CASE REPORT

Diagnosis and implications in the therapeutic management of patient with afebrile neuroleptic malignant syndrome

Rafael Quintes Ducasble Gomes*, Amilton dos Santos-Júnior, Gabriel Augusto de Araujo Silva Dias and Carlos Filinto da Silva Cais

Department of Psychiatry, Faculty of Medical Sciences, University of Campinas (Unicamp), Rua Tessália Vieira de Camargo, 126, Campinas 13083-894, Brazil

*Correspondence address. Department of Psychiatry, Faculty of Medical Sciences, University of Campinas (UNICAMP), Rua Tessália Vieira de Camargo, 126, Campinas 13083-894, Brazil. Tel: +55 19 3521 7206; Fax: +55 19 3521 7206; E-mail: rafaqdgomes@hotmail.com

Abstract

This report aims at raising clinical awareness for the diagnosis of atypical presentations of neuroleptic malignant syndrome (NMS). We describe the case of a female patient with NMS symptoms, except fever, after starting the use of chlorpromazine. The afebrile condition delayed the consideration of NMS by the emergency clinicians who provided her initial assessment. Before this consideration, an anticholinergic agent, not recommended at this condition, was inadvertently prescribed. This might have contributed to the worsening of symptoms. NMS is a life-threatening idiosyncratic reaction most often seen as a complication of antipsychotic treatment. Its clinical spectrum is broad and its diagnosis should be considered even if the patients do not fulfill all the possible described symptoms.

INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a rare idiopathic entity characterized by clinical hyperthermia, muscle rigidity, autonomic dysfunction and changes in the level of consciousness [1]. It is a serious complication of various kinds of medications and occurs in 0.5–1% of patients who take first-generation antipsychotics [2]. Although there are no consistent predisposing factors, its incidence is higher among men and at two peaks of age: under 40 and over 70 [3]. Patients with organic brain disease, psychosis, dehydration and exhaustion have been suggested to develop NMS with more frequency [3]. We present the case of a patient with presumed afebrile NMS related to the use of chlorpromazine. The difficulties in diagnosis, both by the incomplete symptom presentation and by concomitant confounding factors are discussed.

CASE REPORT

A 58-year-old female patient, previously diagnosed with bipolar disorder, Type 1, with past episodes of mania with psychotic symptoms, had been without pharmacologic maintenance treatment and, after visiting a psychiatrist from another health service, she was prescribed chlorpromazine 300 mg/day, without mood stabilizers. On the second day, she developed inappetence, muscle rigidity, prostration and postural instability. The dose was reduced to 100 mg/day on the third day, without response, and the medication was completely withdrawn on the fifth day, when she was referred to the emergency unit of
the Clinical Hospital of the State University of Campinas (Brazil), due to worsening of symptoms.

At admission, when she was initially evaluated by emergency clinicians, she was lucid, oriented, interacting with the examiners, with stereotyped perioral movements and cogwheel rigidity of the upper limbs. Her vital signs were: blood pressure = 216/118 mm of mercury; temperature = 96.26°F; heart rate = 137 beats per minute; respiratory frequency = 24 inspirations per minute; capillary glycemia = 126 mg/dl; oxygen saturation = 95%.

Her laboratory parameters were: creatine phosphokinase = 1238 U/L; leukocytes = 14,320/mL (segmented neutrophils = 86%, metamyelocytes = 1%; lymphocytes = 8%); urea = 73 mg/dl; creatinine = 1.28 mg/dl; sodium = 143 mg/dl; potassium = 4.3 mg/dl; calcium 10.3 mg/dl; magnesium = 1.98 mg/dl; inorganic phosphate = 5.7 mg/dl; international normalized ratio of coagulation = 1.4; aspartate aminotransferase = 53 IU/L; alanine aminotransferase = 56 IU/L; Urinalysis was normal and electrocardiogram only confirmed sinus tachycardia, without other alterations. Brain computed tomography showed no bleeding or fracture signs. The clinical staff who first evaluated the patient initially considered the diagnostic hypothesis of extrapyramidal syndrome due to the use of antipsychotic. The first clinical procedures included the intravenous administration of two ampoules of biperiden (5 mg each) and one of diazepam (10 mg), without improvement of motor symptoms, and with a subsequent development of fluctuating level of consciousness, disorientation and incoherent speech. At this moment, our consultation liaison psychiatric team was called for a joint assessment of the patient. Although she did not have fever, the psychiatrists considered the hypothesis of NMS, as the occurrence of muscle rigidity, hypertension, tachycardia, leukocytosis and increased creatine kinase had followed the previous use of chlorpromazine. The condition was complicated by the development of delirium, which might have been precipitated or aggravated by the use of biperiden, an anticholinergic agent.

She was transferred to a semi-intensive care unit and clinical support measures were initiated. It was introduced lorazepam 2 mg every 4 hours and all other psychiatric medications were suspended. She had a fast clinical improvement and laboratory parameters were normal within three weeks.

DISCUSSION

This article described the case of a patient with a diagnostic hypothesis of afibrile NMS after using chlorpromazine, which was not considered by the emergency clinicians who initially examined her.

Given the absence of fever and of predisposing factors [3, 4], except the psychiatric diagnosis and the recent introduction of an antipsychotic medication, the suspicion of NMS was delayed and confounded with the possibility of isolated extrapyramidal effects induced by chlorpromazine. Nevertheless, chlorpromazine was started without titration, at a relatively high dose.

The administration of an anticholinergic agent for the treatment of extrapyramidal symptoms would be contraindicated if NMS had been considered, as anticholinergics may cause symptoms resembling NMS and may also be associated with the occurrence of delirium [4]. Indeed, the patient developed delirium. This might have been a complication of the NMS itself, possibly precipitated or aggravated by the anticholinergic activity of biperiden [4].

The identification of early signs of NMS reflects on therapeutic actions, beginning by the suspension of the drug with antidopaminergic activity [1, 5]. The differential diagnosis can be difficult, mainly when presentations are not typical, and an evaluation of other clinical conditions, such as infections, inflammatory states, trauma, other neurological diseases, etc., is mandatory [2–5]. Acute extrapyramidal symptoms may be associated with secondary parkinsonism, serotonin syndrome, lethal catatonia, heart stroke, among other conditions [2–5], but they may also be associated with NMS, even without fever. We consider of most importance to expand the suspicion level of professionals, psychiatrists or not. The diagnosis of NMS in its classic presentation is not simple, and it becomes even more difficult in atypical situations [6].

Considering the severity of the condition and its low incidence, we believe it is important to share experiences in order to raise awareness for the importance of early diagnostic suspicion of NMS. Its diagnosis shall be considered for every patient in use of antipsychotics who develops its clinical features, even if none of them are present at a same time.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

No sources of funding.

ETHICAL APPROVAL

No approval is required.

GUARANTOR

Rafael Q. D. Gomes

REFERENCES

1. Modi S, Dharaiya D, Schultz L, Valeras P. Neuroleptic malignant syndrome: complications, outcomes, and mortality. Neurorcr Care 2016;24:97–103. doi:http://dx.doi.org/10.1007/s12028-015-0162-5.
2. Totten VY, Hirschenstein E, Hew P. Neuroleptic malignant syndrome presenting without initial fever: a case report. J Emerg Med 1994;12:43–7. doi:http://dx.doi.org/10.1016/0736-4679(94)90011-6.
3. Lev R, Clark RF. Neuroleptic malignant syndrome presenting without fever: case report and review of the literature. J Emerg Med 1994;12:49–55. doi:http://dx.doi.org/10.1016/0736-4679(94)90012-4.
4. Berman BD. Neuroleptic malignant syndrome: a review for neurohospitalists. Neurohospitalist 2011;41–7. doi:http://dx.doi.org/10.1177/1941875210386491.
5. Danaf JA, Madara J, Dietsche C. Neuroleptic malignant syndrome: a case aimed at raising clinical awareness. Case Rep Med 2015;Article ID 769576. doi:http://dx.doi.org/10.1155/2015/769576.
6. Garrera RJ, Caroff SN, Cohen A, Carroll BT, DeRoos F, Francis A, et al. An international consensus study of neuroleptic malignant syndrome diagnostic criteria using the Delphi method. J Clin Psychiatry 2011;72:1222–8. doi:http://dx.doi.org/10.4088/JCP.10m06438.