

RELATIONSHIP BETWEEN ANTICARDIOLIPIN AND MULTIPLE SCLEROSIS PATIENTS

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Abstract

The presence of anticardiolipin in serum of multiple sclerosis patients has been reported frequently but no clear relationship between anticardiolipin and the clinical neuroimaging features of multiple sclerosis. To analyze the possible role of anticardiolipin antibody in the pathogenesis of multiple sclerosis. We investigated (22) patients with multiple sclerosis of ages 25-45 years. The patients were also compared with (20) healthy individuals.

We found there was a highly significant elevation in the concentration of IgG and IgM anticardiolipin antibody in patient with multiple sclerosis than in control group $P < 0.001$. The prevalence of IgG and IgM anticardiolipin antibody was 36.4% and 27.3% respectively.

There was a highly significant difference between study groups. The findings of this preliminary study show that increased levels of anticardiolipin IgG and IgM associated with exacerbations of multiple sclerosis.

The significance of this association in the pathogenesis of multiple sclerosis remains unknown.

Introduction

Multiple sclerosis (MS), also known as disseminated sclerosis or encephalomyelitis disseminate is an autoimmune condition in which the immune system attacks the central nervous system (CNS), the brain and spinal cord, lead to demyelination [1,2,3]. Disease onset usually occurs in young adult, it is more common in women and has a prevalence that ranges between 2 and 150 per 100000 depending on the country or specific population and this disease was first described in 1835 by Jean Martin Charcot [4, 5, 6].

In multiple sclerosis (MS) case control studies have shown that anticardiolipin antibodies (ACL Ab) are more frequent than in the general population [7, 8, 9].

Patients with ACL Ab (antibody directed against cardiolipin), these are one of the antiphospholipid antibody syndrome (APS) [10].

Whereas cardiolipin (biphosphotidyl glycerol) is an important component of the inner mitochondrial membrane where it constitutes about 20% of the total lipid and it is typically present in metabolically active cells of the heart and skeletal muscle in the membrane of their mitochondria [11].

Multiple sclerosis (MS) and antiphospholipid antibody have many things in common, MS is probably an autoimmune disease and anticardiolipin antibody is seen in some patients especially of neuromyelitic type [12].

In addition bright T2_Imaging foci are occasionally detected in brain MRI (Magnetic Resonance Imaging) of patients with antiphospholipid antibody syndrome (APS) [13]. For unequivocal of antiphospholipid syndrome a patients have both a clinical event (thrombosis and pregnancy loss), antiphospholipid antibody but not the syndrome, can be induced by drugs or infections [14]. The purpose of this study was to determine whether patients with (MS) are positive for ACL.

Patients and Methods

The study included (22) patients with multiple sclerosis of ages 25-45 years and (20) healthy blood donors taken as a healthy control group.

IgG and IgM anticardiolipin antibodies were measured in both serum samples by using Enzyme-Linked Immunosorbent Assay (ELISA). This was performed as described in the leaflet of the kit (AESKULISA, Germany).

Statistical Analysis

Comparison of paired data from the three groups of subjects was done using T-test (t), while correlations between groups were analyzed using Pearson correlation coefficient(r) formula.

Statistical tables including observed frequencies with their percentage.

SPSS and Microsoft Excel Programs were used for T-test and correlation coefficient calculations respectively [15].

Results

The levels of ACL in patient with multiple sclerosis and controls are reported in Tables & Fig. (1).

There was a highly significant elevation in IgM and IgG ACL concentration in patient with multiple sclerosis than in negative and control groups ($P < 0.001$).

The prevalence of IgM and IgG was 36.4% (8 of 22) and 27.3% (6 of 22) respectively. There was highly significant difference between study groups.

Table (1)
Anti-cardiolopin Ab. (IgG) in sera of multiple sclerosis patients.

Diseases	Anti-Cardiolopin Ab. (IgG)	No.	%	Chi-square (χ^2)	
				P-value	Sig.
MS	Positive	6	27.3	0.033	Sig. (P<0.05)
	Negative	16	72.7		

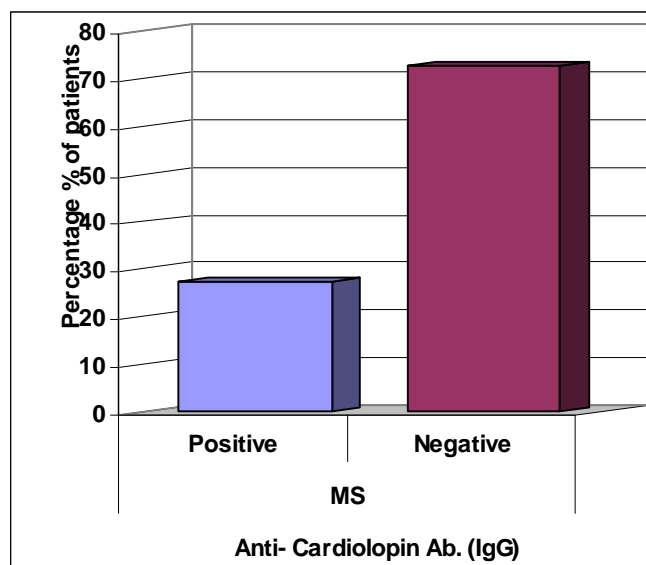


Fig. (1): *Anti-cardiolopin Ab.(IgG) in sera of multiple sclerosis patients.*

Table (2)
Anti-cardiolopin Ab.(IgM) in sera of multiple sclerosis patients.

Diseases	Anti-Cardiolopin Ab. (IgM)	No.	%	Chi-square (χ^2)	
				P-value	Sig.
MS	Positive	8	36.4	0.201	Non Sig. (P>0.05)
	Negative	14	63.6		

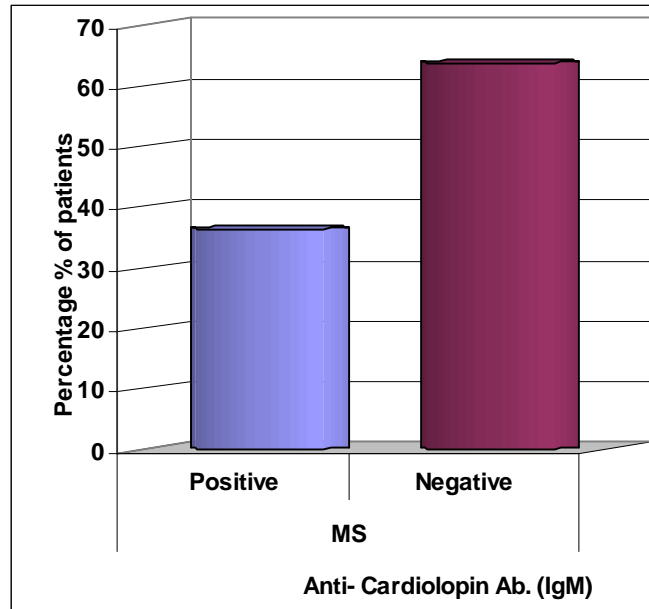


Fig. (2) : *Anti- cardioloopin Ab.(IgM) in sera of multiple sclerosis patients.*

Table (3)
Mean distribution of anti-CLP Ab-IgG (GPL/ml) level among studied group (Control & multiple sclerosis patients).

Studied group	N	Mean	SD	Std. Error	Mini.	Maxi.	Student test (t-test)		
							P-value	Sig.	
Control	20	8.65	2.37	0.53	4	13	-	-	
Anti-CLP Ab. (IgG)	Positive	6	29.83	8.04	3.28	19	43	0.00	HS
	Negative	16	7.75	2.05	0.51	5	12	0.455	NS
Total	42	Positive Vs Negative					0.00	HS	

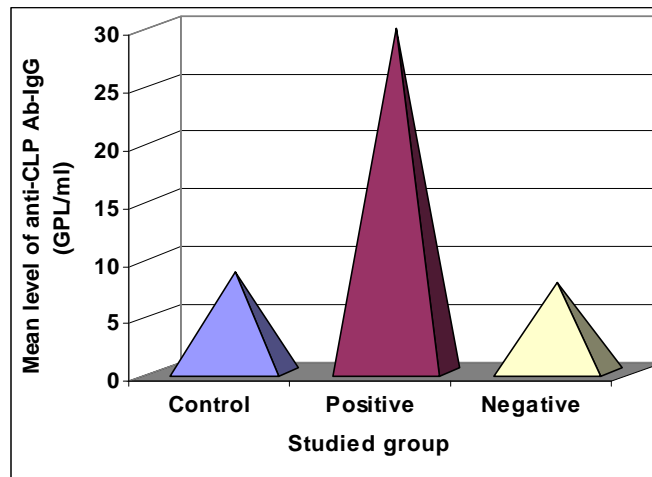


Fig. (3) : Mean distribution of anti-CLP Ab-IgG (GPL/ml) level among studied group (Control & multiple sclerosis patients).

Table (4)
Mean distribution of anti-CLP Ab-IgM (MPL/ml) level among studied group (Control & multiple sclerosis patients).

Studied group	N	Mean	SD	Std. Error	Mini.	Maxi.	Student test (t-test)		
							P-value	Sig.	
Control	20	9.1	2.13	0.48	6	13	-	-	
Anti-CLP Ab. (IgM)	Positive	8	35.75	20.76	7.34	19	62	0.00	HS
	Negative	14	7.21	1.58	0.42	5	10	0.571	NS
Total	42	Positive Vs Negative					0.00	HS	

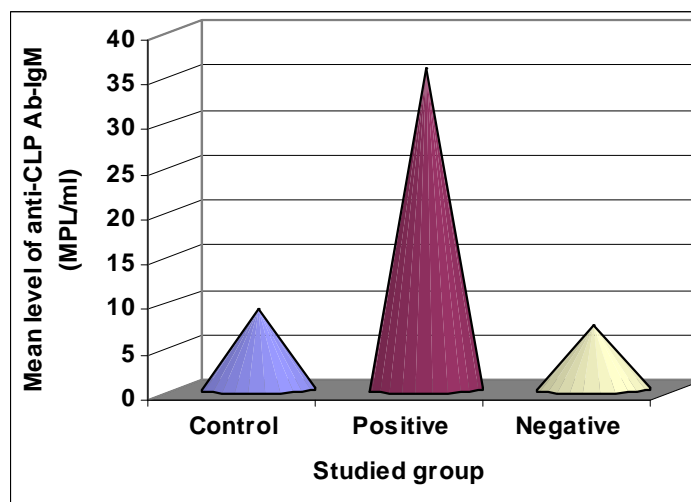


Fig. (4): Mean distribution of anti-CLP Ab-IgM (MPL/ml) level among studied group (Control & multiple sclerosis patients).

Discussion

The central finding of this research as a close association between ACL and certain clinical and neuroradiologic features of (MS). The previous studies failed to detect this association because they did not distinguish clinical states of the patients or used method unable to make this discrimination.

There are few reports on ACL Ab in association with (MS). In one study, the frequency of ACL Ab in patient with (MS) was 88%, in another report found 14 of 32 positive for IgM but only 3 of 32 positive for IgG [16].

In another study, ACL Ab positively was found in 29 patients (32.6%) 15 of the IgG and 4 of the IgM ecotype, through a retrospective study, the investigators shown that ACL Ab are more frequent than in the general population and that ACL Ab positively may be associated with specific clinical characteristics [7].

The greater frequency of other Abs in ACL Ab positive patient suggests that they only reflect a more general autoimmune activation in (MS) [16].

The clinical significance of the findings of this study is unknown, however, there are two broad possibilities: first, that ACL Ab in (MS) may contribute causally to the disease pathogenesis or that ACL are secondary epiphenomenal with no role in promotion of the inflammatory cascade of (MS) [17, 18].

Many antiphospholipid antibodies (APLA) are now known, and certainly many more exist. Therefore it is possible that APLA in (MS) are directed against some specific Ag that could be involved, for example in BBB [19, 20].

A number of available reports document cross-reaction of some ACL with endothelial cells and platelets. [21]

Raising the possibility that the rise of specific types of APLA in the (MS) subjects could trigger exacerbation by further compromise of the BBB. We have shown complex effects of plasma from (MS) patients on brain micro vascular endothelial cell in tissue cellular. [22,23]

It should be stressed that our assay against the four pure phospholipids will detect any PL-binding protein, not necessarily those thus for

identified as APLA. It is possible that we are checking Ags specifically involved in compromise of the BBB, possibly responsible for the endothelial activation that use reported in exacerbation of (MS) [24].

Conclusions

The findings of this preliminary study demonstrate presence of IgG and IgM APLA during exacerbations of (MS). Currently, the significance of these auto antibodies in pathogenesis of (MS) remains unknown.

Longitudinal studies to measure both IgG and IgM classes of APLA in larger cohorts of patients with relapsing-remitting (MS) are necessary to establish the significance of these auto antibodies and assess their pattern of expression before and after treatment with disease modifying agents.

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الخلاصة

أن ظهور أضداد شحميات القلب في مرضى تصلب الأعصاب المنتشر قد تم اثباته ، لكن لا توجد علاقة واضحة بين وجود هذه الأضداد وهذا المرض بحيث يمكن ملاحظتها. ولتحليل الوظيفة المحتملة لهذه الأضداد في امراضية تصلب الأعصاب المنتشر، فقد تمت الدراسة على (22) مريض مصاب بهذا المرض وبأعمار تتراوح بين 25-45 سنة مع إجراء مقارنة بين هؤلاء المرضى مع (20) شخص من النوع السيطرة (الأصحاء).

لقد وجد بأن هناك فرق معنوي من حيث الزيادة في تراكيز أضداد شحميات القلب نوع IgM و IgG بين المرضى المصابين بتصلب الأعصاب المنتشر مقارنة مع السيطرة (الأصحاء) ($P < 0.001$). وقد كانت نسبة الزيادة في تراكيز أضداد IgG و IgM تقدر بـ 36.4% و 27.3% على التوالي. وقد كانت هناك فروق معنوية عالية بين مجاميع الدراسة. لقد أثبتت الدراسة بأن هناك زيادة في تراكيز اَضداد شحميات القلب نوع IgM و IgG مقترنة مع الاصابة بمرض تصلب الأعصاب المنتشر في المرضى والذي يبقى سبباً غير معروف في هذه الامراضية.