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Characterization of Multiple Sclerosis Lesions with the Inclusion of Susceptibility Weighted Imaging on a 3T MRI Scanner in Sri Lankan Patients

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Abstract

Background: Multiple sclerosis (MS) is an under-researched disease in Sri Lanka. Detailed MRI analysis of MS has become possible with the availability of high resolution 3T scanners in the country.

Objectives: To describe the MRI features of MS in Sri Lankan patients and to identify the sensitivity of the Central Vein Sign at 3T.

Methods: A descriptive cross-sectional study was conducted on MS patients presenting for MRI at National Hospital of Sri Lanka, Colombo over a 12-month-period. Imaging was performed on a 3T MRI scanner and interpreted on digital format.

Results: The mean age of symptom onset was 30 years and the male to female ratio was 1:1.6. Periventricular lesions were found in the most patients (98.9%, n=91). Spinal cord lesions were found in 88.0% (n=81) and all these patients showed cervical cord involvement. Contrast enhancement was identified in 24% (n=22) indicating active lesions. A vast majority of lesions showed normal or increased diffusivity (97.8%, n=90). Nearly all the patients had positive central vein sign (98.9%, n=91) and most were periventricular (73.6%, n=502). Mean CVS positivity was 7.41. Optic neuritis was identified in 42.4% (n=39) and unilateral short segment (97.4%, n=38) optic neuritis was the commonest pattern.

Conclusions: Demography and MRI morphology of the Sri Lankan MS patients are similar to that of the Western populations. Identifying the CVS at 3T MRI is feasible and we recommend it to be included in routine MS reporting.

Keywords: *Multiple Sclerosis, Central Vein Sign*

INTRODUCTION

Multiple sclerosis (MS) is an emerging neurological disease in Sri Lanka characterized by the presence of multiple inflammatory demyelinating plaques. Its clinical presentation, laboratory investigations and imaging findings are relatively non-specific and therefore early diagnosis is a challenge. An early

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diagnosis is important since prompt initiation of treatment can significantly improve the prognosis of these patients by limiting the progressive accumulation of disabilities [1][2][3].

There are several other Inflammatory Demyelinating Disorders (IDDs) such as anti-aquaporin 4 antibody Neuromyelitis Optica Spectrum Disorders (NMOSDs) and myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) that may have overlapping clinical presentations. It is vital to distinguish these entities at the onset as their treatments are different. Multiple sclerosis is usually treated with drugs such as interferon beta to reduce inflammation. However, this is ineffective for NMOSD and may even worsen the severity of an attack and instead high dose intravenous corticosteroids is the first line therapy [4]. Delay in diagnosis and appropriate treatment may therefore lead to devastating and disabling clinical attacks [5].

Since no single clinical feature or investigation can provide an accurate diagnosis of MS, a set of diagnostic criteria has been developed which takes into consideration the clinical presentation, CSF oligoclonal band status and MRI findings [6][7][8]. As most MS research has been conducted in the Western countries it remains important to conduct research in Asian countries such as Sri Lanka to guide future revisions of the criteria so that they can be accurately applied to all ethnicities.

Only a few MS related studies have been published in Sri Lanka. Most of them have focused on the clinical aspects [9]. With the development of dedicated neuroimaging units in Sri Lanka and the availability of high resolution 3T MRI scanners, the opportunity for a large Sri Lankan MS study focusing on the MRI findings became feasible. The 2017 McDonald criteria of MS diagnosis heavily relies on neuroimaging with MRI to identify white matter lesions (WMLs) in characteristic locations, to distinguish acute lesions from chronic lesions and for follow up. Laboratory investigations such as AQP4 and MOG antibody status are now being used increasingly to distinguish among IDDs. As many of these antibody tests are not freely available in our country, it is important to be aware of their subtle differences on MRI to aid early diagnosis and treatment[10][11][12].

In this study, the main objective was to describe the neuroimaging features of Sri Lankan MS patients in detail. In addition to routine MRI sequences used for MS imaging, lesions were further evaluated using the SWI sequence, to detect the sensitivity of the central vein sign (CVS). This is important because the CVS has been shown to associate more with MS lesions compared to other types of WMLs, especially at higher field strengths due to the perivenular distribution of inflammation and demyelination [13][14][15][16]. The distribution of spinal cord lesions and the pattern of optic neuritis were also described as these features have also been found to aid in the differentiation between IDDs.

MATERIALS AND METHODS

Sampling

This cross-sectional descriptive study was conducted at the Neuroradiology department (MRI) of the Epilepsy unit at the National Hospital of Sri Lanka, Colombo 10 over a period of 12 months in 2020. This department provides Neuroimaging services to all Neurology wards and clinics at NHSL. All consenting MS patients diagnosed by the Neurologist, undergoing MRI were included. Patients with contraindications to MRI, contraindications to intravenous gadolinium-based contrast media, patients with alternative diagnosis for symptoms other than MS such as NMOSD and MOGAD, patients under the age of 18 years and patients over the age of 50 years were excluded. Simple consecutive sampling was used.

Instrument

Imaging was done on a Siemens 3.0T MAGNETOM Skyra MRI system and reported by an experienced Consultant Radiologist and a Senior Registrar subspecializing in Neuroradiology in DICOM format on a colour calibrated medical grade monitor. Imaging covered the brain, the whole spine and orbits with both pre-contrast and post contrast sequences. Brain imaging included T1W, T2W, FLAIR, DWI, SWI and T1W post gadolinium imaging. Fusion of FLAIR and SWI images using Radiant DICOM viewer to improve CVS identification during reporting. Findings were documented on a Microsoft Excel spreadsheet.

Statistical analysis

Age range, mean, mode and median, male: female ratio, mean age of symptom onset were calculated. The spatial distribution of lesions was tabulated according to periventricular, cortical/ juxtacortical, infratentorial and spinal cord locations. Spinal cord lesions were further sub categorized into cervical, thoracic and conus medullaris regions. The number of lesions were stratified (>10 lesions, 5-10 lesions, <5 lesions) and percentages calculated. The distribution of contrast enhancing lesions, diffusion restricting lesions, lesions with central vein sign and SWI hypointense lesions were tabulated and the percentages calculated. Percentage of patients with MRI evidence of optic neuritis, its location and length were calculated.

RESULTS

Demographic Details

Ninety-two MS patients participated in this study. The mean age at presentation to the neuroradiology department was 33 years, mode was 37 years and median was 33 years. Age range was 18-50 years. The mean age of symptom onset was 30 years. There were 57 (62%) female and 35 (38%) male patients. Male: Female ratio = 1:1.6

Spatial Distribution of lesions

The distribution of brain and spinal cord lesions are summarized in Table 2 and Table 3 respectively. Periventricular brain lesions were identified in 98.9% (n=91) the patients. Cortical and juxtacortical lesions were identified in 91.3% (n=84) the patients. Infratentorial lesions were identified in 65.2% (n=60) the patients. Spinal cord lesions were identified in 88.0% (n=81) the patients. There were 88.0% (n=81) of the patient with cervical cord lesions and 65.2% (n=60) with lesions in the thoracic spine. All the patients with thoracic spinal cord lesions also had cervical cord lesions. Conus medullaris involvement was observed in 2.1% (n=2). All the patients with conus medullaris involvement had cervical spine and thoracic spine lesions. The distribution of brain and spinal cord lesions are summarized in Table 2 and table 3 respectively.

Table 1: Distribution of lesions

Distribution of Brain lesions					
T2W/ FLAIR Brain lesions (100%, n=92)	**Patient % (number)**	**No lesions**	**<5 lesions**	**5-10 lesions**	**>10 lesions**
Periventricular	98.9% (n=91)	1.08% (n=1)	15.2% (n=14)	25% (n=23)	58.6% (n=54)
Cortical/juxtacortical	91.3% (n=84)	8.6% (n=8)	48.9% (n=45)	19.5% (n=18)	22.8% (n=21)
Infratentorial	65.2% (n=60)	34.7% (n=32)	51.0% (n=47)	9.7% (n=9)	4.3% (n=4)
Distribution of Spinal Cord lesions					
Spinal cord lesions 88.0% (n=81)	**Patient % (number)**	**No lesions**	**<5 lesions**	**5-10 or confluent lesions**	
Cervical	88.0% (n=81)	11.9% (n=11)	39.1% (n=36)	48.9% (n=45)	
Thoracic	65.2% (n=60)	34.7% (n=32)	53.2% (n=49)	11.9% (n=11)	
Conus medullaris	2.1% (n=2)	97.8% (n=90)	2.1% (n=2)	0% (n=0)	

Imaging Characteristics

There were 24% (n=22) with contrast enhancing lesions on T1W post gadolinium images. Their distribution is summarized in Table 2.

Table 2: Distribution of Contrast Enhancing lesions

Distribution of Contrast Enhancing lesions	
Location	**Patient % (number)**
Periventricular	33.6% (n=31)
Cortical/ juxtacortical	34.7% (n=32)
Infratentorial	14.1% (n=13)
Spinal cord	19.5% (n=18)

Diffusion restriction was evaluated using DWI and ADC maps. There were 2.1% (n=2) of patients who showed diffusion restricting lesions and 97.8% (n=90) of patients who did not have any diffusion restricting lesions. None of the diffusion restricting lesions showed contrast enhancement. DWI was not performed for the spinal cord lesions due to technical limitations.

Susceptibility weighted imaging was used to assess the presence of central vein sign and hypointense lesions. The central vein sign was identified in 98.9% (n=91) of patients. Their distribution is summarized in Table 3. The total number of hypointense lesions on SWI were 340; The rest of the lesions were isointense to white matter. Percentage of patients with hypointense lesions on SWI was 50% (n=46) and all these lesions were hypointense on T1W (black holes). Their distribution is summarized in Table 3.

Table 3: Distribution of lesions detected on SWI

Distribution of lesions containing CVS	
Location	**Patient % (number)**
Periventricular	73.6% (n=502)
Cortical/ juxtacortical	14.6% (n=100)
Infratentorial	11.7% (n=80)
Spinal cord	Not applicable
Distribution of SWI Hypointense lesions	
Location	**Patient % (number)**
Periventricular	87.0% (n=296)
Cortical/ juxtacortical	9.4% (n=32)
Infratentorial	3.5% (n=12)
Spinal cord	Not applicable

Optic neuritis was identified in 42.4% (n=39). Unilateral optic neuritis was identified in 97.4% (n=38) of them and bilateral optic neuritis was identified in 2.6% (n=1).

Short segment optic neuritis was identified in 84.6% (n=33) and long segment optic neuritis was identified in 10.2% (n=4). In the patients who has short segment optic neuritis, the intra-orbital segment was involved in 48.7% (n=19) and the intra-cranial segment was involved in 35.9% (n=14).

DISCUSSION

MRI features of 92 Sri Lankan MS patients were described in this study. Their mean age at presentation to MRI was 3 years older than the mean age of symptom onset at 30 years. A male to female ratio of 1:1.6 was observed. These values are similar to previous local and international studies [8] [7][7][9].

The highest number of lesions were periventricular. Nearly all patients (98.9%) showed periventricular involvement and most patients (58.6%) had more than 10 lesions. The number of cortical/ juxtacortical and infratentorial lesions were progressively lower. Spinal cord lesions were found in 88.0% (n=81) and all these patients showed cervical cord involvement. More than 5 lesions or a patchy confluent pattern were seen in 48.9% (n=45) of the patients. The thoracic spine was involved in 65.2% (n=60). Only 2.1% (n=2) had conus medullaris involvement and this was in the background of extensive spinal cord lesions in the cervical and thoracic cord. Isolated thoracic cord or conus medullaris involvement was not observed. Overall, a craniocaudal gradient in the number of spinal cord lesions was observed with a decline in lesion number caudally. This is the first Sri Lankan study to describe the distribution of MS lesions within the spinal cord and these findings are consistent with previous international studies [8].

Contrast enhancement which is considered a marker for active lesions was detected in 24% (n=22) of patients. Most of these lesions were observed in the supratentorial compartment (68.5%, n=63). A vast majority of lesions showed normal or increased diffusivity. Only 2.1% (n=2) of patients showed true diffusion restriction. Contrast enhancement was not observed in these lesions. Therefore, it can be concluded that diffusion weighted imaging (DWI) is not a sensitive sequence to detect acute lesions. Furthermore, if diffusion restriction is observed, the possibility of alternative diagnosis such as acute ischemic lesions must be considered first. These findings are also consistent across multiple international studies[7][8].

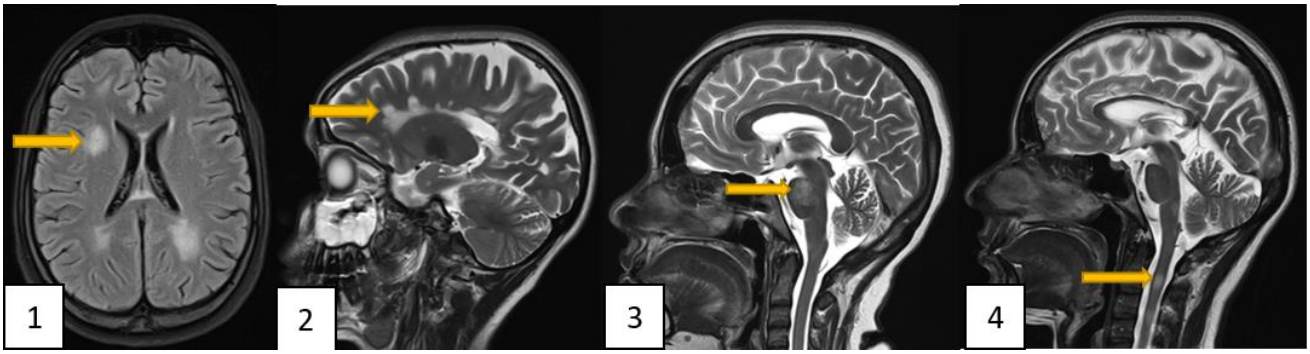

Figure 1: Lesion Locations. Axial FLAIR (1) and Sagittal T2W (2,3,4) images showing hyperintense lesions in juxtacortical white matter (1), periventricular white matter - Dawson's fingers (2), pons (3) and cervical cord (4).

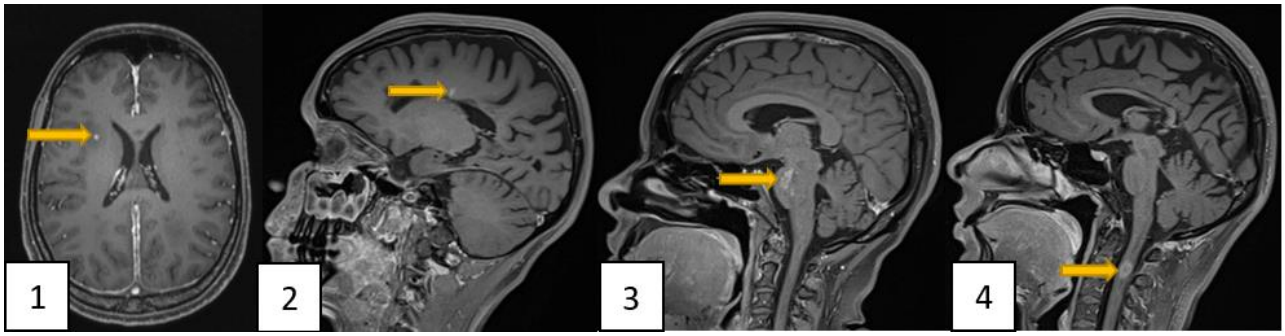

Figure 2: Contrast Enhancement. Axial (1) and Sagittal (2,3,4) post gadolinium images showing active contrast enhancing lesions in juxtacortical white matter (1), periventricular white matter (2), pons (3) and cervical cord (4).

Susceptibility Weighted Imaging at high field strengths is useful to characterize the iron deposition within MS plaques. The main advantage of SWI in MS is to identify the Central Vein Sign. This is because on SWI, the paramagnetic deoxyhaemoglobin within venous blood disturbs the local magnetic field and causes veins to appear hypointense. CVS, if present increases the likelihood of a white matter lesion (WML) to be caused by MS. In our study, nearly all MS patients had positive CVS (98.9%, n=91). Most of the lesions were identified in the periventricular region (73.6%, n=502). This finding has been consistent across multiple other studies[15][17]. Mean CVS positivity was 7.41. In addition to the CVS, 50% (n=46) of the patients showed hypointense lesions on SWI. This signal pattern is thought to be secondary to iron deposition within MS lesions. Most of these lesions were periventricular (87.0%, n=296) and all were hypointense on T1W imaging as well ("black holes").

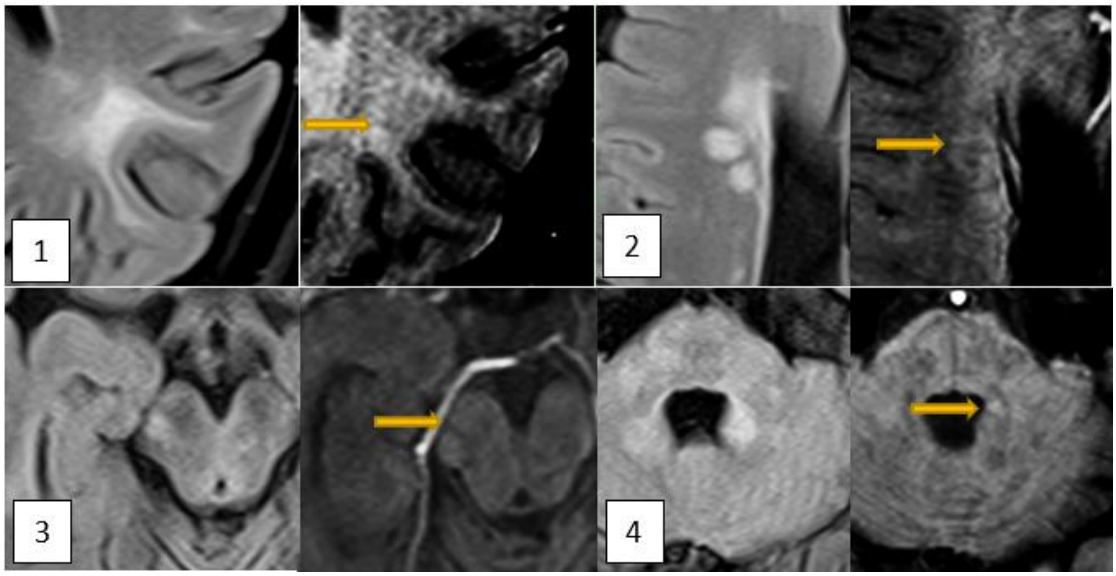

Figure 3: Central Vein Sign. Axial FLAIR and SWI images showing the Central Vein Sign in juxtacortical (1), periventricular (2) and infratentorial (3,4) locations.

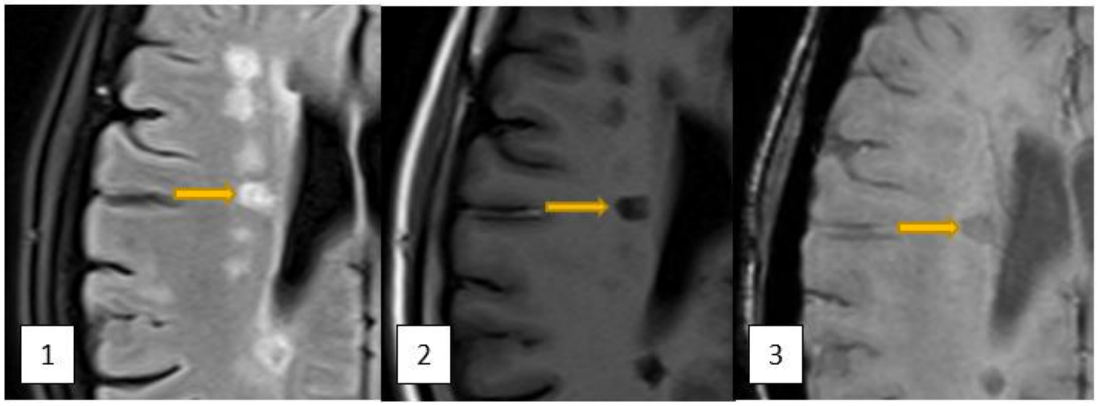

Figure 4: Hypointense SWI lesions. Axial FLAIR (1), T1W (2) and SWI (3). Arrow shows a FLAIR hyperintense periventricular lesion which appears as a black hole on T1W. On SWI, it is still seen as a hypointense lesion, whereas most other lesions seen on FLAIR are not visible.

Optic neuritis can be detected on MRI by identifying optic nerve swelling, increased T2W and FLAIR signal intensity and contrast enhancement. Optic neuritis was identified in 42.4% (n=39) of patients. A vast majority of these cases were unilateral (97.4%, n=38), short segment (84.6%, n=33) and anterior (48.7%, n=19). In contrast to short segment unilateral optic neuritis in MS, AQP4-IgG positive NMOSD patients have been found to develop bilateral, long segment, posterior optic neuritis with chiasmatic extension and MOGAD patients were more likely to develop bilateral, long segment, anterior neuritis[10][11][12].

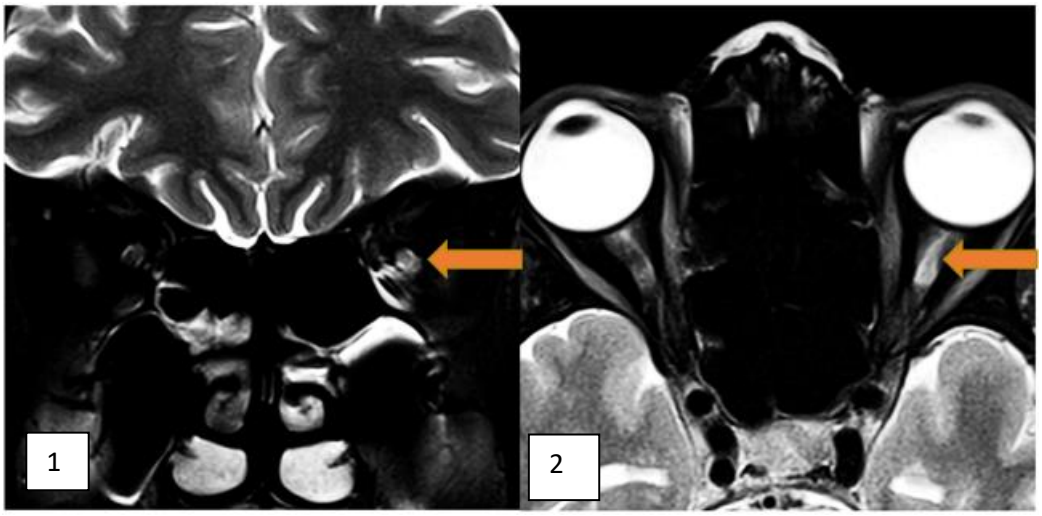

Figure 5: Optic Neuritis. Coronal (1) and Axial (2) T2W images showing anterior short segment hyperintensity of the left optic nerve.

CONCLUSIONS

The demographic features, spatial distribution and MRI morphology of MS lesions in this study were similar to the findings of the Western populations. Since none of the active contrast enhancing lesions showed diffusion restriction it can be concluded that diffusion weighted imaging (DWI) is not a sufficiently sensitive sequence to detect active lesions in MS. Additionally, the presence of diffusion restriction in a WML may indicate an alternate diagnosis such as an acute infarction rather than MS. Nearly all the patients had positive central vein sign and at least 7 such lesions were observed on average.

RECOMMENDATIONS

We recommend the inclusion of the presence, number and location of CVS in routine MRI reporting for MS and other IDDs. It is also recommended that further studies be conducted comparing presence of CVS in MS with other white matter diseases.

LIMITATIONS

Technical limitations resulted in the inability to image spinal cord lesions using SWI and DWI sequences.

Author declaration
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Availability of data and materials
Data will be available from corresponding author on request

Ethics approval and consent to participate
This study was conducted under the approval of the Board of Study in Radiology, PGIM, University of Colombo. Ethics approval for the study was obtained from the Ethics Review Committee, NHSL, Colombo. Informed consent was obtained from the participants and Information Sheet and Consent Form available in English, Sinhala and Tamil languages. Data confidentiality was maintained.

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