

Herpes Simplex Virus Encephalitis

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Herpes simplex virus (HSV) encephalitis (HSVE), which is caused by HSV-1 or HSV-2, is a rare neurologic disorder associated with focal or global cerebral dysfunction. HSVE is a syndrome of altered mental status, fever, and seizures. Advanced practice providers should have a high clinical suspicion of HSVE in any patient presenting with these symptoms to ensure prompt workup and administration of IV acyclovir to help minimize mortality and morbidity.

AT A GLANCE

- Most patients with HSVE typically present with altered mental status for more than 24 hours, fever, new onset of seizures, and/or focal neurologic deficits.
- The gold standard to diagnosis HSVE is results from testing cerebral spinal fluid for quantitative HSV-1/HSV-2 polymerase chain reaction.
- Despite patients receiving antiviral treatment for HSVE, mortality rates remain high, and many HSVE survivors experience severe disability.

KEYWORDS

herpes simplex virus encephalitis; altered mental status; neurologic condition

DIGITAL OBJECT IDENTIFIER

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Encephalitis is an inflammatory condition of the brain with a wide array of etiologies, including bacterial, viral, fungal, parasitic, and, in rare cases, amoebas. Among these, herpes simplex virus (HSV) encephalitis (HSVE) is a rare neurologic disorder caused by HSV-1 or HSV-2 that is associated with focal or global cerebral dysfunction. Although about 78% of the population has HSV-1 or HSV-2 (Singh & Tscharke, 2020), HSVE affects only 2–4 cases per 1,000,000 people worldwide (Rabinstein, 2017). Symptoms can range from altered mental status to fever to headaches and can, at times, progress to seizures. HSVE is the most common fatal sporadic encephalitis in humans, as well as the leading and gravest form of acute viral encephalitis (Klein, 2022). HSVE can occur in all age groups, equally affects men and women, and has no seasonal predilection. In adults, HSVE is associated with significant morbidity and death despite treatment with antiviral therapy; mortality is estimated to be 20%–30% even with prompt diagnosis and treatment (Kumar & Mendez, 2023). The mortality of untreated HSVE is about 70% (Bradshaw & Venkatesan, 2016), and more than 50% of survivors have moderate to severe neuropsychiatric sequelae (Jakob et al., 2012).

Pathophysiology

HSV-1 encephalitis can be caused by a primary infection or reactivation of a latent infection, but encephalitis can occur in either case. The exact pathogenesis is unclear, and factors that precipitate HSVE are unknown (Lakhan, 2021). The hypothesis is that the virus enters the body via a cutaneous or mucosal lesion. The virus travels retrograde from the skin and infects the sensory or autonomic nerve endings at cranial nerve V, which gives rise to the following three divisions: ophthalmic, maxillary, and mandibular. The virus then enters the trigeminal ganglion, located in the medial aspect of the temporal fossa, which can correlate with the neurologic deficits with which patients often present. The virus can then spread to the central nervous system via the meningeal branches of cranial nerve V (Klein, 2022; Lakhan, 2021). During the latent phase, the virus stays in its dormant state where the viral genome is stable, but viral particles assemble. The virus can reactivate spontaneously or following triggering events (e.g., trauma, sunlight, immunosuppression). Of note, patients do not need to have symptomatic mucocutaneous lesions to contract HSVE.

Symptoms

Most patients with HSVE present with altered mental status for more than 24 hours, fever, new onset of seizures, and/or focal neurologic deficits (Klein, 2022). HSVE often affects the temporal lobe and the limbic structures and is