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Case Report

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Neuroleptic Malignant Syndrome Due to Antipsychotic Use in a Geriatric Case

Geriatrik Bir Olguda Antipsikotik Kullanımına Bağlı Gelişen Nöroleptik Malign Sendrom

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ABSTRACT

Neuroleptic malignant syndrome is a serious clinical condition that can develop due to antipsychotic use. In this case report, we discussed a 77-year-old patient with neuroleptic malignant syndrome. A 77-year-old female patient was admitted to the geriatric outpatient clinic with impaired oral intake, mental status change, reduced mobilization, and urinary incontinence that developed in the last week. The patient, who was using dual antipsychotics due to sleep problems, was hospitalized with the diagnosis of neuroleptic malignant syndrome presented with bilateral upper extremity rigidity. The patient, whose serum creatine kinase levels were high, was given intravenous hydration, clonazepam and bromocriptine treatments. A significant improvement was observed in her clinical condition with the treatment. The patient was discharged after 1 week of ward follow-up. Neuroleptic malignant syndrome is a rare clinical condition that can be overlooked. If not diagnosed, it can be fatal. Unnecessary antipsychotic use should be avoided, especially in the geriatric population, and treatment should be started as soon as possible after diagnosis.

Keywords: Antipsychotic, neuroleptic malignant syndrome, rigidity, creatine kinase, elderly

ÖZ

Nöroleptik malign sendrom, antipsikotik kullanımına bağlı olarak gelişebilen ciddi bir klinik durumdur. Bu olgu sunumunda, nöroleptik malign sendrom tanısı alan 77 yaşında bir hastayı ele aldık. Yetmiş yedi yaşında kadın hasta, son bir haftada gelişen oral alım bozukluğu, mental durum değişikliği, mobilizasyonda azalma ve üriner inkontinans şikayetiyle geriatri polikliniğine başvurdu. Uyku problemi nedeniyle ikili antipsikotik kullanan hastada bilateral üst ekstremitede rijidite mevcuttu ve nöroleptik malign sendrom tanısıyla hastaneye yatırıldı. Serum kreatin kinaz düzeyleri yüksek olan hastaya intravenöz hidrasyon, klonazepam ve bromokriptin tedavileri başlandı. Tedaviyle hastanın kliniğinde belirgin iyileşme gözlendi. Hasta, 1 haftalık servis takibinin ardından taburcu edildi. Nöroleptik malign sendrom, gözden kaçabilen nadir bir klinik durumdur. Tanı konulmadığı takdirde ölümcül olabilir. Özellikle geriatrik popülasyonda gereksiz antipsikotik kullanımından kaçınılmalı ve tanı konulduktan sonra mümkün olan en kısa sürede tedaviye başlanmalıdır.

Anahtar Kelimeler: Antipsikotik, nöroleptik malign sendrom, rijidite, kreatin kinaz, yaşlı

INTRODUCTION

A 77-year-old female patient with known dementia, cerebrovascular disease, hypertension, and epilepsy diagnoses applied to the geriatric outpatient clinic due to decreased oral intake, impaired mobilization, altered mental status, and urinary incontinence for the last week. On physical examination, bilateral rigidity was observed in the upper extremities. Muscle strength was 4/5 in the upper extremities and 2/5 in the lower extremities. Other system examinations were normal. Anamnesis revealed that she had been taking olanzapine 5 mg/day and quetiapin 50 mg/day for sleep disorders for the last 3-4 months. She was also taking memantine 20 mg/day, donepezil 5 mg/day, acetylsalicylic acid 100 mg/day, valsartan/hydrochlorothiazide 160/12.5 mg, and levetiracetam 1000 mg/day. Neuroleptic malignant syndrome (NMS) due to antipsychotic use was considered in the patient and she was admitted to the geriatric inpatient clinic. Vital signs showed a temperature of 36

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°C, blood pressure of 125/85 mmHg, pulse of 85/minute, and respiratory rate of 18/minute. The patient's baseline creatinine levels were 0.5 mg/dL, and when she was admitted to the clinic, her creatinine levels were 0.9 mg/dL. Creatine kinase (CK) levels were 408 U/L, C-reactive protein levels were 10 mg/L, and she had no leukocytosis. After the patient was admitted to the clinic, her CK level increased rapidly to 916 U/L. Serum electrolyte levels were normal. Brain magnetic resonance imaging showed chronic ischemic changes but no other pathology. There was no significant stenosis in carotid and vertebral Doppler ultrasonography. Olanzapine and quetiapine treatments were discontinued. A urinary catheter was inserted and intravenous hydration was started. Clonazepam 0.5 mg 3 times daily and bromocriptine 2.5 mg twice daily were started for 5 days. Due to acute kidney injury, the patient's valsartan/hydrochlorothiazide treatment was temporarily suspended. Oral nutritional support was provided. Mobilization exercises were performed under the supervision of a physiotherapist. With the current treatments, renal function tests returned to normal, and CK levels decreased to 36 U/L. Improvement was observed in the patient's oral intake and mental status. Rigidity in the upper extremities decreased and mobilization increased. Table 1 shows the patient's laboratory findings. The patient's general condition and laboratory results improved, and she was discharged from the geriatric inpatient clinic.

CASE REPORT

Neuroleptic Malignant Syndrome

NMS is a rare but potentially life-threatening condition associated with the use of antipsychotic medications. First-generation antipsychotic drugs carry a higher risk of NMS, but they can also occur with second-generation antipsychotics and other dopamine-blocking agents, such as antiemetics (1,2). NMS is not dose-dependent, although higher doses do increase the risk. Additionally, the withdrawal of levodopa or dopamine agonists or a relative deficiency of levodopa due to increased needs (such as during an infection) can also cause NMS (3).

The diagnostic criteria for NMS include a tetrad of symptoms: fever, altered mental status, rigidity, and autonomic instability. Hyperthermia is defined as core body temperature >38 °C (100.4 °F), muscle rigidity is often described as "lead-pipe", and autonomic dysfunction may manifest as tachycardia, hypertension or hypotension, diaphoresis, and incontinence. Mental status change may range from confusion to coma. Other supportive findings are elevated CK and liver transaminases due to muscle breakdown (rhabdomyolysis). CK is typically more than 1000 international units/L and can be as high as 100.000 international units/L (4). Rhabdomyolysis may also cause acute kidney injury. The exclusion of other causes, such as infections, metabolic disorders, or other drug-induced syndromes, also supports NMS diagnosis. The criteria for diagnosing disorders in the diagnostic and statistical manual of mental disorders (DSM V) include exposure to a dopamine-blocking agent within 72 hours prior to symptom development, severe muscle rigidity, and fever. Additionally, other minor criteria include diaphoresis, dysphagia, tremor, incontinence, altered level of consciousness, mutism, tachycardia, elevated or labile blood pressure, leukocytosis, and elevated creatine phosphokinase (5). According to the severity of rigidity, confusion, heart rate and body temperature NMS can be classified as mild/early, moderate or severe (6). Mild NMS presents with mild stiffness, mild catatonia, or confusion, body temperature ⩽38 °C (100.4 °F), and heart rate ⩽100 bpm. Moderate NMS presents with moderate stiffness and worsening catatonia or confusion, body temperature 38 °C -40 °C (100.4 °F -104 °F), and heart rate 100-120 bpm. Severe NMS presents with severe stiffness, often leading to immobility; severe catatonia, confusion, or coma, body temperature ⩾40 °C (104 °F), and heart rate ⩾120 bpm.

DISCUSSION

NMS shares features with several other conditions, making differential diagnosis essential, including serotonin syndrome caused by serotonergic agents (e.g., SSRIs, SNRIs) differentiated by hyperreflexia, clonus, and gastrointestinal symptoms. Malignant hyperthermia is a condition triggered by anesthetic agents, often in genetically predisposed individuals. Central nervous system infections, such as meningitis or encephalitis, may present with fever and altered mental status. Heat stroke is differentiated by environmental exposure to high temperatures without muscle rigidity. Catatonia may present with rigidity and mutism but lacks autonomic instability and hyperthermia. Drug-induced parkinsonism has rigidity and bradykinesia without fever or autonomic dysfunction. The acute dystonic reaction has sudden muscle spasms without systemic symptoms. The anticholinergic syndrome can occur due to drug overdose, with patients often presenting symptoms such as encephalopathy and elevated body temperatures; however, these temperatures are typically not as severe as those seen in NMS. In contrast to NMS, features like diaphoresis, rigidity, and elevated CK levels are absent in anticholinergic syndrome. Instead, symptoms often atypical for NMS, such as flushing, mydriasis, and bladder distension, are commonly observed in these patients (6). In the present case, there was no history of catatonia, psychiatric illness except dementia and anesthetic agent or serotonergic agent exposure. Therefore, the diagnosis of NMS was considered.

The management of NMS involves immediately stopping the offending medication and providing supportive care. Additionally, dopamine agonists such as bromocriptine or amantadine can restore dopaminergic activity, while benzodiazepines may help reduce rigidity. It is also essential to reevaluate the use of antipsychotics and consider non-pharmacologic alternatives or switching to lower-risk medications if antipsychotics are necessary.

Table 1. Laboratory findings of the patient within days

Reference intervals	WBC ($3.8\text{-}11.8 \times 10^3/\mu L$)	CK (5-145 U/L)	AST (5-35 U/L)	LDH (5-248 U/L)	Creatinin (0.5-0.95 mg/dL)
Day 1	7.6	408	18	282	0.99
Day 2	8.8	916	40	255	0.92
Day 3	8.3	194	26	209	0.54
Day 4	8.3	82	21	217	0.54
Day 5	7.5	39	24	255	0.57

WBC: White blood cells, CK: Creatine kinase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase

An older woman with cognitive impairment was diagnosed in an outpatient setting while being treated concurrently with two atypical antipsychotic medications. She presented with symptoms of rigidity, urinary incontinence and impaired oral intake. A rapid increase in CK levels supported the diagnosis. Due to the timely intervention, she made a remarkable recovery.

CONCLUSION

Diagnosing NMS requires high clinical suspicion and awareness among healthcare providers. It is particularly concerning in older adults, who may be more susceptible to the side effects of antipsychotics due to age-related changes in pharmacokinetics and pharmacodynamics. Older adults often take multiple medications (polypharmacy), which increases the risk of drug interactions. Moreover, older adults tend to present with milder or atypical symptoms, leading to misdiagnosis or delayed diagnosis (7). They also face a higher risk of complications, such as renal failure and aspiration pneumonia, as well as increased mortality due to NMS.

Ethics

Informed Consent: Informed consent was obtained from the formal representatives of the patient. The information of the patient's identity was not defined in the manuscript.

Footnotes

Author Contributions

Surgical and Medical Practices: D.D.G., E.A.B., Concept: D.D.G., E.A.B., Design: D.D.G., E.A.B., Data Collection or Processing: D.D.G., E.A.B., Analysis or Interpretation: D.D.G., E.A.B., Literature Search: D.D.G., E.A.B., Writing: D.D.G., E.A.B.

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