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Letter to Editor

Letter to the Editor Regarding "Epstein-Barr Virus and COVID-19 Induced Systemic Inflammatory Response Syndrome and Guillain-Barré Syndrome - A Novel Case Report"

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Dear Editor,

We read with interest the case report *"Epstein-Barr Virus and COVID-19 Induced Systemic Inflammatory Response Syndrome and Guillain-Barré Syndrome – A Novel Case Report"* [1]. The clinical scenario is relevant and reflects the diagnostic complexity increasingly encountered in the context of overlapping infections and immune-mediated neurological disease. However, several limitations substantially restrict the interpretive strength of the authors' conclusions.

The principal limitation is the inability to establish a causal relationship between Epstein-Barr virus, SARS-CoV-2, and Guillain-Barré syndrome. Guillain-Barré syndrome is classically an immune-mediated, post-infectious neuropathy, most often explained by molecular mimicry rather than direct viral neuroinvasion [2]. Although both EBV and SARS-CoV-2 have been independently associated with Guillain-Barré syndrome, the literature consistently emphasizes that detection of a virus alone does not establish causality [3]. In COVID-19–associated cases, neurological symptoms typically develop days to weeks after infection onset, supporting a post-infectious mechanism rather than a para-infectious one [4]. In the present report, the absence of a clearly defined temporal sequence limits etiological inference.

Virological characterization is insufficient to support the claim of "simultaneous infection". EBV DNAemia may represent viral reactivation during acute systemic illness rather than primary infection, a phenomenon well documented in critically ill patients and in the setting of COVID-19 [3]. Similarly, SARS-CoV-2 RT-PCR positivity without cycle threshold values, serial testing, or serological kinetics makes it difficult to determine whether COVID-19 preceded, coincided with, or followed the inflammatory and neurological manifestations. Current reviews stress that careful timing, viral load assessment, and exclusion of alternative triggers are essential when attributing Guillain-Barré syndrome to SARS-CoV-2 [4].

The proposed immunopathological mechanisms are also not substantiated by objective data. Molecular mimicry and immune dysregulation are invoked, yet no

immunological markers, such as antiganglioside antibodies, are reported. These antibodies are frequently discussed in the context of infection-associated Guillain-Barré syndrome and are particularly useful in complex or atypical presentations [2]. Their absence further weakens the mechanistic argument.

Systemic inflammatory response syndrome is presented as a key element linking infection and neuropathy, but its role remains underdeveloped. While hyperinflammatory states and cytokine-mediated immune dysregulation have been proposed as amplifiers of autoimmunity in COVID-19, the report lacks longitudinal inflammatory markers or clinical data demonstrating a sustained or severe inflammatory trajectory temporally related to neurological decline. Finally, although nerve conduction studies support the diagnosis of Guillain-Barré syndrome, the limited electrophysiological detail precludes clear subtype classification. This is relevant, as different subtypes may carry different immunopathological associations [2].

In summary, the novelty of this case resides primarily in the descriptive coexistence of Guillain-Barré syndrome, systemic inflammation, and dual viral detection. However, incomplete temporal resolution, limited virological and immunological characterization, and reliance on associative rather than mechanistic evidence substantially constrains causal interpretation. A more cautious framing that emphasizes diagnostic uncertainty rather than implied etiological linkage would better align the conclusions with the available data.

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