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Letter to the Editor

Before diagnosing postoperative chemical meningitis, all infectious causes must be thoroughly ruled out

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Quick Response Code:

Dear Editor,

We read with interest the article by Ehrlich *et al*. about a 33-year-old female who developed aseptic meningitis following the redoresection for a fourth ventricular epidermoid cyst.[2] The postsurgical course was complicated by recurrent fever, sub-occipital pseudomeningocele, hydrocephalus, leptomeningeal enhancement, neutrophil pleocytosis, and hypoglycorrhachia, why she was repeatedly treated with steroids and antibiotics, despite repeatedly negative cerebrospinal fluid (CSF) cultures, and placement of a ventriculoperitoneal shunt (VPS).[2] Because of recurrent shunt dysfunction, several revisions of the VPS had to be carried out.[2] A second sub-occipital craniotomy and posterior fossa exploration was non-informative.[2] Finally, the patient made an incomplete recovery under long-term treatment with prednisone.[2] The study is appealing but raises concerns that warrant further discussion.

A limitation of the study is that the results of reverse transcription polymerase chain reaction for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were not reported.[2] As the case coincided with the SARS-CoV-2 pandemic, it is crucial that acute infection with SARS-CoV-2, long-COVID, or post SARS-CoV-2 vaccination syndrome are appropriately ruled out. There is also no mention of whether or not a virus panel, including human immunodeficiency virus, was conducted and, if conducted, whether it was informative or noninformative.

A further limitation of the study is that the CSF was tested neither for fungi nor for mycobacterium tuberculosis. There is also no mention whether the CSF was tested for antibodies associated with immune encephalitis. Involvement of the cerebral parenchyma as shown in Figure 4 should prompt the exclusion of encephalitis.

Another limitation of the study is that the patient did not undergo electroencephalography recordings when she developed episodes of confusion 6 weeks after removal of the epidermoid cyst.[2] Aseptic meningitis can be complicated by seizures.[1]

Acute onset right facial palsy and double vision suggest ischemic stroke. We should be informed whether diffusion weighted images, apparent diffusion coefficient maps, and perfusion-weighted images were also performed to rule out a cytotoxic lesion in the context of an ischemic stroke.

Missing are the results of the CSF cytology investigation. Missing is the profile of CSF cytokines, chemokines, and glial factors.

A shortcoming of the report is that the authors constantly switch between the terms "aseptic meningitis" and "chemical meningitis" although they mention in the introduction that chemical meningitis is a subtype of aseptic meningitis. For didactic reasons and for consistency, it can be helpful to use only one term throughout and to explain it the first time it is used.

Overall, the study carries obvious limitations that require re-evaluation and discussion. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Diagnosis of aseptic meningitis requires the exclusion of all possible infectious causes of meningitis.

Ethics approval

Only secondary data were used.

Availability of data

All data are available from the corresponding author.

Author contributions

Josef Finsterer: Design, literature search, discussion, first draft, critical comments, and final approval and FS: Literature search, discussion, critical comments, and final approval.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of Interest

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Authors' reply

We thank the authors for their thoughtful commentary accompanying our paper, "Protracted Course of Chemical Meningitis Following Posterior Fossa Epidermoid Cyst Excision – Case Report."[1] The points raised are well received, and we aim to provide clarity.

The patient received routine Reverse transcription polymerase chain reaction (PCR) SARS-CoV-2 per hospital protocol throughout her hospital admission. The results were negative for all dates. A myriad of attempts have been made in recent medical literature to correlate several conditions to the novel SARS-CoV-2 virus with little evidence of causation. There is no reason to suspect her symptoms were a sequela of such a correlation. Long-COVID and post SARS-CoV-2 vaccination syndrome could not be a part of the differential as the patient never reported testing positive for the virus, and the vaccinations were not yet available.

As indicated by the editorial title, one of the authors' most significant concerns was the absence of an explicit statement regarding the investigation of all possible infectious causes. Cerebrospinal fluid (CSF) cultures were thoroughly investigated in this case by working directly with our Department of Infectious Disease. Although not explicitly outlined in the case report, the mention of "CSF Culture" should be taken to represent testing from intraoperative and lumbar cistern obtained CSF for all possible infectious causes. This includes the following: meningitis/encephalitis panel (*Escherichia coli*, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria*, *Streptococcus agalactiae*, *Streptococcus penuomoniae*, Cytomegalovirus, Enterovirus, Human herpesvirus 6-6, Herpes simplex virus type 1, Herpes simplex virus type 1, Human perechovirus, Varicella zoster virus, and *Cryptococcus neoformans*/*gattii*), bacterial culture (aerobic and anaerobic), fungal culture and smear, Acid-fast bacillus culture + smear, India ink prep, *Mycobacterium tuberculosis* PCR, Cryptococcal antigen PCR, and Venereal disease research laboratory. Additional studies also included CSF analysis for West Nile Virus, Aspergillus, Blastomyces, Histoplasma, Toxoplasma, Lyme Disease, Epstein-Barr, and JC virus. Fungitell and Karius panels were used to analyze blood and urine samples. These analyses returned negative results, including cultures held for extended periods. As a result, the above details were not elaborated on in the published report. We agree that a more careful explanation would have been prudent but would not have led to alternative conclusions.

Similarly, the authors raise concern over the lacking detail regarding the CSF cytology and autoimmune investigation results. Clinical neurologic examination and routine diagnostic tests (Magnetic resonance imaging

[MRI], CSF analysis, and Electroencephalography [EEG]) provide adequate information for an initial assessment of autoimmune encephalitis. Diagnosing possible autoimmune encephalitis is considered when patients meet the following criteria.[2] Subacute onset (rapid progression of fewer than 3 months) of memory deficits, altered mental status, or psychiatric symptoms. At least one of the following: new focal central nervous system findings, new onset of seizures, CSF pleocytosis, MRI findings suggestive of encephalitis. Finally, the exclusion of alternative causes (i.e., toxicology, metabolic, and infectious). The diagnosis and initiation of treatment for autoimmune encephalitis cases are often not dependent primarily on the patient's antibody status. Rather, specific autoantibodies only corroborate a definitive diagnosis secondary to the clinical determination of a "possible" autoimmune etiology.[3]

Additional tests included analyses for oligoclonal bands, myelin basic protein, and CSF flow cytometry. The results of the CSF cytometry included a paucicellular specimen of mostly nonviable cells, nonhematolymphoid cells, and debris. Granulocytes comprised most of the few identified cellular debris, and there was no evidence of abnormal B or T cell populations. All additional test results were negative. While the patient exhibited acute/subacute neurologic symptoms, there was no evidence of CSF pleocytosis or new seizure onset. While admittedly absent from our report, the patient underwent continuous EEG monitoring episodes. Findings lacked evidence of seizure and were consistent with nonspecific encephalopathy and mild diffuse cortical irritability. Most important, instead, is that the patient had a plausible alternative explanation for their presentation — specifically, the history of a partially resected posterior fossa epidermoid cyst. There was no further performed autoimmune testing.

The concern for stroke is valid, though in this particular situation, less likely. Diffusion-weighted imaging was not suggestive of a cerebrovascular event. Most relevant would be the diffuse T2 fluid-attenuated inversion recovery signal [Figure 6] and increasing leptomeningeal enhancement [Figures 3 and 4] throughout the areas of the brainstem and surrounding cranial nerves.

Finally, the authors highlight the constant switching between the terms "aseptic" and "chemical" meningitis. The provocative use of "aseptic" meningitis as opposed to "chemical" meningitis is found most often within the discussion. As described early in the report and acknowledged by the authors as mentioned earlier, chemical meningitis is a subset of the broader category of aseptic meningitis. Given the lack of evidence to suggest a viral or autoimmune etiology, one could consider this case a "chemical" meningitis. However, despite the exhaustive testing, we felt it best to be conservative, given the lack of a definitive diagnosis.

We appreciate the opportunity for thoughtful discourse. We hope the above provides clarity to the respondent authors and future readers.

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