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Case Report

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Neuroleptic Malignant Syndrome-From Emergency Department to Intensive Care Unit

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Abstract

Neuroleptic Malignant Syndrome (NMS) is a medical emergency, characterized by blockage of dopaminergic receptors or a rapid weaning of them. It is represented by stiffness, hyperthermia and autonomic instability. The present case described a 59-year-old man with schizophrenia, medicated with oral olanzapine. He was medicated with intramuscular haloperidol, in the emergency department, in the context of an acute confusional syndrome. Forty-eight hours later he began muscle stiffness, hyperthermia, dystonia, diaphoresis and depression of consciousness. Due to suspicion of NMS, he was admitted to the Intensive Care Unit (ICU), where he underwent pharmacological therapy with bromocriptine, benzodiazepines and supportive treatment. The patient was discharged from the ICU ten days later, with clinical improvement. Early recognition, referral to ICU and targeted supportive and pharmacological treatment are essential in the management of NMS, contributing to a better prognosis.

Keywords: Neuroleptic Malignant Syndrome; Dopaminergic Receptors; Neuroleptics; Haloperidol

Introduction

Neuroleptic Malignant Syndrome was first described in 1956 by J. Frank, shortly after the discovery of antipsychotic medication [1,2]. NMS is considered an idiosyncratic reaction, with a poorly understood pathophysiological mechanism [1,3]. It is thought that the blockade of dopaminergic receptors is the basis of this pathology. It is mainly caused by potent neuroleptics, such as haloperidol, chlorpromazine, fluphenazine. However, despite being less common, it can occur with atypical neuroleptics, such as olanzapine, risperidone and quetiapine, or with other drugs with central antidopaminergic action such as metoclopramide and tricyclic antidepressants. Rapid weaning of dopaminergic agents such as levodopa, used in Parkinson's disease, can also cause this syndrome [1,2,5]. Only 0.1 to 3.2% of patients taking neuroleptics present NMS [1]. It is thought that these cases may be associated with a genetic predisposition, dehydration state, hypersensitivity of dopaminergic receptors, undiagnosed psychiatric illness, administration of a high dose, parenteral or rapid dose increase [4].

Case Report

Male patient, 59 years old, independent, with a history of hypertension, obesity and schizophrenia diagnosed at 34 years old. Usually medicated with amlodipine 10 mg, olanzapine 5 mg, biperiden hydrochloride 4 mg, flurazepam 30 mg. He went to the emergency department (ED) due to diffuse abdominal pain that had lasted 3 days. In the ED, he underwent an analytical and urinary study, without changes, and presented spontaneous resolution of the initial complaints. However, during his stay in the ED, he began experiencing psychomotor agitation. For this reason, he was kept under surveillance. Due to continued agitation, he was medicated with haloperidol 10 mg, intramuscularly, twice

a day, and diazepam 10 mg, intramuscularly, once a day, during the first 48 hours of hospitalization. On the third day, he developed a persistent fever above 38ºC, refractory to antipyretic therapy. The objective examination showed an eye opening on call, non-cooperative and non-communicative, tachypneic, diaphoretic, with generalized muscular spasticity and mental dyskinesia. No other changes to the physical examination. Cranioencephalic computed tomography and lumbar puncture, without changes. Analyzes with 13,500 leukocytes, 1.2 mg/dL of creatinine, hypernatremia with Na+ 156 mEq/mL, C-reactive protein 1.5 g/dL and elevation of creatine phosphokinase (CPK), with a maximum of 2715 IU/mL. After excluding infectious causes, neuroleptic malignant syndrome was suspected and suspended olanzapine, biperiden hydrochloride and haloperidol. He was admitted to the ICU for monitoring, support and treatment. He started fluid therapy, bromocriptine 2.5 mg every 8 hours and oxazepam 15 mg every 8 hours. During the first 3 days in the ICU he maintained the same neurological status, diaphoresis, persistent hyperthermia (Figure 1) and refractory to antipyretic therapy (metamizole, paracetamol, diclofenac) and body cooling measures. He also required oxygen therapy with a maximum FiO2 of 40% due to hypoxemic respiratory failure (RF) and a nasogastric tube (NGT) for feeding. From the fourth day of hospitalization, he showed progressive improvement of neurological status, RF, hyperthermia and rhabdomyolysis (Figure 2). He was transferred to the Internal Medicine ward on the tenth day of hospitalization, conscious, cooperative, with limited speech, without oromandibular dyskinesia or muscular spasticity, hemodynamically stable, apyretic, without RF and without need for NGT.

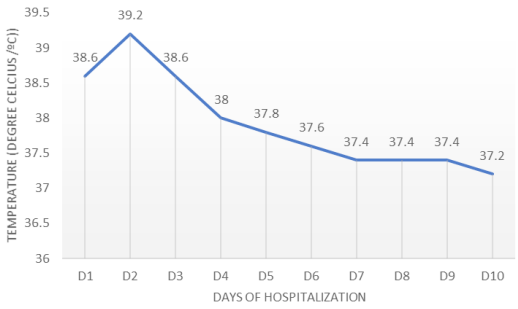

Figure 1: Thermal variation during hospitalization in the ICU.

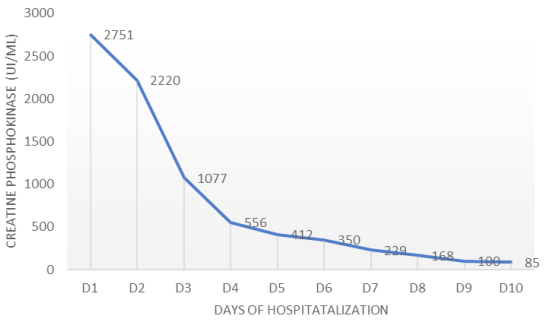

Figure 2: CPK variation during hospitalization in the ICU.

Discussion

NMS is characterized by hyperthermia and marked muscle stiffness. It can be associated with changes in the state of consciousness from delirium to coma, dysphagia, dysarthria, mutism, extrapyramidal signs such as tremor, chorea, akinesia and dystonic movements; autonomic instability such as blood pressure lability, tachycardia, tachypnea, sialorrhea, diaphoresis and urinary incontinence. The most common analytical changes are leukocytosis, elevated CPK in the context of rhabdomyolysis and acute kidney injury, with increased creatinine [2,3,5]. It usually appears 24 hours to 1 week after the start of therapy, however it may appear later or even in patients chronically medicated with antipsychotics [2,3]. Recovery occurs on average 7 to 10 days after trigger discontinuation [2]. Clinical heterogeneity is one of its main characteristics, therefore constituting a complex syndrome. In order to simplify the diagnosis, objective criteria were established in DSM-5 [2]. However, despite this, the list of differential diagnoses is vast, with several entities with similar manifestations that must be screened for, such as serotonin syndrome, hyperthermia malignant, malignant catatonia, central nervous system infections, toxic or metabolic encephalopathy, withdrawal syndrome, non-convulsive status epilepticus [1,2]. The treatment of NMS is based on three main pillars: discontinuation of the drug that triggered it; supportive treatment and in more severe cases, pharmacological therapy [2]. As support, vigorous hydration, body cooling measures, correction of hydro-electrolyte disorders and cardiorespiratory support are recommended; In more severe cases, pharmacological therapy can be administered with dopaminergic agonists such as bromocriptine and amantadine,

which promote the reversal of central dopaminergic blockade. Bromocriptine is administered orally or NGT, at a dose of 2.5 mg, 2 to 3 times a day. In the absence of response, 2.5 mg of bromocriptine can be increased every 24 hours, up to a maximum of 45 mg per day; muscle relaxants such as dantrolene, which prevents the release of calcium in the sarcoplasmic reticulum, being used in cases of severe muscle stiffness with a temperature that is difficult to control [2,4,5]. Dantrolene can be administered as an initial intravenous bolus at a dose of 1 to 2.5 mg/Kg, followed by 1 mg/Kg every 6 hours, up to a maximum of 10 mg/Kg per day. Dantrolene is suspended after clinical improvement, while bromocriptine should be maintained for 10 days in the case of NMS associated with oral neuroleptics and 2 to 3 weeks in the case of depot neuroleptics [5]. Benzodiazepines are the preferred agents for controlling psychomotor agitation.4 patients with NMS have an increased risk of dysphagia and aspiration pneumonia as a result of the altered state of consciousness, and evaluation and, if necessary, introduction of NGS are recommended; due to dehydration and immobilization, thromboprophylaxis with low molecular weight heparin is also suggested due to the greater thromboembolic risk [4,5]. Recurrence of NMS may occur mainly when neuroleptic therapy is resumed with high potency or restarted early. Therefore, in the case of patients who require antipsychotic treatment, neuroleptic therapy should be initiated and titrated cautiously [5]. Early recognition of NMS, referral to ICU and pharmacological treatment with dopaminergic agents and muscle relaxants contributed to a significant reduction in the mortality rate, from 40%, to 10 to 20% [2,4]. Cases of psychomotor agitation are common in the ED. Antipsychotic drugs and, in particular, intramuscular haloperidol are the most commonly used agents in the management of agitation. Although the clinical case portrays a patient chronically medicated with neuroleptics, haloperidol appears to have been the factor that triggered NMS. This is a common case in the ED, which can culminate in a potentially fatal syndrome. Therefore, it is imperative to know the characteristics of drugs, use them rationally and know how to identify and treat their complications.

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