COVID-19 obscuring the diagnosis of ciclosporin-related posterior reversible encephalopathy syndrome

Dear Editor,

We appreciate the opportunity to respond to the letter from Mehri and Finsterer [1] regarding our article about a 16-year-old patient who experienced seizures while on ciclosporine prescribed for a corticoresistant syndrome [2]. The diagnosis of posterior reversible encephalopathy syndrome (PRES) related to anticalcineurin use was challenging to establish due to a concurrent severe acute respiratory syndrome coronavirus 2 infection [2]. The case we published was complex, and we established the diagnosis of PRES only after ruling out other differantial diagnoses. We are pleased to clarify several points and below, we addressed the authors' three questions point-by-point.

Magnetic resonance imaging (MRI) findings

The brain MRI revealed cortico-subcortical abnormalities characterized by diffusion hyperintensity; however, apparent diffusion coefficient maps were not performed. A follow-up MRI conducted six months later demonstrated complete resolution of the lesions described in the initial cerebral MRI (Figure 1), which is a key argument in support of the PRES diagnosis.

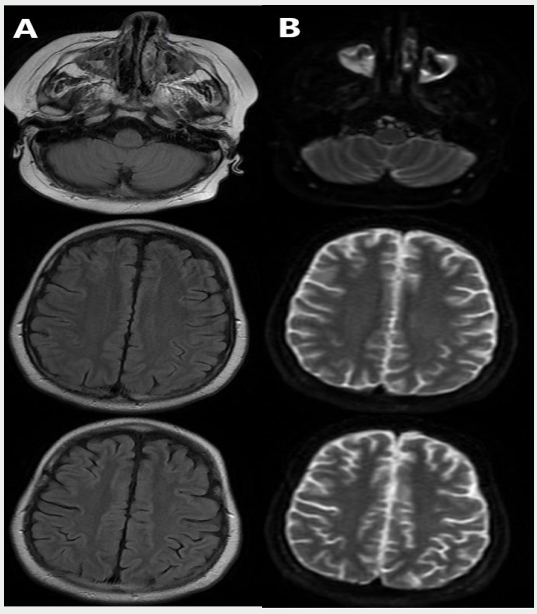

Figure 1. Disappearance of the signal anomalies already described in axial fluid attenuated inversion recovery - weighted (A) and diffusion magnetic resonance imaging (B)

Examination for autoimmune encephalitis

While we considered various differential diagnoses, including infectious etiologies, the presence of leukocytes in the cerebrospinal fluid was absent, and both coronavirus 19 Polymerase Chain Reaction (PCR) and multiplex PCR results were negative.

The diagnosis of autoimmune encephalitis was also evoqued, yet the radiological findings, including lesion distribution, negativity for anti-immune antibodies, and the subsequent resolution of signal abnormalities, effectively ruled out this hypothesis.

As discussed in our article [2], the distribution of lesions in the parietal and frontal regions is atypical for PRES, but on reviewing the literature, frontal lesions are frequent (94%), slightly more than occipital lesions (89%) [3]. Brain edema in areas outside the classic parieto-occipital regions is not uncommon; frontal and temporal lobe involvement can occur in typical PRES findings, and cerebellar edema was seen in up to half of cases [4]. As such, the suggestion has been made to use the term “multifocal” or simply remove “posterior” from “posterior reversible encephalopathy syndrome” [5].

Moreover, contrast enhancement in PRES has been variably reported, typically manifesting as leptomeningeal or gyral cortical enhancement [6]. McKinney et al. [5] reported enhancement in 37.7% of cases studied.

Exclusion of Inflammatory central nervous system (CNS) Diseases

We did not consider inflammatory CNS diseases such as multiple sclerosis or MOG-associated disorders based on the radiological pattern, which did not align with these inflammatory conditions. The clinical presentation lacked indicators of neuromyelitis optica spectrum disorder or medullary syndrome, and the lesion distribution, primarily in cortico-subcortical regions, did not support these diagnoses. Consequently, we did not perform spinal cord sequences or additional tests such as oligoclonal bands, aquaporin-4 antibodies, MOG antibodies, or visual evoked potentials.

The diagnosis of Acute Disseminated Encephalomyelitis was unlikely because the lesions were not confluent, they did not primarily affect the white matter, and there was no significant enhancement of these lesions on imaging.

In summary, the diagnosis of PRES was substantiated by multiple factors, including the recurrence of seizures upon resuming ciclosporin treatment, the radiological appearance showing asymmetric bilateral fluid-attenuated inversion recovery hyperintensities and diffusion in the frontal and parietal regions, and evidence of leptomeningeal contrast enhancement. We effectively ruled out other infectious and inflammatory differential

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diagnoses, and the diagnosis was corroborated by the complete resolution of lesions on follow-up MRI.

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