Evaluation cervical cord changes in the patients with MS and their comparison with vasculitis patients

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Abstract: Multiple sclerosis disease (MS) is a chronic inflammatory demyelinating disease. The aim of this study was to evaluate cervical cord changes and to determine abnormal cervical cord prevalence in the patients with MS and their comparison with vasculitis patients. In a descriptive-analytic study carried out on 50 patients with MS, 40 patients with vasculitis and 50 people as control group in Tabriz Razi hospital, we studied cervical cord changes and the prevalence of cervical cord abnormalities in the patients with MS and vasculitis. From 50 MS patients, only four people had diffused lesions in spine that were all related to Primary Progressive (P-P) type. From the 22 patients with MS, having spinal symptoms during the study, focal lesions were revealed in the cervical cord Magnetic Resonance Imaging (MRI) of eight people (36.4%) whereas the lesions were found in 28 patients with MS who had no spinal symptoms. Diffused lesions were also found in the cervical cord MRI of four patients (18.2%) who had spinal symptoms whereas the lesions were found in the 28 patients with MS who had no spinal symptoms. There was a meaningful and the reverse relations between EDSS mean and transverse cross-section of cervical cord. In every five patients with MS one patient had demyelinated lesions in cervical spine which was more obvious in progressive types and atrophy degree of cervical spine was more in the patients with P-P and Secondary progressive types compared to the patients with relapsing remitting.

[Nikanfar M, Charsouei S, Miabi Z, Sha'afi SH, Hashemilar M, Farhodi M, Ebrahimi A, Khabbazi A, Rikhtegar Ghiasi R. **Evaluation cervical cord changes in the patients with MS and their comparison with vasculitis patients.** *Life Sci J* 2012;9(4):607-613] (ISSN:1097-8135). http://www.lifesciencesite.com. 93

Keywords: Multiple Sclerosis;Cervical Cord Changes; Vasculitis; MRI

1. Introduction

Multiple sclerosis disease (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS) which usually affects optic nerve, brain, spinal cord, brain stem and cerebellum(Rovira and León, 2008 ; Valsasina, 2005).

Spinal cord is commonly involved in MS and its disorders contribute to a part of disabilities of the disease (Rovira and León, 2008 ; Valsasina, 2005). Recently spinal cord has been comprehensively studied and some studies show that patients with MS have a smaller cervical cord cross-section compared to the control group which is in relation with disability. Furthermore several spines Magnetic Resonance Imaging (MRIs) may provide information on the disease progression which is not available through brain MRI. There are reports on cervical cord atrophy in the beginning of the disease as it is detectable in the patients with clinically isolated syndrome (C. I. S) and these findings show the importance of early diagnosis in MS patients as atrophy is equal to irreversible destructive pathology(Tench, 2005; Lin, 2004).

In cases with dubious or negative brain results or in MS onset associated with spinal symptoms, cervical cord MRI can play an important role in early diagnosis of MS (Simon, 2000; Lycklama, 2003; Grossman, 2000).

The validity of cervical spine studies have been emphasized on in the studies carried out in different countries in spite of limitations and controversial reports. As there is no integrated information regarding the prevalence of cervical spine changes and the importance of this region to be studied in MS patients, we decided to study this subject in patients with MS, however in a small population. The aim of this study was to evaluate cervical cord changes and to determine abnormal cervical cord prevalence in the patients with MS and their comparison with vasculitis patients.

2. Material and Methods

In a descriptive-analytic study carried out on 50 patients with MS, 40 patients with vasculitis and 50 people as control group in Tabriz Razi hospital from 2007-2008, we studied cervical cord changes

and the prevalence of cervical cord abnormalities in the patients with MS and vasculitis.

All the studied patients underwent cervical cord MRI with deep T1 and T2 weighted sequences and sagittal and axial sections were obtained using (1.5 Tesla, Signa, the US) unit. The diagnosis of MS was made using Mac Donald criteria and all the selected patients with vasculitis showed brain involvement in MRI.

All MRI images were reported by a neuro-radiologist regarding having any parenchymal lesions or plaques in cervical cord, the number, size, position, being focal or diffused of the lesions specially inT2 view. Other lesions were studied based on the number of the vertebral segments involved. Transverse cross-sections of cervical cord in C4-C5 level were measured by the software of the MRI unit. Diffused lesion is defined as hyper signal areas with indefinite margins which are clearly distinctable from CSF.

MS patients were selected using Mac Donald criteria. Patients with a history of neck trauma, degenerates and diseases of cervical cord and neck surgery were excluded from the study.

Ethical considerations:

No specific therapeutic intervention was done in this study. MRI was performed free of charge. Cervical cord MRI was performed for the patients with vasculitis and brain involvement without spinal symptoms. To avoid the probable complications of IV contrast, MRI was carried out without injection.

Statistical analysis:

All data were analyzed using descriptive and deductive statistics methods by SPSS Ver 11.5. The relation between qualitative data was evaluated using Chi-square test. And the relation between quality and quantity data were evaluated using T-test, Mann Whitney U-test, ANOVA and Kurksal Wallis tests and the relation between the variables were evaluated using Pearson and Spearman correlation coefficient. P<_ 0.05 was considered meaningful.

3. Results

From the 50 patients with MS, 30% were males and 70 % females. From the 40 patients with vasculitis, 22.5% were males and 77.5% female and there were 11 males (22%) and 39 females (78%) in control group. There was no meaningful difference regarding gender distribution between the three groups of patients with MS, vasculitis and the people of control group and all three groups were homogeneous regarding gender (P= 0.424). Gender distribution in different types of MS in patients is brought in table I. The mean age of the patients with MS was 33.86 ± 9.04 years in the range of 18-54 years. The mean age of the patients with vasculitis was 35.10 ± 9.80 years and 34.23 ± 8.45 years for the people of control group. There was no meaningful difference regarding age between the three groups and all three groups were homogeneous regarding age (P= 0.535). The mean age of symptoms onset was 25.62 ± 5.55 years for patients with MS and 29.65 ± 8.25 years in the patients with vasculitis which revealed a meaningful lower age for symptoms onset in patients with MS (P= 0.007). There was no meaningful difference between the different types of MS regarding symptoms onset age (P= 0.482). The mean time between symptoms onset and definite diagnosis in patients with MS was13.06 ± 8.03 months and 8.17 ± 4.96 months in patients with vasculitis which was meaningfully less(P= 0.001).

The most common onset symptoms in patients with MS were optic neuritis (42%), paresthesia (22%) and paraparesia (16%). 11 people (22%) of patients with MS had spinal symptoms (including paraparesia, urinary incontinence and Lehrmit sensory level) in the beginning of the disease and 22 people(44%) within study period. The frequency of spinal cord MRI changes in patients with MS is brought in chart I (abnormal MRI means existence of focal or diffused demyelinated lesions.)

The frequency of spinal cord MRI changes has been summarized in table I according to the MS type.

From the 10 patients with demyelinated lesions in cervical cord, only six people had focal demyelinated lesions, 6 had diffused lesions and two people had focal and diffused demyelinated lesions. The maximum number of focal lesions was three and the maximum number of the involved spinal segments was two, mostly in C4 and C3 levels. Three segments were the most involved segments with diffused demyelinated lesions (mainly in C5 and C3). The frequency of focal lesions in cervical cord MRI is brought in table I according to MS types.

From the total 50 the patients with MS, only four people had diffused lesions in spine that were all related to Primary Progressive(P-P) type. From the 22 patients with MS, having spinal symptoms during the study, focal lesions were revealed in the cervical cord MRI of eight people (36.4%) whereas the lesions were found in 28 patients with MS who had no spinal symptoms. Diffused lesions were also found in the cervical cord MRI of four patients (18.2%) who had spinal symptoms whereas the lesions were found in the 28 patients with MS who had no spinal symptoms.

The mean expanded disability status scale (EDSS) was 3.08 ± 2.15 in all patients with the maximum EDSS of 7.5 and the minimum of 1. There

was a meaningful statistical difference between EDSS and MS types (P< 0.0001) and this meaningful difference is seen in chart II. There was no meaningful difference between the time of being affected by MS and transverse cross-section of cervical cord (P= 0.45, r=-0.109).

There were 40 patients with vasculitis including 19 patients with systemic lupus erythematosis, 12 patients with Behcet syndrome, seven patients with antiphospholipid syndrome and two patients with temporal arthritis in whose cervical cord MRI no parenchymal lesions were found. Cerebral symptoms in patients with vasculitis included seizure, blurred vision and stroke. The youngest patient with vasculitis was 20 years old and the oldest was 64. The youngest age for vasculitis symptoms onset was 18 and oldest was 60.

The mean transverse cross section of spinal cord in C4 and C5 was meaningfully less in patients with MS compared to the patients with vasculitis and the control group (P= 0.006) (Chart III) but there was no meaningful difference between the patients with vasculitis and the control group (P=0.999). But most and least transverse cross-section of spinal cord were 84 mm2 and 66.40 mm2 for the patients with MS, 81 .24 mm2 and 77.47 mm2 for the patients with vasculitis and 80.42 mm2 and 77.69 mm2 for the control group. The mean transverse cross section of cervical cord was meaningfully less in patients with P-P type MS compared to the other types (P<0.0001) which is brought in chart IV. The most and least transverse cross-sections of the cervical cord in P-P type were 77. 60 and 66.44 accordingly, in Secondary progressive(S-P) type 80.20 and 70.30, in Relapsing Remitting(R-R) type 84 and 73.60 mm2.

The mean EDSS for the patients with MS having abnormal MRI was meaningfully more than patients with normal MRI (P= 0.004) which is shown in chart V. There was a meaningful and the reverse relations between EDSS mean and transverse cross-section of cervical cord (P<0.001 and r = -0.623) as disability degree increased when transverse cross-section of cervical cord decreased. This relation is shown in table II by MS types.

The mean transverse cross section of cervical cord was 73.40 ± 4.38mm2 in nine patients with MS having abnormal MRI and 77.23 ± 3.48mm2 for the patients with normal MRI. The mean transverse cross-section of cervical cord was meaningfully less in the patients with abnormal MRI compared to the patients with normal MRI (P= 0.006). The mean transverse section of the cervical cord was 76.70 ± 5.49mm2 in males and 76.74 ± 3.70 mm2 in the females having MS.

Table 1. Gender distribution, Frequency of MRI changes of cervical spinal cord and focal lesions in the spinal cord of MS patients by different types of disease

MS type	Gender		MRI		Local Lesions	
	Male	Female	Normal	Abnormal	Positive	Negative
Relapsing Remitting(R-R)	23	8	28	3	3	6
Secondary progressive(S-P)	1	9	8	2	2	8
Primary Progressive(P-P)	6	3	4	5	3	28

Table 2. Correlation of EDSS with cross-section of cervical cord by different MS types

MS type	R	P_Value
Relapsing Remitting(R-R)	-0.191	0.304
Secondary progressive(S-P)	0.086	0.812
Primary Progressive(P-P)	-0.881	0.002
Total Ms Patients	-0.623	<0.0001

4. Discussions

The frequency of demyelinated lesions in the cervical cord of the patients with MS was 20% which was significantly more in the patients with progressive type compared to the relapsing-remitting type (P= 0.036). This 20% would definitely increase if spinal atrophy is also included. In the study of Filippi et al, from 96 patients with MS only 81 people had abnormal cervical cord images (Filippi, 2000).

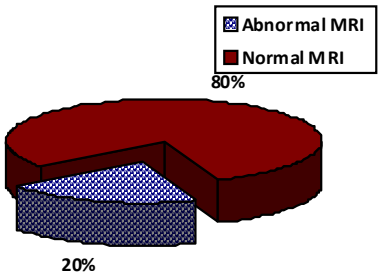

Chart 1.Frequency of MRI changes of cervical spinal cord in MS patients

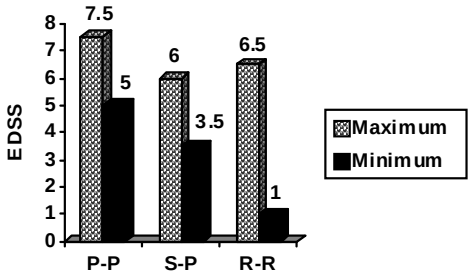

Chart 2. The mean, minimum and maximum of EDSS in MS patients by different MS types

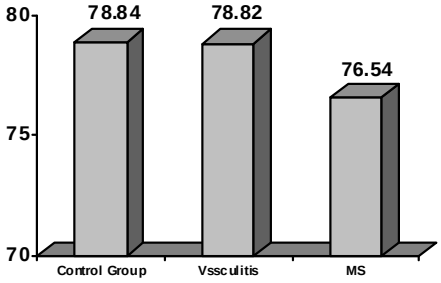

Chart 3. Mean cross-section of cervical cord (mm^2) in the three groups under study

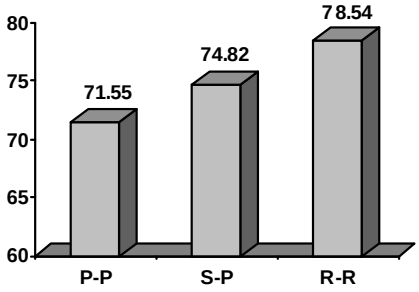

Chart 4. Mean cervical spinal cord profile area (mm^2) by different MS types

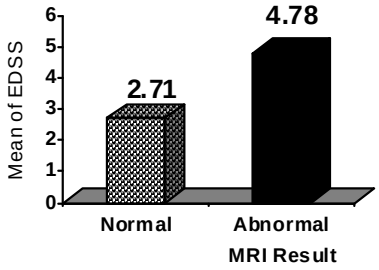

Chart V. Mean EDSS and MRI result of cervical spinal cord in MS patients

In two studies carried out in India and Thailand the frequency of abnormal MRI was accordingly reported as 93.75% and 86.66% and in the study carried out in Thailand the frequency of abnormal cervical cord MRI was 40% (Mani, 1999; Chawalparit, 2006). In the study of BOT, the frequency of focal lesions in entire spine was 70.02%, for the diffused lesions 2.9% and combination of both lesions 9.6%. (Bot, 2004).

In the study of Bonek, demyelinated lesions on the entire spine of the patients with MS were reported as 47-90% (Bonek, 2007). In the study of Chong et al, 29% of the spinal lesions in the patients with MS were in cervical and thoracic regions (Chong, 2006). The time of being affected by MS, the percentage of the MS types being studied, receiving medication or not, MRI unit power and evaluation degree of spine can affect prevalence rate. On the other hand according to the study of Bot et al, almost 50% of spinal lesions are missed when only cervical spine is studied (Bot, 2004).

In our study 11 people had spinal symptoms in the beginning of their diseases which increased to 22 people (two times more) during the study from which 12 people (54.6%) had focal or diffused lesions in their spines. In the study of Bot et al 52% of the patients also had spinal symptoms during this study (Bot, 2004).

The mean duration between the first symptoms of the disease and the definite diagnosis in this study was 13.06 ± 8.03 months for the patients with MS and 8.17 ± 4.96 months for the patients with vasculitis which was a meaningful difference. The early diagnosis of vasculitis compared to MS is due to different reasons such as vasculitis having broader systemic signs, being considered by physicians, MS having more subtle clinical signs and …. In the study of Bot et al the study duration was 18.4 months (Bot, 2004).

As mentioned before, in our study demyelinated lesions in the cervical spine of the patients with progressive type MS are meaningfully more than R-R type.

In the study of Bonek et al, demyelinizated lesions were found in cervical spine 62%, i.e 50% for R-R, 60 % for P-P and 75% for S-P types (Bonek, 2007). These differences are due to MRI power in diagnosing plaques, time duration between symptoms onset and definite diagnosis and other reasons. For instance, our patients being referred earlier, treated or our samples being few might have affected the current study. In Vaithianathar et al study, cervical spine MRI is mentioned to be able to differentiate between different types of MS as in progressive type vertical spine lesion are more frequent than R-R type (Vaithianathar, 2003).

The mean EDSS of the patients in our study in P-P, S-P, R-R types were accordingly 1.61, 4.90, 6.11 which had meaningful relation ($P<0.0001$) which were in accordance with studies of Bonek, Vaithianathar, Benedetti and Zivadinov (Bonek, 2007; Vaithianathar, 2003; Benedetti, 2006; Zivadinov, 2008).

The mean EDSS had a meaningful relation with MRI results in our study ($P= 0.004$) as EDSS was much higher in the patients with abnormal cervical spine compared to the ones with normal cervical spine. These results are also in accordance with the

studies of Benedetti and Vaithianathar (Vaithianathar, 2003; Benedetti, 2006) which indicates that the result of cervical MRI could be helpful in predicting prognosis of the disease.

The study of the mean and transverse cross-section of cervical spine between different types of MS revealed that the patients with progressive, especially P-P, type MS have considerably lower cervical spine cross section compared to the R-R type patients which suggests that cervical spine atrophy is related to the progression of the disease. In the study of Bonek, total spine atrophy was reported in 13-41% of the patients (Bonek, 2007). But the most spinal atrophy was reported in S-P patients, which patient follow-up period would have caused this paradox.

In the present study, R-R type MS patients show no significant difference regarding cervical spine cross-section with the control group. Bot, in his studies, found out that spinal disorders are more frequent in patients with early stage MS (Bot, 2004). Rashid, in his study, showed that R-R type MS has no meaningful impact on cervical spine cross-section (Rashid, 2006). In Agosta study, the grey matter of vertical spine showed atrophy in the patients with R-R type MS compared to the control group (Agosta, 2007). But in the study of Rovaris patients with R-R type MS had no diffused injuries in the cervical spine (Rovaris, 2008). But in the study of Uros Rot this was not confirmed (Rot, 2008). Therefore most of the previous studies confirm the results obtained from our study regarding the cross-section of cervical spine in the patients with R-R type MS. At the mean time it can be said that degenerative changes start from the beginning of the disease and the study of the spine using accurate methods such as MRS can reveal these changes sooner than conventional MRI. Therefore Blamire in his studies suggested that that a combination of MRI and MRS could provide a more complete picture of neuro-degeneration in the spine (Blamire, 2007).

In the present study, 40 patients with vasculitis were also studied regarding cervical spine in whom no parenchymal lesions or obvious atrophy were found which is in accordance with the studies of Flippi, Mani and Rovaris (Filippi, 2000; Mani, 1999; Rovaris, 2002; Rovaris, 2000).

It was concluded in Bot's study that unlike MS, cord lesions are uncommon in inflammatory diseases and these findings can assist with differential diagnosis (Bot, 2002). Studies with paradoxical results also exist showing cervical spine changes in patients with vasculitis (Yesilot, 2007; Ilniczky, 2007; Cakirer, 2003).

In a study Mentzel showed that in some German patients suffering Wagener disease, there were posterior epidural masses in cervical spine (Mentzel, 2003). In a report presented by Mimenza –Alvarado, it has been mentioned that that disorders of brain stem in the patients with lupus are one of the rare CNS involvements (Mimenza-Alvarado, 2002). And in another report presented by Campi on two patients having primary CNS angiitis, it was reported that most of these lesions were small, enhancing and mainly located in the posterior parts of the spine (Campi, 2001).

Lin, in his study, suggested that the beginning of the disease (R-R MS) atrophy is limited to supratentorial area and in S-P stage there are some visible atrophies in the brain and cervical cord and the volume of brain and cervical cord is a valuable index of irreversible pathologic process in MS and considering the volume of supratentorial and lateral ventricles, cerebellum and brain stem is of great importance in evaluating the volume of all cervical cord in patients (Lin, 2003). Rashid suggested in his studies that there is a powerful relation between cervical spine cross-section and the total intracranial volume and that cervical spine cross section is smaller in females (Rashid, 2006). We studied the spinal cord separately from the other variables in our study and cervical spinal section had no meaningful difference in female patients compared to the males.

Other issue is the existence of OSMS, optical spinal MS, in Asians. In a study carried out in Japan, one fourth of the patients with conventional MS had wide longitudinal lesions and it was shown in the study that wide longitudinal cord lesions were meaningfully more common in OSMS patients compared to conventional MS patients and wide longitudinal cord lesions were commonly located in upper and middle parts of the thoracic spine in OS MS patients (Lin, 2003). Chong in a study suggested that the Asian patients have bigger spinal lesions (Chong, 2006). In a study carried out in Japan by Jun-Ichi Kira, it was reported that MS in Asian population is defined by severe and selected involvement of optic nerve and spine and almost 15-40% of MS types are optic spinal types in Japan which are associated with less brain lesions in MRI and longitudinal lesions in several vertebral segments (Kira, 2003). In the present study, also patients with MS had findings in their brains confirming MS. Only 22% of the patients had spinal symptoms in the beginning of their diseases. At the mean time the maximum number of the spinal segments showing demyelinizated lesions was three segments. It should be considered that the patients with MS may refer to us only having spinal symptoms and cervical involvements in MRI.

On the other hand the characteristic appearance of spinal lesions in the patients with MS can be helpful in differentiating MS from other diseases

when the lesions are atypical. For instance contrast agent absorption by leptomeninges, lesions occupying more than half of the cord width, and hypo-intense lesions in spine T1 have been rarely reported, but the physician should be suspicious about vasculitis diseases (Bot, 2004). No pathologic findings were found in the patient with vasculitis in our study in cervical spine so that we can compare their characteristics with the patients with MS, contrast agent was not used on the other hand.

As for patients had been diagnosed by MS using McDonald's criteria, clinical findings and brain MRI, we were not able to evaluate the role of cervical spine MRI changes in approving or disapproving definite MS diagnosis but it is suggested in the study that when the spinal lesion, based on McDonald's criteria, is used, the number of patients not having MS criteria decreased from 35 cases to 16 (Bot, 2004). On the other hand in the mentioned study it was suggested that spinal lesions are independent of brain lesions and there is no powerful relation between brain and spine abnormalities.

In the MS patients of our study, EDSS had a meaningful relation with the cervical spine cross-section and in the patients with smaller cervical spine, disability degree was higher. Brain and spine tissue damage is one of the major causes of disability in MS patients and it has been shown in a study that the most brain and spine atrophy happens in the patients needing walking aid (Blamire, 2007) and in the study carried out by Blamire, using MRS, patients with EDSS= 2.5-7 had spinal atrophy (Blamire, 2007). It can be concluded that neuronal injury in cervical spine is related to the functional disability degree in the patients with MS. The study of cervical spine cross section and the result of cervical MRI in MS patients also revealed meaningful relation between these two variables meaning that cervical spine cross-section of the patients with demyelinated lesions in cervical spine was smaller in the patients without these lesions which may be indicating that patients with cervical spine demyelinated lesions in their spine are more probable to have atrophy in cervical spine followed by disability regression in the future.

Conclusion

In this study, from every five patients with MS one patient had demyelinated lesions in cervical spine which was more obvious in progressive types and atrophy degree of cervical spine was more in the patients with P-P and S-P types compared to the patients with R-R. We found no pathologic finding in cervical spine parenchyma of the patients with vasculitis. It shows that using cervical spine MRI can be helpful in differentiating MS from the inflammatory diseases especially in uncertain conditions. On the other hand existence of demyelinated lesions and atrophy in the cervical spine of the MS patients can also be helpful in differentiating MS types, choosing medication type and predicting clinical status of the patient in the future. Administrating early treatment can also prevent demyelinated lesions and spine atrophy and EDSS increase rate. Although MS patients in our study were definitely diagnosed in advance, it can be said that cervical spine study especially in uncertain MS cases can help clinical findings and brain MRI and reduce the time needed for definite diagnosis and early treatment, disability degree and the speed of disease progression. It is accepted that an increase in the power of MRI unit, diverse and accurate imaging techniques such as MRS, total spine study and increasing the volume of study can affect the obtained results from this study.

Suggestions:

Based on the results obtained from this study, it is suggested that in evaluating imaging results of the patients with suspected MS, spine MRI specially cervical spine should be carried out. Also in uncertain cases which MS disease cannot be differentiated from other diseases such as vasculitis, spinal MRI should be used. It is also suggested that further studies with higher sample volume and total spine studies be carried out.

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9/26/2012