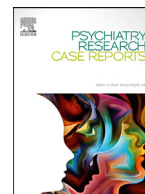




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Concurrent catatonia and COVID-19 infection in a demented patient: A case report

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ABSTRACT

Catatonia is a complex neuropsychiatric syndrome that comprises motor, behavioral and autonomic abnormalities. It occurs in the context of general medical, neurological, and psychiatric conditions. The study of catatonia in the elderly is particularly challenging due to the higher somatic and cognitive comorbidity, poly medication and the higher prevalence of delirium. Catatonia remains underdiagnosed in this population, especially in those with dementia.

We describe a case of an 82-years-old patient with mixed dementia, who developed catatonia for the first time, during her admission to our general medical ward due to SARS-CoV-2 organizing pneumonia. Besides the specific treatment for SARS-CoV-2 organizing pneumonia, catatonia was treated symptomatically with benzodiazepines and memantine with success.

In general, catatonia in older patients tends to have a good prognosis if detected early, its cause treated, the symptoms managed, and complications avoided. We report this case to alert clinicians in medical wards to this condition, to improve its overall diagnosis and treatment rates.

Introduction

Catatonia is a complex neuropsychiatric syndrome that comprises motor, behavioral and autonomic abnormalities (Cuevas-Esteban et al., 2017). It occurs in the context of general medical, neurological, and psychiatric conditions. It can also appear associated with medications and drugs of abuse (Jaimes-Albornoz et al., 2022). The Diagnostic and Statistical Manual - Fifth Edition (DSM-5) classifies catatonia either as a specifier within all mental disorders, as secondary to a general medical condition, or as an unspecified catatonia, when the syndrome is identified but not yet its etiology (American Psychiatric Association (APA) 2013). Depending on the predominant symptoms, catatonia can be divided into two variants: hypokinetic and hyperkinetic (Jaimes-Albornoz et al., 2022).

Clinical recognition of catatonia is of paramount importance since there are specific and definitive treatments (Suzuki et al., 2009). However, its diagnosis, especially in older patients, is challenging particularly because a substantial number of these patients are not in psychiatric settings (Serra-Mestres and Jaimes-Albornoz, 2018). In adults

over the age of 65, a review of 71 cases found that 28.16% of catatonia cases were associated with a general medical condition (Serra-Mestres and Jaimes-Albornoz, 2018). During the COVID-19 pandemic, different medical specialties were called upon to help in the general medical wards, which made it possible for psychiatrists to come in contact with said catatonic patients.

Data on the prevalence of catatonia in the elderly is scarce (Cuevas-Esteban et al., 2017, Jaimes-Albornoz et al., 2022, Takács et al., 2017), even more so in the case of catatonia in elderly with COVID-19 (Vazquez-Guevara et al., 2021). Only a few reports specifically explore catatonia in older patients (Cuevas-Esteban et al., 2017). From these reports a recent meta-analysis stands out, which showed an overall pooled mean prevalence of catatonia of 9.2% among older subjects diagnosed with a variety of psychiatric and medical conditions (Solmi et al., 2018).

We describe a case of catatonia in a patient with multiple medical conditions, including COVID-19. This report intends to alert clinicians in medical wards to this condition, in order to improve its overall diagnosis and treatment rates.

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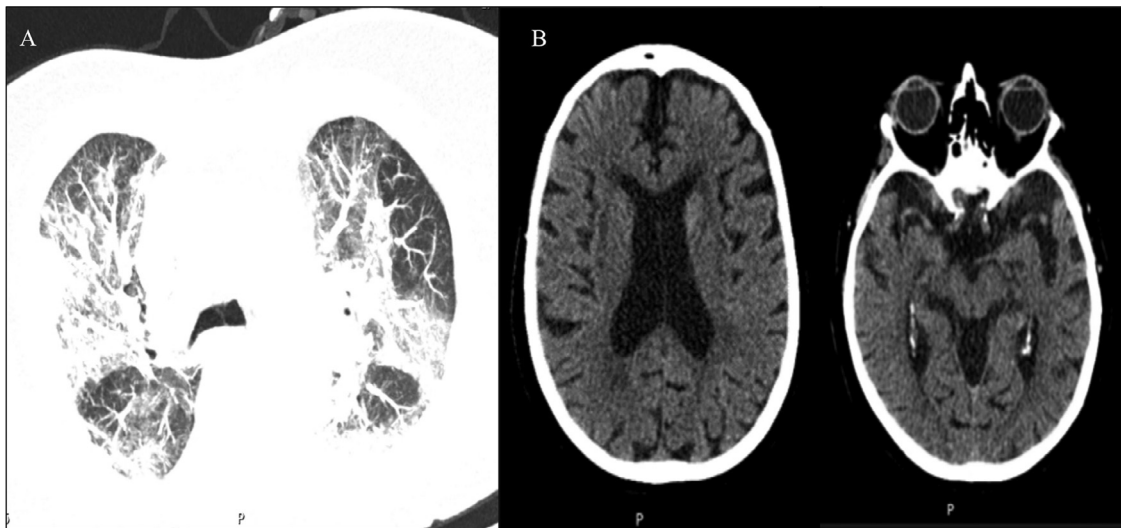


Fig. 1. A. Lung CT scan: SARS-CoV-2 organizing pneumonia. B. Cranial CT scan: Chronic ischemic microvascular leukoencephalopathy and generalized brain atrophy.

Case presentation

We present the case of an 82-years-old woman, with two higher education degrees, who is currently living in a nursing home due to her inability to perform basic activities of daily living independently (e.g., bathing and eating). She had been previously diagnosed with hypertension, dyslipidemia and mixed Alzheimer's and vascular dementia. She also has a history of a single major depressive episode in later life. Her usual medication was sertraline 50mg/day, amisulpiride 50mg/day, memantine 10mg/day, bromazepam 1,5mg/day, mexazolam 0,5mg/day, acetylsalicylic acid 150mg/day, ramipril 1,25mg/day and esomeprazole 20mg/day.

The patient was hospitalized in the first trimester of 2021 in an internal medicine ward especially dedicated to COVID-19 patients' care, due to prostration, diarrhea, and dyspnea in the context of SARS-CoV-2 infection.

Two days after she tested positive for COVID-19, and six days prior to hospital admission, she was prostrated, had one fall (without head injury), and had temporal and spatial disorientation for periods of time. The day before admission, her health condition worsened, with the patient declining food, and reducing her speech to a minimum. She was then admitted to the internal medicine ward due to SARS-CoV-2 organizing pneumonia with 50–60% parenchymal involvement with partial respiratory insufficiency, for which she was medicated with prednisolone 1mg/kg/day and with oxygen therapy via a venturi mask (FiO₂ 60%). Her usual medication was stopped in the Emergency Room, where she stayed for one day before being admitted to the inpatient unit. Her cranial CT scan showed a pattern of chronic ischemic microvascular leukoencephalopathy and generalized atrophy, without any acute lesion (Fig. 1)

On the second day, after admission to the inpatient unit, the medical team found the patient lying immobile on the bed, mute, and with a bizarre posture. On demand, a formal psychiatric evaluation was later performed by the team's psychiatrist. These signs, together with mutism and food refusal previously described in the day before admission, strongly suggested the diagnosis of catatonia. The Bush Francis Catatonia Rating Scale (BFCRS) (Takács et al., 2017) was used to formally assess catatonia. The BFCRS is a 23-item rating scale with operationalized definitions of catatonic symptoms. The first 14 items are used as a screening tool. Two or more catatonic signs on the first 14 items (evaluated in a dichotomous way, as present or absent) warrants further assessment with the complete BFCRS, where each catatonic sign

is rated from 0 to 3. The patient scored 8 on the screening scale and 17 on the severity scale (Table 1). She showed mutism, motor slowing, immobility, posturing and waxy flexibility. The patient was formally diagnosed with catatonia associated with a medical condition. During the first days of admission, an asymptomatic sinus bradycardia with normal QTc interval and poor R-wave progression was documented in the electrocardiogram (~35–45 bpm), without any other relevant changes on the echocardiogram and on the twenty-four-hour Holter monitoring. The etiology of that bradycardia remained unknown. After discussion with the cardiology unit, the patient was referred to a cardiology consultation with the possible intention of implanting a pacemaker if bradycardia persisted after discharge. Memantine was reintroduced at its previous outpatient dose of 10mg/day, and lorazepam 1,5mg/day was started. We had to be particularly careful with the dose of lorazepam to minimize potential adverse effects as the patient had SARS-CoV-2 organizing pneumonia with partial respiratory insufficiency and bradycardia. Her condition improved in the subsequent days.

During her hospital stay, she had a urinary infection, caused by a highly sensitive *Escherichia coli*, and a vaginal candidiasis as comorbidities, for which she was medicated with oral cefuroxime and clotrimazole cream, respectively.

After thirty days, on the day of her discharge, she scored 7 on the screening scale and 12 on the severity scale, mainly due to grimacing, posturing and waxy flexibility. The respiratory disease improved, and she was discharged, medicated with lorazepam 1mg/day, memantine 10mg/day, pantoprazole 40mg/day and a prednisone tapering schedule, without the need for further oxygen therapy. Tapering off the dose of lorazepam from 1,5mg/day to 1mg/day after the discharge was a collaborative decision made with a cardiologist. Considering the patient is improving from catatonia, the underlying etiologies of catatonia seemed already resolved, and the patient remained bradycardic, this decision intended to reduce the risk of adverse events in outpatient, namely the risk of falls or excessive diurnal somnolence.

One month after discharge, in a psychiatry follow-up appointment, she scored 3 on the screening scale and 10 on the severity scale, due to stereotypy, grimacing and passive obedience. Lorazepam was adjusted to 2mg/day.

Two months after discharge, she showed no signs of catatonia and lorazepam was then firstly reduced to 1mg/day and later discontinued. Memantine was also titrated to 20mg. Due to the persistence of sinus bradycardia, a pacemaker was implanted.

Table 1
Punctuations in Bush-Francis Catatonia rating scale.

BFCRS	Inpatient (day 2)	Inpatient (day 19)	Follow-up (day 45)	Follow-up (day 90)
1. Immobility/stupor	1	1	1	0
2. Mutism	1	0	0	0
3. Staring	1	0	0	0
4. Posturing/catalepsy	2	2	2	0
5. Grimacing	2	2	1	0
6. Echopraxia/echolalia	0	0	0	0
7. Stereotypy	0	0	1	0
8. Mannerisms	0	0	0	0
9. Stereotyped & meaningless repetition of words & phrases	0	0	0	0
10. Rigidity	1	1	0	0
11. Negativism	0	0	0	0
12. Waxy flexibility	3	0	0	0
13. Withdrawal	1	1	0	0
14. Excitement	0	0	0	0
15. Impulsivity	0	0	0	0
16. Automatic obedience	2	1	2	0
17. Passive obedience (mitgehen)	0	3	3	0
18. Muscle resistance (gegenhalten)	0	0	0	0
19. Motorically Stuck (ambitendency)	3	0	0	0
20. Grasp reflex	0	0	0	0
21. Perseveration	0	0	0	0
22. Combativeness	0	0	0	0
23. Autonomic abnormality	0	1	0	0
Score total	17	12	10	0

Discussion

In this case report, we describe a case of a patient with mixed dementia, who presented with catatonia and COVID-19 infection and underwent inpatient treatment in an internal medicine ward.

The study of catatonia in the elderly is particularly challenging due to the higher somatic and cognitive comorbidity, poly medication and the higher prevalence of delirium among this population (Cuevas-Esteban et al., 2017). These particularities may explain why catatonia remains underdiagnosed in this population, especially in those with dementia (Younes et al., 2019). In this group, its prevalence is unclear, etiology tends to be multifactorial, and there is a greater risk of complications, if undiagnosed or untreated (Alisky, 2004). Two studies have reported rates of catatonia in patients with dementia of 4.7–12.6% (using the DSM-5 and the BFCRS, respectively) (Alisky, 2004), and 42.8% (using Fink and Taylor and DSM-5 criteria) (Serra-Mestres and Jaimes-Albornoz, 2018), however these studies were conducted in acute psychogeriatric settings, not in general medical wards. In more than half of the cases of catatonia in dementia, catatonia was associated with a medical condition (Takács et al., 2017).

Catatonia has been described as a sequel of many disparate processes of neuronal injury, including cerebrovascular accidents, head injury, HIV encephalitis, brain tumors, and multiple sclerosis (Serra-Mestres and Jaimes-Albornoz, 2018). Lesions of the frontal lobe, parietal lobe, limbic system, diencephalon, and basal ganglia can be associated with catatonia. Consequently, there is a common anatomical basis for catatonia and all the major dementias, including Alzheimer's disease, vascular dementia, Lewy body dementia, corticobasal degeneration, frontotemporal dementia, and Parkinsonian dementia (Alisky, 2004).

As in this case report, a multifactorial etiology to catatonia has been reported in various publications in the older adults' age group (Jaimes-Albornoz et al., 2022). We hypothesize that the COVID-19 infection is likely to have precipitated catatonia, particularly in a patient with a previous diagnosis of mixed dementia, a history of a previous major depressive episode and a recent abrupt suspension of memantine (NMDA receptor antagonist) and benzodiazepines. In fact, the available literature suggests that catatonia tends to be present in demented patients alongside with other disorders, be they medical or psychiatric (Serra-Mestres and Jaimes-Albornoz, 2018). Some authors admit that COVID-19 infections may contribute to accelerating the development of or al-

tering the course of pre-existing neuropsychiatric disorders which is in line with recent literature (Quincozes-Santos et al., 2021). Additionally, as will be described below, NMDA receptor antagonists, such as memantine or amantadine, and benzodiazepines can be used as a treatment option for catatonia (Jaimes-Albornoz et al., 2022, Carroll et al., 2005), which might suggest that the abrupt suspension of these drugs, days before the admission to the inpatient unit, may also have favored the worsened of catatonia in our patient. This hypothesis is in line with the literature which suggest that abrupt discontinuation of certain drugs, namely benzodiazepines and NMDA receptor antagonists, may contribute to catatonia onset or worsening (Jaimes-Albornoz et al., 2022).

The hypokinetic variant of catatonia is the most frequently found variant in depressive disorders and general medical conditions and is characterized by reduced movement, mutism, and withdrawal (Serra-Mestres and Jaimes-Albornoz, 2018). In a study of psychiatrically hospitalized older adults, the hypokinetic variant predominated in over 50% of cases (Takács et al., 2017). In a study of catatonia among elderly patients, the most frequent signs were immobility/stupor (83–100%), posturing (67–70%), mutism (33–80%), staring (50–100%), rigidity (67–90%), and withdrawal (50–80%) (Serra-Mestres and Jaimes-Albornoz, 2018). Our patient also exhibited the hypokinetic variant, being the preeminent catatonic signs the ones described above.

One important aspect to discuss is the challenging differential diagnosis between catatonia and delirium. In fact, both conditions present with prominent psychomotor abnormalities, particularly in the case of catatonia and hypoactive delirium. Additionally, the causes of both delirium and medical catatonia greatly overlap (Serra-Mestres and Jaimes-Albornoz, 2018) and both conditions co-occur relatively frequently in older people (Jaimes-Albornoz et al., 2022). There are, however, relevant differences in their pharmacological management. The treatment of choice in catatonia, lorazepam, is rarely the treatment of choice in delirium, except when caused by a benzodiazepine withdrawal. The most widely used symptomatic treatment of choice in delirium, antipsychotics, is generally to be avoided in the management of catatonia (Serra-Mestres and Jaimes-Albornoz, 2018). In our patient, probably the initial presentation, characterized by prostration and fluctuant temporal and spatial disorientation, was compatible with a delirium diagnosis. Catatonia only became evident a few days later. A recent systematic review (Oldham and Lee, 2015) recommended identifying

and treating the etiology of both conditions by initially trying/ giving a challenge test with lorazepam, avoiding the use of high-potency antipsychotics, and taking the necessary measures to prevent and treat complications.

Catatonia is associated with neurochemical abnormalities, namely low GABA activity in frontal cortex, low dopamine (D2 receptor) activity in basal ganglia, high glutamate NMDA activity in parietal cortex, or a combination of these (Carroll et al., 2005). These neural aspects explain why catatonia responds not only to treatment with benzodiazepines (GABA-A agonists), particularly lorazepam, but also diazepam, clonazepam, and oxazepam (Alisky, 2004), but also to glutamate antagonists, such as memantine and amantadine. The low dopamine activity in basal ganglia may explain, at least partially, why antipsychotics should be avoided in most catatonic patients (Jaimes-Albornoz et al., 2022), particularly in older adults.

The management of catatonia has three main steps: first, the treatment of the underlying cause; second, symptomatic treatment; and third; the prevention of complications (Jaimes-Albornoz et al., 2022, Serra-Mestres and Jaimes-Albornoz, 2018). After addressing the cause, regarding symptomatic treatment, general treatment recommendations on catatonia are derived from case reports or observational studies (Zaman et al., 2019). Some authors suggest a treatment algorithm for catatonia, where GABA-A agonists such as lorazepam and diazepam are first-line treatments. If these treatments fail, ECT and glutamate antagonists, such as memantine and amantadine, are the second- and third-line treatments, respectively (Carroll et al., 2007). In general, treatment can be dramatically effective, with a complete resolution of signs in 60–80% of acute cases (Serra-Mestres and Jaimes-Albornoz, 2018), even in older patients. In our patient, the treatment for COVID-19 organizing pneumonia, together with the reintroduction of memantine and benzodiazepine therapy, produced a complete resolution of catatonia. Had this approach not been successful, we would have considered electroconvulsive therapy (ECT) after respiratory failure resolution. In a recent report of catatonia among COVID-19 patients (Sakhardande et al., 2022), the authors emphasized that, in the absence of respiratory compromise, ongoing close monitoring of the COVID-19 disease can allow for concurrent administration of parenteral benzodiazepines, such as lorazepam, and ECT safely in catatonia.

Regarding follow-up, the patient will continue living in a nursing home and maintain regular outpatient appointments with geriatric psychiatry and internal medicine in our hospital.

Catatonia in older patients tends to have a good prognosis if detected early, its cause treated, the symptoms managed, and complications avoided (Serra-Mestres and Jaimes-Albornoz, 2018). Prolonged catatonia is associated with adverse events that can be life-threatening (Serra-Mestres and Jaimes-Albornoz, 2018).

Regarding limitations, we recognize that the absence of complete access to the patient's previous medical reports and the fact that the mental state examination had taken place in a non-psychiatric setting with the constraints arising from the particularities of COVID-19 units, namely, the need for personal protective material and the necessity of reducing the time of exposure to the patients during clinical evaluation, may have limited the accuracy of some clinical elements.

However, we tried to mitigate such factors by obtaining medical information from a collateral source of information, namely, a close relative, by interviewing the patient at different moments and, finally, by the successive application of BFCRS, to better characterize catatonia in this case report.

In conclusion, it is important to keep in mind the possibility of catatonia and look for it proactively, especially when dealing with older patients admitted in general medical wards, due to acute medical complications, particularly when they have a history of previous psychiatric disorders and a diagnosis of dementia. If recognized and treated without delay, the prognosis is excellent. Further studies are required to clarify the relation between catatonia and dementia, and, also, the role of a COVID-19 infection in catatonia.

Authors contribution

PCP: Substantial contribution for the draft of the manuscript. Clinical follow-up of the patient.

CC: Substantial contribution for the draft of the manuscript.

MR: Clinical follow-up of the patient. Case review and critical review of the paper.

MS: Clinical follow-up of the patient. Case review and critical review of the paper.

MJE: Case review and critical review of the paper.

LP: Substantial intellectual contribution. Case review and critical review of the paper.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

Data confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Patient consent

The authors received written consent from the patient to publish the report and the information has been deidentified to protect anonymity.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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