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Commentary

Delirium: A suggestive sign of COVID-19 in dementia

Huali Wang

Dementia Care and Research Center, Beijing Dementia Key Lab, NHC Key Laboratory of Mental Health, National Clinical Research Center for Mental Disorders, Peking University Institute of Mental Health (Sixth Hospital), Beijing 100191, China

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Approximately 40% - 60% of people with dementia in residential care facilities experience behavioral and psychological symptoms (BPSD), such as agitation, psychosis, or apathy [1]. During the COVID-19, older adults with dementia were likely to develop behavioral changes [2]. Among multiple factors contributing to the behavioral disturbances in unprecedented times, delirium was not well recognized in dementia, especially among those without respiratory failure [3,4]. In the *EClinicalMedicine*, Tino Emanuele Poloni and colleagues report a retrospective study of delirium superimposed on dementia during the COVID-19 outbreak peak in a dementia facility in Italy [5].

Based on a review of the medical charts of 57 residents with positive SARS-CoV-2 infection in the residential care facility, Poloni et al. found that delirium occurred as the initial presentation in about 38.7% of the subjects. Hypoactive (52.4%) delirium was slightly more prevalent than hyperactive (47.6%) delirium. The prevalence of delirium increased with age. Persons with moderate and severe dementia had a higher prevalence of delirium than those in the advanced dementia stage. In the study facility, residents with delirium-onset COVID-19 had higher mortality than those who did not manifest delirium at onset (mortality rate: 52.4% *vs.* 8.3%, OR=17.0, 95% CI: 2.8−102.7). Besides, the male gender and multiple comorbidities increased the risk of COVID-19 mortality [5].

Previous studies have reported neurological manifestations among patients infected with the SARS-CoV-2 virus [6]. Neuropsychiatric changes may characterize either acute or long-term brain dysfunction. The inflammatory process in the central nervous system (CNS), prodromal hypoxia, acute pain, impaired attention, and cognitive-communication deficits due to coronavirus infection may contribute to delirium [3,4]. Therefore, it was not surprising that Poloni et al. found a high prevalence of delirium among people with dementia and COVID-19.

However, during the COVID-19 pandemic, delirium data were minimal so far, partly because ICU care in hospitals placed more emphasis on respiratory failure rather than neuropsychiatric presentations in critically ill patients. Additionally, when healthcare professionals wore protective shields and facial masks, the communication between them and patients was kept too brief to suffice for mental status assessment. Meanwhile, patients with hypoactive delirium, which constituted a majority of delirium-onset COVID-19, were likely to be missed and did not receive appropriate attention [7]. In the Lombard dementia facility, when the residents manifested with acute behavioral changes and were suspected with delirium, the staff would conduct the assessment with the Confusion Assessment Method (CAM) [5]. Routine evaluation of delirium in dementia was noteworthy and should be scaled up in more facilities.

Why is timely detection of the delirium-onset COVID-19 infection of great clinical significance? On the one hand, if unrecognized, the cases might have contributed to the spread of the infection in the high-risk facilities. On the other hand, delirium imposed a higher risk of mortality [5,8]. If misdiagnosed, patients with delirium might fail to receive adequate care, such as maintaining ventilation and monitoring immune response [9]. The longer the delay, the worse the prognosis. Using the DICE (describe-investigate-create-evaluate) approach, assessing the underlying causes might aid the differential diagnosis between delirium and the aggravation of BPSD [1]. The aggravated behavioral disturbance was often precipitated by external stimuli, such as a change in surroundings and caregivers. If environmental adjustment and changes of the caregiving process could be precluded in residential care facilities, diagnostic priority should be given to delirium, and further lab investigation of lymphocytes and coronavirus testing should be administered.

As noted, Poloni et al. observed a very low prevalence of delirium among people with dementia who attended the house call service and the emergency room [5]. It remained inconclusive why the initial presentations of co-morbid dementia and COVID-19 differed between residential care facility and homebound settings. It might be partly explained that the domestic caregivers were not well trained to recognize early signs of acute behavioral changes, especially the hypoactive manifestation [10]. Therefore, training home caregiver would be necessary for the timely detection of delirium as the initial presentation of COVID-19.

Delirium in older people with dementia may represent a prodromal phase of COVID-19. Therefore, in clinical practice, it is particularly important to increase access to the CAM screening and

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E-mail addresses: huali_wang@bjmu.edu.cn, cpig2005@126.com

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encourage prompt pharyngeal swab testing in high-risk settings, such as dementia care facilities. Further investigations on the mechanism of the COVID-19 on CNS are warranted.

Declaration of Competing Interest

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