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Concomitant multiple sclerosis and another autoimmune disease: Does the clinical course change?

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ABSTRACT

Objectives: Multiple Sclerosis is a demyelinating disease that can cause different symptoms by the autoimmune involvement of myelin. CD4+ and CD8+ T-cells as well as B-cells play important roles in MS pathophysiology. Co-existence of other autoimmune diseases and multiple sclerosis has been reported previously in the literature. It is not clear whether this co-existence may change the clinical course of MS or not. In this study we aim to evaluate the prevalence of other autoimmune diseases among patients with MS and if they may play any role in the clinical course of the patients.
Patients and methods: Twenty four patients with multiple sclerosis and another simultaneous autoimmune disease were detected among 1700 patients referred to the MS clinic of Sina Hospital during two years. Sex, age, duration of MS and the autoimmune disease as well as the type of the latter were recorded. For evaluation of disease progression a control group was randomly selected from the same patients referred to the clinic. EDSS was measured and recorded in both groups.
Results: The prevalence of concomitant autoimmune disease and multiple sclerosis was 0.014. The mean age of the patients was 35.04 ± 6.45 years. There were 18 different autoimmune diseases in the first group. The mean duration of MS and concomitant autoimmune disease were 5.91 and 9.80 ± 7.1 years respectively. The mean of EDSS in these patients was 1.62 ± 1.12 and in the control group was 3.33 ± 1.89. One patient had developed secondary progressive course in the first group. The statistical difference between these groups based on EDSS, was significant (P-value: <0.001). The median of EDSS in the first group was 1.5 and in the second one was 2.5. The mean of annual relapse rate in the first group was 0.60 and in the second one was 0.62 (P-value: 0.71).
Conclusion: The present study shows that several other autoimmune diseases may coexist with MS and their presence may modify the course of the disease. This should be re-evaluated in multicenter prospective long term studies.

1. Introduction

Multiple Sclerosis (MS) is a chronic demyelinating disease of the nervous system that may cause various signs and symptoms by autoimmune involvement of the brain and spinal cord [1]. The disease has both inflammatory and neurodegenerative nature which complicates understanding its etiology and pathophysiology [2]. Myelin destruction, inflammation and axonal loss are prominent pathological hallmark of the disease [3]. BothCD4+ and CD8+ T-cells as well as B-lymphocytes are involved in this inflammatory process and mediate tissue injury to the central nervous system [4,5]. Co-existence of two or more autoimmune diseases in a single patient has been reported frequently in various immune mediated diseases. MS is not an exception and several other auto-immune diseases such as myasthenia gravis, rheumatoid arthritis, immune thrombocytopenic purpura (ITP), and systemic lupus erythematosus (SLE) have been reported in patients with MS. This study was designed to evaluate demographic characteristics of MS when occurs concomitantly with another immune mediated disease of any type in Iranian patients.

2. Methods and material

2.1. Participant

The subjects were detected out of 1700 patients referred to the outpatient clinic of our MS research center throughout 2 years.

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Table 1
Types and percentages of concomitant autoimmune diseases.

Type of Autoimmune disease	Frequency	Percent
Vitiligo	1	4%
Autoimmune hepatitis	2	8%
Asthma	1	4%
Eczema	3	12%
Behcet	1	4%
Psoriasis	3	12%
Alopacia Areata	1	4%
Rheumatoid Arthritis	3	12%
Systemic Lupus Erythematous	1	4%
Idiopathic Thrombocytopenic Purpura	1	4%
Henoch Schonlein Purpura	1	4%
Scleroderma	1	4%
Graves disease	1	4%
Hashimoto thyroiditis	1	4%
Leukocytoclastic vasculitis	1	4%
Diffuse proliferative glomerulonephritis	1	4%
Crohn's disease	1	4%
Ulcerative Colitis	1	4%

In this observational open label study twenty eight patients with MS and another simultaneous autoimmune disease were detected. All medical records and documents were evaluated after signing the informed consents in the last appointment or follow up. Diagnosis of MS was based on Mc Donald's criteria (2010) by two neurologists and the diagnosis of other autoimmune disease was made by rheumatologist, pulmonologist or hematologist depending on the case and confirmed by appropriate lab data. Special attention was considered to ensure that neurological lesions of the MS patients was not the result of their autoimmune disease and finally, the simultaneous diagnosis of both diseases was confirmed by specialists of different fields. Sex, age, duration of MS and the autoimmune disease as well as the type of the latter were recorded.

For evaluation the course of disease in these patients a comparison was performed with control group.

The control group was randomly selected from the patients who were referred to the clinic according to their sex, age and duration of the disease. The patients were matched for age, sex and duration of the disease. However; the patients were under different drugs. Expanded Disability Status Scale (EDSS) was measured and recorded by a trained neurologist in both groups.

We used independent samples *t*-test to analyze the data. A *p*-value of less than 0.05 was considered to be significant.

3. Results

Out of 1700 patients 28 patients had MS and another immune mediated disease. Four patients were excluded from the study (three patients with ITP and one with sarcoidosis) because it was supposed that their second diseases have been developed due to use of different kinds of interferon beta preparations. These patients have been reported previously (ITP [6] and sarcoidosis [7]) and we only included the patients that their co-existed disease was not a complication of biological therapy. It should be mentioned that different disease modifying drugs (DMD)s especially interferons and alemtuzumab can induce autoimmune disorders including ITP [6,8], sarcoidosis [7], SLE [9,10] and thyroiditis [11] in patients with MS.

The prevalence of concomitant MS and other autoimmune disease was 0.014 in our study.

One patient was male and the others were female. The mean age of the patients was 35.04 ± 6.45 years and the mean duration of MS was 6.45 year in both groups. There were 18 different autoimmune diseases in the first group (Table 1).

The mean duration of concomitant autoimmune disease was 9.80 ± 7.1 years and the range of duration was from 0.3 to 30 years.

Table 2
Different Characteristics of MS in two groups.

	MS patients with concomitant autoimmune disease	MS patients without concomitant autoimmune disease
Mean of age (yr)	35.04 ± 6.45	34.50 ± 7.44
Mean of EDSS	1.62 ± 1.12	3.33 ± 1.89
Median of EDSS	1.5	2.5
Mean of Annual Relapse Rate	0.60	0.62
Mean of time from diagnosis (yr)	5.87	5.79

Table 3
Types of DMDs in two groups.

	MS patients with concomitant autoimmune disease	MS patients without concomitant autoimmune disease
Interferon beta 1a weekly (Intramuscular)	12	9
Interferon beta 1a three times per week (Subcutaneous)	4	4
Interferon beta 1b	5	5
Azathioprin	3	4
Methotrexate	–	2

The priority of MS or autoimmune disease onset was different among our patients.

In 15 patients (62%) the autoimmune disease onset was prior to MS onset and in 4 patients (16%), MS developed earlier than autoimmune disease. In 5 patients (20%) there was no any priority and the onset of these two different diseases was approximately concomitant (in less than one year).

For evaluation of disease progression comparison was performed between two mentioned groups.

In the first group, one patient had developed secondary progressive course; however, in the other one, six patients were secondary progressive. It should be noted that all of 48 patients enrolled to this study had been relapsing remitting type in the onset of MS.

The mean of EDSS in the first group was 1.62 ± 1.12 and in the second one was 3.33 ± 1.89. The statistical difference between these groups based on EDSS, was significant (P-value: <0.001).

The median of EDSS in the first group was 1.5 and in the second one was 2.5.

The mean annual relapse rate (ART) in the first group was 0.60 and in the second one was 0.62. The statistical difference between these groups based on ART, was not significant (P-value: 0.71). The mean of time from diagnosis in the first group was 5.87 years and in the second group was 5.79 years without significant differences (P-value: 0.08) (Table 2).

As mentioned above, DMDs were different in two groups. Table 3 shows the types of DMDs in both groups.

4. Discussion

Co-existence of MS and other autoimmune diseases have been frequently reported in the literature. The diseases have been different and may be predominantly B or T-cell mediated.

In previously reported cases, MS may precedes or develop after the other autoimmune disease. In later cases one of the major concerns is development of immune mediated diseases after biological treatment for MS. Actually induction of autoimmune diseases have been reported in various biological agents [12–14] in many conditions. Even central nervous system (CNS) demyelinating like lesions have been reported in anti-Tumor Necrosis Factor (anti-TNF) agents [15]. We excluded the cases who developed an autoimmune dis-