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นิพนธ์ต้นฉบับ **Original Article**

The Study of Acute Transverse Myelitis in Ratchaburi Hospital

การศึกษาของโรคไขสันหลังอักเสบเฉียบพลัน ในโรงพยาบาลราชบุรี

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ABSTRACT

Introduction: Epidemiological studies on acute transverse myelitis (ATM) in Thailand are scarce. The aim of study was to describe demographic, clinical and para-clinical features of patients with ATM in Ratchaburi. A further objective was to determine the aetiologies of ATM.

Methods: All patients diagnosed with ATM between September 1, 2009 and September 30, 2014 were retrospectively identified, using the Transverse Myelitis Consortium Working Group (TMCWG) criteria.

Results: A total of 32 patients diagnosed with ATM (21 females, 65.6%) were included. Of these patients, 53.1% (n =17) had idiopathic ATM, 25% (n = 8) had clinically isolated syndrome (CIS), 9.3% (n = 3) had multiple sclerosis (MS), 6.3% (n = 2) had neuromyelitis optica (NMO) and 6.3% (n = 2) had postinfectious myelitis (PIM). The Idiopathic group had more mean age, mean score level of disability and oligoclonal bands (OCB) negative than other groups, including the Idiopathic group which had OCB negative. The OCB negative group had more mean age, mean score level of disability than OCB positive group. The multisegmental lesions and longitudinally extensive myelitis had more mean score level of disability than partial myelitis (p-value < 0.05). After 3 months of follow-up, 40.6% (n = 13) of the patients had severe disability. The majority of severe disability patients had an multisegmental or extensive cord lesion detectable with spinal MRI.

Conclusion: Majority of acute transverse myelitis (ATM) was idiopathic group, had more mean age, mean score level of disability than other groups. The multisegmental lesions and longitudinally extensive myelitis with spinal MRI had more disability rate.

Keywords: Acute transverse myelitis, Ratchaburi Hospital

บทคัดย่อ

วัตถุประสงค์: การศึกษาเพื่อดูลักษณะอาการทางคลินิก ชนิด และสาเหตุของผู้ป่วยโรคไขสันหลังอักเสบเฉียบพลันในโรงพยาบาลราชบุรี

วิธีการวิจัย: ศึกษาผู้ป่วยที่ถูกวินิจฉัยเป็นโรคไขสันหลังอักเสบเฉียบพลันในโรงพยาบาลราชบุรี ระหว่าง วันที่ 1 กันยายน 2552 ถึง 30 กันยายน 2557 ตามเกณฑ์การวินิจฉัยโรคไขสันหลังอักเสบเฉียบพลัน (TMCWG)

ผลการศึกษา: ผู้ป่วยโรคไขสันหลังอักเสบเฉียบพลัน 32 คน เป็นเพศหญิง 21 คน ประกอบด้วย ผู้ป่วยโรคไขสันหลังอักเสบเฉียบพลันชนิดไม่ทราบสาเหตุ 17 คน (ร้อยละ 53.1) ผู้ป่วย clinically isolated syndrome (CIS) 8 คน (ร้อยละ 25) ผู้ป่วย multiple sclerosis (MS) 3 คน (ร้อยละ 9.3) ผู้ป่วย neuromyelitis optica (NMO) 2 คน (ร้อยละ 6.3) และผู้ป่วย postinfectious myelitis (PIM) 2 คน (ร้อยละ 6.3) อายุเฉลี่ย คะแนนประเมินพิการเมื่อเข้ารับการรักษา และหลังการรักษา 3 เดือนของกลุ่ม Idiopathic หรือ oligoclonal bands (OCB) negative สูงกว่ากลุ่มอื่นๆ หรือ OCB positive อย่างมีนัยสำคัญทางสถิติ ผลคลื่นสนามแม่เหล็กของไขสันหลังแบบ multisegmental และ longitudinally extensive myelitis จะมีคะแนนประเมินพิการเมื่อเข้ารับการรักษา และหลังการรักษา 3 เดือน สูงกว่าแบบ partial myelitis อย่างมีนัยสำคัญทางสถิติ ติดตามหลังการรักษา 3 เดือน พบว่าผู้ป่วย 13 คน (ร้อยละ 40.6) มีความพิการรุนแรง และมีผลคลื่นสนามแม่เหล็กของไขสันหลังแบบ multisegmental หรือ longitudinally extensive myelitis

สรุป: ผู้ป่วยโรคไขสันหลังอักเสบเฉียบพลันส่วนใหญ่เป็นชนิดไม่ทราบสาเหตุ โดยมี อายุเฉลี่ย คะแนนประเมินพิการ สูงกว่ากลุ่มอื่น ถ้าผลคลื่นสนามแม่เหล็กของไขสันหลังแบบ multisegmental หรือ longitudinally extensive myelitis จะมีอัตราความพิการมากกว่า

คำสำคัญ: โรคไขสันหลังอักเสบเฉียบพลัน โรงพยาบาลราชบุรี

Introduction

ATM is a neurological disorder involving focal inflammation of the spinal cord which may have different aetiologies. It forms part of a subgroup of acute myelopathies for which inflammation within the spinal cord is an essential factor for diagnosis.[1]

The estimated incidence rate of the disorder is 1 to 4 new cases per million inhabitants, it affects individuals of all ages, and it is a major cause of disability around the world.[2] Clinically, ATM is characterized by acute onset of motor and sensory symptoms with spinal cord-like distribution, usually associated with bladder dysfunction. Approximately 50% of patients with this condition are unable to walk upon reaching their maximum level of disability,[3] and a third recover poorly and remain severely disabled.[4]

In 2002, the Transvere Myelitis Consortium Working Group (TMCWG) proposed diagnostic criteria for idiopathic ATM and ATM secondary to or associated with a specific diseases.[2] These criteria have allowed us to harmonise classifications and ensure use of standard language in clinical practice. They also serve as guidelines for recognizing cases

of inflammatory myelitis for inclusion in studies.

Systemic and complete evaluation in a patient with acute inflammatory myelopathy will help minimize the possibility of diagnostic errors and delays in starting treatment that may affect clinical recovery and prognosed over both the long and short term.

The aim of this study is to describe demographic, clinical, and paraclinical characteristics of patients with ATM in Ratchaburi. Objective was to determine the different aetiologies of ATM and distinguish between idiopathic and secondary diseases by using TMCWG criteria.

Patients and methods

Participants

All patients diagnosed with ATM by neurologists between September 1, 2009 and September 30, 2014 were identified using medical in database.

Patients were examined and evaluated according to TMCWG criteria. All patients underwent brain and spinal MRI scans with and without gadolinium contrast. MRI scans were performed using a 1.5T scanner. Spinal MRI findings were devided into 3 categories according to the length of the lesions: partial myelitis (asymmetrical lesion affecting only 1 or 2 spinal cord segments); longitudinally extensive transverse myelitis (LETM) (central lesion extending 3 or more spinal cord segments); and multisegmental spinal cord lesions. Brain MRI findings were classified according to the Barkhof / Tintore criteria.[5-6] Routine CSF studies and PCR testing were performed to check for Herpes Simplex. Flavivirus, Varicella-Zoster virus, Cytomegalovirus, Epstein-Barr virus and Enterovirus were only performed in suspected cases.

Oligoclonal bands (OCBs) and the IgG index in CSF were analysed using isoelectric focusing. All patients were checked with HIV, syphilis, chlamydia and mycoplasma. Tests to detect and measure autoantibodies, lupus anticoagulant, anticardiolipin antibodies.

Data from only those patients who meet the ATM diagnostic criteria established by the TMCWG were included in this study (Table 1).

Classification

After inclusion of eligible patients and analysis of clinical and paraclinical results, patients were divided into 2 major groups, an idiopathic ATM group and secondary ATM group. For a diagnosis of secondary ATM, requirements were that the cases should meet all inclusion criterias and also present with one of the diseases listed among the exclusion criteria (Table 1).

Universally accepted standard criteria were used to diagnose multiple sclerosis (MS),[7-8] clinically isolated syndrome (CIS),[7-8] neuromyelitis optica (NMO),[9] acute disseminated encephalomyelitis (ADEM),[10] postvaccinal myelitis (PVM),[11] postinfectious myelitis (PIM)[12] and rheumatic diseases.[13-15]

Data regarding sex; age; date of symptom onset; any infections, vaccinations or trauma in the month prior to symptom onset; history of radiation treatment; score level of disability (mild 1-2, moderate 3, severe 4-5), on which 1, having minor symptoms and signs but fully capable of manual

work; 2, able to walk ≥ 10 m without assistance; 3, able to walk ≥ 10 m with a walker or support; 4, bedridden or chairbound (unable to walk ≥ 10 m with a walker or support); 5, requiring assisted ventilation for at least part of the day. Evaluate score at admission and after 3 months follow up.

Statistical analysis

Categorical variables were expressed as percentage and numeric variables as mean ± standard deviation. The Mann-Whitney test was used to analyse continuous independent variables. The level of statistical significance was set at p-value < 0.05

Results

All 32 patients were diagnosed with ATM during the study period: 21 women (65.6%) and 11 men (34.4%) with a mean age of onset 38.6 ± 17.4 years (range, 18-70). Of these patients, 53.1% (n = 17) had idiopathic ATM, 25% (n = 8) had CIS, 9.3% (n = 3) had MS, 6.3% (n = 2) had NMO and 6.3% (n = 2) had PIM.

The different aetiologies and main clinical and paraclinical characteristics are summarized in Table 2. Different types of MRI spinal cord lesions showed in Figure 1.

The Idiopathic group has mean age, mean score level of disability at admission and after 3 months follow-up more higher than other groups, include the Idiopathic group which had OCB negative (p-value < 0.05) in Table 3, 4. The OCB negative group has mean age, mean score level of disability at admission and after 3 months follow up more higher than OCB positive group (p-value < 0.05) in Table 5.

Table 1 Criteria for idiopathic ATM.

Inclusion criteria	Exclusion criteria
Development of motor or sensory deficit or autonomic dysfunction arising from spinal injury	History of spinal radiation within the preceding 10 years Vascular spinal lesions
Extra-axial aetiology ruled out by imaging study Inflammation discovered due to pleocytsis in CSF or through gadolinium contrast study of spinal lesion	Infectious disease
Progression to maximum deficit between 4 hours and 21 days.	Rheumatic disease[a] Demyelinating disease[a] or infectious and / or postvaccinal myelitis[a]

[a] Does not rule out secondary ATM

Table 2 Aetiology and demographic, clinical, and paraclinical characteristics of ATM cases included in the study (n = 32)

	Idiopathic ATM (n = 1 7)	**CIS (n = 8)**	**MS (n = 3)**	**NMO (n = 2)**	**PVM/PIM (n = 2)**
Demographic data					
Mean age of onset	49	38	30	34	42
Male / female	5/12	3/5	1/2	1/1	1/1
Clinical presentation					
Monosymptomatic	10	8	2	0	1
Myelitis	**7**	0	1	2	1
Polysymptomatic	0	0	0	0	0
Spinal MRI					
Partial myelitis	0	6	3	0	1
LETM	3	0	0	2	1
MSL	14	2	0	0	0
Brain MRI					
Normal	17	3	0	1	2
Lesions in white matter	0	5	3	1	0
OCB in CSF					
Positive (13)	2	8	3	0	0
Negative (19)	15	0	0	2	2
Level of disability					
Mild to moderate	7	8	3	0	1
Severe	10	0	0	2	1

MSL: multi-segment lesions; PIM: Postinfectious myelitis;
PVM: postvaccinal myelitis; NMO: neuromyelitis optica.

Table 3 Comparative of age, score level of disability between idiopathic and others groups (n = 32)

	Idiopathic (n = 17)		Others (n = 15)		t	P-value
	$\overline{X}$	S.D.	$\overline{X}$	S.D.		
Age (years)	49.00	5.18	36.27	5.65	6.65	.000
Score at admission	3.59	.52	2.93	.88		.014
Score at 3 months follow up	3.41	.79	2.53	.83		.005

Table 4 Comparative of OCB positive and negative between idiopathic and others groups (n = 32)

ATM	OCB		Chi sqare	P-value
	negative	positive		
Idiopathic	15 (88.2)	2 (11.8)	12.52	.001
Others	4 (26.7)	11 (77.3)		

Table 5 Comparative of age, score level of disability between OCB positive and negative groups (n = 32)

	Positive (n = 13)		Negative (n = 19)		P-value
	$\overline{X}$	S.D.	$\overline{X}$	S.D.	
Age (years)	38.92	9.37	45.84	6.44	.020
Score at admission	2.77	.73	3.63	.59	.004
Score at 3 months Follow up	2.38	.77	3.42	.77	.003

Table 6 Comparative of score level of disability between Partial myelitis, Multisegmental lesions and Longitudinally extensive myelitis by MRI spinal cord (n = 32)

	Partial myelitis (n = 10)		LETM and MSL (n = 22)		P-value
	$\overline{X}$	S.D.	$\overline{X}$	S.D.	
Score at admission	2.70	.48	3.55	.74	.004
Score at 3 months follow up	2.20	.42	3.36	.85	.001

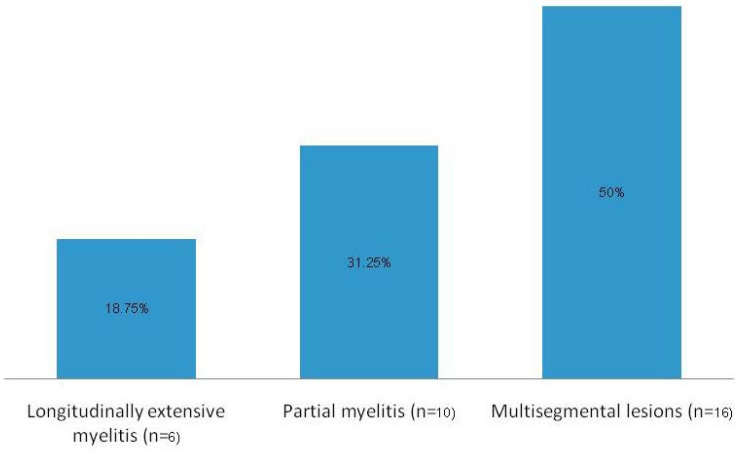

Figure 1 Different types of MRI spinal cord tesions

The multisegmental lesions and longitudinally extensive myelitis had more mean score level of disability than partial myelitis (p-value < 0.05) as shown in Table 6. After 3 months follow up 40.6% (n = 13) of the patients had severe motor disability. The severe motor disability was mostly found in multisegmental lesions and longitudinally extensive myelitis group.

Discussion

ATM is an inflammatory neurological disorder with a variety of aetiologies. Given that specific diseases associates with ATM may have different treatments, a complete evaluation is needed in order to diagnose the disorder's aetiology.

In 2005, De Seze et al. delivered a multi-centre retrospective study carried out in France and including 288 patients. Also applying TMCWG criteria, these authors found that only 16% of cases of ATM were idiopathic. ATM secondary to demye-linating disease represented 29% of the cases (MS 12% and NMO 17%) and was the main cause of ATM.[3]

In current study 5 years in Ratchaburi Hospital include Ratchaburi and near by province population within referral health care system, identify 32 patients with ATM. A full aetiological examination showed that the most common type of ATM was idiopathic.

Understanding that demyelinating ATM was caused by genetic, some by infectious agents, some by autoimmune reactions, some by exposure to chemical agents and some by unknown factors. The following observations have been drawn from existing epidemiological studies:

1. Occurs with much greater frequency at above 40^{o} latitude than closer to the equator. However, prevalence rates may differ significantly even within a geographic area, where latitude and climate are fairly consistent.

2. Occurs more common among Caucasians (particularly those of northern European ancestry) than other ethnic groups.

3. Indicating that ethnicity and geography interact in some complex way to impact prevalence figures in different parts of the world.

Significant results from the CSF studies included the fact that all patients with MS and CIS were positive for OCBs. The test is high sensitivity for diagnosing of MS,[7] but is not specific. The role - played by OCBs as factor predicting CIS conversion to MS is now well known,[16-19] although their role in determining long-term prognosis requires further clarification.

This study showed more about idiopathic ATM, But it is extremely important to perform an exhaustive aetiological assessment so as to identify the different diseases that may be associated with ATM.

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