



Meningitis-retention syndrome: Clinical features, frequency and prognosis

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ABSTRACT

Background: Meningitis-retention syndrome (MRS) is a peculiar combination of aseptic meningitis (AM) and acute urinary retention without other neurological symptoms. MRS has not been well recognised, and the prevalence of MRS in patients with AM is unknown.

Objective: To investigate the frequency and clinical features of MRS.

Methods: Clinical and laboratory features of patients with MRS who were consecutively admitted to the Chiba Rosai Hospital between 2009 and 2017.

Results: Of the 37 patients with AM, MRS was observed in three (8%). In MRS patients, the mean latency between the onset of meningeal symptoms (headache and/or fever) and the three clinical course milestones (the onset of voiding difficulty, urinary retention and recovery of no residual urine volume) were 8, 9.3 and 18 days, respectively. Patients with MRS frequently showed elevated cerebrospinal fluid adenosine deaminase levels and decreased cerebrospinal fluid/serum glucose ratios. All patients with MRS recovered without a specific treatment, and the mean hospital stay was 18 days.

Conclusions: MRS may be more common than is generally considered. The long-term prognosis of MRS was good, and it was a self-limiting condition. However, it is likely to be underreported or misdiagnosed. Therefore, it is important to recognise that patients with AM may have MRS.

1. Introduction

Meningitis-retention syndrome (MRS) is a peculiar combination of acute urinary retention and aseptic meningitis (AM) [1,2]. Although AM is a common neurological disorder, MRS has not been well recognised, and information on its clinical features is scarce and limited. Moreover, the prevalence of MRS is unknown [2]. There have been no surveys of the proportion of patients with AM who present with MRS. In the present study, we reported the frequency and clinical features of MRS in a general hospital setting.

2. Materials and methods

2.1. Patients

This was a retrospective study based on a review of the medical records of patients diagnosed with AM who were admitted to the neurological department of the Chiba Rosai Hospital (a 400-bed acute care general hospital that serves a population of 280,000) between October 2009 and September 2017. All patients were aged > 15 years because those aged < 14 years are admitted to the paediatric

department in this hospital. Patients were diagnosed with AM if they had symptoms or signs of meningeal inflammation without any evidence of cerebral parenchymal involvement (altered consciousness or personality, epileptic seizures, or focal neurologic signs), if their initial cerebrospinal fluid (CSF) white blood cell (WBC) count was > 5/mm³ and if their CSF bacterial culture was negative and cure was achieved without any antibiotic treatment apart from antiviral therapy [3,4]. Patients who were treated with antibiotics during hospitalisation were excluded. Patients with postoperative meningitis, another focus of infection in addition to meningitis, known immunodeficiency, collagen disease or autoimmune disease were also excluded. The inclusion criteria of MRS, modified from Sakakibara et al. [2], were presenting with acute AM and urinary retention appearing simultaneously or after the occurrence of AM and documentation of all signs by a neurologist. Patients with a history of urological disorders or urogenital infection or those receiving any drug inducing urinary retention, such as anticholinergic agents, were excluded because these conditions can induce urological symptoms. This study was approved by the ethical committee of our hospital.

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2.2. Laboratory tests

Blood cell counts and routine blood chemistry tests including C-reactive protein (CRP) and analysis of CSF samples, bacterial culture and determination of WBC count and protein and glucose levels were conducted on admission. CSF/serum glucose ratios were also calculated. Additional CSF analysis [tests for viruses, fungi, or adenosine deaminase (ADA)] was performed at the discretion of the treating neurologist. The limit of ADA detection in CSF was 2.0 U/L. ADA levels in CSF under the limits of detection were expressed as 0.

2.3. Brain imaging

Patients underwent computed tomography and/or magnetic resonance imaging (MRI) of the brain before lumbar puncture. One pregnant patient with AM did not undergo neuroimaging examination.

2.4. Treatments

General treatment, such as hydration and reduction of fever, was considered essential. Each responsible neurologist made the final decision regarding the use of intravenous acyclovir.

2.5. Statistical analyses

Differences in the proportions were tested using Fisher's exact test, and the differences in the means were tested using Student's or Welch's *t*-test. $P < .05$ was considered statistically significant. Statistical analyses were performed using a statistical add-in software of Excel (Statcel 2, OMS Publishing, Saitama, Japan).

3. Results

3.1. Frequency

Among 3346 patients admitted to our department during the observation period, AM was observed in 37 (1.1%; 16 men and 21 women; mean age, 33 years). We excluded five patients because one lacked a record of bacterial culture, two were treated with antibiotics by the first physician, one was treated with antibiotics for a complicated urinary tract infection and one had insufficient medical records for analysis. No patient had more than one episode of AM during the retrospective study period.

3.2. Clinical presentation

Clinical features of patients with AM without urinary retention and MRS are provided in Table 1. Initial symptoms of AM were headache (31/37), fever (22/37), nausea (4/37) and myalgia (2/37). Headache was presented in 37/37 (100%) patients and vomiting and/or nausea in 15/37 (88%) during the clinical course. All patients had fever ($\geq 37^\circ\text{C}$) during the clinical course. Neck stiffness was observed in 18/37 (60%) patients on admission. Among the 19 patients without neck stiffness on admission, nine showed neck stiffness after admission and the remaining 10 had no neck stiffness during the clinical course. No cutaneous and mucosal lesions were noted in the three patients with MRS.

3.3. Laboratory testing and neuroimaging

On admission to hospital (median, 5 days from onset), mean CSF WBC counts were $154/\text{mm}^3$ in patients with AM without urinary retention and $56/\text{mm}^3$ in patients with MRS. HIV enzyme-linked immunosorbent assay was performed in 35 of 37 patients, and all results were negative. Brain computed tomography and/or MRI detected no specific changes in any patient with AM who underwent neuroimaging. A CSF/serum glucose ratio of < 0.5 was found in seven of 34 patients

with AM without retention and in all three patients with MRS. The mean CSF/serum glucose ratio in patients with MRS (0.41) was significantly lower than that in patients with AM without urinary retention (0.54). Two of the three patients with MRS and 16 of the 34 patients with AM without urinary retention underwent the analysis of CSF ADA levels. Two of the three patients with MRS had elevated ADA levels (mean, 23.5 U/L); these were significantly higher than those of patients with AM without urinary retention (mean, 3.5 U/L).

3.4. Treatment and prognosis

Two of the 37 patients received intravenous acyclovir. All patients with AM, including those with MRS, recovered without a specific treatment. The average time from the onset of meningeal irritation or fever to the initiation of recovery from these symptoms in MRS patients (14 days) was significantly longer than that for AM patients without urinary retention (7.6 days). The mean number of hospital days was 18 for patients with MRS, which was longer than that for patients with AM without urinary retention (7.7 days).

In the three patients with MRS, average latencies between the onset of headache or fever and voiding difficulty or urinary retention were 8.0 and 9.3 days, respectively. One of the three patients with MRS did not have urinary symptoms on admission and developed urinary retention after admission. In two of the three patients with MRS, a Foley catheter was inserted into the bladder at our hospital. In two of the three patients with MRS, at 14 and 23 days after the onset of meningitis (4 and 11 days after urinary retention), the Foley catheter was removed and the patients could urinate without assistance. In one patient with MRS who underwent the insertion of a Foley catheter in another hospital before admission to our hospital, the Foley catheter was removed on the day of admission (8 days after the onset of meningitis), but urinary retention continued. The patient underwent clean intermittent bladder catheterisation and could urinate without assistance with residual urine 8 days after urinary retention, and her residual urine volume was 0 milliliter at 11 days after urinary retention (17 days after the onset of meningitis).

4. Discussion

We found that the occurrence of MRS was not uncommon (8% of patients with AM) and presented the clinical course of MRS: the mean duration between the onset of meningeal symptoms (headache and/or fever) and urinary retention was 9.3 days, and the average duration between the onset of meningeal symptoms and recovery of the residual urine volume was 18 days. The duration between the onset of meningeal symptoms and the start of recovery from these symptoms in MRS was significantly longer than in AM without urinary retention; moreover, the hospitalisation days tended to be higher in MRS patients than in AM patients without urinary retention.

In 2005, three adult Japanese patients who developed acute occurrences of AM with urinary retention that lasted for several weeks were reported; this syndrome was named 'MRS' [1]. Although one of these three patients had a mild disturbance of consciousness, the other two had no other neurological abnormalities except for slightly brisk lower extremity deep tendon reflexes. MRS has been reported in patients with AM mostly in Japan. However, it has been recently reported also in other countries. The definition of MRS is somewhat confusing. Several previous patients who were reported as having MRS did have typical MRS: patients with consciousness disturbance indicative of meningoencephalitis [5] or those with abnormal MRI findings indicative of acute disseminated encephalomyelitis (ADEM) [6]. Because of this confusion and the fact that most patients with MRS are reported as single cases, the frequency of MRS in AM has not been previously known. However, in the present study, 8% of patients with AM presented with MRS; thus, MRS is more common than was previously believed. MRS is not well known outside Japan; viral meningitis is

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