

## Commentary

Herpes simplex virus (HSV) and varicella zoster virus (VZV) remain the most frequent agents involved in sporadic infectious encephalitis in the western world.<sup>[1,2]</sup> Two major advances have considerably improved the management of herpes simplex encephalitis (HSE). Indeed, two large randomized controlled trials performed in the mid-1980s highlighted that the use of intravenous acyclovir in suspected encephalitic syndromes reduces the 6-month mortality rate of HSE from around 70% to 10-20%.

On the other hand, HSV DNA amplification by PCR analysis of CSF supported earlier and more practical diagnosis of HSE since the early 1990s.<sup>[3]</sup>

While the overall prognosis of HSE has been dramatically improved, mortality still remains unacceptably high and sequelae in survivors that greatly impair quality of life are frequent.<sup>[4]</sup> Contemporary guidelines emphasize that acyclovir treatment should be commenced on

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clinical suspicion of encephalitis. The importance of rapid administration of acyclovir already on suspicion is further corroborated by a French study reporting that a delay between admission to the hospital and initiation of acyclovir is the main predictor of outcome.<sup>[5]</sup> Encephalitis is among one of the most challenging syndromes and suspicion and subsequent initiation of antiviral therapy is hindered by the non-specific clinical presentation of the disease.<sup>[6,7]</sup> There are several misconceptions regarding the classical triad of fever, altered consciousness and focal neurological deficits. For instance acute personality change, psychosis or delirium may not be recognized as a variant of altered consciousness. In addition, seizures need to be rated as consequence of a parenchymal involvement, and hence alternative manifestation of a focal neurological deficit. In the current three cases, the authors report potential pitfalls in the work-up, which masked an encephalitic syndrome and delayed administration of acyclovir.<sup>[8]</sup> The first patient presented with recurrent seizures in the setting of post-traumatic epilepsy. Subsequent aphasia and impaired consciousness were classified as postictal state. While fever in this patient developed later, it needs to be stressed that elderly, immunocompromised and radiated patients may be anergic and do not develop fever. Elderly patients may already be impaired with pre-existing cognitive impairment, as it was the case in patient 2. Here, pre-existing dementia masked delirium as the leading symptom of encephalitis. Eventually, negative HSV PCR results and lack of cerebrospinal fluid (CSF) inflammation have been reported in the literature during the first three days from symptom onset or in immunocompromised individuals. When the first PCR is negative or signs of inflammation in CSF are lacking but encephalitis is still suspected, the continuation of acyclovir treatment and repeat spinal tap is warranted. Importantly, in such cases a second spinal tap and HSV PCR or serology may support the diagnosis of HSE.<sup>[9]</sup>

The presented cases are of relevance in clinical practice, as they point at potential variants that need to be considered when patients with focal neurological deficits, impaired consciousness, first-ever seizures or changes of seizure patterns in pre-existing epilepsy are encountered.

## References

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