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Case Report

Herpes simplex encephalomyeloradiculitis initially presents with urinary retention

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Abstract: Herpes simplex virus (HSV) infections necessitate careful management of urinary dysfunction and retention, which are underestimated conditions. Here, we present a rare case of HSV encephalomyeloradiculitis in a 76-year-old man, whose initial symptoms included urinary dysfunction and retention that alone lasted for approximately 1 week. Unlike in meningoencephalitis, high fever and headache were absent; however, the patient subsequently developed cauda equina syndrome and consciousness disturbance. Gadolinium-enhanced spinal MRI suggested enhanced cauda equina at the L2/3 level. Upon admission, he was treated for meningoencephalitis with acyclovir and steroid pulse therapy. Subsequent cerebrospinal fluid analysis result was positive for HSV DNA. A brain MRI conducted 1 week after admission displayed high-intensity lesions in the white matter of the right temporal lobe, confirming HSV encephalomyeloradiculitis. These treatments were highly effective and gradually improved the patient's condition. He was discharged 1 month after hospitalization, and the urinary catheter was removed 2 weeks later. HSV infections can cause life-threatening encephalomyeloradiculitis. Therefore, both neurologists and urologists must pay attention to their occurrence and characteristics in clinical settings.

Key words: herpes simplex virus, encephalomyeloradiculitis, urinary retention, cauda equina syndrome

Introduction

Urinary retention frequently originates from neurological infections. Acute infectious encephalitis is characterized by brain inflammation resulting from infections, such as herpes simplex virus (HSV) encephalitis. Throughout the acute phase, it presents with central nervous system manifestations, such as fever, altered consciousness, seizures, and neurological deficits, with urinary dysfunction observed commonly, albeit rarely as the initial neurological symptom. Depending on the etiology of urinary retention, acute infectious encephalitis can be categorized into disorders of the peripheral nervous system (e.g., Elsberg syndrome, sacral herpes, and polyradiculitis), central nervous system (e.g., myelitis, brainstem encephalitis, and meningitis-urinary retention syndrome), or a combination of both[1)2)]. Studies have indicated a correlation between HSV infection-related mortality and urinary retention[3)]. This necessitates the careful management of urinary dysfunction and retention in HSV infection. Herein, we present a rare case of HSV encephalomyeloradiculitis characterized by urinary dysfunction and retention as the initial symptoms, contrary to meningoencephalitis characterized by high fever and headache. Thereafter, gait disturbance ensued, followed by impaired consciousness. This case manifested as cauda equina syndrome or sacral radiculitis in the early disease stages and eventually progressed to HSV encephalomyeloradiculitis.

Case report

A 76-year-old man received treatment for hypertension. He had no history of genital herpes. Approximately 8 days before admission, he reported mild temperature within 37°C and difficulty with urination; headache symptoms were absent. These symptoms persisted, with the additional onset of moderate unsteadiness during ambulation. Three days before admission, the patient was barely able to urinate on his own and sought medical attention at a local clinic because of urinary dysfunction; 400 m/ of residual urine was detected in his bladder. On the day before admission, a subsequent clinic visit suggested an increased residual urine volume of 1,000 m/. Consequently, the patient was referred to the urology department of our hospital for urinary retention management. An indwelling bladder catheter was inserted, and the patient was discharged for monitoring. He managed to walk independently. The subsequent day, he

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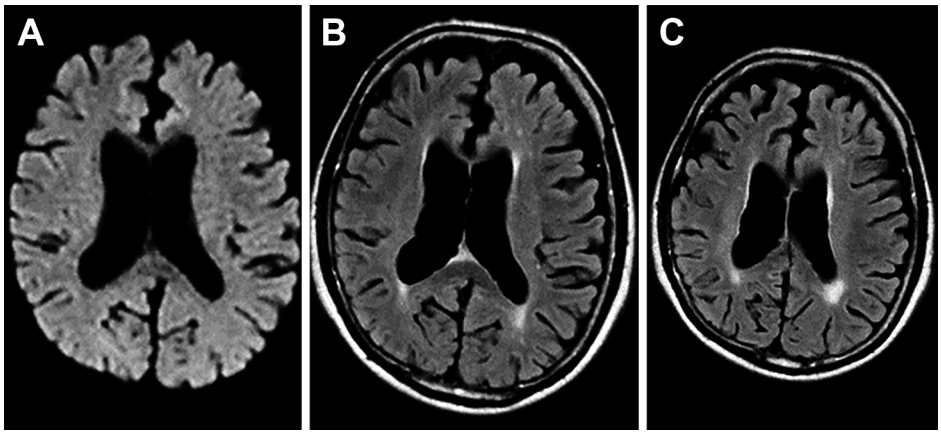

Fig. 1 Axial view of brain MRI on day 1 after admission.
(A) Diffusion-weighted imaging displays no apparent abnormalities. (B, C) Fluid-attenuated inversion recovery images display mild atrophy of the cerebral cortex (B) and mild periventricular white matter lesions (C).

developed a fever of 38°C and experienced further difficulty with independent ambulation, prompting referral to a neurologist. He was subsequently hospitalized for thorough evaluation and intervention.

On the same day, his level of consciousness deteriorated mildly. Moreover, he exhibited disorientation and confused speech (assessed by the Glasgow Coma Scale; E4V4M6). Initial vital signs were recorded as follows: heart rate, 68 beats/min; respiratory rate, 24 breaths/min; blood pressure, 137/70 mmHg; body temperature, 38.2°C; and oxygen saturation, 96% with room air. Erosions or vesicular lesions were absent in the vulvae. Neurological examination suggested mild neck stiffness, no muscle weakness in the limbs, hyporeflexia in both lower extremities, and no pathological reflexes. Mild dyscoordination was evident in his lower extremities, characterized by decomposition in the heel-knee test. Additionally, he could not stand or walk independently because of lower limb ataxia. Hypoesthesia was observed around the anus, along with the loss of vibratory sensation in both lower limbs. Moreover, he presented with bowel incontinence. Blood examination indicated normal inflammatory response values, with a white blood cell count of 7,920/μl (neutrophils, 73.3%; lymphocytes, 15.3%; monocytes, 11.1%; and basophils, 0.3%) and C-reactive protein concentration of 0.24 mg/l (reference range, <0.3 mg/dl). Serum liver function enzyme, creatinine, and electrolyte concentrations were within normal limits. Nasopharyngeal swab tests for SARS-CoV-2 RNA and influenza antigens (A and B) returned negative results. Cerebrospinal fluid (CSF) analysis suggested lymphocyte-dominant pleocytosis with 541 nucleated cells/mm^3 (471 mononuclear cells/mm^3 and 70 polymorphonuclear cells/mm^3), elevated protein concentration (373 mg/dl; reference range, 15–45 mg/dl), and normal glucose level (44 mg/dl, with a serum glucose concentration of 98 mg/dl). Diffusion weighted images and fluid-attenuated inversion recovery (FLAIR) images of brain MRI depicted no apparent abnormalities (Fig. 1). Spinal gadolinium (Gd)-enhanced MRI indicated no abnormal signal area or enhancement effect in the thoracic spinal cord (Fig. 2A); however, an enhancement effect was observed in the cauda equina at the L2/3 level (Fig. 2B, D). Based on his clinical presentation and the results of laboratory and imaging investigations, possible encephalomyeloradiculitis, including HSV encephalitis, was diagnosed. On the admission day, the treatment was commenced for meningoencephalitis with acyclovir (10 mg/kg IV q8h) for 21 days, ceftriaxone sodium (2 g IV q12h) for 7 days, and high-dose intravenous methylprednisolone (1,000 mg) for 3 days as steroid pulse therapy.

On day 4 after admission, the patient became afebrile and had normal conversations; his impaired consciousness improved. However, we observed a decline of 23/30 points in the Mini-Mental State Examination (MMSE) and 7/18 points in the Frontal Assessment Battery (FAB), indicating compromised higher brain functions. Notably, anterograde amnesia, attention deficits, and frontal lobe dysfunction persisted at considerably reduced levels. Upon admission, laboratory analysis detected HSV DNA in the CSF via polymerase chain reaction, confirming HSV-induced encephalomyeloradiculitis, warranting the continued administration of acyclovir. One week after admission, CSF examination suggested decreased mononuclear leukocytosis, with 380 nuclear cells/mm^3 (337 mononuclear cells/mm^3 and 43 polymorphonuclear cells/mm^3). However, brain FLAIR MRI suggested hyperintense lesions in the white matter of the right temporal lobe, alongside cerebral sulci narrowing and brain parenchymal swelling, consistent with encephalitis (Fig. 3B, C). Two weeks after admission, CSF analysis indicated a decline in mononuclear leukocytosis, with 118 nuclear cells/mm^3 (110 mononuclear cells/mm^3 and 8 polymorphonuclear cells/mm^3), reduced protein levels (133 mg/dl), and no CSF HSV DNA. Subsequent follow-up MRI 2 weeks later suggested regression of

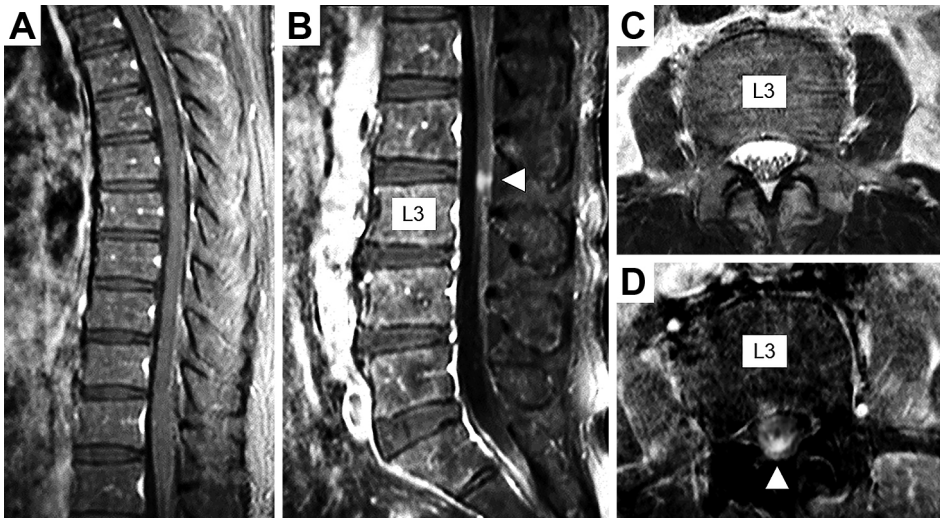

Fig. 2 Spinal magnetic resonance imaging (MRI) on day 1 after admission.
(A, B) Sagittal view of spinal gadolinium (Gd)-enhanced MRI images; (A) No abnormal signal areas or enhancement effects were observed in the thoracic spinal cord. (B) Enhancement effect in the cauda equina at the L2/3 level, indicated by the arrowhead. (C, D) In axial T_2-weighted and Gd-enhanced T_1-weighted images; the cauda equina without abnormalities (C) and high signal enhancement effects in the cauda equina at the L2/3 level (D).

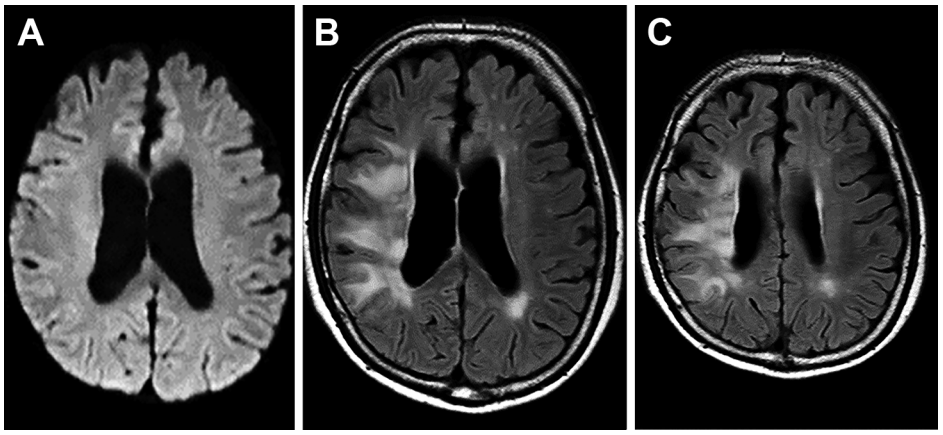

Fig. 3 Axial view of brain magnetic resonance imaging 1 week after admission.
(A) Diffusion weighted imaging displays no apparent high signal intensity. (B, C) Fluid-attenuated inversion recovery images display high-intensity lesions in the white matter of the right temporal lobe, along with narrowing cerebral sulci and swollen brain parenchyma, indicating encephalitis.

hyperintense lesions in the right temporal lobe (Fig. 4B, C). Alongside pharmacotherapy, rehabilitation efforts were initiated, which gradually improved the ataxic gait disorder. By 3 weeks after hospitalization, the patient demonstrated near-normal ambulation, concomitant with improved higher brain functions to a level compatible with the activities of daily living (MMSE, 28/30 points; FAB, 16/18 points). Discharge occurred 1 month after hospitalization. Additionally, urinary retention was ameliorated, leading to the removal of the urinary catheter 2 weeks after discharge.

Discussion

This case presents a rare instance of HSV infection characterized solely by urinary retention, persisting for over 1 week, eventually leading to encephalitis. Alongside early-onset urinary retention, symptoms, such as gait disturbance, hypoesthesia around the anus, and diminished vibration sensation in the lower limbs, were observed during examination. They indicated cauda equina syndrome. Spinal Gd-enhanced MRI illustrated contrast enhancement at the L2/3 level within the cauda equina, suggesting the onset of radiculitis in the cauda equina (Fig. 2B, D). Initially, bilateral nerve root inflammation

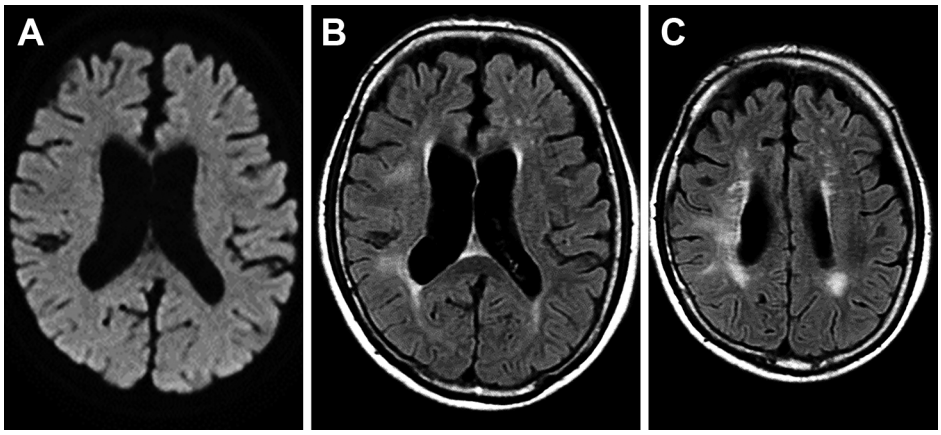

Fig. 4 Follow-up magnetic resonance imaging 2 weeks after admission.
(A) Diffusion weighted imaging did not show any abnormal signals during the course. (B, C) Fluid-attenuated inversion recovery images suggest almost diminished high-intensity lesions in the right temporal lobe (B). A few residual white matter lesions around the right ventricles (C).

resembling cauda equina syndrome was evident in the cauda equina; however, it evolved into encephalitis with disease progression, characterized by altered consciousness and higher brain dysfunction. A brain FLAIR MRI conducted 1 week after admission depicted a hyperintense lesion in the white matter of the right temporal lobe, suggesting encephalitis.

Encephalomyeloradiculitis is a rare neurological disorder associated with underlying etiologies, which has been documented in cases attributed to acute disseminated encephalomyelitis (ADEM), HSV, coronavirus disease 2019, adenovirus, tick-borne viruses, chikungunya virus, Epstein–Barr virus, and other pathogens[4)–11)]. Considering the broad neurotropism of HSV, infection with this virus can cause numerous neurological symptoms, encompassing encephalitis, meningitis, myelitis, and infrequently, myeloradiculitis and polyradiculitis[12)]. Notably, HSV encephalomyeloradiculitis, characterized by concurrent encephalitis and myeloradiculitis, is exceedingly rare, as demonstrated in this case. Naito et al. described a patient who experienced acute encephalitis and urinary retention almost simultaneously; despite initially improved consciousness after acyclovir therapy, they observed subsequent progression to brainstem encephalitis, transverse myelitis, and lumbosacral polyradiculitis[5)].

The prevailing symptoms of HSV encephalitis, observed in over 50% of cases, encompass fever, confusion, impaired mental faculties, headache, altered consciousness, and seizures[13)]. Notably, HSV encephalitis presents alongside urinary retention, with its onset coinciding with or following the symptoms of encephalitis[5)14)15)]. Previous investigations have attributed HSV encephalitis-related urinary retention to a confluence of conditions, including myelitis, myeloradiculitis, encephalomyeloradiculitis, ADEM, brainstem encephalitis, and pelvic neuropathy. They affect various segments of the micturition neuroregulatory system and culminate in urinary retention (Fig. 5). Urinary retention was the only neurological symptom for approximately 1 week before admission; nonetheless, the progressive clinical presentation in our case was similar to Ellsberg syndrome during admission. Ellsberg syndrome is hypothesized to be an infectious syndrome characterized by acute or subacute bilateral lumbosacral radiculitis. It typically presents as cauda equina syndrome featuring symptoms, such as sensory disturbances, weakness in the lower extremities, saddle anesthesia, and urinary retention[2)]. During admission, our patient presented with urinary retention, sensory disturbance in the lower extremities, mild saddle anesthesia, and bowel incontinence. Spinal Gd-enhanced MRI suggested a contrast effect on the cauda equina (Fig. 2B, D). Our case represents a disorder of the lower micturition center (S2–S4) (Fig. 5). HSV infection supposedly targeted the nerves surrounding the sacral spinal cord initially. The pathogenesis of HSV encephalitis involves both direct virus-mediated cell lysis and immune-mediated pathological changes; however, it is poorly understood. Hence, the pathological mechanism underlying the subsequent development of encephalitis in this case remains unclear[13)]. However, we could not differentiate between HSV types 1 and 2. Ellsberg syndrome is often caused by HSV-2, which tends to be associated with meningitis[2)16)]. Encephalitis caused by HSV-2 differs from typical lesions in the medial temporal lobe on HSV-1. Moreover, atypical cases, such as this case, have been reported[17)]. Thus, we hypothesized that HSV-2 was reactivated in the sacral spinal cord, initially causing urinary retention, which progressed to cauda equina syndrome and meningitis, and finally to encephalitis. However, differentiating between herpes types 1 and 2 may not facilitate patient management. Meningitis-urinary retention syndrome is a benign inflammatory neurological syndrome associated with aseptic meningitis leading to urinary retention; however, the patients lack prominent neurological symptoms, such as altered consciousness, epilepsy, and aphasia, or spinal cord symptoms,

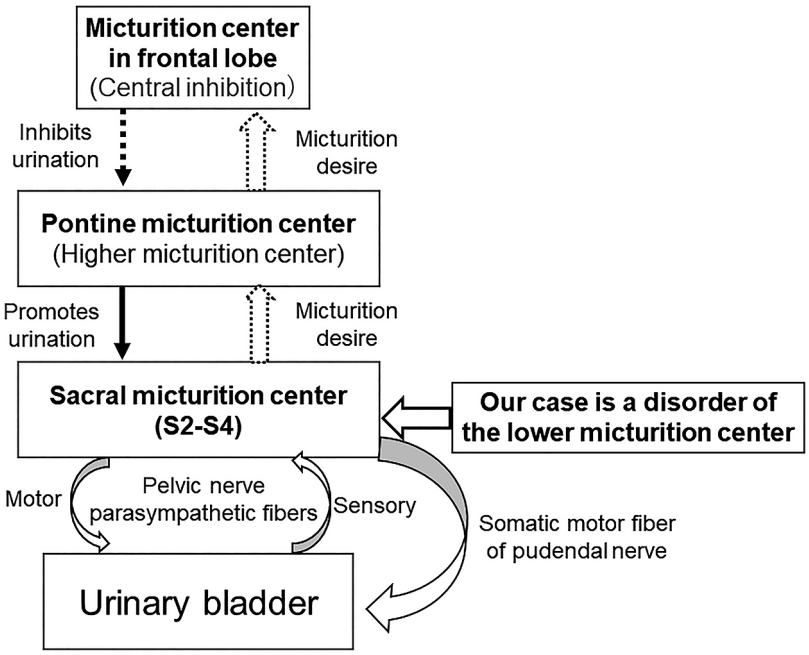

Fig. 5 Neural control of urination, depicting the peripheral-spinal cord-brainstem-basal ganglia/frontal lobe pathway.

such as abnormal gait or sensory deficits[1)18)]. Therefore, diagnosing meningitis-urinary retention syndrome was not applicable in this case.

A previous report documented urinary retention caused by myeloradiculitis preceding aseptic encephalitis, similar to the present case, although not an HSV infection[19)]. Sasaki et al. described three men who experienced acute urinary retention after high fever and headache, subsequently developing aseptic encephalomyeloradiculitis[19)]. One patient exhibited meningeal Gd-enhancing effects in the conus medullaris and cauda equina. In our case, the patient did not exhibit symptoms, such as high fever or headache, which typically suggest encephalitis onset at first. Nevertheless, in all cases, the patients did not initially exhibit severe encephalitis symptoms, such as impaired consciousness; rather, urinary retention or dysuria was the primary neurological symptom, lasting approximately 1 week, as observed in this case[19)]. The authors hypothesized that encephalomyeloradiculitis, presenting with a relatively favorable clinical course and initial urinary retention, is an ADEM variant or a benign and distinctive form of parainfectious immune-mediated disease. However, in our case, CSF testing results were positive for HSV DNA, suggesting syndrome-like conditions arising from various etiologies.

In conclusion, this case report illustrated that HSV infection induces sacral radiculitis in the early stages, subsequently progressing to encephalitis. HSV is a common etiological agent of mucocutaneous infections; however, it can cause life-threatening encephalitis. Encephalomyeloradiculitis rarely manifests with urinary retention initially. By solely concentrating on urinary retention, and disregarding neurological symptoms, clinicians may compromise timely and appropriate intervention. This in turn can cause fatal outcomes for the patient. Hence, both neurologists and urologists must acknowledge these conditions in clinical settings. Further clinical and pathophysiological investigations are imperative to elucidate the mechanisms underlying these syndromes.

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COI：The authors declare that there is no conflict of interest relevant to this article.

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