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ORIGINAL COMMUNICATION

Meningitis-retention syndrome

An unrecognized clinical condition

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Abstract *Background* A combination of acute urinary retention and aseptic meningitis has not been well known. This combination can be referred to as *meningitis-retention syndrome (MRS)*, when accompanied by no other abnormalities. *Objective* To describe the results of a uro-neurological assessment in our patients with MRS. *Methods* In three patients (two men, one woman; age, 34–68 years), we performed urodynamic studies and relevant imaging and neurophysiological tests, in addition to cerebrospinal fluid (CSF) examination. *Results* All three patients developed acute urinary retention along with headache, fever and stiff neck. None had obvious neurological abnormalities, other than a slightly brisk reflex in the lower extremities. One had previously experienced generalized erythematous eruptions, but none had pain, hypalgesia or skin eruptions in the sacral dermatomes suggestive of Elsberg syndrome (infectious sacral polyradiculitis; mostly genital herpes). Brain/spinal/lumbar plexus MRI scans and nerve conduction studies were normal. CSF examination showed mild mononuclear pleocytosis, increased protein content, and normal to mildly decreased glucose content in all patients; increased myelin basic protein suggestive of central nervous system demyelination in one; and increased viral titers in none. Urodynamic study revealed, during the voiding phase, an underactive detrusor in all patients and an unrelaxing sphincter in one. These clinical manifestations were ameliorated within 3 weeks. *Conclusions* We reported three cases of MRS, a peculiar syndrome that could be regarded as a mild variant of acute disseminated encephalomyelitis (ADEM). Urinary retention might reflect acute shock phase of this disorder. Although MRS has a benign and self-remitting course, management of the acute urinary retention is necessary.

Key words meningitis-retention syndrome · urinary retention · aseptic meningitis · acute disseminated encephalomyelitis (ADEM) · Elsberg syndrome · underactive detrusor

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Introduction

Acute urinary retention is a symptom of urological emergency. Whereas urinary retention in elderly men is mostly attributed to prostate hypertrophy, urinary retention in childhood, young adults and in women is very uncommon [1], which may have a neurological etiology [2]. Spina bifida occulta is such a disorder that causes urinary retention without marked neurological abnormality, other than sacral hypesthesia [3]. Although aseptic meningitis is a common neurological disorder, a combination of acute urinary retention and aseptic meningitis has not previously been well known. This combination can be referred to as *meningitis-retention syndrome (MRS)*, when accompanied by no other ab-

normalities. To our knowledge, only a few case reports of this syndrome are available, most of them having been reported in Japan [4–8] and the underlying pathophysiology of MRS remains unclear. We here describe the results of a uro-neurological assessment in our three patients with MRS.

Case reports

Case 1

A 46-year-old man began an acute febrile illness with headache. Four days later, he developed abdominal distention. Transurethral catheterization revealed 800 ml of residual urine, and an indwelling balloon catheter was inserted into the bladder. The patient had no constipation or erectile dysfunction. He had no skin eruption including the perineal area. Neurological examination showed a marked stiff neck, a positive Kernig sign, slightly brisk lower extremity reflexes, and he had fine postural tremor of the fingers. Sensation was normal including the perineal area. Laboratory examination showed no leukocytosis or increased C-reactive protein. There was no abnormality in blood chemistry and urinalysis except for a serum glucose level of 125 mg/dl. The cerebrospinal fluid (CSF) examination showed mononuclear leukocytosis of 290/mm^3, increased protein content of 80 mg/dl, and a mildly decreased glucose level of 41 mg/dl (33 % of serum glucose). Bacterial smears and cultures, including tuberculosis and cryptococcus, were negative. The CSF enzyme immunoassay showed negative IgM antibodies of herpes simplex type-1 (HSV-1) and herpes zoster viruses (VZV). IgG antibodies of HSV-1 and VZV were 0.46 (normal < 0.2) and negative, respectively. There was no increase in adenosine deaminase, myelin basic protein (MBP), or oligoclonal bands (OCB) in the cerebrospinal fluid. Magnetic resonance imaging (MRI) scans of the brain and the spinal cord were normal. From the laboratory findings, particularly of decreased CSF glucose level, we initially suspected meningitis due to HSV-1 or cryptococcus, and started 1500 mg/day of aciclovir and 400 mg/day of fluconazole, respectively. Five days later, his headache and fever ameliorated, although there was no evidence in cultured cryptococcus or virus titer change in the follow-up CSF examination. After pulling out the balloon catheter, the patient became able to urinate. However, he still had voiding difficulty and we performed a urodynamic study on the 11th hospital day.

After voluntary voiding, he had a post-micturition residual volume of 100 ml (normal < 30 ml). A double-lumen 8F catheter (for use with saline infusion and intra-vesical pressure measurements) was inserted into the bladder. We performed a medium-fill (50 ml/min) electromyography (EMG)-cystometry with a urodynamic computer (Janus; Lifetech Inc, Houston, TX, USA) and an electromyographic computer (Neuropack Sigma; Nihon Kohden Inc, Tokyo, Japan), simultaneously recording the detrusor pressure, which is the difference between the intra-vesical and intra-abdominal (rectal) pressures, sphincter EMG via a concentric needle electrode in the external anal sphincter muscle, and urinary flow via a uroflowmeter. The methods and definitions used for the urodynamic study conformed to the standards proposed by the International Continence Society [9]. Sphincter EMG revealed normal voluntary contraction of the sphincter. During bladder filling, he had a first sensation at 130 ml (100 ml < normal < 300 ml) and a bladder capacity of 500 ml (200 ml < normal < 600 ml); we then stopped infusing saline into the bladder. He did not show detrusor overactivity during filling even after provoking the maneuver by coughing. When we asked him to void, however, he was unable to contract his bladder at all (underactive detrusor). The sphincter EMG activity persisted on voiding (unrelaxing sphincter), which normally disappears completely. He did not have prostatic hypertrophy by digital examination and abdominal echography. In order to ameliorate the voiding difficulty, he was taught clean, intermittent self-catheterization (CISC) twice a day. We also started 150 mg/day of bethanechol chloride (cholinergic agent) and 0.2 mg/day of tamsulosin hydrochloride (alpha-blocker). These treatments gradually ameliorated his voiding difficulty, and a week later, his residual urine volume became less than 30 ml.

Case 2

A 68-year-old woman began to have an acute fever, headache, appetite loss, and at the same time, urinary frequency and a lower abdominal pain. Transurethral catheterization showed 500 ml of urine, and an indwelling balloon catheter was inserted. She had no constipation. She had no skin eruptions, including in the perineal area. On neurological examination, she was inactive, slightly drowsy, and had a mildly stiff neck. She had normal deep tendon reflexes. Sensation was normal, including in the perineal area. Laboratory findings were normal except for mild liver dysfunction (AST 59; normal < 40 IU/l, ALT 66; normal < 45 IU/l, LDH 469; normal < 442 IU/l), but her abdominal CT findings were normal. The CSF examination was performed on the 7th hospital day, which showed mononuclear leukocytosis of 108/mm^3, an increased protein content of 97 mg/dl, and a mildly decreased glucose level of 41 mg/dl (45 % of serum glucose). At that time, her headache and fever resolved spontaneously. Bacterial smears and cultures were negative. The CSF complement fixation test revealed negative titers of HSV-1, VZV, Coxsackie's, echo, mumps, measles, rubella, adeno, or cytomegaloviruses.

However, there was increased MBP of 212 pg/ml (normal < 102) with negative OCB in the CSF. MRI scans of the brain and the spinal cord, and nerve conduction studies of the extremities were normal.

We performed cystometry on the 4th hospital day, although we did not perform a sphincter EMG in the patient. During bladder filling, she had a normal first sensation at 180 ml and a bladder capacity of 280 ml, without evidence of detrusor overactivity. When we asked her to void, however, she was unable to contract her bladder at all (underactive detrusor). Urethral pressure profilometry revealed low urethral closure pressure of 10 cm H_2O (41 < normal < 82). She did not have apparent urological disease by intravenous pyelography and cystoscopy. After the urodynamics, she still had voiding difficulty with post-micturition residuals of 360 ml. In order to ameliorate voiding difficulty, she was taught CISC three times a day. We also started 10 mg/day of distigmine bromide (cholinergic agent). These treatments gradually ameliorated her voiding difficulty, and only 5 days later, her residual urine volume became less than 30 ml.

Case 3

A 34-year-old man, who had taken 2 g/day of salazosulfapyridine for ulcerative colitis for the past 14 years, had an acute generalized erythematous eruption that disappeared spontaneously on the following day. However, on that day, he began to have an acute fever, mild headache, and nausea. Two days later, he developed abdominal distention and one episode of fecal incontinence. Transurethral catheterization revealed 1000 ml of urine left behind, and an indwelling balloon catheter was inserted into the bladder. He had no constipation or erectile dysfunction. Neurological examination showed a marked stiff neck and slightly brisk lower extremity reflexes. Sensation was normal, including the perineal area. Laboratory examination showed mild leukocytosis of 12,900/mm^3, but normal C-reactive protein. There was no abnormality in blood chemistry and urinalysis, and serum immunoglobulin concentrations (G, A, M) were normal. The CSF examination showed mononuclear leukocytosis of 38/mm^3, increased protein content of 71 mg/dl, and a normal glucose level of 57 mg/dl (61% of serum glucose). Bacterial smears and cultures were negative. HSV-DNA assay (PCR method) in the CSF revealed a negative result. There was negative OCB in the CSF. Plain and gadolinium-enhanced MRI scans of the brain, spinal cord, and lumbar plexus, and nerve-conduction studies of the extremities were normal. From the history of skin eruption, we initially suspected viral meningitis and started 1,500 mg/day of acyclovir. Five days later, his headache and fever were ameliorated. However, after the balloon catheter was pulled out, he still had urinary retention and he was taught CISC four times a day. At this time, parainfectious myelitis was suspected and 1,000 mg/day of methylprednisolone was administered for 3 days. Four days later, he became able to urinate. His residual urine volume became less than 50 ml, and CISC was stopped. However, he still had voiding difficulty and we performed a urodynamic study on the 12th hospital day.

We then performed free-flowmetry. The patient had a voluntary voided volume of 350 ml, and his average flow rate was low (6 ml/s.; normal > 10). The maximum flow rate could not be obtained because of an artifact. He had post-micturition residuals of 20 ml. We then performed EMG-cystometry. During bladder filling, he had a normal first sensation at 190 ml and a bladder capacity of 460 ml, without evidence of detrusor overactivity or a low-compliance detrusor. When we asked him to void, however, he was unable to contract his bladder at all (underactive detrusor), although the sphincter EMG activity ceased. He did not have apparent obstructive urological disease. Only 2 days after the urodynamic study, his voiding difficulty disappeared completely.

Discussion

Clinical manifestations of our three MRS patients are mostly the same as those of the six cases in the literature [4–8] (Table 1). All patients had symptoms and signs of meningeal irritation such as headache, stiff neck, and a positive Kernig sign, except for the patient reported by Fukagai et al. [6], who had drowsiness without meningeal irritation. The CSF examination showed mononuclear pleocytosis of 38–370/mm^3 and normal to increased protein content (up to 260 mg/dl), and normal to mildly decreased glucose content (up to 33% of that in the serum). All viral titers studied in the CSF and the serum were negative, including HSV-1, VZV, Coxsackie's, echo, mumps, measles, rubella, adeno-, and cytomegaloviruses, although the other viral titers were not studied. Other than aseptic meningitis, these patients did not have marked neurological abnormalities such as epilepsy, aphasia, gait difficulty, or sensory impairment. Nevertheless, it seems likely that the urinary retention in the patients has a neurologic etiology, since none had urological abnormalities such as urinary tract infection, genital prolapse, or apparent prostatic hypertrophy, and there was a strong chronological association in that the urinary retention appeared simultaneously or just after the occurrence of the aseptic meningitis.

Urodynamic study results showed that all patients studied had an underactive detrusor, which results in an inability to contract the bladder properly on voiding, with two patients having an unrelaxing sphincter (a case of Ohe [5] and case 1 of our patients). An underactive

Table 1 Patients with meningitis-retention syndrome and the results of uro-neurological assessment

year	author	age	sex	neurological symptoms and signs						urinary dysfunction				cerebrospinal fluid						MRI/CT		treatment	prognosis	
		(years)		fever	head-ache	stiff neck/ Kernig sign	drow-siness	lower extremity	superficial sensation reflexes	FS (ml)	BC (ml)	UD	US	cell (/mm^3)	P:M	protein (mg/dl)	glucose (mg/dl) CSF: serum	MBP	OCB	brain	spinal cord		menin-gitis (weeks)	reten-tion (weeks)
1985	Kanno	34	F	+	+	+	–	brisk	numbness		460	+		40			44:94 (47 %)					bethanechol	3	6
1990	Ohe	24	F	+	+	–	–	N	N	170	210	+?	+	312	0:100	260				N		aciclovir, prazosin, CIC, bethanechol	2	2
1996	Fukagai	46	M	+	–	–	+	N	N	96	220	+?		143	19:81							aciclovir, distigmine	6	10
1999	Shimizu	13	M	+	+	+	–	N	N	N	N	+		60	1:99	N	N					CIC, bethanechol	4	5
		18	F	+	+	+	–	N	N	N	N	+		109	34:66	76	N			N	N	aciclovir, CIC, bethanechol	3	4
2002	Zenda	32	F	+	+	+	–	N	N	110	205	+		370	3:97	116	39:86 (45 %)					CIC, urapidil distigmine	3	8
2005	present cases	46	M	+	+	+	–	brisk	N	130	500	+	+	290	2:98	80	41:125 (33 %)	–	–	N	N	aciclovir, tamsulosin, CIC, bethanechol	2	3
		68	F	+	+	+–	+–	N	N	180	280	+		108	5:95	97	41:92 (45 %)	+	–	N	N	distigmine	2	3
		34	M	+	+	+	–	brisk	N	190	460	+		38	1:99	41	57:93 (61 %)		–	N	N	aciclovir, steroid pulse,CIC	1	2

N normal; *FS* first sensation; *BC* bladder capacity; *CSF* cerebrospinal fluid; *CIC* clean, intermittent self-catheterization; *UD* underactive detrusor; *US* unrelaxing sphincter; *nsMUP* neurogenic sphincter motor unit potential; *MBP* myelin basic protein; *OCB* oligoclonal band

detrusor is regarded as the major cause of voiding dysfunction in neurological diseases [10], although it is occasionally seen in neurologically intact women being evaluated for urinary incontinence due to physical stress. An underactive detrusor originates from various sites of lesions in the neural axis, with lower motor neuron lesions being the most common. Elsberg syndrome (infectious sacral polyradiculitis) is such a disease, causing an underactive detrusor with minimal neurological abnormalities, i. e., pain, hypalgesia and skin eruption in the sacral dermatomes [11, 12, 13, 14]. CSF abnormalities may also occur, although meningeal irritation such as headache is not a feature of this disease [12, 14]. The causes of this disease are mostly viral, particularly HSV and VZV infections (genital herpes) [12–14]. However, the neurological, neurophysiological, and serological findings indicate that this condition is unlikely in MRS patients. Upper motor neuron lesions that affect the brain or spinal cord also cause an underactive detrusor, particularly in the acute shock phase [10]. Acute disseminated encephalomyelitis (ADEM) is such a disease that causes meningeal irritation and an underactive detrusor, and in a subset of patients, lower urinary tract (LUT) dysfunction is the only sequel of this disease [15]. Therefore, the LUT innervation is selectively vulnerable in such cases. As described above, encephalitic features are absent in most cases of MRS. However, three of the MRS patients (a case of Kanno et al. [4] and cases 1 and 3 of our patients) had brisk lower extremity reflexes suggestive of myelitis. In its typical form, ADEM appears after vaccination or exanthematous infections, and serological and pathological studies have suggested that ADEM is of parainfectious or of autoimmune origin [16, 17]. In one of the MRS patients (case 2 of our patients), MBP was increased, which is suggestive of central nervous system demyelination. From these results, it seems possible that MRS is a mild variant of ADEM, which selectively affects the LUT innervation. Although MRS is a rare clinical condition, both neurologists and urologists may encounter it. Since MRS has a benign and self-remitting course (duration of 2–10 weeks), effectiveness of steroid treatment is still unclear. Management of the acute urinary retention is necessary to avoid over distension bladder injury.

In conclusion, we reported three cases of MRS, a peculiar syndrome that could be regarded as a mild variant of ADEM. Urinary retention might reflect acute shock phase of this disorder. Although MRS has a benign and self-remitting course, management of the acute urinary retention is necessary.

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