Yonago Acta medica 2008;51:83–88

Urinary Retention as an Initial Symptom of Acute Meningo-Encephalo-Radiculitis in Epstein-Barr Virus Infection

Yasumasa Asai, Ryosuke Fujita, Hiroyuki Nakayasu, Kaori Suzuki, Taizo Kaneto* and Kenji Nakashima†

*Clinic of Neurology, Tottori Prefectural Central Hospital, Tottori 680-0901, *Clinic of Neurology, Tottori Medical Center, Tottori 689-0203 and †Department of Neurology, Institute of Neurological Sciences, Tottori University Faculty of Medicine, Yonago 683-8503 Japan*

A 48-year-old man presented with urinary retention followed by disturbance of consciousness, areflexia, ophthalmoplegia, muscle weakness, and atrophy. Epstein-Barr virus DNA by PCR was positive in his cerebrospinal fluid. The cerebrospinal fluid revealed elevated myelin basic protein and an oligoclonal band. Magnetic resonance imaging showed high signal intensity in the pons, basal ganglia, and cerebral white matter on T2-weighted imaging and fluid-attenuated inversion recovery imaging. His consciousness, ophthalmoplegia, and muscle weakness almost full recovered. In this patient, the inflammation is thought to have begun as sacral radiculitis, and then extended to encephalitis, and brachial and lumbar radiculoneuritis.

Key words: acute disseminated encephalitis; Guillain-Barré syndrome; meningo-encephalo-radiculitis; urinary retention

Acute disseminated encephalomyelitis (ADEM) is a monophasic inflammatory demyelinating disorder of the central nervous system, typically occurring after infection or vaccination. The disease is characterized by multifocal white matter lesions on neuroimaging. The polysymptomatic presentation reflects the demyelinating lesions and consists of various combinations of motor, sensory, visual, and cognitive symptoms.

Guillain-Barré syndrome (GBS), which is an acute immune-mediated polyneuropathy with a monophasic course, is classified as acute inflammatory demyelinating polyneuropathy and acute motor axonal neuropathy. The cardinal clinical features of GBS are weakness, paresthesia, and hyporeflexia. Albuminocytological dissociation is one of the diagnostic findings in GBS. Central nervous system involvement in GBS has been reported (Baker, 1943; Morley and Reynolds, 1966; Blennow et al., 1968; Gamstorp, 1974; Amit et al., 1986; Laarman et al., 1987; Amit et al., 1992; Okumura et al., 2002; Pfausler et al., 2002; Tsugawa et al., 2004; Chikakiyo et al., 2005). Blennow et al. introduced the term "encephalomyelo-radiculo-neuropathy" to describe this combined involvement. However, there are a few reports of both GBS and ADEM occurring simultaneously (Amit et al., 1986, 1992). In these reports, the term "acute severe central and peripheral nervous system combined demyelination" was used to replace the combination of GBS and ADEM. Guillain (1936) has refused to recognize this syndrome as belonging to any condition with a spinal fluid pleocytosis (Pfausler et al., 2002). However, Baker (1943) proposed that GBS might involve any part of the peripheral or the central

Abbreviations: ADEM, acute disseminated encephalomyelitis; CSF, cerebrospinal fluid; GBS, Guillain-Barré syndrome; Ig, immunoglobulin; MER, meningo-encephalo-radiculitis; MRI, magnetic resonance imaging

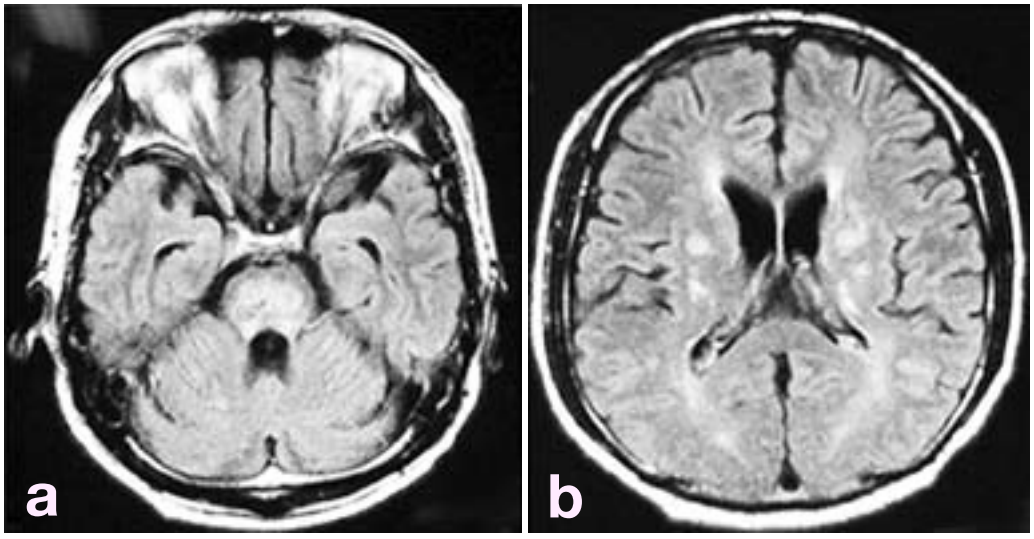

Fig. 1. Brain MRI showed high signal intensity in the pons, basal ganglia, cerebral white matter on T2 weighted imaging (**a**) and fluid attenuated imaging (**b**).

nervous system, which would include "encephalomyelo-radiculitis". We use the term meningoencephalo-radiculitis (MER), because meningoencephalitis and radiculitis was obvious and myelitis was uncertain in our patient.

During the course of ADEM and GBS, micturitional disturbance is commonly seen. Lumbosacral myelitis in ADEM and lumbosacral radiculoneuritis in GBS appear to be the main causes of micturitional disturbance. Local lumbosacral radiculitis can cause micturitional disturbance, a condition known as Elsberg syndrome (Hemrika et al., 1985). Even in the presence of Elsberg syndrome, micturitional disturbance as a first symptom of MER is rare (Laarman et al., 1987; Tsugawa et al., 2004; Sasaki et al., 2006). We report a case of MER with Epstein-Barr virus (EBV) infection presenting urinary retention as an initial symptom.

Patient Report

A 48-year-old Japanese man had joint pain in his knee and elbow, lumbago and headache in mid-March, 2006. Five days after the onset, he had urinary retention, and a urinary catheter was inserted intermittently. He was taken to hospital because of the presenting urinary retention and high fever nine days after onset. He developed consciousness disturbance on Day 2 after hospitalization (10 days after onset).

On physical examination, his body temperature was 38.5°C, blood pressure was 155/80 mmHg, and pulse was regular (100/min). There were no cardiac murmurs, rhonchus or crackles. Neurological examination revealed disorientation and a stiff neck. He also could not walk because of muscle weakness in his lower limbs. Deep tendon reflexes were absent in his lower limbs. Neither sensory loss nor paresthesia was observe d. A urinary catheter was inserted because of difficult micturition.

A hematological investigation showed an elevated white blood cell count of 15,440/μL. The blood urea nitrogen level was 65.6 mg/dL, creatinine level was 1.71 mg/dL, natrium level was 131 mEq/L, and C-reactive protein level was 2.78 mg/dL. Titers of antibody herpes simplex virus (HSV), varicella-zoster virus (VZV) and cytomegalovirus (CMV) were not elevated in his serum. Titers of Epstein-Barr virus (EBV) virus capsid antigen immunoglobulin M (IgM) were < 10 (normal range < 10), virus capsid antigen IgG 80 (normal range < 10), early antigen IgG < 10 (normal range < 10), Epstein-Barr nuclear antigen 20 (normal range < 10) in his serum. Results of cerebrospinal fluid (CSF) examination revealed the following: 492 cells/mm^3 (polymorphonuclear : mononuclear = 1:122), protein level of 299 mg/dL, IgG index 0.79, myelin basic protein (343 pg/mL, control < 102). Oligoclonal band was positive. Viorogical analysis of

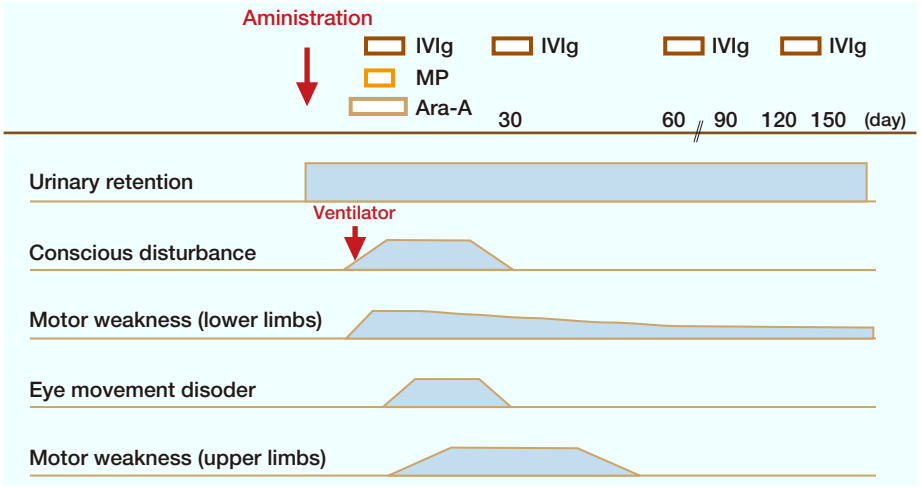

Fig. 2. The clinical course of the present patient. Ara-A, vidarabine; IVIg, intravenous immunoglobulin; MP, methylprednisolone.

CSF revealed the presence of EBV DNA by PCR, but no HSV, VZV and CMV DNA in the CSF. Magnetic resonance imaging (MRI) showed a normal brain on Day 9 after hospitalization (17 days after onset). Gadolinium enhancement was not done. Single photon emission tomography did not show hypoperfusion or hyperperfusion. Electroencephalography showed a 6- to 7-Hz slow wave. On Day 2 (10 days after onset), viral encephalitis was the tentative diagnosis, and vidarabine was administered intravenously. However, he developed consciousness disturbance and presented tonic seizure and tetraplegia, so steroid pulse therapy (methylprednisolone 1000 mg × 3 days) and immunoglobulin (2.5 g × 5 days) were added. He was incubated and required mechanical ventilation. On Day 5 (13 days after onset), total ophthalmoplegia presented, and deep tendon reflexes in all limbs and bilateral oculocephalic reflexes were absent. Immunoglobulin (27.5 g × 5 days) was administered because of the suspected Fisher syndrome on Day 12 (20 days after onset). In the clinical course, diffuse muscle atrophy in the upper and lower limbs was present. On Day 34 (42 days after onset), his consciousness gradually recovered. Ophthalmoplegia and muscle weakness were almost full recovered and he could walk a few steps. However, he performed intermittent self-catheterization because of voiding difficulties. Orthostatic hypotension was not shown in a head-up tilt test. Coefficient of variation of RR intervals was 1.22%. A sweat test indicated no sweat on his trunk and lower limbs. Phenylephrine eye drops test showed mild mydriasis. Antibody activities against ganglioside GM1, GM2, GM3, GD1a, GD1b, GD3, GT1b, GQ1b, GA1, Gal-C and GalNAc-GD1a were all negative. Fifty days after onset, an electrophysiological examination was performed. Distal complex motor action potential amplitudes were 11.7/8.3 (right/left) mV in his median nerve and 0.8/0.7 mV in his tibial nerve. Motor nerve conduction velocities were 56.5/57.5 mV in his median and 48.6/45.0 mV in his tibial nerve. Terminal latencies were 3.9/4.2 m/s in his median and 6.6/6.8 m/s in his tibial nerve. Sensory nerve action potential velocities were 69.9/64.2 m/s in his median and 38.0/44.0 m/s in his sural nerve. F-wave latencies were 28.7/27.9 ms in his median nerve and 53.9/42.6 ms in his right tibial nerve. Urodynamic study was performed for 82 days after onset. When 210 mL of water was infused he complained first of a desire to void. Bladder volume at maximum desire to void was 430 mL. Atonic cystometrogram was presented.

He was transferred to another hospital for further rehabilitation for 168 days after onset. Brain MRI showed high signal intensity in the pons, basal ganglia, cerebral white matter on T2 weighted imaging and fluid attenuated imaging 6 months after onset (Fig. 1). Cervical, thoracic and lumbar MRI were normal. Clinical course was shown in Fig. 2.

Table 1. Clinical comparison among our patient and those reported in literature on urinary retention preceding meningoencephalitis with GBS or meningo-encephalo-radiculitis as the first symptom

	Laarman et al. (1987)	Tsugawa et al. (2004)	Sasaki et al. (2006)			Present patient
			Patient 1	Patient 2	Patient 3	
Age (year)	30	14	34	51	46	48
Sex	Male	Male	Male	Male	Male	Male
Cerebrospinal fluid						
Precedent infection	MC	CPB	ND	ND	ND	EBV
Cell (/mm^3)/protein (mg/dL)	145/100	53/51	704/274	387/805	227/173	492/299
Ganglioside antibody	ND	+	–	–	–	–
Oligoclonal band	ND	–	–	–	ND	+
Myelin basic protein	+	+	+	+	+	+
NCV and/or EMG						
EMG	Denervation					
Motor conduction velocity		ND	NP	NP		Low amplitude
Sensory conduction velocity			NP	NP		
F wave			ND	NP		Delay of latency
Brain MRI	ND	NP	NP			
High intensity area				BG, brain stem	BG, thalamus	BG, DWM
Spinal MRI	ND	NP		NP	ND	NP
Enhanced			Conus, equina			

BG, basal ganglia; CPB, campylobactor; DWM, deep white matter; EBV, Epstein-Barr virus; EMG, electromyography; GBS, Guillain-Barré syndrome; MC, mycoplasma; MRI, magnetic resonance imaging; NCV, nerve conduction velocity; ND, not detected; NP, not performed.

Discussion

The patient presented urinary retention as the first symptom, followed by MER. There are some reports that urinary retention may precede meningoencephalitis in GBS or meningo-encephalo-radiculitis as an initial symptom (Laarman et al., 1987; Tsugawa et al., 2004; Sasaki et al., 2006) (Table 1). Tsugawa et al. (2004) reported GBS with meningo-encephalitis in a patient presenting urinary retention and muscle weakness as in initial symptoms. Laarman et al. (1987) reported a case of meningo-encephalitis and Guillain-Barré type ascending sensorimotor paralysis. In their case, headache and fever were shown as first symptoms, followed by difficult micturition 10 days after onset and consciousness disturbance 12 days after onset. The condition of our patient was similar to that described in these 2 reports; however, urinary retention as a first symptom was not emphasized in these previous reports. Sasaki et al. (2006) reported 3 male patients with meningo-encephalo-radiculitis presenting with acute urinary retention. It was inferred that they may represent a variant of ADEM. The reports of Laarman et al. (1987) and Tsugawa et al. (2004) also showed peripheral disorder, suggesting the co-existence of GBS. However, demyelination of central nervous system by brain and spinal MRI was uncertain. On the other hand, in the report by Sasaki et al. (2006), central nervous system disorder was presented by MRI, but disorder of peripheral nervous system was uncertain. Our patient presented muscle atrophy during the course of his condition, low amplitude of tibial, delay of right sural sensory nerve and tibial F-wave latency. Brain MRI showed high signal intensity in the pons, basal ganglia and cerebral white matter on T2 weighted imaging and fluid attenuated imaging. Thus disorder of both the central nervous system and peripherall nervous system was cer-

tainly shown in the present patient.

The etiology of urinary retention in our patient is thought to be a variant of the Elsberg syndrome that is generally regarded as a form of lumbosacral radiculopathy (Hemrika et al., 1985). The most common etiologies are viral infections, particularly genital herpes (HSV type 2) (Black et al., 1983; White et al., 1984; Hemrika et al., 1996; Lepori et al., 1992; Herbaut et al., 1990; Eberhardt et al., 2004). EBV has also been reported as a cause of sacral myeloradiculitis (Sperber et al., 1973). Additionally, EBV has also been reported as a cause of myeloradiculitis and encephalomyeloradiculitis (Merelli et al., 1997; Majid et al., 2002; Phowthongkum et al., 2007). Elevated CSF cell count is often observed in these conditions as in our case. To the best of our knowledge this is the first reported case of acute meningo-encephalo-radiculitis in EBV, in which urinary retention was an initial symptom. Although it remains to be determinated the pathomechanism of radiculitis and/or encephalitis in Epstein-Barr virus infection, our case report would serve as an aid to clarify this pathomechanism.

In the autonomic system examination, the sympathetic and parasympathetic nervous systems were both impaired. Postsynaptic impairment was suggested from the eye drops test. However, brain stem disorder also might affect urinary retention. It is important to keep in mind that urinary retention can be the initial sign of acute central or peripheral demyelination.

References

1 Amit R, Shapira Y, Blank A, Aker M. Acute, severe, central and peripheral nervous system combined demyelination. Pediatr Neurol 1986;2:47–50.

2 Amit R, Glick B, Itzchak Y, Dgani Y, Meyeir S. Acute severe combined demyelination. Childs Nerv Syst 1992;8:354–356.

3 Baker AB. Guillain-Barre's disease (encephalomyelo-radiculitis): a review of 33 cases. Lancet 1943;63:384–398.

4 Black D, Stewart J, Melmed C. Sacral nerve dysfunction plus generalized polyneuropathy in herpes simplex genitalis. Ann Neurol 1983;14:692.

5 Blennow G, Gamstorp I, Rosenberg R. Encephalo-radiculo-neuropathy. Dev Med Child Neurol 1968;10:485–490.

6 Chikakiyo H, Kunishige M, Yoshino H, Asano A, Sumitomo Y, Endo I, et al. Delayed motor and sensory neuropathy in a patient with brainstem encephalitis. J Neurol Sci 2005;234:105–108.

7 Eberhardt O, Kuler W, Dichgans J, Weller M. HSV-2 sacral radiculitis (Elsberg syndrome). Neurology 2004;63:758–759.

8 Gamstorp I. Encephalo-myelo-radiculo-neuropathy: involvement of the CNS in children with Guillain-Barré-Strohl syndrome. Dev Med Child Neurol 1974;16:654–658.

9 Guillain G. Radiculoneuritis with acellular hyperalbuminosis of the cerebrospinal fluid. Arch Neurol Psychiat 1936;36:975.

10 Hemrika DJ, Schutte MF, Bleker OP. Elsberg syndrome: a neurologic basis for acute urinary retention in patients with genital herpes. Obstet Gynecol 1986;68:37S–39S.

11 Herbaut AG, Nogueira MC, Wespes E. Urinary retention due to sacral myeloradiculitis: a clinical and neurophysiological study. J Urol 1990;144:1206–1208.

12 Laarman GJ, Hoekstra JBL, Donker DNJ, Verbrugh HA, Hekker AC. Meningo-encephalitis and Guillain-Barré type ascending sensorimotor paralysis associated with mycoplasma pneumoniae infection. Neth J Med 1987;31:66–71.

13 Lepori P, Marcacci G, Gaglianone S. Elsberg syndrome: radiculomyelopathy and acute urinary retention in patient with genital herpes. Ital J Neurol Sci 1992;13:373–375.

14 Majid A, Galetta S, Sweeney C, Robinson C, Mahalingam R, Smith J, et al. Epstein-Barr virus myeloradiculitis and encephalomyeloradiculitis. Brain 2002;125:159–165.

15 Merelli E, Bedin R, Sola P, Gentilini M, Pietrosemoli P, Meacci M, et al. Encephalomyeloradiculopathy associated with Epstein-Barr virus: primary infection or reactivation? Acta Neurol Scand 1997;96:416–420.

16 Morley JB, Reynolds EH. Papilledema and Landry-Guillain-Barré syndrome. Case report and review. Brain 1966; 89:205–222.

17 Okumura A, Ushida H, Maruyama K, Itomi K, Ishiguro Y, Takahashi M, et al. Guillain-Barré syndrome associated with central nervous system lesions. Arch Dis Child 2002;86:304–306.

18 Pfausler B, Engelhardt K, Kampfl A, Spiss H, Taferner E, Schmutzhard E. Post-infectious central and peripheral nervous system diseases complicating Mycoplasma pneumoniae infection. Eur J Neurol 2002;9:93–96.

19 Phowthongkum P, Phantumchinda K, Jutivorakool K,

Suankratay C. Basal ganglia and brainstem encephalitis, optic neuritis, and radiculomyelitis in Epstein–Barr virus infection. J Infect 2007;54:141–144.
20 Sasaki M, Ohara S, Hayashi R, Iwahashi T, Tsuyuzaki J. Aseptic meningo-encephalitis presenting initially with urinary retention. J Neurol 2006;253:908–913.
21 Sperber A, Tessler AN, Berezeller P. Infectious mononucleosis with acute urinary retention. Urology 1973;2:456–457.
22 Tsugawa T, Nikaido K, Doi T, Koga M, Susuki K, Kubota T, et al. Guillain-Barré syndrome with meningoencephalitis after Campylobacter jejuni infection. Ped Infect Dis J 2004;23:966–968.
23 White WB, Hanna M, Stewart JA. Systemic herpes simplex virus type 2 infection: proctitis, urinary retention, arthralgia, and meningitis in the absence of primary mucocutaneous lesions. Arch Intern Med 1984;144:826–827.

Received June 24, 2008; accepted August 22, 2008.

Corresponding author: Yasumasa Asai, MD