to have increased psychomotor activity, superficial emotion and persecution delusions in thought content. Abstraction and appreciation of the status were defective with a loose association of ideas and lack of an internal view. The patient was hospitalized with an initial diagnosis of acute psychotic disorder based on the mental examination findings and DSM-V criteria. Drug therapy with amisulpride 200 mg/day was initiated, which was increased to a dose of 400 mg/day within 4 days. On the 7th day of the hospitalization, because the relatives of the patients refused the treatment and wanted the patient to be discharged, the patient was discharged from the hospital after explaining all the risks associated with this early discharge. After the discharge, it has been learned that the health condition of the case deteriorated but the patient has not received any treatment and the relatives took him to a traditional practice which was prayed by a person who is not a professional. Therefore, the NMS diagnosis and treatment of the patient had delayed. Five days after the discharge, the patient was admitted to the emergency department with the complaints of muscle rigidity, sweating, mutism, and changes in consciousness and blood pressure. Laboratory tests revealed leukocytosis of 12.1 K/mcL (white blood cell reference range: 4.5–11.0 K/mcL), creatine phosphokinase (CPK) elevation up to 3747 U/L (reference range: 21–232 U/L), creatinine (Cr) elevation up to 1.4 mg/dL (reference range: 0.6–1.1 mg/dL), C-reactive protein (CRP) elevation up to 11.5 mg/L (reference range: 0-5 mg/dL), and phosphorus (P) elevation up to 3 mg/dL (reference range: 4-7 mg/dL). Other laboratory results were normal. The patient, who had discontinued the drug therapy 5 days ago, had the vital signs of 132 beats/minutes of heart rate, 110/60 mmHg of blood pressure and 38.7°C (101°F) of body temperature. Physical examination revealed muscle rigidity in both upper limbs and the dryness of mucosal membranes. The patient was consulted by the departments of Infectious Diseases and Neurology in order to differential diagnosis, especially central nervous system infection or another neurological pathology, Serotonin Syndrome, catatonia. The results of cerebrospinal fluid, video-EEG, and cranial MRI were normal. The possibility of an organic cause was found to be low. NMS is a clinical picture that overlaps with the Serotonergic Syndrome because of fever and the presence of changes in mental status. Serotonergic syndrome was ruled out by leukocytosis, rigidity, high CPK level and absence of antidepressant use. In differential diagnosis of catatonia, NMS has appeared sudden start of mental changes and presented motor rigidity, fever and autonomous dysregulation whereas catatonia was slower onset and presented posturing, automatisms, negativism, rarely hyperkinesias (11)**.** Sudden start of mental changes and motor rigidity were also presented in our case. Then, patient was diagnosed to have NMS based on DSM-V criteria. Because of dehydration and renal dysfunction and electrolyte imbalance, fluid replacement was started immediately, followed by lorazepam for intermittent episodes of aggressiveness. On the 10th day of the treatment, vital signs became stable with the all laboratory tests returning to normal values (CPK: 197 U/L, Cr: 0.6 mg/Dl, white blood cells 6.4 K/mcL, and P: 4.7 mg/dL). However, despite the improvement of laboratory tests, patient still had muscle rigidity, psychotic sign and agitation. Therefore, bilateral ECT treatment under general anesthesia every other day was planned. Informed content was obtained from the relatives of the patient after giving information about the procedure. Bilateral ECT treatment under general anesthesia every other day was performed for a total of 10 times. Following the ECT procedure, muscle rigidity, psychotic sign and agitation improved. On the 32nd day of the hospitalization, CGIS and PANSS were found to be 3 (mild) and 57, respectively. The clinical picture of NMS was improved and the patient became euthymic following the ECT treatment. Olanzapine (2.5 mg everyday) was initiated which was increased to 20 mg/day in 1 week, followed by discharging the patient with scheduled outpatient visits.

DISCUSSION

Amisulpride is a second-generation neuroleptic agent associated with less extrapyramidal symptom (EPS) due to selective action at limbic cortical dopamine D2/D3 receptors (12). However, there are also amisulpride-related NMS, acute dystonic reaction, akathisia and parkinsonism case reports in the literature (13, 14). Within amisulpride-related EPS, three NMS cases were reported, two of which fulfill all the three sets of diagnostic criteria. Our case also met all of the diagnostic criteria for NMS. In the majority of cases, NMS occurred after dose increase in the literature. As in line with those of previous cases, NMS occurred after dose increase in our case. Unfortunately, the case was diagnosed with NMS 5 days later because of the attitude of the relatives and the case had a life-threatening condition. In the literature, mortality has been also reported in a case with NMS related to amisulpide (15). Consequently, the ECT procedure was applied quickly due to the life-threatening condition (16).

There are many risk factors for the development of antipsychotic-related NMS, including dehydration, malnutrition, infection, organic brain disease, extrapyramidal system disorders like Parkinson Disease, Huntington and sympathoadrenal hyperactivity, high neuroleptic doses, rapid dose titration and parenteral drug administration,

agitation, alcohol, polypharmacy (especially lithium), and previous history of NMS (17-19). In the present case, there were dehydration, malnutrition, agitation and rapid dose as the risk factors. The patient was evaluated for according to Naranjo's Adverse drug reaction probability scale(20). In this scale, a score of ≥9 is accepted as definite; a score between 5 and 8 is accepted as probable; a score between 1 and 4 is accepted as possible and a score of 0 is considered as doubtful for side effects. When we assessed our patient according to this scale, he had a total of 7 points, with the pre-existence of amisulpride-related NMS in the literature (1 point), the absence of a causal factor that could lead to NMS other than the drug (2 points), the resolution of the side effect when the drug was discontinued (1 point), the occurrence of the dystonia after the administration of the suspected drug (2 points) and the confirmation of the side effect with objective evidences (1 point). According to Naranjo's Adverse drug reaction probability scale, NMS most probably occurred as a result of the use of amisulpride.

We initially started to the fluid replacement and supportive therapy to the patient after the necessary medical consultations to the appropriate departments because of the existence of dehydration and malnutrition signs as well as the alterations in CK, creatinine and electrolyte levels in laboratory tests. Supportive therapy is especially important for the prevention of lethal complications which can occur because of the NMS. ECT was also used in addition to the supportive therapy. ECT is a rapid and effective treatment for NMS and it was shown to decrease the complication incidence and obtain rapid improvement when it was used in the early periods of the syndrome (21-23). In addition to ECT, bromocriptine and dantrolene can be used to treat NMS (24). The potential effect of ECT is related to increased dopaminergic activity in the central nervous system. Indeed, bromocriptine and amantadine are also dopaminergic agents. After the treatment, clinical state of the patient improved without any complication (25).

Consequently, it should be noted that although amisulpride is a good antipsychotic agent with its safety profile, it may lead to NMS. Being alert about the possibility of NMS due to amisulpirid treatment, early recognition of NMS signs and symptoms and having knowledge about ECT as an effective treatment will help clinicians for decreasing the mortality associated with amisulpiride induced NMS.

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