COVID-19 is more likely to be complicated by autoimmune encephalitis than PRES

Dear Editor,

We read with interest the article by Mrabet et al. [1] about a 16-year-old boy with nephrotic syndrome due to minimal change disease (MCD) since the age of 13, who was switched to cyclosporine due to side effects from glucocorticoids. Five days later, the boy suffered a tonic-clonic seizure for the first time, so the cyclosporine was discontinued and valproic acid was started [1]. As he tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the magnetic resonance imaging (MRI) showed leptomeningeal enhancement, the patient was diagnosed with encephalitis as a result of SARS-CoV-2 infection [1]. After discharge, the patient was well for 10 days, so treatment with cyclosporine was resumed [1]. One day later, however, the patient suffered a second tonic-clonic seizure, so cyclosporine was discontinued again [1]. As the cerebral lesions showed progression on a second MRI, cyclosporine-induced posterior reversible encephalopathy syndrome (PRES) was diagnosed [1]. The study is excellent, but three points should be discussed.

The first point is that the diagnosis of PRES remains questionable [1]. Imaging has provided no evidence that the lesions shown in Figures 1 and 2 of Mrabet et al's paper [1] are indeed PRES. The fact that the lesions were multifocal and that their appearance on apparent diffusion coefficient (ADC) maps is not documented argues against PRES [1]. Since PRES is characterized by vasogenic edema, and since the latter shows up in the form of diffusion-weighted imaging (DWI) and hyperintensity of the ADC, it would have been mandatory to indicate the hyperintensity of the described lesions on the ADC maps. For the diagnosis of PRES, it is also necessary to document the resolution of the lesions over time.

The second point is that the examination for autoimmune encephalitis (AIE) was inadequate [1]. The cerebrospinal fluid (CSF) analysis should also have included lactate, oligoclonal bands, immunoglobulin (Ig)G, IgA and IgM, a comprehensive viral panel including SARS-CoV-2, AIE-associated antibodies as well as interleukins, chemokines and glial markers [2]. Since neither a viral panel nor AIE-associated antibodies were determined, it cannot be ruled out that the multilocular MRI lesions represent encephalitis rather than PRES. The fact that the patient had a viral infection, that there was meningeal enhancement, that the typical distribution of PRES lesions is the occipital lobe and that the blood pressure was normal argues in favour of encephalitis [3]. A normal CSF cell count does not rule out infectious or immunologic encephalitis.

The third point is that demyelinating diseases, such as multiple sclerosis, myelo-oligodendrocyte glycoprotein (MOG)-associated disorders (MOGAD), neuromyelitis optica (NMO)-spectrum disorders (NMOSD), acute disseminated encephalomyelitis, acute hemorrhagic necrotizing encephalopathy or acute hemorrhagic leukoencephalitis has not been adequately excluded. There are no reports of visual evoked potentials, NMO antibodies, aquaporin-4 antibodies, MOG antibodies or MRI of the cervical and thoracic spine. To confirm or rule out a demyelinating disease of the central nervous system, it would have been imperative to perform all these examinations and evaluate their results.

In summary, PRES should only be diagnosed when DWI and ADC maps are hyperintense, seizures should only be attributed to cyclosporine when all other causes of seizures have been thoroughly ruled out, and a comprehensive CSF analysis should be performed when cerebral lesions are unclear.

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