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SPECTRUM OF ACQUIRED DEMYELINATING DISORDERS OF THE CENTRAL NERVOUS SYSTEM IN ADULTS IN A TERTIARY CARE HOSPITAL

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Background: Acquired demyelinating disorders of the central nervous system are diverse group of conditions characterized by destruction or disturbance of myelin sheath in the central nervous system i.e. brain and spinal cord. These vary in their causes, clinical presentations, and prognosis. **Objective:** To study the spectrum of acquired demyelinating disorders of central nervous system in adults in a tertiary care hospital of Pakistan. **Materials and Methods:** This is a retrospective cross sectional descriptive study carried out at department of Neurology, King Edward Medical University/ Mayo hospital, Lahore. Study period was one year from March 2012 till February 2013. Medical records of the patients with history of focal or multifocal neurological deficits suspected of demyelinating disorders were reviewed. Those fulfilling the diagnostic criteria for specific demyelinating disorder were included in the study. Clinical, laboratory and radiological features were recorded on a specific proforma designed for the study. Results were analyzed using SPSS version 17. **Results:** During this period seventy one patients with various demyelinating disorders were diagnosed. There were 39 (55%) males and 32(45%) females with M: F ratio of 1.2:1. The mean age at presentation was 29.5+ 9.3 years. Thirty four (48%) patients were diagnosed as clinically isolated syndrome (CIS), 23(32%) as multiple sclerosis (MS), 8(11.2%) as neuromyelitis optica (NMO), and 2(2.8%) as acute disseminated encephalomyelitis (ADEM). There was one case (1.5%) of each of the following disorders: progressive multifocal leukoencephalopathy (PML); vitamin B12 deficiency with dorsal myelopathy; post cardiac arrest hypoxic/ischemic symmetrical demyelination affecting basal ganglia; and central pontine myelinolysis (CPM). Out of the 34 cases of CIS, 17(50%) cases presented as transverse myelitis, 14(41%) optic neuritis, 2(6%) cerebellitis, and 1(3%) multifocal CIS. Among 23 cases of multiple sclerosis, 17(74%) had relapsing and remitting course (RRMS), 4(18%) primary progressive (PPMS), and 2(9%) secondary progressive course (SPMS). **Conclusion:** Demyelinating disorders are not uncommon in our local population. Inflammatory demyelinating disorders are more common than non-inflammatory causes. Multifocal clinically isolated syndrome (CIS) remained the most common form of inflammatory demyelination especially transverse myelitis followed by optic neuritis. Frequency of relapsing remitting multiple sclerosis was 74% and neuromyelitis optica was 11.2% in our local population. ADEM was rare (< 2.8%) in our adults population.

KEY WORDS: Clinically isolated syndrome (CIS), multiple sclerosis (MS), neuromyelitis optica (NMO), acute disseminated encephalomyelitis (ADEM), progressive multifocal leukoencephalopathy (PML)

INTRODUCTION

The term demyelination describes a loss of myelin with relative preservation of axons.¹ The etiology of acquired demyelinating disorder is multi-factorial.¹ However, traditionally known major group in this category comprised of immune mediated inflammatory demyelination with resultant wide spectrum of clinical syndromes such as multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM).²⁻⁷ Other less common causes of acquired demyelinating disorders include infections (such as progressive multifocal leukoencephalopathy), drugs and toxins (such as tin, lead, isoniazid and radiation), nutritional deficiencies (such as B12 deficiency), and acquired metabolic disturbances (such as osmotic demyelination causing pontine and extra-pontine myelinolysis).⁸⁻¹² These demyelinating disorders are recognized by their clinical presentation which may be monofocal or multifocal onset, course such as monophasic or polyphasic/relapsing, and specific neuro-imaging features of brain and spinal cord. Other investigations such as cerebrospinal fluid analysis, serum electrolytes, serum B12 and toxic screening may help in reaching the correct diagnosis.^{13,14} Consensus definitions and criteria are available for the diagnosis of most inflammatory demyelinating disorders such as MS, ADEM and NMO.¹⁵⁻¹⁷ We undertook this study to find out the spectrum of acquired demyelinating disorders of central nervous system in adults in a tertiary care hospital of Pakistan.

MATERIALS AND METHODS

This is a retrospective cross sectional descriptive study carried out at department of Neurology, King Edward Medical

University/Mayo hospital, Lahore. Study period was one year from March 2012 till February 2013. Medical records of the patients with history of focal or multifocal neurological deficits suspected of demyelinating disorders were reviewed. Inclusion criteria were: age >13 years; both sexes (male and female) and; symptoms/signs and MRI findings consistent with an acquired demyelinating disorder. Multiple sclerosis was diagnosed according to revised McDonald's diagnostic criteria 2010.¹⁶ Clinically isolated syndrome (CIS) was defined as first acute clinical episode of CNS symptoms (without encephalopathy) with a presumed inflammatory demyelinating cause without any prior history of a demyelinating event. CIS was further classified into monofocal onset when the symptoms localized to a single site in CNS such as optic neuritis, transverse myelitis, isolated hemiplegic syndrome etc and multifocal onset when the symptoms localized to multiple CNS sites but without history of encephalopathy and fever. Neuromyelitis optica was diagnosed according to the revised diagnostic criteria by Wingerchuk et al. (2006).¹⁷ Acute disseminated encephalomyelitis (ADEM) was diagnosed and classified according to International Pediatric MS Study Group-Consensus Definitions criteria with multifocal CNS white matter involvement associated with encephalopathy. Progressive multifocal leukoencephalopathy (PML) was diagnosed on the basis of clinical history, evidence of immunosuppression, and MRI findings suggestive of PML. Central pontine and extrapontine myelinolysis was diagnosed with evidence of white matter lesion on MRI brain in the setting of severe hyponatremia and its rapid correction. Exclusion criteria included: (1) age <13 years; (2) Ischemic demyelination (i.e. lacunar infarcts, Biswenger's disease and age related periventricular ischemic leukoencephalopathy); (3) Radiation induced white matter lesions; (4) Reversible posterior leukoencephalopathy syndrome (RPLS); and (5) Leukodystrophy. Those fulfilling the diagnostic criteria for specific demyelinating disorder were included in the study. Clinical, laboratory and radiological features were recorded on a specific proforma designed for the study. Results were analyzed using SPSS version ¹⁷.

RESULTS

During this period seventy one patients with various demyelinating disorders were diagnosed. There were 39 (55%) males and 32 (45%) females with M: F ratio of 1.2:1. The mean age at presentation was 29.5+ 9.3 years. Thirty four (48%) patients were diagnosed as clinically isolated syndrome (CIS), 23 (32%) as multiple sclerosis (MS), 8 (11.2%) as neuromyelitis optica (NMO), and 2 (2.5%) as acute disseminated encephalomyelitis (ADEM) {Table 1}. There was one case (1.5%) of each of the following disorders: progressive multifocal leukoencephalopathy (PML); vitamin B12 deficiency with dorsal myelopathy; post cardiac arrest hypoxic/ischemic symmetrical demyelination affecting basal ganglia; and central pontine myelinolysis (CPM). Out of the 34 cases of CIS, 17 (50%) cases presented as transverse myelitis, 14 (41%) optic neuritis, 2 (6%) cerebellitis, and 1 (3%) multifocal CIS (Table 2). Among 23 cases of multiple sclerosis, 17 (74%) had relapsing and remitting course (RRMS), 4 (18%) primary progressive (PPMS), and 2 (9%) secondary progressive form (SPMS) {Table 3}.

Table 1. Spectrum of demyelinating disorders (N=71)

Diagnosis of demyelinating disorder	Frequency n (%)	Males n (%)	Females n (%)	M:F
C.I.S	34 (48)	21 (61),	13 (39)	1.6:1
MS	23 (32)	11 (48)	12 (52)	1 : 1
NMO	08(11.2)	03(37.5)	05(62.5)	1:2.6
ADEM	02(2.8)	01(50)	01(50)	1:1
PML	01(1.5)	01(100)	0	1:0
B12 deficiency dorsal cord demyelination	01(1.5)	01(100)	0	1:0
Osmotic demyelination (CPM)	01(1.5)	01(100)	0	1:0
Hypoxic/ischemic demyelination	01(1.5)	0	01(100)	0:1

CIS, clinically isolated syndrome; MS, multiple sclerosis; NMO, neuromyelitis optica; ADEM, acute disseminated encephalomyelitis; PML= progressive multifocal leukoencephalopathy

DISCUSSION

This is the first study from Pakistan addressing the whole spectrum of acquired demyelinating disorders (inflammatory and non-inflammatory) of the central nervous system in adults. In our study the mean age at presentation was 29.5+ 9.3 with F: M ratio of 1.2:1. In a prospective, population-based sample of 1424 patients with multiple sclerosis in South-East Wales, the age at onset was 31. 2 years in male, 29.3 in female and F:M ratios were highest <16 years of age and declined with increasing age, with a male excess in those over 50.¹⁸ In our study the most common form of acquired demyelinating disorder was inflammatory demyelination. More over, the most common form of inflammatory demyelination was CIS (50%) followed by multiple sclerosis (34%) and ADEM (2.5%). In comparison, Wu J.S et al. in their study retrospectively reviewed 842 cases over 12 years and showed that MS was the most common demyelinating disorder (83.5%) followed by CIS (10.9%) and ADEM (1.9%).¹⁹ The high incidence of CIS in our study may be due to short period of review which was one year. With longer follow up some of the CIS cases may show conversion to definite MS or NMO as studies has shown that 30 to 70% of persons experiencing CIS later develop MS.²⁰ In a Dutch study on acquired demyelinating disorder (ADS) in children, most patients presented with polyfocal ADS without encephalopathy (30%), followed by polyfocal ADS with encephalopathy (24%), optic neuritis (ON, 22%), monofocal ADS (16%), transverse myelitis (3%), and neuromyelitis optica (3%).²¹ In our study, most common presentation of CIS was monofocal with transverse myelitis in 50% of cases followed by optic neuritis (41.2%) and cerebellitis (5.9%) respectively. In our study frequency of polyfocal CIS was only 2.9%. The most common presentations of acquired demyelination of the CNS in Canadian children were optic neuritis (ON; n = 51, 23%), acute disseminated encephalomyelitis (ADEM; n = 49, 22%), and transverse myelitis (TM; n = 48, 22%).²² Most common type of MS, according to the course of disease, was relapsing and remitting form (74%) in our study. This is slightly lower than previously reported (80-85%).²³ In contrast, the frequency of primary progressive MS was 18% in our study which is in accordance with previous reports (15-20%).²⁴ The frequency of NMO was 11.8% in our study which is generally considered a rare disease in white populations and occurs much more commonly in nations with a predominately nonwhite population. The frequency of NMO was 6.8% in São Paulo and 20.5% in Rio de Janeiro, and mainly seen in persons of African descent in a Brazilian multiple sclerosis (MS) survey performed from 1995-1998.²⁴ Selective involvement of the optic nerves and spinal cord has been reported up to 15-40% from Japan and 36% from Hong Kong.^{25, 26} In contrast, in countries consisting predominately of a white population, NMO comprised less than 2% of all demyelinating disorders.¹⁸ F:M ratio was 2.6 : 1 in our study but much higher preponderance in female up to 9:1 in relapsing form of NMO has been reported.²⁷ The other types of acquired non inflammatory demyelinating disorders were rare in our study. To our knowledge there has been no published study till to date addressing the overall spectrum of acquired demyelinating disorders in adults with inclusion of both inflammatory and non-inflammatory causes of demyelination.

Table 2. Frequency of various presentations of clinically isolated syndrome (n=34)

Diagnosis	Frequency of CIS (n=34) n(%)	Overall frequency of demyelinating disorders (n=71) n(%)
Transverse Myelitis	17(50%)	17(24%)
Optic Neuritis	14(41.2%)	14(20%)
Cerebellitis	02(5.9%)	02(2.8%)
Multifocal	01(2.9%)	01(1.4%)

CONCLUSION

In conclusion, the demyelinating disorders are not uncommon in our local population. Inflammatory demyelinating disorders are more common than non-inflammatory demyelination. Monofocal CIS remained most common form of inflammatory demyelination especially transverse myelitis followed by optic neuritis. Frequency of RRMS was 74% and NMO 12% in our local population. ADEM was rare (< 2.5%) in our adults population. However, larger studies over longer period are required to confirm these findings and to observe the further conversion of CIS cases into MS or NMO.

Table 3. Frequency of various types of multiple sclerosis (n=23)

Types of MS	Frequency n (%)	Males n (%)	Females n (%)	M:F
RRMS	17(74)	08 (47),	09 (53)	1.1:1
PPMS	04 (18)	03(75)	01(25)	3 :1
SPMS	02(8)	0	02(100)	0:2

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