Psychiatria Danubina, 2023; Vol. 35, Suppl. 2, pp 412-414
Conference paper
Case report

NEUROLEPTIC MALIGNANT SYNDROME WITH UNDERLYING CATATONIA – A CASE REPORT

Chloé Gilson, Denis Jacques & Thomas Dubois
Université Catholique de Louvain, Psychosomatic Medicine Unit, CHU Mont-Godinne, Yvoir, Belgium

* * * * *

INTRODUCTION

Catatonia and neuroleptic malignant syndrome (NMS) share similarities in their symptomatology and both respond to benzodiazepines or electroconvulsive therapy (ECT). In this case report, we discuss the distinction between the two diagnoses and the treatment of catatonia.

CASE REPORT

A 51-year-old man was admitted in neurology for an NMS with an underlying catatonic presentation.

He suffered from a schizoaffective disorder, stabilized with carbamazepine, clotiapine, trazodone, procyclidine, quetiapine, lormetazepam, and lithium.

His treatment had been modified the weeks preceding his admission in neurology; discontinuation of carbamazepine, clotiapine, quetiapine and lithium and addition of 10 mg olanzapine per day and 10 mg haloperidol per day. The patient then developed an NMS with confusion, muscular rigidity, tremor, agitation, insomnia, hyperthermia, extrapyramidal syndrome, and increased CRP and CPK rates.

Once the NMS had been treated in the intensive care unit by discontinuation of psychotropic drugs, hydration and injection of intravenous benzodiazepines, catatonic symptoms persisted with confusion, oppositional behaviour, aggressiveness, agitation, mutism, poor or incoherent speech, echolalia, staring, stereotypies, psychomotor retardation, postural maintenance, and delusion.

Neurologists excluded various disorders including autoimmune encephalitis, neurodegenerative disorder, and extrapyramidal disorder.

Low doses of clozapine were initially used to treat catatonia but worsened the symptoms and was rapidly discontinued. Administration of lorazepam 2.5 mg three times a day and amitriptyline 30 mg daily modestly improved catatonic symptoms. Indication of ECT was established given the partial response observed but the delays were long.

The patient developed complications due to catatonia (inhalation pneumonia, gastrostomy, bed sores). He was transferred to a nursing home due to major motor deconditioning with amyotrophy secondary to prolonged immobility.

SUBJECTS AND METHODS

We conducted a literature review on PubMed, PyscArticles and PsycInfo. The keywords used were catatonia, neuroleptic malignant syndrome, and differential diagnosis.

RESULTS

The question of the link between catatonia and NMS remains unresolved. Five hypotheses emerge in the literature, ranging from the hypothesis that they form one single entity to the hypothesis that they are two distinct entities (Vesperini et al. 2010).

According to Lang et al. 2015, catatonia and NMS can be distinguished descriptively (Table 1). Therefor we can affirm the presence of catatonia in this patient.

What is the treatment for catatonia?

First, any underlying pathology must be treated. Indeed, catatonia can be caused by a multitude of pathologies including mental disorders (psychotic disorder, bipolar disorder, depression, etc.), organic disorders (infectious, metabolic, neurological, etc.), and drug-related disorders (intoxication, withdrawal, side effects).

Then, lorazepam is the first-line treatment, 1 to 2 mg daily. In case of insufficient response, the dose should be repeated every 3 to 4 hours up to 8 to 24 mg per day. In most cases, catatonia disappears within 3 to 7 days. There is no consensus on how long benzodiazepines should be pursued, but prolonged prescribing may be justified, as some patients relapse on discontinuation of benzodiazepines (Sienaert et al. 2019).

Mormando et al. 2020 recommend parenteral administration given the pharmacodynamic advantages (slower distribution, higher serum concentrations, and prolonged clinical effect) and the frequent inability to administer oral medications to a catatonic patient.

Zolpidem can be used as an alternative to lorazepam with doses ranging from 7.5 to 40 mg per day (Sienaert et al. 2019).

A lorazepam-diazepam protocol has also been suggested with an initial dose of 2 mg of lorazepam injected intramuscularly. If the patient does not respond, a second dose is administered after 2 hours. If this remains unsuccessful, an intravenous drip of 10 mg diazepam in 500 mL normal saline at a rate of 1.25 mg/h for 1 day is prescribed (Sienaert et al. 2019).

Table 1. Diagnostic criteria for catatonia and neuroleptic malignant syndrome

DSM 5 diagnostic criteria for catatonia	
The clinical picture is dominated by 3 (or more) of the following symptoms: ▪ Stupor (ie, no psychomotor activity; not actively relating environment) ▪ Catalepsy (ie, passive induction of a posture held against gravity) ▪ Waxy flexibility (ie, slight, even resistance to positioning by examiner) ▪ Mutism (ie, no, or very little, verbal response (exclude if known aphasial)) ▪ Negativism (ie, opposition or no response to instructions or external stimuli) ▪ Posturing (ie, spontaneous and active maintenance of a posture against gravity ▪ Mannerism (ie, odd, circumstantial caricature of normal actions) ▪ Stereotypy (ie, repetitive, abnormally frequent, non-goal-directed movements) ▪ Agitation, not influenced by external stimulu ▪ Grimacing ▪ Echolalia (ie, mimicking another's speech) ▪ Echopraxia (ie, mimicking another's movements)	
Diagnostic criteria for neuroleptic malignant syndrome according to an international consensus of experts using the Delphi method (Gurrera et al. 2011)	
Diagnostic criteria	Priority score
Exposure to dopamine antagonist, or dopamine agonist withdrawal, within past 72 hours.	20
Hyperthermia (> 100.4°F or > 38°C on at least 2 occasions, measured orally)	18
Rigidity	17
Mental status alteration (reduced or fluctuating level of consciousness)	13
Creatinine kinase elevation (at least 4 times the upper limit of normal	10
Sympathetic nervous system lability, defined as at least 2 of the following: ▪ Blood pressure elevation (systolic or diastolic ≥ 25 % above baseline) ▪ Blood pressure fluctuation (≥ 20 mm Hg diastolic change or ≥ 25 mm HG systolic change within 24 hours) ▪ Diaphoresis ▪ Urinary incontinence	10
Hypermetabolism, defined as heart-rate increase (≥ 25 % above baseline) and respiratory-rate increase (≥ 50 % above baseline)	5
Negative work-up for infectious, toxic, metabolic or neurologic causes	7
Descriptive distinction between catatonia and neuroleptic malignant syndrome (Lang et al. 2015)	
Signs more predictive of NMS: ▪ Diaphoresis ▪ Rigor ▪ Fever ▪ Tremor ▪ Laboratory evidence of muscle injury ▪ Leukocytosis	
Signs more predictive of catatonia: ▪ Negativism ▪ Posturing ▪ Waxy flexibility ▪ Stupor ▪ Stereotypy	

Schizophrenia may predict a poorer response to benzodiazepines (Mormando et al. 2020).

Some authors suggest the use of NMDA antagonists (amantadine, memantine) as an alternative to benzodiazepines, but evidence for their efficiency is anecdotal (Sienaert et al. 2019).

ECT is the treatment of choice in case of insufficient response to benzodiazepines and should be initiated without delay. It is even considered the first-line treatment in severe cases (such as malignant catatonia, a form of catatonia associated with autonomic nervous system dysfunction and hyperthermia) and should be

introduced early to prevent medical complications (Mormando et al. 2020).

Longer duration of untreated catatonia probably predicts poorer response to ECT. ECT should be continued until complete remission and may be combined with benzodiazepines. Rapid withdrawal from benzodiazepines before or during ECT may result in recurrence of catatonic symptoms (Sienaert et al. 2019).

To date, there is no protocol on how to proceed in cases of catatonia resistant to benzodiazepine or ECT treatment.

The use of antipsychotics in catatonia is controversial and the literature regarding this subject calls for prudence. For most of authors they are contraindicated as they appear to not be effective and risk to worsen catatonia, induce malignant catatonia or NMS, especially first generation antipsychotics (Sienaert et al. 2019). Mann et al. (2013) recommend suspension of neuroleptics in case of suspected malignant catatonia.

Some evidence suggests that second-generation antipsychotics may be useful in the treatment of simple or mild catatonia (Mann et al. 2013). If used, this treatment may be in conjunction with benzodiazepines and careful monitoring of worsening catatonia or the development of NMS (Mormando et al. 2020).

Other authors suggest a beneficial effect of second-generation antipsychotics in schizophrenia-induced catatonia. Antipsychotics with weak D2 receptors blockade (clozapine, olanzapine, quetiapine) or partial D2 agonism (aripiprazole) should be preferred (Sienaert et al. 2019).

DISCUSSION

A review of the literature does not allow to confirm or invalidate a link between catatonia and neuroleptic malignant syndrome. The answer to this question is important, given the suggestion of a link has led to the contraindication of neuroleptics for the treatment of catatonia (Vesperini et al. 2010).

CONCLUSION

From the data currently available in the literature, experts agree on the treatment of catatonia in favour of an initial treatment with lorazepam and management with ECT for severe cases or those refractory to lorazepam after a certain number of days (Mormando et al. 2020).

Acknowledgements: *None.*

Conflict of interest: *None to declare.*

Contribution of individual authors:

Gilson Chloé: literature research and analysis, data interpretation and manuscript writing.
Jacques Denis: article design and proofreading.
Dubois Thomas: article design and proofreading.

References

1. *American Psychiatric Association: DSM 5: Manuel diagnostique et statistique des troubles mentaux (traduit par Crocq MA & Guelfi JD). Elsevier Masson, Issy-les-Moulineaux, 2015*
2. *Gurrera RJ, Caroff SN, Cohen A, Carroll BT, DeRoos F & Francis A: An international consensus study of neuroleptic malignant syndrome diagnostic criteria using the Delphi method. J Clin Psychiatry 2011; 72:1222-1228*
3. *Lang FU, Lang S, Becker T & Jäger M: Neuroleptic malignant syndrome or catatonia? Trying to solve the catatonic dilemma. Psychopharmacol 2015; 232:1-5*
4. *Mann SC, Caroff SN, Ungvari G & Campbell EC: Catatonia, malignant catatonia and neuroleptic malignant syndrome. Curr. Psychiatry Rev 2013; 9:111-119*
5. *Mormando C & Francis A: Catatonia revived: a unique syndrome updated. Int Rev Psychiatry 2020; 32:403-411*
6. *Sienaert P, Van Harten P & Rhebergen D: The psychopharmacology of catatonia, neuroleptic malignant syndrome, akathisia, tardive dyskinesia, and dystonie. Handb Clin Neurol 2019; 165:415-428*
7. *Vesperini S, Papetti F & Pringuey D: Are catatonia and neuroleptic malignant syndrome related conditions? Encephale 2010; 36:105-110*

Correspondence:
Chloé Gilson, MD
Université Catholique de Louvain, Psychosomatic Medicine Unit, CHU Mont-Godinne
Rue Dr Gaston Therasse 1, 5530 Yvoir, Belgium
E-mail: chloe.gilson@student.uclouvain.be