

The Influence of Covid-19 Infection on Neurocognitive Disorders

DANIELA GABRIELA GLĂVAN^{1,2}, VICTOR GHEORMAN^{1,3},
MĂDĂLINA ALDEA¹, FELICIA MILITARU^{1,3}, ION UDRIȘTOIU^{1,3}

¹Department of Psychiatry, University of Medicine and Pharmacy of Craiova, Romania

²Psychiatry Clinic II, Neuropsychiatry Clinical Hospital, Craiova, Romania

³Psychiatry Clinic I, Neuropsychiatry Clinical Hospital, Craiova, Romania

ABSTRACT: Neurocognitive disorders are a group of disorders characterized by an impaired cognition which has not been present since birth or very early life and represents a decline from a previous attained level of functioning. The case we studied is M.E., a 62 years female, married, from rural area, working as a tailor, without any psychiatric history. She develops psychiatric symptoms during Covid-19 infection and treatment, in November 2020. The patient has been admitted in psychiatric care, in that time, for about one month, for a persistent confusion state during and after this event. These symptoms diminish the patient's level of functioning and seemed to be related with the Covid-19 infection or treatment. Psychological investigation underlines a MMSE 14, severe impairment in attention, short-term and long-term memory. CT evaluation presents normal relation except a moderate general atrophy, according with patient's age. Differential diagnosis will be discussed. The treatment has proven its effectiveness, the patient regaining her ability to orientate, could do housework, good improvement in attention and short-term memory. We emphasize that there is correlation between the Covid-19 infection and confusive state and delirium in patients, as a comorbidity, followed in many cases by chronic progressive neurocognitive disorder, especially in elderly.

KEYWORDS: Covid-19 infection, delirium, confusion, neurocognitive disease.

Introduction

The neurocognitive disorders include multiple etiological subtypes. The main subtypes are “due to Alzheimer’s disease”, “vascular”, “with Lewy’s bodies”, “due to Parkinson’s disease”, etc. [1].

Often, the neurocognitive disorder evolves unnoticed by the patient and his relatives and sometimes only the presence of delirium draws attention over the underlying pathology.

Considering the advanced age of affected individuals, burdened by a diversity of chronic medical comorbidity, besides the effectiveness, the practitioners must be concerned about the tolerability and safety of medications used to treat cognitive impairments.

There is a question raised among the specialists about Covid-19 infection and treatment and how it affects individuals from psychiatry and neurology point of view.

We already know that Covid-19 has neurotropism and the most common symptoms are: headache, anosmia, ageusia and might evolve to cerebrovascular disease, encephalopathy [2,3].

Case Study

Patient Description

The patient, M.E., a 62 years old female did not have a psychiatric history and, during the Covid-19 infection, developed a psychotic symptomatology and cognitive impairment-mystical delusional ideas, auditory and visual hallucinations, disturbance in attention and memory, associated with short confusing states, psychomotor agitation.

These symptoms determined the transfer of the patient from an Infectious Diseases Section to the Psychiatric Clinic Support Covid-19 of the Neuropsychiatry Hospital from Craiova.

The patient caregivers gave a written informed consent accepting the publication of these data.

Psychiatric and Medical History

There was no known familial history of mental illness. We already knew that the patient had no psychiatric history, but had a cardiovascular history (Hypertension, Ischemic Cardiomyopathy) and was admitted and treated for a Covid-19 infection 12 days earlier in the Infectious Diseases Section of a Hospital from Dolj County.

Chronic medical comorbidities included hypertension; chronic ischemic heart disease; generalized and unspecified atherosclerosis;

SARS-CoV-2 infection. **Covid-19 treatment** conducted in the Infectious Diseases section included Dexamethasone 8mg/2mlx1/day, 10 days; Azithromycin 250mgx2/day, 10 days; Favipiravir 1600mg/12h in the first day, then 600mg/12h for 10 days; Enoxaparine 40mg x1/day, s.c.

Psychiatric examination in admission, revealed a 62 M.E. female patient with disheveled aspect, restless gestures, hyperactivity with episodic psychomotor agitation, which led to difficult interaction with the medical staff. Perceptual disturbances such as hallucinations, illusions and false recognitions were experienced by the patient, also impaired concentration and memory, difficulties in focusing attention, associated with the cognitive disorder and internal stimuli such as auditory hallucinations were noticed.

Orientation was disturbed according to time and place. The form of thought was illogical and incoherent and even incomprehensible, with mystical ideas-she believed that she was „sent here by the God to save us”. The patient was unable to control impulses due to cognitive and psychotic disorders and had no awareness and no understanding about being ill.

During the physical examination, the woman appeared partial conscious; with the following vital signs-BP=200/104mmHg, HR=93b/min, t=36,3 C, SaO2=98%. In evaluation, the cardiovascular system revealed no issues, with normal heart sounds and no added sounds or murmurs. In respiratory system there were present nasal congestion, cough, rales/rhonchi,

wheezing. There was no abdominal pain and the patient denied changes in stool frequency and consistency for the gastro-intestinal system.

During the neurological exam, we observed discreetly gait and balance disorders, positive Babinski’s reflexes bilaterally, diminished patellar and Achilles’s reflex, mild dysarthria, adiadochokinesia, dyscalculia, dysgraphia, dyslexia, mild mixed dysphasia, positive Noica signs.

Blood and Serologic Tests

Psychometric scales (Table 1) in admission revealed a 14 points MMSE (out of 30 maximum points) with time and space orientation alterations, registration and recall of information disturbances. GAFs scale was 18 meaning an adaptive disability more than 70%.

Blood tests revealed anemia; hepatic cytolysis and the presence of inflammatory syndrome.

Table 1. Evolution of psychometric scales in admission and discharge.

Scale	MMSE	GAF
Admission	14	18
Discharge	20	40
	+ 6	+ 22
EVOLUTION	significant improvement	significant improvement

Neuroimaging and Thoracic Scan

A native brain CT scan examination proved moderate cerebral atrophy with secondary dilatation of the liquid spaces (Figure 1).



Figure 2. Cranial CT scan showing moderate cortical atrophy.

The thoracic CT scan examination revealed typical aspects for Covid-19 pneumonia, with ground-glass opacities, vascular enlargement, bilateral abnormalities, lower lobe involvement with posterior predilection in about 25% of the lung surface.

Positive and Differential Diagnosis

Psychiatric Diagnoses (according to DSM-V) were: delirium due to multiple aetiologies; neurocognitive disorder, in observation for Alzheimer Disease [1].

The patient presented a disturbance in attention and cognition, which developed over a short period of time and represents a change in baseline attention and awareness and tends to fluctuate during the course of a day.

The disturbances are not better explained by another pre-existing condition and are caused by more than one etiological medical condition and medication side effects.

We took in consideration several other mental disorders:

- Psychotic disorders and bipolar disorders with psychotic features-have in common with delirium underlying cognitive disorders vivid hallucinations, delusions, language disturbances, agitation. We think about psychotic disorders due to dexamethasone treatment.
- Acute stress disorder precipitated by Covid-19 infection-might associate fever, anxiety, dissociative symptoms, such as depersonalization, delusions.
- Other cognitive disorders, the most difficult differential diagnosis issue when evaluating confusion in older adults is emphasizing the difference between delirium and dementia. Delirium might also be overlaid to a prior neurocognitive disorder that may not had been recognized or might be followed by persistent cognitive disorder.
- Medication induced delirium can be due to dexamethasone administration, while delirium due to a medical condition can follow the Covid-19 encephalopathy.

Our diagnosis was delirium due to multiple etiologies, **consisting of combined** dexamethasone use, Covid-19 encephalopathy and an underlying undiagnosed neurocognitive disorder.

Treatment

The patient completed treatment for Covid-19 infection (corticosteroid therapy in anti-inflammatory doses and antivirals) before the psychiatric admission.

The treatment during the psychiatry admission included Risperidonum (oral solution) -1mg/ml, 1mg x 2/day, Pramiracetamum-600mg x 2/day, Acidum valproicum-300mg x 2/day, Lorazepam-1mg x 2/day, in association with high vitamin doses.

The patient also continued the treatment of the other medical comorbidities.

Future proposed follow-up: Patient evaluation in 3-6 months and if the Alzheimer Disease diagnosis is confirmed, initiating anticholinesterase inhibitor treatment +/- Memantine, according to the existing national therapeutic protocols approved by the Romanian Ministry of Health.

Continuing the treatment for other medical conditions.

We expected, as a result the amelioration of the cognitive impairment symptoms with confusing status remission-(we proposed to re-evaluate the patient in 3 months in order to confirm the neurocognitive disease, and follow-up monthly after discharge), the remission of psychotic symptoms and improving the patient's compliance in taking the medicine and increasing her self-autonomy.

The actual results included the amelioration of cognitive status and maintaining the progress achieved in cognitive functioning, remission of psychotic associated symptoms, remission of confusive state and improving the self-motivation in respecting the prescribed regimen and medications for cardio-vascular disease and psychiatric illness.

Evaluation in Three Months after Discharge

As we expected, there was a remission of psychotic symptoms and confusive state, but there was a persistence of the cognitive impairment (MMSE-23, GAF-50).

During these 3 months, the treatment was maintained with Pramiracetamum 600mg x 2/day, Risperidonum, which was gradually reduced and stopped after 1 month, Valproic acid and Lorazepam were also gradually stopped.

After re-evaluation the Alzheimer Disease diagnosis was confirmed and the treatment with Rivastigminum patches and Memantinum 10mg was continued, with gradually increasing doses.

Discussion

Sometimes there is quite difficult to evaluate confusive symptoms in term to etiologies especially in elderly patients.

During the Covid-19 pandemics a lot of patients with SARS-CoV-2 virus which were admitted in Psychiatric II Clinic had psychotic and confusive symptoms, which made us think if there is any correlation between the infection or the treatment and confusive state.

International studies also confirm that delirium is present in 70% of the patients admitted in ICU units, with Covid-19 infection, especially in prolonged hospitalization, and with a higher percentage of women.

The same authors consider that cognitive impairment is high in Covid-19 patients and is related to the risk of complications and may persist after discharge [4-8,10].

The confusive states and neurodegenerative diseases often coexist in the same patients and negatively impact each other [8-10].

Neurocognitive disorders must be treated by multiple specialties in collaboration, especially because the prevalence of delirium is proved to be higher in hospitalized individuals.

The cognitive improvement was objectified based on both psychometric measured tests and subjective experiences.

The prevalence of delirium is low in the community (1-2%), but in hospitalized individuals ranges to 14-24% and is estimated to arising during hospitalization range from 6 to 56%.

Most patients with delirium have a full recovery if the symptoms are early recognized and treated [5].

Usually, the evolution of delirium is strictly related to the underlying condition and the treatment of this condition, the mortality being evaluated to about 40% [1,2,10].

There are studies which confirm that 5% of the neurological events associated with this respiratory virus are ischemic strokes [11].

Another recent study confirms that 62% of their admitted patients had a cerebrovascular event, of which 74% were represented by ischemic stroke [6].

Encephalitis was present in several cases of Covid-19 infection, associated with confusion and treated successfully with mannitol, with consciousness recovery [12].

Some authors consider that patients should be evaluated early for neurological and psychiatric symptoms, so the intervention can be promptly [13,14].

According to them 20% of the persons infected with Covid-19 had psychiatric pathologies in the following 14-90 days after the diagnosis, the incidence of newly diagnosed dementia being 1.6%, in elderly [14,15].

Conclusion

Taking in consideration the frequency of delirium and confusive state in patients with Covid-19 infection we consider that there in a correlation between them.

We expect that a big proportion of the patients, especially elderly, might develop a chronic neurocognitive disorder after the SARS-CoV-2 infection, as a comorbidity, impairing their socio-familial functionality and autonomy.

On the other hand, there are the patients already diagnosed with cognitive disorders, which are susceptible to infection and a more rapidly deterioration because of the Covid-19 infection and the comorbidities associated with it.

An early neurological and psychiatric management and diagnosis could improve the prognosis for this kind of patients.

Conflict of interests

None to declare.

References

1. Wilson JE, Mart MF, Cunningham C, Shehabi Y, Girard TD, MacLulich AMJ, Slooter AJC, Ely EW. Delirium. *Nat Rev Dis Primers*, 2020, 6(1):90.
2. Román GC, Spencer PS, Reis J, Buguet A, Faris MEA, Katrak SM, Láinez M, Medina MT, Meshram C, Mizusawa H, Öztürk S, Wasay M; WFN Environmental Neurology Specialty Group. The neurology of COVID-19 revisited: A proposal from the Environmental Neurology Specialty Group of the World Federation of Neurology to implement international neurological registries. *J Neurol Sci.*, 2020, 414:116884.
3. Maury A, Lyoubi A, Peiffer-Smadja N, de Broucker T, Meppiel E. Neurological manifestations associated with SARS-CoV-2 and other coronaviruses: A narrative review for clinicians. *Rev Neurol (Paris)*, 2021, 177(1-2):51-64.
4. Ragheb J, McKinney A, Zierau M, Brooks J, Hill-Caruthers M, Iskander M, Ahmed Y, Lobo R, Mentz G, Vlisides P. Delirium and neuropsychological outcomes in critically ill patients with COVID-19: a cohort study. *BMJ Open*, 2021, 11:e050045.
5. Helms J, Kremer S, Merdji H, Schenck M, Severac F, Clere-Jehl R, Studer A, Radosavljevic M, Kummerlen C, Monnier A, Boulay C, Fafi-Kremer S, Castelain V, Ohana M, Anheim M, Schneider F, Meziani F. Delirium and encephalopathy in severe COVID-19: a cohort analysis of ICU patients. *Crit Care*, 2020, 24(1):491.

6. Varatharaj A, Thomas N, Ellul MA, Davies NWS, Pollak TA, Tenorio EL, Sultan M, Easton A, Breen G, Zandi M, Coles JP, Manji H, Al-Shahi Salman R, Menon DK, Nicholson TR, Benjamin LA, Carson A, Smith C, Turner MR, Solomon T, Kneen R, Pett SL, Galea I, Thomas RH, Michael BD; CoroNerve Study Group. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *Lancet Psychiatry*, 2020, 7(10):875-882.
7. Brummel NE, Jackson JC, Pandharipande PP, Thompson JL, Shintani AK, Dittus RS, Gill TM, Bernard GR, Ely EW, Girard TD. Delirium in the ICU and subsequent long-term disability among survivors of mechanical ventilation. *Crit Care Med*, 2014, 42(2):369-377.
8. Mcloughlin BC, Miles A, Webb TE, Knopp P, Eyres C, Fabbri A, Humphries F, Davis D. Functional and cognitive outcomes after COVID-19 delirium. *Eur Geriatr Med*, 2020, 11(5):857-862.
9. Geriatric Medicine Research Collaborative. Delirium is prevalent in older hospital inpatients and associated with adverse outcomes: results of a prospective multi-centre study on World Delirium Awareness Day. *BMC Med*, 2019, 17(1):229.
10. Zazzara MB, Penfold RS, Roberts AL, Lee KA, Dooley H, Sudre CH, Welch C, Bowyer RCE, Visconti A, Mangino M, Freidin MB, El-Sayed Moustafa JS, Small KS, Murray B, Modat M, Graham MS, Wolf J, Ourselin S, Martin FC, Steves CJ, Lochlainn MN. Probable delirium is a presenting symptom of COVID-19 in frail, older adults: a cohort study of 322 hospitalised and 535 community-based older adults. *Age Ageing*, 2021, 50(1):40-48.
11. Li Y, Li M, Wang M, Zhou Y, Chang J, Xian Y, Wang D, Mao L, Jin H, Hu B. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. *Stroke Vasc Neurol*, 2020, 5(3):279-284.
12. Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19. *Brain Behav Immun*, 2020, 88:945-946.
13. Wu Y, Xu X, Chen Z, Duan J, Hashimoto K, Yang L, Liu C, Yang C. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*, 2020, 87:18-22.
14. Mukaetova-Ladinska EB, Kronenberg G, Raha-Chowdhury R. COVID-19 and neurocognitive disorders. *Curr Opin Psychiatry*, 2021, 34(2):149-156.
15. Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. *Lancet Psychiatry*, 2020, S2215-0366:30462-30464.

*Corresponding Author: Mădălina Aldea, Department of Psychiatry,
University of Medicine and Pharmacy of Craiova, 2, Petru Rareș St, Craiova 200349,
e-mail: filfanmadalina@gmail.com*