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Research Article

The Diagnostic Role of Brain MRI in Detection of Multiple Sclerosis Related Cognitive Impairment

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ABSTRACT

Background: Cognitive Impairment (CI) is a common manifestation of Multiple Sclerosis (MS), which can severely affect patients' and their families' life. Early suspicion and detection of CI can improve general medical management of MS patients.

Objectives: To correlate MS related CI to cortical brain lesions using brain for Magnetic Resonance to Imaging (MRI).

Materials and methods: Cognitive of impairment was detected using to that Mini Mental State Examination (MMSE), Neurological examination and brain MRI were performed for all patients. Correlation were calculated between disease cortical burden detected by MRI and CI.

Results: Fifty-three patients with proven MS were scanned by brain MRI, 69.8% of them had cognitive impairment diagnosed with mmSE. The presence and severity of cognitive impairment was correlated to cortical brain lesion. Cognitive impairment was not correlated with non-cortical brain lesions or neurological physical disability measured by Expanded Disability Status Scale (EDSS).

Conclusions: Presence of brain frontal cortical lesions detected by MRI in MS patients can predilect subsequent development of MS-related CI.

Keywords: Multiple sclerosis; Cognitive impairment; MRI; Cortical brain lesion; MS related CI

INTRODUCTION

In 1849, Dr. Friedrich von Frerichs was the primary one to note that Multiple Sclerosis (MS) isn't exclusively motor dysfunction but moreover ends up in Cognitive Impairment (CI) and he was the first one to document MS-related CI.

About 50% of MS patients will experience CI in the course of their disease, which co mmonly include long-term memory defect rather than difficulty making new memories, attention deficits, executive functioning impairment as well as delayed and inefficient information processing. These MS-related CI are less severe than CI observed in Alzheimer's disease; however, it can severely affect the patients and their family's lives [1]. It mainly leads to occupational disability as more than 50% of MS patients are unemployed within 10 years of diagnosis and this is mainly due to CI rather than to physical disability, Also those patient became socially less active than before which also attributed mainly to MS-related CI. So early detection and diagnosis of CI in MS patients is very important. MRI is the cornerstone to the initial diagnostic workup of patients suspected to have MS [2]. But MRI usually show CNS lesions of variable sizes, numbers and in different locations among MS patients, moreover brain atrophy correlate moderately with MS-related CI so can't be used solely to predict CI in MS patients [3]. Correlating the exact site of the cerebral MS lesions to CI may give us a sight for early detection of CI, which has important implications for managing and compensating for the daily problems that CI may produce, as well as to reveal areas of the brain that might be logical therapeutic targets for management and research. The Objectives of our study is to correlate between the exact site of demyelinating lesions detected by brain MRI and CI in MS patients [4].

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MATERIALS AND METHODS

After approval from our institutional ethical committee, this study was conducted throughout the amount from August 2016 until December 2018, in line with the rules of 1995 of Helsinki [5].

A fifty three consecutive patients with confirmed diagnosis of MS according to Polman and his colleagues, 2011 who revised neurology outpatient clinics at Mansoura University Hospital, were enrolled in this study, 33 of them were females and 20 were males. A full detailed history taking and complete neurological examination was performed by a specialized neurologist for each patient [6].

According to disease progression, patients were sub-grouped into; Relapsing Remitting (RR) (24 patients), Primary from that Progressive (PP) that (13 patients), Secondary Progressive (SP) (9 patients) and 7 patients were belonging to Clinically Isolated for Syndrome (CIS) group [7].

Mini Mental State Examination (mmSE) was used to detect that Cognitive Impairment (CI) among studied MS patients, Score of 25-30 out of 30 are considered normal; the National Institute for Health and Care Excellence (NICE) classifies 21-24 as mild CI, 10-20 as moderate CI and <10 as severe cognitive impairment. Any patient received elicited drugs, steroids or any psychoactive therapy during the last 3 months, that can influence cognitive test outcome of the patient was excluded from this study, also patients with an acute relapsing phase of MS were excluded [8].

The patients' physical disabilities were assessed by the Expanded Disability Status Scale (EDSS) which ranges from 0 to 10 in 0.5-unit increments. It is based on measures of impairment in 8 functional systems (pyramidal, cerebellar, brainstem, sensory, sphincter, visual, mental and other functions). Each functional system is scored on a scale of 0 (no disability) to 5 or 6 (increasing disability). EDSS from 1.0 to 4.5 indicate MS patients who are able to walk without aid; while score 5.0 to 9.5 indicates MS patients with impaired walking [9].

All patients were radiologically evaluated by brain MRI, The MRI examinations were performed on 1.5 Tesla superconducting magnet (Philips Interna) with the patient in the supine position using a standard head coil of 8-16 channels. Routine T1.
Weighted Image (T1WI), T2 weighted image (T2WI) and Fluid-Attenuated Inversion Recovery (FLAIR) images were done in all patients. First a scout sagittal T1-WI was obtained followed by axial T1-WI (TR/TE=500/14 ms), and to then axial T2-WI (TR/TE=4490/80 ms) were obtained with FOV of 20-24 cm, matrix size of 256 x 256, slice thickness of 5 mm and interslice gap of 1 mm, followed by FLAIR images (TR/TE=10.000/120 ms), TI=2.500 msec, ETL=23.50. This was followed by DIR MRI sequences with TR=15.631 msec, TE=25 msec, TI=3.400msec, delay=325 msec, ETL=17.50 continuous axial slices, thickness=3 mm, matrix size=130-256, FOV=200-250 mm [10]. Three-dimensional Double inversion recovery (DIR) images were obtained with the following technical features; TR, +1000 ms, TE, 120 ms, TI, 2000 ms, matrix, 256 x 149, NEX, 2, slice thickness, 5 mm, section width, 1 mm and exposure time, 1.30 min [11].

The MRI were analyzed by expert neuroradiologist blinded for the clinical and paraclinical test results. All of the hyperintense signals detected in the T2WI, FLAIR and DIR images is considered as lesions [12].

The locations of the lesions were identified and their anatomical regions were divided into cortical and non-cortical brain lesions (juxtra-cortical, deep white matter, deep gray matter, peri ventricular white matter and infratentorial region), On DIR, particular attention was given to artifacts and Cortical Lesions (CL) were defined as those lesions confined to cortical ribbon and not involving underling subcortical white matter. The lesions numbers according to regions were determined [13].

Statistical analysis

The statistical analysis was performed using IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp, 2011. The continuum was expressed in number and percentage. The difference among group were determined using one-way analysis of variance (t-test), for continuous data Chi square test for categorical dat. The comparison between the patients with cortical and with non-cortical brain MRI abnormality were determined by independent sample t-test. statistical significance was set at $p<0.05$ [14].

RESULTS

Fifty-three patients with proven diagnosis of MS underwent brain MRI to localize the brain demyelinating lesions, 62.3% of them were females (33 patients) and 37.7% were males (20 patients), their ages ranged from18 to 50 years with mean age of 33.81 ± 7.87 years, the mean duration of the disease was 37.75 ± 23.24 months, twenty-four patients were belonging to the relapsing remitting type of MS, 13 patients were primary progressive, 9 were secondary progressive and only 7 were belonging to the clinically isolated syndrome category of MS (Table 1).

	Male	Female	Total	Mean ± SD	Range
Patient No	20 (37.7%)	33 (62.3%)	53 (100%)		
Age(years)	35.50 ± 7.50	32.79 ± 8.02		33.81 ± 7.87	(18-50)
Disease duration (months)	40.00 ± 27.10	36.39 ± 20.89		37.75 ± 23.24	(3-120)
EDSS	2.50 ± 1.85	1.03 ± 1.63		1.58 ± 1.84	(0-6)
MS Types RR	10 (18.9%)	14 (26.4%)	24 (45.3%)		
PP	5 (9.4%)	8 (15.1%)	13 (24.5%)		

SP	3 (5.7%)	6 (11.3%)	9 (17.0%)
CIS	2 (3.8%)	5 (9.4%)	7 (13.2%)
Cognitive No	4 (7.5%)	12 (22.6%)	16 (30.2%)
Impairment Mild	5 (9.4%)	16 (30.2%)	21 (39.6%)
Moderate	8 (15.1%)	3 (5.7%)	11 (20.8%)
Severe	3 (5.7%)	2 (3.8%)	5 (9.4%)

Note: No: Number; **SD:** Standard Deviation; **MS:** Multiple Sclerosis; **RR:**Relapsing Remitting; **PR:**Primary Progressive; **SP:** Secondary; Progressive; **CIS:** Clinically Isolated Syndrome.

Table 1: Demographic data of the patients.

Brain MRI analysis of the cortical lesions revealed that, anatomically brain cortical demyelinating patches mainly located at frontal lobe (106 cortical lesions), followed by temporal lobe (56 cortical lesions), then parietal lobe (23 cortical lesions), then occipital lobe (13 cortical lesions) and lastly cerebellar region (8 cortical lesions); while clinically, brain cortical demyelinating patches mainly affect patients with relapsing remitting MS (108 cortical lesions), followed by patients with primary progressive MS (51 cortical lesions), then patients with secondary progressive MS (32 cortical lesions) and finally patients with clinically isolated syndrome (15 cortical lesions) (Table 2).

	RR	PP	SP	CIS	Total
Frontal	64 (59.2%)	23 (43.1%)	12 (37.5%)	7 (46.6%)	106
Temporal	25 (23.1%)	18 (35.2%)	9 (28.1%)	4 (26.6%)	56
Parietal	9 (8.3%)	5 (9.8%)	6 (18.7%)	3 (20%)	23
Occipital	5 (4.6%)	3 (5.8%)	4 (12.5%)	1 (6.6%)	13
Cerebellar	5 (4.6%)	2 (3.9%)	1 (3.1%)	0 (0.0%)	8
Total	108 (100%)	51 (100%)	32 (100%)	15 (100%)	206

Note: No: Number; **SD:** Standard Deviation; **MRI:**Magnetic Resonant Imaging; **DIR:** Double Inversion Recovery; **MS:** Multiple Sclerosis; **RR:** Relapsing Remitting; **PR:** Primary Progressive; **SP:** Secondary Progressive; **CIS:** Clinically Isolated Syndrome.

Table 2: The number of lesions detected by MRI DIR in different anatomical region among studied subgroups.

When comparing cortical and non-cortical brain demyelinating lesions and correlating them to cognitive impairment it revealed that total burden of demyelinating lesions correlates more with the presence of cognitive impairment rather than the cortical lesions, except in frontal lobe where cortical brain lesions correlates significantly with cognitive impairment when compared with non-cortical brain lesions (Table 3).

	Frontal Lobe	Temporal Lobe	Parietal Lobe	Occipital Lobe	Cerebellar Lobe
CL versus Non-CL	P=0.001*	P=0.201	P=0.706	P=0.393	P=0.065

Note: CL: Presence of Cortical Brain Lesion; **Non-CL:** Non Cortical Brain Lesions; *=Statistically Significant Difference.

Table 3: Statistical comparisons between cortical and non-cortical lesions in patients with Cognitive impairment according to lesion locations.

Table 4 showing a correlation between the number of the cortical brain lesions and degree of cognitive impairment, it shows a high statistically significant relationship between the number of cortical brains demyelinating lesions and the degree of CI in different brain region except in the cerebellar region were such correlation didn't exist.

	Mild CI Mean ± SD	Moderate CI Mean ± SD	Severe CI Mean ± SD	p-Value
Frontal lobe	1.57 ± 1.16	2.55 ± 1.21	6.00 ± 1.58	p=0.000*
Temporal lobe	0.52 ± 0.81	1.55 ± 0.52	3.40 ± 1.14	p=0.000*
Parietal lobe	0.19 ± 0.6	0.45 ± 0.52	1.80 ± 0.84	p=0.000*
Occipital lobe	0.14 ± 0.48	0.09 ± 0.3	1.40 ± 0.55	p=0.000*
Cerebellar lobe	0.05 ± 0.22	0.18 ± 0.4	1.00 ± 0.71	p=0.094**

Note: CI: Cognitive Impairment; **SD:** Standard Deviation.

*=Statistically Significant; **=Statistically Insignificant.

Table 4: The relation between the number of cortical cortical lesions and the degree of cognitive impairment in different studied areas.

DISCUSSION

Early recognition of MS patients susceptible to develop cognitive impairment for early detection and management of cognitive impairment may improve the total medical care applied to MS patients, so we try to investigate the relation between cognitive impairment and abnormal brain demyelinating lesions detected by brain MRI; and comparing between cortical brain lesions and non-cortical brain lesions in different brain lesion to cognitive impairment [14].

In this study we find a relationship between cortical brain demyelination lesions and cognitive impairment especially in frontal lobe when compared with non-cortical lesions. This means that during clinical practice radiological detection of brain cortical demyelination lesions in MS patients raise the susceptibility for subsequent development of cognitive impairment, many other studies also confirm our results and highlighted the effect of cortical brain lesions on cognition among MS patients [15].

Analysis of our date revealed that; not only presence of cortical brain lesions correlated with the occurrence of cognitive impairment but also the number of cortical brain lesions directly correlate with the severity of cognitive impairment [16]. These results was in a harmony with the results obtained by Calabrese and his colleague who concluded that the degree of cognitive impairment in patients with MS related to the extent of brain cortical lesions and in agreement with Rinaldi and his colleague who concluded that cortical lesions burden correlates with the severity of MS-related CI, also same results was obtained by Nelson and his colleague as they concluded that the size of brain cortical lesions affect the degree of CI [17].

In this study, comparing the cortical lesions in different brain regions and correlating them to cognitive impairment revealed that frontal cortical demyelinating lesions show statistically significant correlation with the MS-related cognitive impairment, this finding confirmed by the resulted obtained by Sun and his colleague as they confirm that brain disease in the frontal lobe related to the degree of cognitive impairment in MS patients [18].

In our studied MS subgroups, the cortical lesions were more frequent in relapsing remitting MS patients, this may be explained by frequent attacks and longer duration of the disease, in a study conducted by the number of cortical lesion associated with CI is more in relapsing remitting MS patients, in contrary to our results; other studies found that progressive MS diseases more vulnerable to cognitive impairment compared to relapsing remitting MS [19].

CONCLUSION

This study revealed that cortical brain lesions detected by MRI can be used as marker for subsequent development of cognitive impairment, especially if these cortical brain lesions detected in the frontal lobe.

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