Original Article

The Role of Antineutrophil Cytoplasmic Antibodies in Patients with Systemic Lupus Erythematosus

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Summary:

Background: *A recently demonstrated antineutrophil cytoplasmic antibodies (ANCA) are reported to have a role in the pathogenesis of systemic lupus erythematosus (SLE) which is associated with variable number of autoantibodies, most commonly having specificity for the cellular nuclear antigens.*

Objectives: *To study the prevalence of ANCA in SLE patients and their possible association with most common clinical manifestations of the disease.*

Patients and methods: *the study was conducted on 35 SLE patients attended the Renal Clinic in the Private Nursing Hospital/Medical City /Baghdad during the study period and compared with age and sex matched healthy control group. Enzyme linked immunosorbant assay was used for the detection of ANCA subspecificities antiproteinase 3 (anti-PR3) and antimyeloperoxidase (anti-MPO) antibodies.*

Results and conclusion: *Anti-PR3 was detected in 34.3% and anti-MPO in 2.8% of patients.ANCAs were associated with certain clinical manifestations of SLE , particularly vasculitis (PO.0005), neuropsychiatric manifestations (PO.0005) and serositis (P<0.025). Whether ANCAs plays a direct role in the pathogenesis of SLE or it only represents an epiphenomenon remains to be elucidated.*

Keywords: *ANCA and SLE.*

Introduction:-

It is generally accepted that systemic lupus erythematosus (SLE) is associated with variable number of autoantibodies, most commonly specific for the cellular nuclear antigens (1,2,3). Among those are the ANA and anti-ds DNA, which are thought to play a crucial role in the pathogensis of SLE. Moreover, a recently demonstrated antineutrophilic cytoplasmic antibodies (ANCA) are reported to add another Jigsaw piece to the pathogenesis of this mysterious disease (4,5).

These ANCA represent a group of antibodies directed against cytoplasmic components of neutrophil granulocytes and monocytes (6). The main primary (azurophilic) granuless proteins are the enzyme myeloperoxidase (MPO) and the serine proteases, elastase, cathepsin-G and proteinase-3 (PR3) (7).

In this study, we tried to shed light on the prevalence of ANCA in SLE patients with special emphasis on subspecificities antimyelperoxidase (anti-MPO) and antiproteinase-3 (anti-PR3) and possible association of these antibodies with the most common clinical manifestations of the disease:-

Patients:

The study was conducted on 35 patients with SLE who fulfilled four or more of the ACR criteria for the classification of SLE, 10 of them were associated with secondary vasculitis, and compared with age and sex matched healthy control group.

Methods:

Enzyme linked immunosorbant assay (ELISA) was used for the detection of anti-MPO and anti-PR3 subspecificities of ANCA.

Microplates are coated with highly purified MPO and PR3 antigens respectively, and the principles of the tests based on the formation of sandwich complex and enzymatic color reaction.

1-Anti-PR3 ELISA kit (Biomaghreb no .80518)
2-Anti-Mpo ELISA kit (Biomaghreb no .80519)

Results:

Our study showed that anti-PR3 antibodies were detected in 12 (34.3%) patients with SLE, while anti-MPO antibodies were detected in only one (2.8%) patient, but ANCA were not detected in healthy controls (table 1 and figure 1).

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Table 1: Detection of anti-PR3 and anti-MPO levels in study groups

Study group	Rate of detectable ANCA levels			
	Anti-PR3 level cut off = 5 IU/ml		Anti-Mpo level cut off= 5 IU/ml	
	N	%	N	%
SLE (n=35)	12	(34.3)	1	(2.8)
Healthy controls (n=35)	0	(0)	0	(0)

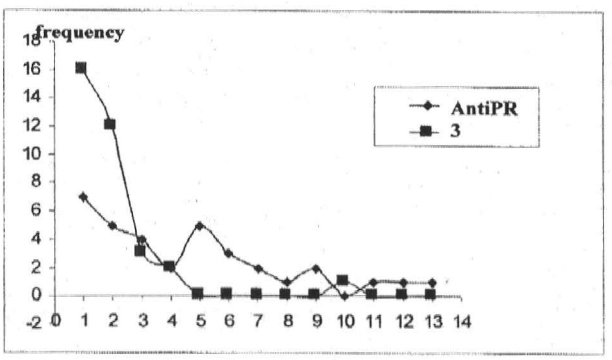

Figure 1: Frequency curve showing distribution of anti-PR3 and anti-Mpo among SLE cases

Table 2: Detection of anti-PR3 and anti-Mpo in SLE patients according to clinical manifestation

		Prevalence of detectable ANCA level					
		Anti-PR3			Anti-Mpo		
		N	%	P(X^2)	N	%	P(X^2)
1	**Renal**			P>0.4 [NS]			>0.5 [NS]
	Absent (n=9)	4	(44.4)		0	(0)	
	Present (n=26)	8	(30.7)		1	(3.8)	
2	**Vasculitis**			<0.0005 very high sig.			>0.5 [NS]
	Absent (n=25)	4	(16)		1	(4)	
	Present (n=10)	8	(80)		0	(0)	
3	**Neuro-psychiatric**			<0.0005 very high sig.			>0.5 [NS]
	Absent (n=26)	2	(7.7)		1	(3.8)	
	Present (n=9)	7	(77.7)		0	(0)	
4	**Musculo-skeletal**			>0.05 [NS]			<0.025 sig.
	Absent (n=5)	0	(0)		1	(20)	
	Present (n=30)	12	(40)		0	(0)	
5	**Constitutional**			>0.5 [NS]			>0.5 [NS]
	Absent (n=7)	2	(28.5)		0	(0)	
	Present (n=28)	10	(35.7)		1	(3.5)	
6	**Haematologic**			>0.5 [NS]			>0.3 [NS]
	Absent (n=20)	6	(30)		1	(5)	
	Present (n=15)	6	(40)		0	(0)	
7	**Serositis**			<0.025 sig.			>0.5 [NS]
	Absent (n=26)	6	(23)		1	(3.8)	
	Present (n=9)	6	(66.6)		0	(0)	

* All patients with SLE presented with mucocutaneous features

The rate of detectable anti-PR3 was significantly higher among those patients with secondary vasculitis (80%, PO.0005), neuropsychiatric manifestations (77.7%, P<0.0005), and those with serositis (66.6%, PO.025). Detectable levels were also observed in patients with other clinical manifestations, but in low percentages, as musculoskeletal manifestations (40%) (P>0.05) and renal manifestations (30.7%) (P>0.4), (Table-2)

Discussion:

Our study showed that there was no significant discrepancy in the clinical manifestations of SLE patients with other studies in Iraq and abroad (8,9).

Serum level of anti-PR3 was detected in 34.3% of patients, which is inconsistent with other studies reported abroad where anti-PR3 antibodies were either detected in low percentage, or not detected at all (10,11,12,13,14,15,16). This difference is probably due to genetic, environmental, or other precipitating factors.

On the other hand, there was an interesting correlation between the detectable levels of anti-PR3 and the clinical manifestation of SLE, and this was demonstrated by the statistically higher levels of anti-PR3 antibodies among those patients with secondary vasculitis (P,0.0005). This is may be because the hallmark of SLE is the inflammation of small sized blood vessels. Moreover, an interesting correlation was observed between the detectable anti-PR3 levels and neuropsychiatric manifestations (77.7%), and it was also statistically significant (PO.0005). These findings agreed with a similar study reported by Sanna-G et.al.(17).

Whether anti-PR3 plays a direct role in pathogenesis of SLE, or it is only an epiphenomenon remains to be elucidated.

Anti-Mpo antibodies detected in only one (2.8%) patient with SLE, and this result agreed with many other similar studies done abroad (12,14,15).

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