Neurodegenerative Diseases

Editorial

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A Pivotal Time

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Neurodegenerative Diseases, founded two decades ago by Roger M. Nitsch and Christoph Hock [1], holds a crucial position in filling the gap between fundamental research and clinical applications. It is a great honor to succeed the esteemed founding editors and the accomplished former editor, Paul G. Unschuld, who have elevated the journal to its current level.

The field of neurodegenerative diseases is currently experiencing a pivotal time. After the devastating COVID-19 killing countless older adults with neurodegenerative diseases and social isolation being imposed on older survivors, a new disabling condition known as long COVID has emerged, affecting the cognition of young and older adults. Besides the sad consequences of COVID-19, there is a recent hope with the revolutionizing disease-modifying therapies that are becoming available for patients with Alzheimer's disease (AD). Interestingly, the founder editors of *Neurodegenerative Diseases* made a significant contribution to the development of disease-modifying therapies for AD [2].

The SARS-CoV-2 pandemic had a worldwide impact (Fig. 1), destabilizing the healthcare systems and leaving a bitter taste as it neglected millions of older adults, particularly those with neurodegenerative diseases, even in the most developed countries, due to the lack of resources and knowledge. In April 2020, I remember evaluating at the Geneva University Hospitals' ICU during a busy Friday evening a 75-year-old nuclear engineer with Parkinson's disease, who was struggling with a severe SARS-CoV-2 infection. Remarkably, after 15 days of intubation, he was finally feeling better and able to breathe without respiratory assistance, allowing him the privilege to enjoy the Kiddush of Shabbat, the blessings performed at the beginning of the Friday evening Shabbat dinner; an unusual celebration for an ICU. Prepared with love by his wife, who was unfortunately prohibited from entering to the ICU for "safety" reasons, the patient was slowly eating and gave hope to his son, who stood by his father's side, reciting together prayers welcoming the Shabbat. It was his last Shabbat. The religious man died 24 h later from a COVID-19 encephalopathy, one of the most devastating neurological complications of COVID-19 [3]. On the next Monday, when I shared this sad news with my team, the young neuropsychologist, who had been diligently caring for the patient for 15 days, was totally devastated, falling into a deep burnout. Few months later, the same neuropsychologist experienced a mild SARS-CoV-2 infection but then suffered from a severe long COVID rendering her unable to care for her patients for several months. This story underscores how the pandemic has not only impacted patients and families but has also affected healthcare providers. Numerous reports have highlighted the alarming death rate among healthcare workers, either directly from SARS-CoV-2 infection [4] or from the indirect consequences of overwhelming pressure leading some to suicide [5]. Today, many questions remain unanswered regarding the consequences of COVID-19 on neurodegenerative diseases [6]:

- Does the excess mortality among patients with neurodegenerative diseases stem from vulnerability of specific neurodegenerative conditions?

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Fig. 1. Pisa (Italy) during the COVID-19 pandemic.

- Are the patients with early-stage neurodegenerative conditions infected by SARS-CoV-2 at an accelerated risk of rapidly progressive neurodegenerative processes?
- Are long COVID patients more susceptible to developing any kind of neurodegenerative diseases?

Exploring these timely questions will provide invaluable insights into the pathophysiology of neurodegenerative diseases. At the same time, a long-awaited hope for patients suffering from AD has transformed into reality through the first-ever clinical trial showing the clinical benefits of a disease-modifying therapy – the anti-amyloid drug lecanemab. The groundbreaking drug has demonstrated a 27% reduction of cognitive decline in patients in the early stages of AD, while removing amyloid plaques, in comparison to patients on placebo [7]. However, the treatment is not without concerns, particularly with a novel neurological complication known as amyloid-related imaging abnormalities [8]. This inflammatory complication disproportionately affects patients with cerebral amyloid angiopathy [9] and individuals with specific APOE4 genotype [10], potentially leading to catastrophic brain hemorrhages, especially in cases where patients receive intravenous thrombolysis for ischemic stroke [11]. Identifying patients at higher risk of amyloid-related imaging abnormalities and safeguarding them from co-prescription of potentially dangerous drugs, such as thrombolysis or even anticoagulants, remains an ongoing challenge for the clinical and research communities [12]. To explore these emerging questions surrounding the anti-amyloid drugs, we will soon announce a special call for papers in *Neurodegenerative Diseases*. This novel experience of disease-modifying therapies for AD patients will undoubtedly extend its benefits to other neurodegenerative diseases, particularly through the strategic targeting of early stages of neurodegenerative diseases (even at the presymptomatic phase) using appropriate biomarkers. Furthermore, the deep reasoning on the clinical infrastructure required for delivering such treatments, which significantly impact healthcare systems, will enhance our clinical practice for upcoming disease-modifying drugs for other neurodegenerative diseases.

The transitions from the pre- to post-COVID-19 era, as well as the pre- and post-disease-modifying therapies for neurodegenerative diseases are associated with profound societal challenges. While the brain sadly became the unexpected target of an upper airway infection, revolutionary treatments for neurodegenerative diseases are around the corner. That places *Neurodegenerative Diseases* at a pivotal time to explore the emerging perspectives that will shape the future of our patients.

Statement of Ethics

Written informed consent was obtained from the patient's next of kin for publication of the details of the medical case.

Conflict of Interest Statement

The author has no conflicts of interest to declare.

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