

HSV Encephalitis

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I. Epidemiology

- most common cause of fatal sporadic encephalitis in the U.S.; 2000 cases annually, or 10-20 percent of annual viral encephalitis cases
- no seasonal variation
- bimodal age distribution; more than 80% of cases develop in patients less than 20 or greater than 50 years of age
- HSV-1 accounts for 90% of adult and childhood cases, whereas HSV-2 is responsible for most neonatal cases
- if untreated, fatality approaches 90% and most survivors have serious neurological impairments
- with appropriate treatment, fatality may be 20-30%, with only about 40-60% of survivors regaining normal neurological function

II. Clinical Presentation

- acute onset (<1 week) of focal neurologic findings
 - altered mentation, cranial nerve deficits, hemiparesis, dysphasia, aphasia, ataxia, focal seizures
- behavioral changes
 - hypomania (early), amnesia, Kluver-Bucy syndrome, subtle personality changes
- fever is common
- “atypical” presentation- mild cases of febrile encephalopathy in the absence of focal neurologic features, CSF pleiocytosis, or imaging abnormalities

III. Pathogenesis

- most cases are due to reactivation of latent virus, though primary infections may lead to encephalitis as well
 - immediate CNS invasion via trigeminal nerve or olfactory tract following primary HSV
 - CNS invasion following recurrent HSV infection (viral reactivation with subsequent spread)
 - reactivation of latent HSV within the CNS
- encephalitis during a primary HSV infection is much more common in children
- brain necrosis (in the temporal lobes in most cases) is probably both virus-mediated and indirectly immune-mediated

III. Labs and Studies

- CSF
 - can be normal early on, but typically shows lymphocytic pleiocytosis, elevated RBC's, and elevated protein; low glucose is uncommon
 - HSV DNA PCR- very high specificity and sensitivity, now considered the gold standard
 - o false negative can be due to fluid collected too early (24-48 hrs), too late (10-14 days), after acyclovir
 - viral culture- only positive in 4-5% of cases
- Head CT
 - poor sensitivity early in disease
 - may remain normal for the first 4-5 days, but about 50% will have abnormalities on noncontrasted CT

- Head MRI
 - most sensitive and specific imaging method for HSV encephalitis
 - typical early changes of focal edema in medial aspects of temporal lobes, insular cortex, and cingulate gyrus
- SPECT
 - highly specific, focal hyperperfusion may be an indicator of poor outcome
- EEG
 - focal findings in greater than 80% of cases

IV. Treatment

- must be started EARLY to prevent mortality and limit the severity of postencephalitic behavioral and cognitive impairments; the only predictor of outcome that can be influenced is the level of consciousness at the time of initiation of therapy
- acyclovir 10 mg/kg IV q 8°
 - slow infusion and with a fluid bolus to prevent crystal nephropathy
- duration should be no less than 14-21 days
- second line would be vidarabine or foscarnet if unable to tolerate acyclovir
- patients age and level of consciousness at the onset of treatment are the primary determinants of outcome



References:

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3. Schmutzhard, E. Virus Infections of the CNS With Special Emphasis on Herpes Simplex Infections. *Journal of Neurology* 2001; 248:469-477.