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Clinical Study

Etiological, clinical, and radiological features of longitudinally extensive myelopathy in Chinese patients

Weihe Zhang *, Yujuan Jiao, Lei Cui, Lei Liu, Linwei Zhang, Jinsong Jiao *

Department of Neurology, China-Japan Friendship Hospital, 2 Yinghua, Dongjie, Hepingli, Beijing 100029, China

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ABSTRACT

Longitudinally extensive myelopathy (LEM) is a rare spinal syndrome, and was mostly assessed in western populations. In order to investigate the etiological, clinical, and radiological features of LEM in Chinese patients, we retrospectively analyzed eighty-nine (40 men and 49 women, median age 45.9 ± 15.7 years) patients with LEM hospitalized in China-Japan Friendship Hospital. LEM comprised autoimmune inflammatory myelitis (n = 53), metabolic and compressive disorders (n = 13), vascular diseases (n = 10), neoplastic diseases (n = 7), infectious diseases (n = 4), and syringomyelia (n = 2). Neuromyelitis optica spectrum disorders (NMOSD) was the most common cause of transverse myelopathy identified in LEM (38/89 [42.7%]) characterized by intractable vomiting and hiccups and painful tonic spasms. Subacute combined degeneration and anterior spinal artery syndrome accounted for the largest non-transverse LEM, which selectively affected the spinal dorsal and/or lateral columns and the spinal anterior region, respectively. Radicular pain was common in anterior spinal artery syndrome. Postrema (n = 15, 39.5%) and cervical (n = 31, 81.6%) lesions were significantly increased in NMOSD versus non-NMOSD (n = 7, 13.7% and n = 34, 66.7%, respectively, $p < 0.05$]. Axial T2-weighted MRI indicated that 46 (51.7%) patients exhibited complete lesions; 43 (48.3%) patients exhibited non-transverse lesions, mainly unilateral or symmetrical tract lesions. Twenty-four (51.1%) LEM patients exhibited distinct gadolinium contrast enhancement. In this Chinese cohort, LEM was primarily attributed to NMOSD. While the etiological distribution in the non-NMOSD group was different from western populations, clinical and imaging features may facilitate a differential diagnosis.

1. Introduction

Longitudinally extensive myelopathy (LEM) refers to a substantial spinal cord lesion that spans three or more vertebral segments on MRI. LEM is a relatively rare spinal cord syndrome, with varying incidence rates [1–3]. Based on the transverse section area involved, the syndrome is divided into two groups: complete (transverse myelopathy, referred to as LETM), which is classically associated with neuromyelitis optica spectrum disorders (NMOSD), or partial (non-transverse myelopathy) [4,5]. However, LEM is not caused by NMOSD in all patients [6], and other conditions may mimic the clinical and imaging features of NMOSD, which may obscure its diagnosis and treatment. Most LEM studies to date have focused on Caucasian populations [1,2]; our group has previously published several patients with longitudinally extensive spinal cord lesions in a small cohort [7]. Nevertheless, to our knowledge, no studies have specifically assessed the clinical and imaging features of LEM in Chinese patients. The aim of this study was to determine the etiological distribution of LEM patients via a retrospective assessment of a large series of consecutive Chinese patients. The clinical and radiological characteristics associated with each etiology were subsequently assessed to establish a disease spectrum and identify differential features associated with this condition.

2. Materials and methods

2.1. Patients

Eighty-nine (40 men and 49 women) patients with LEM, confirmed by spinal cord T2-weighted MRI, who were hospitalized at the China-Japan Friendship Hospital (Beijing, China) between January 2011 and April 2015 were consecutively enrolled. LEM was defined as spinal cord lesion that extended over three or more vertebrae on T2-weighted MRI scans. The 2015 International consensus diagnostic criteria were used for NMOSD with or without aquaporin-4 (AQP4) antibody [8]. The 2010 revised McDonald

* Corresponding authors. Tel.: +86 010 84205259; fax: +86 01084205442.
E-mail address: z_weihe@hotmail.com (W. Zhang).

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criteria [9] were used for the assessment of patients with multiple sclerosis (MS). The following parameters were retrospectively analyzed: demographic data (age and gender), etiological classification, clinical and imaging features. The study was approved by the Institutional Review Board of China-Japan Friendship Hospital.

2.2. Laboratory data

An AQP4-IgG test was conducted using a cell-based assay (AQP4-IgG test kit from EUROIMMUN (Beijing, China) by an independent medical inspection agency. Serum specimens were collected during the acute phase or clinical relapse in 49 patients. The cerebrospinal fluid (CSF) cell count, glucose concentration, and protein levels were recorded, as well as oligoclonal bands via isoelectric focusing electrophoresis. Serum and CSF antibodies against herpes simplex virus, adenovirus, cytomegalovirus, varicella-zoster virus, Epstein-Barr virus, and enterovirus were considered when necessary. Polymerase chain reaction testing of the CSF was performed in one suspected patient with tuberculosis. We recorded the serum immunoglobulin E (IgE) level and antigen (e.g., mite, mold, and pollen)-specific IgE, as well as serum and CSF neurological paraneoplastic antibodies (anti-Hu, anti-Yo, anti-Ri, anti-CV2, anti-amphiphysin, and anti-Ta/Ma2), which were determined based on clinical requirements.

2.3. Imaging data

The spinal cord MRI used a SignaHDX-3.0T (General Electric, Fairfield, CT, USA) or GYROSCAN-1.5T (Philips, Amsterdam, Holland) nuclear magnetic resonance scanner. MRI scanning included the cervical, thoracic, and lumbar spine. T1-weighted MRI sequences with and without gadolinium were obtained. T2-weighted MRI sequences were used to obtain sagittal and axial images. We delineated the affected area as transverse sections of complete and partial lesions, the involved spinal cord segments (the number of vertebral segments), and their location in the sagittal image (cervical, thoracic, or lumbar). In the partial lesion subgroup, we also recorded the lesion location on the axial image (anterior, posterior, or symmetrical tract lesion). Forty-seven of 89 patients underwent gadolinium enhancement scanning.

2.4. Statistical analysis

All statistical analyses were performed using SPSS 22.0 software (IBM, Armonk, NY, USA). Statistical significance was set at $p < 0.05$. The age of onset and affected vertebrae were analyzed using Student's t-tests. Differences in the sex ratio and other clinical and imaging parameters between groups were analyzed using Fisher's exact tests. Atopic myelitis (AM), acute disseminated encephalomyelitis (ADEM), spinal dural arteriovenous fistula (SDAVF), neoplastic myelopathy, and syringomyelia subgroups were excluded because of small sample size.

3. Results

3.1. Etiological distribution and clinical features of LEM

In our cohort, LEM was divided into six categories based on etiological analysis, as seen in Table 1. Clinical data are summarized in Table 2. Thirty-eight of 89 (42.7%) patients met the diagnostic criteria for NMOSD. These patients were predominantly female, and had a median age of onset of 42.9 ± 14.8 years. The AQP4-IgG was positive in 22 of 36 NMOSD patients. Twelve patients exhibited one or more systemic diseases, including Sjögren syndrome (SS), systemic lupus erythematosus (SLE), Hashimoto's thyroiditis (HT), chronic Hepatitis B (inactive phase), and Churg-Strauss syndrome. Thirty-six patients exhibited an acute or subacute onset, and two patients were chronic. Thirteen patients presented with intractable vomiting and hiccups (IVH, 1- to 2-day duration), and six patients exhibited painful tonic spasms; 15 patients presented with radicular pain, and 21 patients exhibited early sphincter disorder.

Table 1
Etiology of longitudinally extensive myelopathy in Chines patients (n = 89)

Etiological distribution	Num. (%)
Autoimmune inflammatory	**53 (59.6)**
Neuromyelitis optica and spectrum disorders	38 (42.7)
Isolated longitudinally extensive transverse myelitis	6 (6.7)
Multiple sclerosis	4 (4.5)
Atopic myelitis	3 (3.4)
Acute disseminated encephalomyelitis	2 (2.2)
Metabolic and degenerative	**13 (14.6)**
Subacute combined degeneration	8 (9.0)
Compressive myelopathy	5 (5.6)
Vascular	**10 (11.2)**
Anterior spinal artery syndrome	7 (7.9)
Spinal dural arteriovenous fistula	3 (3.4)
Neoplastic	**7 (7.9)**
Paraneoplastic myelopathy	3 (3.4)
Radiation myelopathy	2 (2.2)
Intramedullary metastases	1 (1.1)
Leukemia-related myelopathy	1 (1.1)
Infectious	**4 (4.5)**
Infectious mononucleosis-associated myelitis	1 (1.1)
Neurolisteriosis-associated myelitis	1 (1.1)
Mycobacterium tuberculosis-related myelitis	1 (1.1)
Syphilitic myelitis	1 (1.1)
Syringomyelia	**2 (2.2)**

Three women and one man exhibited multifocal lesions in the first brain MRI that fulfilled the Barkhof criteria for MS [10], including 1 relapsing-remitting (RR) and three primary progressive (PP) MS patients. Two of four MS patients tested positive for oligoclonal bands in the CSF. Three AM patients exhibited an atopic condition with limb paresthesia, serum hyper-IgE-emia, and mite antigen-specific IgE positivity. Two patients were diagnosed with adult ADEM. Both patients exhibited concurrent multiple brain lesions and a monophasic course during the previous four-year follow-up. The remaining six LETM patients were not classified into any of these diseases and were referred to as isolated LETM (iLETM).

Eight patients with subacute combined degeneration (SCD) presented subacute or chronic sensational ataxic gait and spastic paraplegia; three patients had lower serum vitamin B12, two patients had atrophic gastritis, one patient received gastric surgery, and two patients were vegans. Four of the five compressive myelopathy patients presented with severe root pain.

In terms of vascular etiology, six men and one woman, were diagnosed with anterior spinal artery syndrome (ASAS). These patients were aged 31–76 years, and six of the seven ASAS patients manifested acute radicular pain followed by paraplegia and urinary retention. Three middle-aged men who presented with chronic progressive spastic paraplegia with mild sensory and sphincter disorders were classified as SDAVF.

Seven patients exhibited neoplastic myelopathy, including three patients with paraneoplastic myelopathy (PM). All PM patients manifested subacute-to-chronic myelopathy, small cell lung cancer, breast cancer, or prostate cancer, which was identified before or after the onset of PM. Seropositive anti-Hu antibody was also detected in the small cell lung cancer patient. Two radiation myelopathy patients received high doses of irradiation for esophageal cancer. Further, one 37-year-old woman with intramedullary metastases secondary to small cell lung cancer and one 32-year-old woman with leukemia-related myelopathy secondary to acute myelocytic leukemia exhibited an acute onset and serious sphincter disorders.