

Commentary

Ivana Vachalová, Leila Kyavar and Josef G. Heckmann report three cases of atypical presentations of Herpes Simplex Virus (HSV) encephalitis:^[1] intestinal initial

symptoms, quinolone-related consciousness disorders, and diabetes. All cases were finally diagnosed as HSV encephalitis using Polymerase Chain Reaction (PCR)

test. All the three patients had abnormalities of the initial cerebrospinal fluid (CSF), even if mild. All patients had delayed diagnosis due to their atypical presentation and authors report sequels: the first one suffered from neuropsychological impairments and was not able to return to work, the second one showed marked neurocognitive impairment, needing moderate home care, and the third one needs professional care at home. It is crucial to insist on the shortest delay for initiating the acyclovir treatment. Mailles *et al.*,^[2] recently reported sequels in 40% of encephalitis case. They identified in their two studies^[2,3] HSV as having an important cause fatality rate: fatality rate of 5% during the acute phase of the infection, with an additional 7% during the three years following the infection. Also, HSV is clearly associated with a poor outcome: 40% of HSV encephalitis patients present with long-term sequels.

Ivana Vachalová *et al.*,^[1] are fully right when saying that it is important to perform lumbar puncture very early and immediately treat .

Clinical presentation of HSV encephalitis is not limited to symptoms related to temporal or frontal lobe injuries. Those three cases demonstrate that it is mandatory to obtain CSF for analysis in case of febrile neurological symptoms, whatever they are. HSV PCR is then a key point of this analysis, keeping in mind that it is possible to observe negative PCR during the first four days after the onset of neurological symptoms.^[4] Acyclovir is the key point for the initial anti-infective treatment, as could be antibiotics against *Listeria*^[5] in endemic areas.

Another key point in case of suspected HSV encephalitis is an alternate diagnosis: auto-immune encephalitis can mimic HSV cases.^[6] An HSV-like encephalitis with negative PCR in CSF should be tested for specific auto-antibodies, more so if it is a case occurring in a young woman. The Californian team^[7] identified anti- N-Methyl-D-Aspartate Receptor (NMDAR) encephalitis as more than 4 times as frequently as HSV-1, West Nile Virus, or Varicella Zoster Virus in young adult women; and the English group^[8] reported anti-NMDAR

encephalitis as being 8% of the encephalitis included in their cohort.

HSV encephalitis is difficult to diagnose when presenting with atypical symptoms, and it is important to keep in mind the frequency of auto-immune encephalitis mimicking HSV.

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