Abundance of Pleocytosis Alone Is Insufficient To Exclude Encephalitis Caused by Herpes Simplex Virus in Children

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We have witnessed a rise in the number of requests for herpes simplex virus (HSV) PCR on cerebrospinal fluid (CSF) specimens in our pediatric hospital. Not infrequently, the indications for testing are questionable. Thus, we read with interest the study by López Roa et al. evaluating criteria for limiting its use, whereby samples were accepted for analysis if they had >10 cells/mm³ or were from an immunocompromised patient or a child aged <2 years (1). We remain wary, however, of the claim that such restrictive criteria would not compromise the sensitivity of detection of herpes simplex encephalitis (HSE). Here, we report a case of HSE to illustrate our concerns.

A 2.5-year-old boy was brought to our emergency department with a 24-h history of fever, vomiting, dysphagia, and brief episodes of teeth-clenching. He was febrile (38.2°C), dysarthric, and drooling, with otherwise normal examination results. A CSF examination was normal, including a leukocyte count of 1 cell/mm³. He was admitted with a presumptive diagnosis of primary seizure disorder. His seizures remained uncontrolled despite anticonvulsant therapy, and he required intubation and transfer to the pediatric intensive care unit due to deteriorating mental status. Lumbar puncture repeated at 48 h revealed 11,000 red blood cells/mm³, 150 leukocytes/mm³, protein > 3.2 g/liter, and normal glucose. Intravenous acyclovir was initiated pending HSV PCR results. Both CSF samples were positive for HSV-1 at 162 copies/ml (initial specimen) and 44,418 copies/ml (second specimen).

The availability of HSV PCR has contributed to establishing that the spectrum of disease in HSE is broader than previously thought and that many instances lack “classical” clinical, laboratory, electroencephalographic, or imaging features (2, 3). Consequently, the interpretation of an entire constellation of parameters should guide clinical suspicion and microbiologic testing for HSE, without which cases may be missed, particularly in children presenting early disease manifestations (3). Regarding pleocytosis, the 2012 International Encephalitis Consortium consensus statement affirms that “CSF may be devoid of cells in immunocompromised patients and early in the course of infection” (4). Furthermore, case series of nonneonatal pediatric HSE estimate that many as 4% to 26% of children (not restricted to those < 2 years old) in whom HSE is subsequently confirmed (2, 5–7).

We agree that there is a pressing need to establish judicious criteria for the use of HSV PCR; however, the absence of pleocytosis alone is not a reliable negative predictor of disease and does not warrant HSV PCR request rejection, especially in pediatrics. This diagnostic indicator must be interpreted in the context of all clinical, laboratory, and imaging findings. Moreover, although HSE is rare, timely identification and appropriate management are primordial to prevent death and to minimize morbidity. The development of criteria for HSV PCR testing that fully account for the diagnostic complexity of HSE is essential to safely guide clinicians and thereby improve the appropriateness of HSV PCR testing requests.

REFERENCES

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