Consider cerebral tuberculosis as differential of SARS-CoV-2-associated acute, haemorrhagic, necrotising encephalitis

Josef Finsterer1*, Daniel Matovu1,2, Ana C. Fiorini2,3,4 and Fulvio A. Scorza1,2

Letter to the Editor

With interest we read the article by Ermilov et al. about a young male in his twenties, born to a consanguineous marriage, who developed a spontaneous pneumothorax after having been hospitalised in a primary infectious hospital for moderate COVID-19 [1]. Work-up for the cause of pneumothorax revealed “infiltrative pulmonary tuberculosis in the phase of disintegration and seeding” [1]. Consecutively the patient developed impaired consciousness and epilepsy which was attributed to fatal acute, haemorrhagic, necrotising encephalitis (AHNE) [1]. It was concluded that “the death of the patient, as well as the severity of the disease, was largely due to COVID-19”. The study is appealing, but raises concerns which require comments.

We do not agree with the notion that SARS-CoV-2 was definitively responsible for AHNE. As long as cerebral tuberculosis had not been appropriately excluded, as long as SARS-CoV-2 was not documented in the CSF or the cerebrum, and as long as upregulation of cytokines, chemokines, and glial markers had not been documented in the CSF, a causal relation between AHNE and SARS-CoV-2 remains speculative. Arguments against SARS-CoV-2 as the cause of AHNE are that in a recent review about the neurological and neuroimaging findings of 584 patients with COVID-19, AHNE has not been mentioned [2] and that AHNE had only been rarely reported in association with SARS-CoV-2 [3].

Regarding cerebral tuberculosis, neither the cerebrospinal fluid (CSF) intra vitam nor the brain at autopsy had been investigated for Mycobacterium tuberculosis by culture, histology, immune histology, or PCR [1]. Excluding cerebral tuberculosis is crucial given the findings of generalised cerebral vasculitis, which occurs in up to one-quarter of the patients with intra-cranial tuberculosis [4].

Missing is the visualisation of the cerebral vessels by conventional angiography, computed tomography angiography (CTA), or by magnetic resonance angiography (MRA) [1]. Since the patient presented with generalised cerebral vasculitis on autopsy [1], it would have been useful to document cerebral vasculitis on imaging of the cerebral vasculature. It would have been also necessary to exclude aneurysm formation, which can be a complication of tuberculous cerebral vasculitis [5].

A further limitation is that no explanation of the cause of tremor three years prior to admission had been provided. Since tuberculosis is a chronic disease, it is conceivable that tremor was already a clinical manifestation of cerebral tuberculosis. It is also conceivable that tremor was in fact a focal seizure given the occurrence of focal seizures during hospitalisation.

Though the figure caption of figure-1 promises to show a diffusion-weighted imaging (DWI), only T2/TIRM images are presented. Missing is also a susceptibility-weighted imaging (SWI) to document the bleeding. Furthermore, an explanation for the narrowing of the subarachnoid space on MRI should be provided. We should be told if this was an artefact, due to meningitis, or due to cerebral oedema. Missing is the treatment the patient received for tuberculosis.

*Correspondence: fipaps@yahoo.de

1 Neurology & Neurophysiology Center, Postfach 20, 1180 Vienna, Austria
Full list of author information is available at the end of the article
Overall, the interesting study has several limitations which challenge the results and their interpretation. Attributing AHNE to the SARS-CoV-2 infection is speculative as long as cerebral tuberculosis has not been convincingly excluded.

Abbreviations
AHNE: Acute, haemorrhagic, necrotising encephalitis; CSF: Cerebro-spinal fluid; CTA: Computed tomography angiography; DWI: Diffusion-weighted imaging; MRA: Magnetic resonance angiography; SWI: Susceptibility-weighted imaging.

Acknowledgements
None.

Author contributions
AF, AF, FS: literature search, discussion, critical comments, final approval, JF: design, literature search, discussion, first draft, critical comments. All authors read and approved the final manuscript.

Funding
None received.

Availability of data and materials
All data reported are available from the corresponding author.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Neurology & Neurophysiology Center, Postfach 20, 1180 Vienna, Austria. 2 Disciplina de Neurociência, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), Rua Pedro de Toledo, 697 - Vila Clementino, São Paulo, SP 04039-00, Brazil. 3 Programa de Estudos Pós-Graduado Em Fonoaudiologia, Pontifícia Universidade Católica de São Paulo (PUC-SP), São Paulo, Brazil. 4 Departamento de Fonoaudiologia, Escola Paulista de Medicina/Univesidade Federal de São Paulo (EPM/UNIFESP), R. Botucatu, 740 - Vila Clementino, São Paulo, SP 04023-062, Brazil.

Received: 15 December 2021   Accepted: 23 May 2022

References
1. Ermilov VV, Dorofeev NA. Clinical and morphological features of SARS-CoV-2 associated acute hemorrhagic necrotizing encephalopathy: case report. Egypt J Neurol Psychiatr Neurosurg. 2021;57(1):158. https://doi.org/10.1186/s41983-021-00413-1.
2. Mohan N, Fayyaz MA, Del Rio C, Khurana NKRS, Vaidya SS, Salazar E, Joyce J, Ali AA. Neurological manifestations and neuroimaging findings in patients with SARS-CoV-2: a systematic review. Egypt J Neurol Psychiatr Neurosurg. 2021;57(1):68. https://doi.org/10.1186/s41983-021-00322-3.
3. Ghosh R, Dubey S, Finsterer J, Chatterjee S, Ray BK. SARS-CoV-2-associated acute hemorrhagic, necrotizing encephalitis (AHNE) presenting with cognitive impairment in a 44-year-old woman without comorbidities: a case report. Am J Case Rep. 2020;16(21): e925641. https://doi.org/10.12659/AJR.925641.
4. Synmon B, Das M, Kayal AK, Goswami M, Sarma J, Basumatary L, Bhownick S. Clinical and radiological spectrum of intracranial tuberculosis: a hospital based study in Northeast India. Indian J Tuberc. 2017;64(2):109-18. https://doi.org/10.1016/j.ijtb.2016.11.011.
5. Liu W, Li C, Liu X, Xu Z, Kong L. Case of subarachnoid hemorrhage caused by tuberculous aneurysm. World Neurosurg. 2018;110:73–8. https://doi.org/10.1016/j.wneu.2017.10.128.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.