Int. j. adv. multidisc. res. stud. 2025; 5(4):479-480

Received: 28-06-2025
Accepted: 08-07-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

The diagnosis of neurosarcoidosis requires evidence of non-necrotizing granulomatous inflammation by biopsy

Josef Finsterer
Department of Neurology, Neurology & Neurophysiology Center, Vienna, Austria

DOI: https://doi.org/10.62225/2583049X.2025.5.4.4629
Corresponding Author: **Josef Finsterer**

Letter to the Editor

We read with interest the article by Mehramiri *et al*. about a 51-year-old woman who presented with persistent, throbbing, non-positionable holocranial headache accompanied by recurrent nausea, non-hemorrhagic vomiting and dizziness for eight months, which developed one month after SARS-CoV-2 infection (SC2I) [1]. One month prior to admission, the patient also developed esotropia of the right eye, limited eye movement in the same eye, mild left hemiparesis, dysphagia and ataxia [1]. As angiotensin-converting enzyme (ACE) was elevated in the cerebrospinal fluid (CSF), neurosarcoidosis was suspected and the patient was treated with methyl prednisolone, which had little effect [1]. The study is noteworthy, but several points should be discussed.

The first point is that it was not reported which viruses, bacteria, protozoa or helminths were excluded as the cause of the clinical presentation by the panel test used [1]. Was the CSF was tested for SARS-CoV-2, HIV, JC, Zika, herpes simplex, varicella zoster, Coxsackie virus, parechovirus, West Nile, Japanese encephalitis, mumps, measles. Enterovirus, polio and Epstein-Barr virus [2]? Have bacterial infections with meningococci, pneumococci, Haemophilus influenza and Listeria monocytogenes been ruled out?

The second point is that neither the CSF nor the serum were examined for immune encephalitis-associated antibodies [1]. Since SARS-CoV-2 infection can be complicated by autoimmune encephalitis [3], it would have been crucial to exclude this particular differential diagnosis.

The third point is that no cerebral angiography, either as magnetic resonance angiography (MRA) or digital subtraction angiography (DSA), had been performed [1]. Since SC2I can be complicated by reversible cerebral vasoconstriction syndrome, dissection, aneurysm-associated subarachnoid hemorrhage, intracerebral hemorrhage, and cerebral vasculitis [4], it would have been imperative to rule out these differential diagnoses by cerebral angiography. Since the headache can also be caused by venous sinus thrombosis (VST) and VST can be a complication of SC2I [5], magnetic resonance venography with contrast should also have been performed.

The fourth point is that sarcoidosis was not confirmed by biopsy [1]. The diagnosis of sarcoidosis is based on three main criteria: a compatible clinical presentation, evidence of non-necrotizing granulomatous inflammation in one or more tissue samples, and exclusion of other causes of granulomatous disease [6, 7].

As long as these criteria are not met, neurosarcoidosis should not be diagnosed. ACE may also be elevated in psychosis, tuberculosis, atypical mycobacteria, histoplasmosis, coccidiodomycosis, allergic alveolitis, berylliosis, Hodgkin's lymphoma, lung cancer, asbestosis and silicosis.

The fifth point is that no long-term follow-up has been reported [1]. Since methylprednisolone was of little benefit, reexamination of the patient, especially a second lumbar puncture, would have been essential. We should know whether the patient survived or not. If he died, we should know whether the autopsy confirmed neurosarcoidosis or whether the actual cause was discovered.

To summarize, this interesting study has limitations that affect the results and their interpretation. Addressing these limitations could strengthen the conclusions and support the message of the study. The diagnosis of neurosarcoidosis requires not only a clinical presentation suggestive of neurosarcoidosis, but also biopsy confirmation of granulomatous inflammation and exclusion of all possible differential diagnoses.

Declarations
Ethical approval: Not applicable.

Consent to participation: Not applicable.

Consent for publication: Not applicable.

Funding: None received.

Availability of data and material: all data are available from the corresponding author.

Completing interests: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contribution: JF was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval. JGM: contributed to literature search, discussion, correction, and final approval.

Acknowledgements: None.

Keywords: SARS-CoV-2 Infection, COVID-19, Neurosarcoidosis, Pleocytosis, Headache

References
1. Mehramiri A, Heidari M, Bahadoram M, Akade E. Severe headache as the first presentation of post-COVID-19 brain and spinal cord injury resembling neurosarcoidosis. Postep Psychiatr Neurol. 2024 Sep; 33(3):196-200. Doi: 10.5114/ppn.2024.144608
2. Abdullahi AM, Sarmast ST, Singh R. Molecular Biology and Epidemiology of Neurotropic Viruses. Cureus. Aug 11, 2020; 12(8):e9674. Doi: 10.7759/cureus.9674
3. Vasilevska V, Guest PC, Szardenings M, Benros ME, Steiner J. Possible temporal relationship between SARS-CoV-2 infection and anti-NMDA receptor encephalitis: a meta-analysis. Transl Psychiatry, Mar 8, 2024; 14(1):139. Doi: 10.1038/s41398-024-02831-0
4. Siegler JE, Dasgupta S, Abdalkader M, Penckofer M, Yaghi S, Nguyen TN. Cerebrovascular Disease in COVID-19. Viruses, Jul 21, 2023; 15(7):1598. Doi: 10.3390/v15071598
5. Ostovan VR, Foroughi R, Rostami M, Almasi-Dooghaee M, Esmaili M, Bidaki AA, *et al*. Cerebral venous sinus thrombosis associated with COVID-19: A case series and literature review. J Neurol. 2021 Oct; 268(10):3549-3560. Doi: 10.1007/s00415-021-10450-8
6. Crouser ED, Maier LA, Wilson KC, Bonham CA, Morgenthau AS, Patterson KC, *et al*. Diagnosis and Detection of Sarcoidosis. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med, Apr 15, 2020; 201(8):e26-e51. Doi: 10.1164/rccm.202002-0251ST
7. Ibitoye RT, Wilkins A, Scolding NJ. Neurosarcoidosis: A clinical approach to diagnosis and management. J Neurol. 2017 May; 264(5):1023-1028. Doi: 10.1007/s00415-016-8336-4