

# Urinary retention in an elderly patient - a complication of HSV type 1 encephalitis in association with other factors.

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### Abstract

Herpes simplex encephalitis (HSE) is a challenging viral infection with high morbidity, especially in the elderly. Rarely is it complicated by urinary retention, which is a urological emergency. Other studies have observed that reversible acute urinary retention due to herpes simplex virus infection occurs when there is an involvement of meninges or sacral spinal ganglia. However, the pathophysiology and association of urinary retention with HSE are not well understood. Also, urinary pathologies with herpes encephalitis are less recognized. We present an 89-year-old woman, who developed acute urinary retention during treatment for HSE. Catheterization for four weeks alleviated her urinary complication. In the absence of relevant urological history, neurological damage to the central nervous system (CNS) and or peripheral nervous system (PNS) due to HSV-1 seems to be the most likely reason for urinary retention. Catheterization is the treatment of choice, and patients usually recover within 4-6 weeks. Hence, we further emphasize that urinary retention is a rare and less recognized complication of HSE Type 1 encephalitis, but the possibility of recovery is high.

Keywords: Acute urinary retention, Herpes virus type 1 encephalitis, Herpes simplex encephalitis, viral encephalitis

#### Introduction

Herpes Simplex virus accounts for 10-20% of cases of sporadic encephalitis worldwide<sup>4, 24</sup>. Herpes simplex virus (HSV) 1 affects all age groups, whereas HSV 2 most typically occurs as a disseminated infection in neonates <sup>10</sup>. Despite the availability of efficacious antiviral treatment, Herpes encephalitis has a significant mortality rate of about 35% <sup>16</sup>, and about 50% of the patients develop disability [10]. HSV encephalitis presents with some acute imaging features that assist in diagnosis. MRI findings usually contain perivascular edema along with hemorrhagic necrosis in the mesiotemporal, orbitofrontal and insular cortex<sup>7,23</sup>. Necrosis extends from grey to white matter, and gross destruction of the temporal and frontal lobes is often present<sup>7, 23</sup>. Additionally, HSV type 2 encephalitis is more commonly associated with ischemic changes related to multifocal large vessel vasculitis 7.

The infectious cycles of HSV 1 and 2 begin with lytic replication in the somatic cells, leading to primary infection and later secondary transmission<sup>8, 21</sup>. These neurotropic viruses establish latent infection, which most commonly affects the sensory ganglia<sup>7</sup>. According to previous studies, about one-third of HSV-1 encephalitis cases develop due to primary infection and rarely due to reactivation<sup>11</sup> or immune-mediated pathological changes<sup>1, 11, 15</sup>.

HSV-1 can cause encephalitis, keratitis, herpetic stomatitis, and several peripheral nervous system disorders<sup>13, 21</sup>. The peripheral nervous system, particularly the neurons around the urinary tract, is commonly involved with HSV2 and VZV; involvement is not described adequately with HSV-1. Therefore, we describe a case of acute urinary retention as a rare and less recognized complication of HSE. Clean intermittent catheterization is the most common treatment because it allows the bladder to void spontaneously and avoid stretch-related detrusor injury. An 89-year-old woman presented with complaints of fever, confusion & weakness. On admission, she had altered mental status & her highest recorded temperature was 102.5 °F. Neurological examination revealed disorientation to time, place, and people. There were no focal signs and no signs of meningeal irritation present. The rest of the physical examination was unremarkable. Her initial Computed Tomography (CT) scan revealed diffuse atrophy and ischemic microvascular changes; however, there was no acute ischemic change. Computed Tomography Angiography (CTA) was normal. Lab results showed leukocytosis, and the Respiratory Virus Panel (RVP) test was positive for Rhinovirus. She was commenced on broadspectrum antibiotics empirically. After six days, the patient's condition did not improve, and a repeat CT revealed a lowdensity area in the right insular cortex extending into the temporal lobe. HSV Encephalitis was suspected, and an MRI of the brain and cerebrospinal fluid (CSF) study was done. The MRI demonstrated a large area of abnormally increased T2/ FLAIR (Fluid Attenuated Inversion Recovery). The signal intensity was mostly in the right temporal lobe and the external capsule lesions that were highly suspicious for herpes encephalitis (Figure). Her CSF analysis showed a protein level of 242 mg/dl, a white blood cell (WBC) count of 93, a red blood cell (RBC) count of 1,010, and a glucose level of 68 mg/dL. IV acyclovir 10mg/kg every 12 hours was commenced. Her condition improved gradually, and she became more alert. Although cultures were negative, a CSF polymerase chain reaction (PCR) was found to be positive for HSV-1 DNA.

Although her initial symptoms and signs started to trend in the right direction with treatment, she developed acute urinary retention during her hospital stay. She could not pass urine by herself, and urological consultation was obtained. The impression was that urinary retention in women voiding normally prior to CNS infection is usually self-limiting with no significant sequelae. Bladder rest with catheterization was started with the instruction to avoid narcotics, sedatives, hypnotics, anticholinergics, and antihistamines. Her urinary symptoms gradually improved.





**Figure 1:** Diffuse cortical atrophy. Enlargement along with an abnormally increased T2/FLAIR signal intensity predominantly involving the right temporal lobe(A) and external capsule(B).

#### **Discussion:**

Herpes encephalitis was diagnosed in our patient due to the main clinical features of fever and altered mental status along with acute loss of consciousness after starting empirical vancomycin. Herpes simplex encephalitis preferentially involves the temporal lobe. However, extratemporal involvement is also well described in the literature<sup>6,</sup> <sup>13</sup>. In our case, the initial CT scan was nonspecific, but a subsequent CT scan after six days revealed a low-density area in the right insular cortex extending into the temporal lobe. MRI detected a hyperintense area in the right temporal lobe with leptomeningeal enhancement suspicious of an inflammatory process. PCR results were positive for HSV type 1, and CSF analysis revealed findings consistent with the viral infection. MRI and CSF PCR findings in our case were indicative of HSV encephalitis, consistent with previous studies<sup>2, 3, 14, 22</sup>. There are considerable difficulties in understanding the pathogenesis of acute urinary retention in a patient with HSV-1 encephalitis<sup>13</sup>. VZV is the cause of urinary retention 35% of the time, while HSV-2 is rarely reported as a cause. However, previous studies have not well described urinary retention followed by HSV-1 infection<sup>13</sup>. Previous literature suggested that acute urinary retention following HSV encephalitis could be due to neurological damage to the central and or peripheral nervous system<sup>13</sup>. Another consideration for deterioration in our patient was HSV-associated CNS vasculitis. While this complication is more commonly reported with varicella-virus, there are rare reports of HSV-associated vasculitis, particularly in neonates9.

However, in an elderly woman, multiple cofactors can be associated with the development of urinary retention in addition to CNS infections. Recent anesthesia, sedatives, hypnotics or anticholinergic medications, and multiple co-morbidities like HIV, diabetes mellitus, and neurologic disorders may play a role<sup>20</sup>. Also, a lack of ambulation can contribute to urinary retention. Although viral encephalitis has been reported to cause acute urinary retention, it is rarely reported with HSE, especially with the type 1 herpes simplex virus. In those reports, HSE-associated urinary retention developed due to concomitant herpes radiculitis, brain stem encephalitis, ADEM, and Elsberg syndrome. Localized sacral radiculitis followed by herpes simplex virus type 1 infection involves sacral 2-3 dorsal root ganglia. This causes sensory symptoms, detrusor areflexia with loss of bladder sensation without motor dysfunction <sup>17</sup>. Herpes simplex brainstem encephalitis may cause urinary retention with detrusor hyporeflexia and normal sphincter function. The pathophysiology can be due to the involvement of the pontine micturition center, which is seen in MRI as a bilateral pontine segmental lesion. Encephalitis, myelitis with a combination of detrusor hyperreflexia and impaired contractile function (DHIC) is common in ADEM (Acute disseminated encephalomyelitis). Another cause of urinary retention stated in the previous case reports is meningeal retention syndrome (MRS) which presents with aseptic meningitis and acute urinary retention. The site of lesion for both ADEM and MRS is in the spinal cord <sup>17</sup>. Additionally, Ellsberg syndrome, a rare cause of urinary retention, is generally regarded as a unique form of lumbosacral radiculopathy. Ellsberg syndrome is clinically characterized by urinary retention, constipation, erectile dysfunction, pain or loss of sensation in the anogenital region, and weakness of leg muscles in various combinations<sup>19</sup>.

In our patient, the neurological examination was normal. Motor or sensory neuropathies, along with gait disturbances, were all absent. Our case supports the hypothesis describing the involvement of the preferential parasympathetic pelvic nerve in HSE. Also, other factors such as her age and lack of ambulation during her prolonged hospital stay may have contributed to urinary retention. The absence of brainstem deficit, back pain, lateralizing signs, and sensory-motor or reflex findings usually indicates involvement of the pontine micturition center, spinal cord, cauda equine, or peripheral nervous system<sup>17</sup>. Catheterization is the mainstay of treatment because it allows the bladder to empty normally and avoids stretchrelated bladder wall injury. If the patient does not improve within 12 weeks, the next step would be a urodynamic study. We usually do not perform urodynamic studies before catheterization because most studies showed spontaneous recovery following catheterization. Consistent with previous case reports, urinary function recovery was also observed in our case following catheterization for four weeks <sup>5, 12, 14, 18</sup>. Most HSE patients require catheterization in the early phase of presentation due to an altered level of consciousness. Bladder involvement during HSE infection, along with other contributing factors, is under-reported and requires further studies to confirm the nature of the association.

In summary, our case emphasizes recognizing urinary retention as a complication of HSE and other comorbid conditions in elderly patients.

#### **Conclusion:**

Our case depicts the importance of prompt suspicion of viral encephalitis and prompt initiation of treatment. We emphasize that acute retention of urine in elderly women may occur as a complication of HSV-1 encephalitis in the presence of other contributory factors. Immediate management with catheterization can lead to significant recovery.

#### References

1. Armangue, T., Spatola, M., Vlagea, A., Mattozzi, S., Cárceles-Cordon, M., Martinez-Heras, E., et al.: Frequency, symptoms, risk factors, and outcomes of autoimmune encephalitis after herpes simplex encephalitis: a prospective observational study and retrospective analysis. The Lancet. Neurology. 17, 9, 760– 772. (2018). https://doi.org/10.1016/S1474-4422(18)30244-8.

2. Baskin, H.J., and Hedlund, G.: Neuroimaging of herpesvirus infections in children. Pediatric radiology. 37, 10, 949–963. (2007). https://doi.org/10.1007/s00247-007-0506-1.

3. Bradshaw, M.J., and Venkatesan, A.: Herpes Simplex Virus-1 Encephalitis in Adults: Pathophysiology, Diagnosis, and Management. Neurotherapeutics. 13, 3, 493–508. (2016). https://doi.org/10.1007/s13311-016-0433-7.

4. Byun, Y.H., Ha, E.J., Ko, S.-B., and Kim, K.H.: Decompressive craniectomy for herpes simplex encephalitis complicated by frank intracerebral hemorrhage: a case report and review of the literature. BMC neurology. 18, 1, 176. (2018). https://doi.org/10.1186/s12883-018-1181-6.

5. Fukuoka, T., Nakazato, Y., Miyake, A., Tamura, N., Araki, N., and Yamamoto, T.: A case of urinary retention in the early stages of herpes simplex virus type-1 encephalitis. Clinical neurology and neurosurgery. 157, 17–18. (2017). https://doi. org/10.1016/j.clineuro.2017.03.011.

6. Haanpää, M., and Paavonen, J.: Transient urinary retention and chronic neuropathic pain associated with genital herpes simplex virus infection. Acta obstetricia et gynecologica Scandinavica. 83, 10, 946–949. (2004). https://doi.org/10.1111/ j.0001-6349.2004.00500.x.

7. Hauer, L., Pikija, S., Schulte, E.C., Sztriha, L.K., Nardone, R., and Sellner, J.: Cerebrovascular manifestations of herpes simplex virus infection of the central nervous system: a systematic review. Journal of neuroinflammation. 16, 1, 19. (2019). https://doi.org/10.1186/s12974-019-1409-4.

 Held, K., and Derfuss, T.: Control of HSV-1 latency in human trigeminal ganglia--current overview. Journal of neurovirology.
 6, 518–527. (2011). https://doi.org/10.1007/s13365-011-0063-0.

Joshi, P.: Multiple strokes associated with herpes simplex virus type-2 infection: case report. Journal of neurovirology.
 22, 2, 251–253. (2016). https://doi.org/10.1007/s13365-015-0385-4.

10. Kennedy, P.G.: Herpes simplex virus and the nervous system. Postgraduate medical journal. 60, 702, 253–259. (1984). https://doi.org/10.1136/pgmj.60.702.253.

11. Kennedy, P.G.E., Rovnak, J., Badani, H., and Cohrs, R.J.: A comparison of herpes simplex virus type 1 and varicellazoster virus latency and reactivation. The Journal of general virology. 96, Pt 7, 1581–1602. (2015). https://doi.org/10.1099/ vir.0.000128.

12. Kusuhara, T., Nakajima, M., Inoue, H., Takahashi, M., and Yamada, T.: Parainfectious encephalomyeloradiculitis associated with herpes simplex virus 1 DNA in cerebrospinal fluid. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 34, 9, 1199–1205. (2002). https://doi.org/10.1086/339811.

13. Mancino, P., Dalessandro, M., Falasca, K., Ucciferri, C.,

Pizzigallo, E., and Vecchiet, J.: Acute urinary retention due to HSV-1: a case report. Le infezioni in medicina. 17, 1, 38–40. (2009).

14. Nakamura, K., Terasaki, T., Tsuchiya, T., Oita, J., and Yamaguchi, T.: [Herpetic simplex encephalitis followed by myelopathy]. No to shinkei = Brain and nerve. 45, 6, 553–558. (1993).

15. Piret, J., and Boivin, G.: Innate immune response during herpes simplex virus encephalitis and development of immunomodulatory strategies. Reviews in medical virology.
25, 5, 300–319. (2015). https://doi.org/10.1002/rmv.1848.

16. Raschilas, F., Wolff, M., Delatour, F., Chaffaut, C., De Broucker, T., Chevret, S., et al.: Outcome of and prognostic factors for herpes simplex encephalitis in adult patients: results of a multicenter study. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 35, 3, 254–260. (2002). https://doi.org/10.1086/341405.

17. Sakakibara, R., Yamanishi, T., Uchiyama, T., and Hattori, T.: Acute urinary retention due to benign inflammatory nervous diseases. Journal of neurology. 253, 8, 1103–1110. (2006). https://doi.org/10.1007/s00415-006-0189-9.

18. Sakakibara, R., Hattori, T., Fukutake, T., Mori, M., Yamanishi, T., and Yasuda, K.: Micturitional disturbance in herpetic brainstem encephalitis; contribution of the pontine micturition centre. Journal of neurology, neurosurgery, and psychiatry. 64, 2, 269–272. (1998). https://doi.org/10.1136/jnnp.64.2.269.

19. Sasaki, M., Ohara, S., Hayashi, R., Iwahashi, T., and Tsuyuzaki, J.: Aseptic meningo-radiculo-encephalitis presenting initially with urinary retention: a variant of acute disseminated encephalomyelitis. Journal of neurology. 253, 7, 908–913. (2006). https://doi.org/10.1007/s00415-006-0131-1.

20. Selius, B.A., and Subedi, R.: Urinary retention in adults: diagnosis and initial management. American family physician. 77, 5, 643–650. (2008).

21. Steiner, I., and Benninger, F.: Update on herpes virus infections of the nervous system. Current neurology and neuroscience reports. 13, 12, 414. (2013). https://doi. org/10.1007/s11910-013-0414-8.

22. Wasay, M., Mekan, S.F., Khelaeni, B., Saeed, Z., Hassan, A., Cheema, Z., et al.: Extra temporal involvement in herpes simplex encephalitis. European journal of neurology. 12, 6, 475–479. (2005). https://doi.org/10.1111/j.1468-1331.2005.00999.x.

23. Weisberg, L.A., Greenberg, J., and Stazio, A.: Computed tomographic findings in acute viral encephalitis in adults with emphasis on herpes simplex encephalitis. Computerized medical imaging and graphics : the official journal of the Computerized Medical Imaging Society. 12, 6, 385–392. (1988). https://doi.org/10.1016/0895-6111(88)90082-1.

24. Whitley, R.J., and Gnann, J.W.: Viral encephalitis: familiar infections and emerging pathogens. Lancet (London, England). 359, 9305, 507–513. (2002). https://doi.org/10.1016/S0140-6736(02)07681-X.