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Research Article

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Evaluation of Antiserum Level of EBV-VCA Antibodies in Acute Attack in Patients with Multiple Sclerosis

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Abstract

Introduction: MS is considered as one of the most common causes of disability among young people. As no definite treatment has been recognized for this disease yet, the patients are confused due to the life struggles with regard to the chronic clinical conditions, influencing their quality of life and health. Thus, finding the factors exacerbating the MS and trying to eliminate these factors are crucial. Thus, this research was conducted to evaluate the antiserum level of EBV-VCA antibodies in acute attack in patients with multiple sclerosis.

Method and materials: In this descriptive, cross-sectional research, 30 patients with multiple sclerosis admitted to neurologic clinic due to acute MS, were included. Anti-serum level of EBV-VCA antibodies was measured by ELISA method.

Results: The research results revealed that out of total 30 patients, 3 patients (10%) had positive serum EBV-VCA IgM, 5 suspected cases (16.7%) were doubtful and 22 patients (73.3%) were negative in this regard. No significant relationship was found between serum level of EBV-VCA IgG and acute MS attack (P>0.05).

Conclusion: The results of the research and comparison of these results with those of some other studies suggest that there is no significant relationship between serum level of IgM EB-VCA and acute attack of multiple sclerosis.

Keywords: Multiple Sclerosis; EBV; MS Attack; EB-VCA IgM

Introduction

Multiple sclerosis (MS) is a chronic inflammatory and demyelinating disorder of the central nervous system. This disease is one of the most common neurological diseases. It has four main patterns (relapsing-recovering), (progressive-secondary), (primary-progressive), (relapsing-progressive) [1].

MS is clinically defined as involvement of different parts of the central nervous system at different times, provided that other multifocal diseases of the central nervous system are excluded. The first symptoms usually emerge before the age of 55, its peak is seen between the ages of 20 and 40, and its prevalence in women is two times more than that in men [2]. The myelin layer is attacked by the immune system in this disease, leading to lesions of the nervous system, axonal degeneration and brain atrophy [3]. Multiple sclerosis symptoms include paresthesia, dysfunction in walking, reduced or loss of vision, diplopia, etc. [2]. In some types of MS, patients often experience exacerbated and mitigated (relapsing and suppression) symptoms due to the process of inflammatory demyelination and axonal degeneration, and inadequate structural restoration and improvement in function. Symptoms of this disease are periodical in patients [4].

MS is considered as one of the most common causes of disability among young people [5]. As no definite treatment has been recognized for this disease yet, the patients are confused due to the life struggles with regard to the chronic clinical conditions, influencing their quality of life and health [6]. Thus, finding the factors exacerbating the MS and trying to eliminate those factors are crucial. This disease requires adopting strategies for its treatment and prevention due to imposing high health care costs on the health system of the community and causing physical disabilities and psychological disorders. Thus, focusing on studies looking for finding the etiology of this disease seems to be an essential issue. While etiology of MS has remained unknown, it is believed that the genetic, immunological and environmental factors to be involved in its development [7].

It is stated that viral infections may trigger or exacerbate organ-specific autoimmune diseases [8]. For a long time, viruses have been introduced as a suspected environmental factor, involved in the onset of autoimmune diseases in patients who are genetically predisposed for these diseases. Seroepidemiologic studies have reported that EBV is associated with SLE, rheumatoid arthritis and MS. The potential role of this virus in the development of multiple sclerosis was first introduced in 1979. While this relationship has not been confirmed yet, the patients with multiple sclerosis have showed higher seropositive than healthy people at their age. Patients with MS also have a higher antigen level of EBV, which has not been seen for other viruses such as CMV and HSV, and VZV.

EBV affects 95% of adults around the world. This virus is periodically re-activated and this makes EBV a candidate for accompanying the relapsing-recovering episodes of MS [9]. It has been well indicated that the clinical exacerbation of MS occurs at systemic acute infection time with multiple viral and bacterial agents (three times) [10, 11].

Thus, as Epstein-Barr virus (EBV) is one of the most important viruses, whose involvement in MS and the onset of this disease' attacks has been proven by several studies and as each MS acute attack, regardless of recovery in symptoms, will reduce the function and increase EDSS in patients with MS, if a new infection or relapse of EBV is proven (increased EB-VCA IgM titer) as a risk factor in new attacks of MS relapse, MS can be prevented by its immediate and timely treatment, leading to reduced hospitalization costs and prevention of increased EDSS in patients with MS.

Method and Materials

This cross-sectional research was conducted on 30 patients with MS admitted to a neurologic clinic with an acute MS attack. They were randomly selected.

Inclusion criteria

People whose MS disease has already been diagnosed by a neurologist and they admitted to the center due to acute attack of this disease and acute attack of this disease or its relapse was approved by a neurologist.

Exclusion criteria

1. Patients in the CIS stage or recently-diagnosed cases
2. Patients with other autoimmune diseases
3. Use of corticosteroids
4. Use of immunosuppressive drugs

First, among the patients visiting neurology clinic, whose MS diseases was diagnosed before by a neurologist and admitted by a neurologist concerning relapse of the disease, 30 patients were randomly selected and their blood samples were taken at the reference laboratory and their EBV-VCA antibody titer was measured and their questionnaire was completed. Finally, the positive or negativeness of the patients' serum was analyzed in terms of the mentioned antibodies.

In order to determine the type and titration of Anti EBV IgM in the reference laboratory, 5 cc of venous blood was taken from the patient and its serum was isolated. It was prepared for testing (antibody titration determination by using ELISA method) after pouring it in a disposable container and keeping at suitable temperature (0 to 8 °C). All patients were referred to a reference laboratory for sampling in order to eliminate the laboratory error. Based on the reference range IgG of the reference laboratory: 0.8> IgM & IgG (Unit / ml) was considered negative, 0-1.2 was considered suspect, and 1.2< was considered positive. Vasculitis results of the tests and VEP of patients were also recorded in the questionnaire.

Finally, after collecting the required data from all subjects, the analysis was done. In this regard, SPSS 21 software was used. To evaluate the relationship between the two variables, Spearman's correlation coefficient was used and the significance level was considered to be 0.05. Frequency percentage was calculated for the quantitative variables.

Results

In this research, 76.7% of the patients were at the age range of 20-40 years and 63.3% and 36.7% were percentages of female and male, respectively.

It was found that 30% of the patients had less than 5 attacks. The most recent type of attack was paresthesia in the studied patients and the result of the vasculitis test was normal in 100% of patients.

IgM		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	negative	22	73.3	73.3	73.3
	suspected	5	16.7	16.7	90.0
	positive	3	10.0	10.0	100.0
	Total	30	100.0	100.0	

*10% of the patients had positive IgM serum level.

*83.3% of patients had positive IgG level.

Table 1: Frequency distribution of serum EBVCA IgM in the studied group.

Correlations			IgM	Rec attack Type
Spearman's rho	IgM	Correlation Coefficient	1.000	-0.259
		Sig. (2-tailed)	0.000	0.168
		N	30	30
	Recent attack Type	Correlation Coefficient	-.259	1.000
		Sig. (2-tailed)	0.168	0.000
		N	30	30

*No significant correlation was found between acute MS and Anti EBVCA IgM serum level (P>0.05).

Table 2: Correlation between EBVCA IgM serum level and MS attack.

Discussion

Given the global increase in the prevalence of multiple sclerosis and its debilitating and progressive nature, affecting mostly the young population, and given the fact that the etiology and triggers of the onset of the attacks and the definitive treatment of this disease have not been recognized yet, MS has become a great challenge for medical community. This disease annually imposes much cost, both financially and in terms of quality of life, on community and patients. Thus, it is important to conduct studies to find answer to the questions asked on this disease. Various environmental factors, such as smoking and vitamin D deficiency, and probably some microbial agents, such as EBV, have been proposed in etiology of multiple sclerosis [7].

Correlations			IgG	Recent attack t
Spearman's rho	IgG	Correlation Coefficient	1.000	-0.191

		Sig. (2-tailed)	0.000	0.313
		N	30	30
	Recent attack t	Correlation Coefficient	-0.191	1.000
		Sig. (2-tailed)	0.313	0.000
		N	30	30
* No significant correlation was found between acute MS and Anti EBVCA IgG serum level (P> 0.05)				

Table 3: Correlation between EBVCA IgG serum level and acute MS attack.

As attacks of this disease lead to development of disability and increased EDSS in patients, if we can identify the triggers of the onset of these attacks, we can prevent these attacks or increase in axonal degeneration of patients and its development into disability stage. The current research was conducted to evaluate the triggering factors of MS attacks. After performing the examinations, serum level of EBVCA IgM, indicating an acute infection with EBV, showed no significant correlation with acute MS (Only 10% of patients had positive EBVCA IgM) (p>0.05). Moreover, the serum level of EBVCA IgG showed no significant correlation with acute MS.

In a research conducted by Khaki, et al. in Iran, the presence of anti-EBV (IgG and IgM), HHV-6, measles, mumps, and para-influenza was examined in the serum of the patients with MS and they were compared with the control group. They found a correlation between the prevalence of MS and measles and mumps anti-virus antibodies. It might indicate the role of these viruses in triggering the initial response (IgM) or re-activation of the virus [12]. In addition, almost all EBV and para-influenza IgM of patients were negative in their research Our research also revealed that 90% of patients were negative in terms of EBVCA IgM serology.

Kiriyama T, et al. in Japan evaluated CSF and serum samples by PCR and ELISA methods to find the recent infection with HSV and EBV viruses. The research results suggest that anti-EBV or anti HSV antibodies significantly increased in serum and CSF, and immunohistochemistry studies on biopsy samples taken from the demyelination waste (3 cases) were reported to be negative which indicates that there is no relationship between the recent infection (positive anti EBV antibodies) and MS [13]. The correlation between the recent infection (serum IgM antibody) and multiple sclerosis attacks was not also proven in our research.

In a case control study conducted in Zahedan to evaluate the role of EBV re-activation and MS development, Ramroodi et al. found that the serum level of anti-nuclear IgM and IgG antibodies was higher in patients than that in control group. In addition, 68.7% of patients had EBV reactivation and the rate of nuclear DNA of virus was higher in MS patients with acute attack of disease, confirming the hypothesis that states this virus is involved in MS attacks [14]. The results of this research are inconsistent with those of our research.

In a research conducted in Denmark in 2007, TR Nielsen et al evaluated the relationship between antibody levels against EBV and other risk factors of MS, such as female gender, smoking, and HLA DR2, and with regard to the association between EB-VCA antibody and non-viral risk factors of MS, they concluded that EBV was seriously associated with the etiology of MS [15].

Comabella et al. (2010) found that immune response of production of anti-EBNA IgG in patients with MS increased compared to that in healthy subjects, so increased IgG response to EBNA is associated with MS and EBV virus is considered as trigger in the occurrence of MS [16]. In a research conducted in England in 2011, Farrell et al. showed that the correlation between increased titration (EBNA-1 IgG) and increased lesions in MRI indicates that MS has a direct correlation with the level of EBNA-1 IgG [17].

Conclusion

It suggests that increased titration is associated with disease development (increase in plaques). While some recent have been conducted recently to evaluate the etiologic role of EBV on multiple sclerosis, the number of studies conducted on the relationship between MS attack and EBV is limited and further studies are required in this regard. The result of our research suggests uncertainty in the relationship between MS attacks and EBV. Based on the results obtained, no significant relationship was found between serum level of EBVCA IgM and MS attacks. This research suffers from some limitations such as low number of samples and lack of genetic compatibility of samples (HLA Typing), so further research is required in this regard.

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