

LETTER TO THE EDITOR

Reply: Concentric demyelination pattern in COVID-19-associated acute haemorrhagic leukoencephalitis: a lurking catastrophe?

Ross W. Paterson,^{1,2,3} Rachel L. Brown,^{1,4} Vinojini Vivekanandam,⁵ Alexander J. M. Foulkes,^{1,6} Maria Thom,¹ Sarah Wiethoff,^{1,7} Laura Benjamin,^{8,9} Gerry Christofi,⁵ Patricia McNamara,⁵ Jasper Morrow,^{1,5} Thomas D. Miller,¹⁰ Ross Nortley,^{1,11} Ruth Gerales,^{11,12} David Attwell,¹³ Guru Kumar,² Alex D. Everitt,¹⁴ Nicholas W. S. Davies,¹⁵ S. Anand Trip,^{1,16} Eli Silber,¹⁷ Robin Howard,^{5,18} Richard J. Perry,⁸ David J. Werring,⁸ Anna Checkley,¹⁹ Nicky Longley,¹⁹ Jennifer Spillane,^{5,18} Michael P. Lunn,¹ Chandrashekar Hoskote,²⁰ Hans Rolf Jäger,^{1,20} Hadi Manji,^{1,5,†} and  Michael S. Zandi^{1,5,†} for the UCL Queen Square National Hospital for Neurology and Neurosurgery COVID-19 Study Group[‡]

[†]These authors contributed equally to this work.

[‡]Appendix 1.

- 1 University College London, Queen Square Institute of Neurology, London, UK
- 2 Darent Valley Hospital, Dartford, Kent, UK
- 3 UK Dementia Research Institute, London, UK
- 4 UCL Institute of Immunity and Transplantation, London, UK
- 5 National Hospital for Neurology and Neurosurgery, University College London Hospitals NHS Foundation Trust, Queen Square, London, UK
- 6 Watford General Hospital, Watford, Hertfordshire, UK
- 7 Center for Neurology and Hertie Institute for Clinical Brain Research, Eberhard-Karls-University, Tübingen, Germany
- 8 Stroke Research Centre, UCL Queen Square Institute of Neurology, London, UK
- 9 University of Liverpool, Brain Infections Group, Liverpool, Merseyside, UK
- 10 Lister Hospital, Stevenage, Hertfordshire, UK
- 11 Wexham Park Hospital, Frimley Health NHS Foundation Trust, Berkshire, UK
- 12 University of Oxford, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Oxford, UK
- 13 UCL, Department of Neuroscience, Physiology and Pharmacology, London, UK
- 14 Imperial College Healthcare NHS Trust, London, UK
- 15 Chelsea and Westminster Hospital, London, UK
- 16 Northwick Park Hospital, Harrow, London, UK
- 17 King's College Hospital, Denmark Hill, London, UK
- 18 Guy's and St Thomas' NHS Foundation Trust, London, UK
- 19 Hospital for Tropical Diseases, University College London Hospitals NHS Foundation Trust, London, UK
- 20 Lysholm Department of Neuroradiology, National Hospital for Neurology and Neurosurgery, University College London Hospitals NHS Foundation Trust, Queen Square, London, UK

Correspondence to: Dr Michael S. Zandi, PhD, FRCP,
University College London Queen Square Institute of Neurology
London WC1N 3BG
UK
E-mail: m.zandi@ucl.ac.uk

We are grateful to [Karapanayiotides and colleagues \(2020\)](#) for their description of a 57-year-old patient with acute haemorrhagic leukoencephalitis (AHLE) and concentric demyelination suggestive of Baló's disease, and for adding insights into the neurological manifestations of COVID-19. The authors are correct to point out that the mechanisms underpinning the features in all of our collective patients remain to be determined, and the role of direct infection, hypoxia, immune-mediated injury and metabolic processes all warrant further exploration. The authors are also correct in describing the difficulty in applying historical terminology to the clinical pictures that we are now seeing in COVID-19, and that new terminologies need to be considered.

In Patient 17, the clinical picture of rapid progression, unilateral significant brain swelling with oedema and ensuing coma—with evidence of brainstem dysfunction, and resolution with decompressive craniectomy and corticosteroids, fitted best clinically with previous descriptions of haemorrhagic leukoencephalitis (AHLE) ([Love *et al.*, 2008](#)). We acknowledge that neither the biopsied tissue, nor the imaging, showed any evidence of haemorrhage. Whereas the former might potentially be a tissue sampling issue, it is unlikely that any significant haemorrhage would have been missed on the susceptibility-weighted MRI sequence done preoperatively, although this may have developed with time. For Patient 17, an 'aggressive hyper-acute disseminated encephalomyelitis' might therefore have been a more appropriate term.

Data availability

Data availability is not applicable to this article as no new data were created or analysed in this study.

Funding

R.W.P. is supported by an Alzheimer's Association Clinician Scientist Fellowship and by the UK Dementia Research Institute. R.L.B. is supported by a Medical Research Council Clinical Research Training Fellowship (555106). S.W. is supported by the Ministry of Science, Research and the Arts of Baden-Württemberg and the European Social Fund of Baden-Württemberg (31-7635 41/67/1). D.A. is supported by a European Research Council Advanced Investigator Award (BrainEnergy, 740427) and a Wellcome Trust Senior

Investigator Award (219366/Z/19/Z). D.J.W. and R.J.P., have received support for the Stroke Investigation in North and Central London (SIGNAL) project from the NIHR UCL/UCLH Biomedical Research Centre. R.W.P., R.N., S.A.T., J.M.M., M.P.L., and M.S.Z. are supported by the NIHR UCL/UCLH Biomedical Research Centre.

Competing interests

C.C. has sat on an advisory panel for Roche. A.V. and the University of Oxford hold patents and receive royalties for antibody tests. M.S.Z. has received lecturing fees for Eisai and UCB pharma. All other authors report no competing interests.

Supplementary material

[Supplementary material](#) is available at *Brain* online.

Appendix I

The UCL Queen Square National Hospital for Neurology and Neurosurgery COVID-19 Study Group includes the authors and the following: Tehmina Bharucha, Dipa L. Jayaseelan, Rhian E. Raftopoulos, Laura Zambreanu, Anthony Khoo, Krishna Chinthapalli, Elena Boyd, Hatice Tuzlali, Gary Price, Benjamin McLoughlin, Soon Tjin Lim, Puja R. Mehta, Viva Levee, Stephen Keddie, Wisdom Yong, Gary Hotton, Christopher Carswell, Michael Yoong, Jemeen Sreedharan, Jonathan M. Schott, Arvind Chandratheva, Robert Simister, Simon F. Farmer, Francesco Carletti, Catherine Houlihan and Angela Vincent.

Affiliations are detailed in the [Supplementary material](#).

References

- Karapanayiotides T, Geka E, Prassopoulos P, Koutroulou I, Kollaras P, Kiourtzieva E, et al. Concentric demyelination pattern in COVID-19-associated acute haemorrhagic leukoencephalitis: a lurking catastrophe? *Brain* 2020; 143: e100.
- Love S, Louis DN, Ellison DW. *Greenfield's neuropathology*. 8th edn. London: Hodder Arnold; 2008.