

CASE REPORT

Delirium in critically ill patients with COVID-19 pneumonia

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Abstract

The ICU delirium is a predictor of mortality, length of stay in hospital, time on ventilation, and long-term cognitive impairment. There is a well-established association between acute respiratory distress syndrome (ARDS) and ICU delirium. However, the profile and disease progression trajectory of COVID-19 patients with ICU delirium has not been studied. This case series reviews our institution's experience in COVID-19 patients with ICU delirium. Of all four patients, two of them died in hospital, and the other two survived to the hospital discharge. The disease progressions were tracked, as well as the ICU delirium. Potential life-threatening complications and organ failure symptoms were also presented. To improve the patients' overall health outcome, Haloperidol was prescribed with careful consideration.

Keywords

Delirium; COVID-19; ICU

1. Introduction

In December 2019, Wuhan (in Hubei Province, China) witnessed an outbreak of novel coronavirus infections, which is named COVID-19 caused by SARS-CoV-2. SARS-CoV-2 is the seventh identified coronavirus known to be contagious in humans. It has caused high mortality, which is similar to the contagious coronaviruses that are already identified, such as severe acute respiratory syndrome coronavirus (SARS-CoV) [1–4] and Middle East respiratory syndrome coronavirus (MERS-CoV) [5, 6]. SARS-CoV-2-infected patients are categorised as severe COVID-19 if they suffer from 1) respiratory distress and respiratory rate ≥ 30 per minute; 2) oxygen saturation $\leq 93\%$ at rest; 3) $\text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg ($\text{PaO}_2/\text{FiO}_2^*$ [atmospheric pressure (mmHg)/760] ≤ 300 mmHg, used if elevation is more than 1,000 meters); or 4) $> 50\%$ progression of pulmonary lesions within 24–48 hours. Critical COVID-19 patients are defined if 1) they suffer from respiratory failure and require mechanical ventilation; 2) shock occurs; or 3) they have other organs dysfunction and require ICU treatments. It is noteworthy that severe and critical patients may present a low/moderate grade fever or even no apparent fever during the disease course, which causes difficulties in the diagnosis of severe and critical cases [7]. Per the “Novel Coronavirus Pneumonia Diagnosis and Treatment Protocol”, critical COVID-19 patients should be admitted to the ICU as soon as possible. At present, an increasing number of studies have shown that the majority of patients admitted to the ICU experience delirium [8–10], with an incidence rate ranging from 11% to 80% and reaching up to 80%, especially in patients treated with mechanical ventilation. Given the

above findings, ICU delirium is expected to occur in severe COVID-19 patients. Previous studies described ICU delirium as a disturbed status of consciousness, attention, cognition and sleep-wake cycle. Under most conditions, the experience during the delirious period is kept in patients' memories and leaves them distress in their remission stage, or even in the last days and hours of life [8, 9]. However, the characteristics of ICU delirium occurring in COVID-19 patients remain uncertain. ICU delirium is related to the prognosis of critical patients and may lead to prolonged mechanical ventilation, prolonged ICU care, prolonged hospitalization, a direct increase in workload for clinical health-care professionals, increased difficulty in disease diagnosis, an increase in in-hospital mortality, and sequelae involving short-term or long-term cognitive dysfunction after discharge in some patients. Therefore, given the high incidence and poor prognosis related to delirium in severe COVID-19 patients, the profile of patients with ICU delirium, the progression of COVID-19, and the other complications is needed.

We enrolled patients with critical COVID-19 caused by COVID-19 infection in Guanggu Campus, Tongji Hospital, Wuhan, China. Delirium was assessed daily using the validated Confusion Assessment Method for the ICU (CAM-ICU) and Richmond Agitation and Sedation Scale (RASS) by registered psychiatrists, both of which were commonly used to evaluate ICU delirium [11]. There are two steps to determine the presence of delirium. Firstly, we evaluated the RASS score. The RASS scores less than -4 were not tested with CAM-ICU, due to the lack of consciousness. Then the CAM-ICU was implemented to compute the status of delirium. In this case series, four patients with critical COVID-19 were

confirmed to have ICU delirium.

2. Case 1

An 84-year-old male patient was admitted to the ICU presenting with shortness of breath and fever for 3-4 days. He was confirmed with critically ill COVID-19 infection and reported a 10-year hypertension history. On presentation to the ICU, his body temperature was 36.5 °C, his heart rate was 100 beats per minute (bpm), his blood pressure was 120/70 mmHg, and his respiratory rate was 29 breaths per minute. His oxygen saturation was 98% using a non-invasive ventilator. His RASS score was +1 on admission. He was overtly combative, struggling out of a protective restraint, and refused medicine and ventilation on day 3 with a RASS score of +4. He exhibited slurred speech, did not follow the doctor's order and had difficulty focusing on conversation. A CAM-ICU was used and yielded a positive result. Four days later, a decrease in the mean arterial pressure (MAP) and a clinical deterioration were observed. The patient received urgent tracheal intubation for acute respiratory distress syndrome (ARDS) on day 11. Although chest radiography indicated a temporary improvement in the lungs over the course of treatment, he ultimately died from septic shock and multiple organ failure on day 27 after admission.

3. Case 2

A 79-year-old female patient was admitted to the ICU due to COVID-19, end-stage renal disease and acute myocardial injury (hs-cTnI 75.4 pg/mL). She had a history of percutaneous transluminal coronary intervention (PCI) and chronic total occlusion. Her body temperature was 35.4 °C, her heart rate was 90 beats per minute, her blood pressure was 117/59 mmHg, and her respiratory rate was 20 breaths per minute. Her PaO₂ pressure was maintained at 95-100 mmHg while receiving oxygen through a face mask at a rate of 5 litres per minute. She received daily continuous renal replacement therapy (CRRT) during medication. Sixteen days after admission, her ability to direct and focus was reduced. Her RASS score was +2, and the CAM-ICU result was positive, with PaO₂/FiO₂ > 300 mmHg. Three days later, she experienced a heart attack (non-ST-segment elevation acute coronary syndrome) and died from cardiac shock.

4. Case 3

A 69-year-old male patient was admitted to the ICU due to critical COVID-19. He had chronic obstructive pulmonary disease (COPD), chronic heart failure and a history of postoperative lung cancer. His body temperature was 37.3 °C, his heart rate was 65 beats per minute, his blood pressure was 168/98 mmHg, and his respiratory rate was 22 breaths per minute. His arterial blood pressure (ABP) was PaO₂/FiO₂ 288.48 mmHg, his PaCO₂ pressure was 86.5 mmHg, and his pH was 7.218 while receiving oxygen through a face mask at a rate of 3 litres per minute. He refused medication and Bilevel Positive Airway Pressure (BiPAP) ventilation and threw the ventilator. His RASS score changed from 1 to 3, and the CAM-

ICU result was positive. One day later, he received mechanical ventilation to correct respiratory failure. He was discharged from the ICU 22 days after intubation.

5. Case 4

An 81-year-old male patient was admitted to the ICU due to COVID-19 pneumonia. He reported hypertension and coronary artery disease. His body temperature was 38.2 °C, his heart rate was 87 beats per minute, his blood pressure was 132/67 mmHg, and his respiratory rate was 24 breaths per minute. Oxygen saturation was 94% with oxygen at a rate of 5 litres per minute. Two days after admission, endotracheal intubation was performed. After 16 days of ventilation, he was extubated and given non-invasive ventilation by an oral-nasal mask. On day 21, the patient was agitated and difficult to calm down. His RASS score increased from 0 to 2, and he showed difficulty with speech. The neurological examination was unremarkable. The CAM-ICU result was positive. His RASS score decreased to 0 in 2 days. Chest radiography and a laboratory examination indicated a continuous improvement in his condition. The patient was discharged from the ICU after 1 week.

6. Discussion

It is commonly known that there is an association between ARDS and delirium [12]. Indeed, the appearance of delirium is a common phenomenon both in critically ill [13] and in elderly patients [14]. Although there were no significant findings that the older patients suffer more from the delirium in adult ICU setting [15], the delirium plays a negative impact on the cognitive function in the later life of ICU admitted patients [16].

In our research, delirium occurred in all of these cases, which could not be simply explained by the history of cognitive impairment. In this four case series, majority of patients (3/4) had complication issues. Two of them have pre-existing hypertension; one had PCI; one had heart failure and lung cancer. There was no clear association pattern between age and ICU delirium duration. The case 4 was the oldest patient in this series, however, he had seven days delirium duration and he was alive. Both cases 1 and 2 died in hospital only have 3 days duration. After we evaluated the patient's delirium status and consulted with an experienced psychiatrist, all four patients were prescribed Haloperidol, although some physicians argued that there was no significant difference between Haloperidol and placebo [17]. Due to the small sample size and study limitation, we cannot perform any formal statistical analysis.

Limitations exist in our case report. For one thing, we only described the observation of delirium in these infected patients, and lacked the association between delirium and COVID-19. It is still possible that the occurrence of delirium in such patients might not be directly related to COVID-19, but, a complication caused by this disease. Regrettably, we could neither summarize the characteristics, nor show the specificity of delirium in these COVID-19 patients because of a large heterogeneity among themselves. It is worth ascertaining whether this type of delirium is different from those of other

patients in ICU. For another, the mechanisms and risk factors of delirium in these four cases were not clear. Only organ dysfunction in case 2 seemed to accelerate delirium, which was consistent with seven risk factors in COVID-19 mentioned by Kotfis K *et al.* [18]. It needs to investigate whether the risk factors of these four cases were included in those reported by Kotfis K *et al.* or not. A controlled design is needed to compare the similarities and differences between the delirium of COVID-19 patients and those of other ICU or non-ICU patients.

7. Conclusions

ICU delirium can be presented in the critical COVID-19 patients. It is a good practice to provide treatment to control the ICU delirium, especially when we are dealing with this highly contagious infection disease.

AUTHOR CONTRIBUTIONS

Shengqing Li planned the study and was responsible for the overall content as a guarantor. Hai Zou and Wanfeng Xiong conducted the survey and submitted the study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by Huashan Hospital Ethics Committee (HS-2020).

ACKNOWLEDGMENT

I would like to express my gratitude to all those who helped me during the writing of this manuscript.

FUNDING

This study was supported by Shanghai Talent Development Fund (2020070).

CONFLICT OF INTEREST

The authors report no declarations of interest.

REFERENCES

- [1] Richman DD, Whitley RJ, Hayden FG. *Clinical virology*. 4th edn. Washington, DC: ASM Press. 2016.
- [2] Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, *et al.* A novel coronavirus associated with severe acute respiratory syndrome. *The New England Journal of Medicine*. 2003; 348: 1953-1966.
- [3] Kuiken T, Fouchier RA, Schutten M, Rimmelzwaan GF, van Amerongen G, van Riel D, *et al.* Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome. *The Lancet*. 2003; 362: 263-270.
- [4] Drosten C, Günther S, Preiser W, van der Werf S, Brodt HR, Becker S, *et al.* Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *The New England Journal of Medicine*. 2003; 348: 1967-1976.
- [5] de Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, *et al.* Middle East Respiratory Syndrome Coronavirus (MERS-CoV): announcement of the coronavirus study group. *Journal of Virology*. 2013; 87: 7790-7792.
- [6] Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *The New England Journal of Medicine*. 2012; 367: 1814-1820.
- [7] Wang W, Faselino M, Cattau B, Goldman N, Kong W, Frederick MA, *et al.* Joint profiling of chromatin accessibility and CAR-T integration site analysis at population and single-cell levels. *Proceedings of the National Academy of Sciences*. 2020; 117: 5442-5452.
- [8] Klankluang W, Pukrittayakamee P, Atsariyasing W, Siriusawakul A, Chanthong P, Tongchai S, *et al.* Validity and reliability of the Memorial Delirium Assessment Scale-Thai version (MDAS-T) for assessment of delirium in palliative care patients. *The Oncologist*. 2020; 25: e335-e340.
- [9] Hosie A, Davidson PM, Agar M, Sanderson CR, Phillips J. Delirium prevalence, incidence, and implications for screening in specialist palliative care inpatient settings: a systematic review. *Palliative Medicine*. 2013; 27: 486-498.
- [10] van Zyl LT, Seitz DP. Delirium concisely: condition is associated with increased morbidity, mortality, and length of hospitalization. *Geriatrics*. 2006; 61: 18-21.
- [11] van den Boogaard M, Wassenaar A, van Haren FMP, Slooter AJC, Jorens PG, van der Jagt M, *et al.* Influence of sedation on delirium recognition in critically ill patients: a multinational cohort study. *Australian Critical Care*. 2020; 33: 420-425.
- [12] Hsieh SJ, Soto GJ, Hope AA, Ponea A, Gong MN. The association between acute respiratory distress syndrome, delirium, and in-hospital mortality in intensive care unit patients. *American Journal of Respiratory and Critical Care Medicine*. 2015; 191: 71-78.
- [13] Chen T, Chung Y, Chang H, Chen P, Wu C, Hsieh S, *et al.* Diagnostic accuracy of the CAM-ICU and ICDSC in detecting intensive care unit delirium: a bivariate meta-analysis. *International Journal of Nursing Studies*. 2021; 113: 103782.
- [14] Zhao W, Hu Y, Chen H, Wang X, Wang L, Wang Y, *et al.* The effect and optimal dosage of dexmedetomidine plus sufentanil for postoperative analgesia in elderly patients with postoperative delirium and early postoperative cognitive dysfunction: a single-center, prospective, randomized, double-blind, controlled trial. *Frontiers in Neuroscience*. 2020; 14: 549516.
- [15] Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, *et al.* Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *Journal of the American Medical Association*. 2001; 286: 2703-2710.
- [16] Davis DHJ, Muniz-Terrera G, Keage HAD, Stephan BCM, Fleming J, Ince PG, *et al.* Association of delirium with cognitive decline in late life: a neuropathologic study of 3 population-based cohort studies. *JAMA Psychiatry*. 2017; 74: 244-251.
- [17] Girard TD, Exline MC, Carson SS, Hough CL, Rock P, Gong MN, *et al.* Haloperidol and ziprasidone for treatment of delirium in critical illness. *The New England Journal of Medicine*. 2018; 379: 2506-2516.
- [18] Kotfis K, Williams Roberson S, Wilson JE, Dabrowski W, Pun BT, Ely EW. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. *Critical Care*. 2020; 24: 176-184.

How to cite this article: Hai Zou, Wan-Feng Xiong, Sheng-Qing Li. Delirium in critically ill patients with COVID-19 pneumonia. *Signa Vitae*. 2021;17(2):216-218. doi:10.22514/sv.2021.013.