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Full Length Research Paper

Association of ribosomal anti-P antibodies with different parameters of lupus

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Systemic Lupus Erythematosus is an autoimmune multisystem disorder with protean manifestations and variable behavior. The main objectives of this study are to verify the association of ribosomal anti-P antibodies with neuropsychiatric lupus manifestations and to find out the relationship of ribosomal anti-P antibodies with other autoimmune parameters of lupus. Ribosomal anti-P antibodies were evaluated in the serum of 41 systemic lupus erythematosus (SLE) patients as well as ANA, dsDNA, anti-Sm, anti-SSA, anti-SSB, anti-histone by an indirect ELISA technique. Apart from Immunological tests, we also studied hematological parameters and biochemical parameters. Of the 41 SLE patients, ribosomal anti-P antibodies were significantly elevated in the sera of 6 lupus patients suffering from severe depression, anxiety, headache and lupus psychosis. Immunological parameters like ANA, dsDNA were positive in 100% of the Anti-Rib-P positive patients; but 66.6% were positive for SSA, only 33.3% for Sm, and none of them were positive for anti-histone and SSB. Biochemical parameters like urea, creatinine were higher than the normal range in 66.6% of the anti-P positive lupus patients, suggestive of lupus nephritis.

Key words: Systemic lupus erythematosus, ribosomal anti-P antibodies, lupus nephritis, enzyme linked immunosorbent assay, neuropsychiatric manifestations, psychosis.

INTRODUCTION

Systemic lupus erythematosus is an autoimmune disease characterized by the production of an array of autoantibodies. These autoantibodies are directed mainly against intracellular antigens, but also against cytoplasmic antigens (Elkon et al., 1985; Francouer et al., 1985). Among cytoplasmic antibodies, ribosomal anti-P antibodies are the most prominent one; located within the large 60S subunit of the eukaryotic ribosome. Ribosomal anti-P antibodies react with three highly conserved phosphorylated proteins P0, P1, and P2 having 38, 19 and 17 kDa molecular masses, respectively (Zampieri et al., 2001).The anti-P immunodominant epitope has been identified as a single linear sequence within the 22 amino acid carboxy-terminal peptide common to the three P protein; however, conformational determinants on P proteins also mediate antibody binding (Elkon et al., 1986; The and Isenberg, 1994).

Anti-Ribosomal P antibody is specific to neuropsychiatric SLE and is detected predominantly during active state; as they have the potential to induce cell or tissue immune mediated dysfunction (The and Isenberg, 1994; Nojima et al., 1992). Neuropsychiatric manifestations are common in 40 to 90% of the SLE patients (Nojima et al., 1992). The reason is that they act as potent inhibitors of protein synthesis and of cellular functions in the living cell cultures. The molecular mechanism by which anti-P antibodies induced depression is still unknown. It is believed that this antibody binds to the olfactory and limbic region result in varying degrees of neuropsychiatric SLE (Bonfa and Elkon, 1986; Sibely et al., 1992). It has been shown

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Abbreviations: ANA, Antinuclear antibodies; **SSA/SSB**, Also referred as Ro, La; **Sm**, After the name Smith; **CRP**, C - Reactive Protein; **ESR**, Erythrocyte sedimentation rate; **C3/C4**, Complement proteins.

Table 1. Comparative analysis between anti-P positive and anti-P negative lupus patients.

Parameter	Anti-Rib-P+ (n=6)	Anti-Rib-P- (n=35)	P-value
Women	66.60%	97.10%	0.032
ANA+	100%	91.40%	0.75
dsDNA+	100%	60%	0.16
Anti-Sm+	33.30%	31.40%	0.99
Anti-SSA+	66.60%	48.50%	0.7
Anti-SSB+	0%	14.20%	0.62
Anti-histone+	0%	14.20%	0.62
Low C3	16.60%	25.70%	0.89
Low C4	83.30%	57.10%	0.47
Lupus nephritis	66.60%	34.20%	0.3
Photosensitivity	100%	54.20%	0.1
Arthritis	33.30%	31.40%	0.34
Anemia	50%	45.70%	0.97
Elevated ESR	100%	65.70%	0.23

that the P-proteins are post-transitionally modified during the Fas ligand-induced apoptosis. The P1 and P2 proteins are completely dephosphorylated whereas P0 is only partially (Sibely et al., 1992; Khoshbin et al., 1999; West, 1994).

Neuropsychiatric syndromes associated with systemic lupus erythematosus are common but diverse in etiology and presentation. Cognitive dysfunction is prevalent among these syndromes but exhibit a significant degree of heterogeneity both within and between patient variability (Nakamura, 1997; Caponi et al., 1995). Here, we attempt to investigate the correlation between anti-Rib-P and lupus.

MATERIALS AND METHODS

A total of 41 SLE patients, fulfilling the 1982 revised ACR criteria for the classification of SLE were included in the study. Informed consent was also obtained from each patient. An indirect ELISA was used for the quantitative measurement of IgG class autoantibodies directed against ribosomal P proteins (Rayno and Reichlin, 1995; (Bonfa et al., 1994). Ribosomal P antibodies are directed against a common epitope of three phosphoproteins (P0, P1, P2), which are major compounds of the 60S subunit of ribosomal RNP complexes (Hay and Isenberg, 1993; Schneebaum et al., 1991; Koren et al., 1992). The assay was based on microplates coated with ribosomal P proteins P0, P1, and P2 (Sato et al., 1991; Chu et al., 1991; Elkon et al., 1990). Other autoimmune parameters were also performed by an indirect ELISA technique using commercially available kit (Orgentec diagnostic, Germany). C-Reactive protein and rheumatoid arthritis factor were detected by routinely available agglutination kit. Here P-value is applied.

RESULTS

Of the 41 SLE patients, 6 were positive for anti-Rib-P antibodies. Figure 1 shows that these positive patients comprised 2 men and 4 women with the mean age of 23.3 years (range: 12-32 yr). Immunological parameters like ANA, dsDNA, were positive in 100% of the anti-Rib-P positive patients, anti-Sm in 33.3%, SSA (Ro) in 66.6%, while SSB (La) and anti-histone were negative in all. CRP was positive in 33.3% and rheumatoid arthritis factor in 66.6% of the anti-Rib-P positive patients.

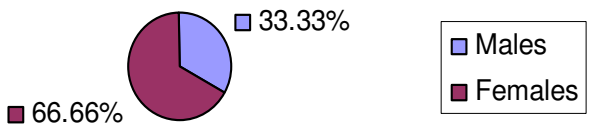

Figure 1. Percentage of males and females in anti-Rib-P positive patients.

Renal disorders occur in 66.6% of the anti- Rib-P positive patients; characterized by proteinuria and red cell cast. Hematological disorders include normocytic normochromic anemia (50%), elevated ESR (100%) while total Leukocyte count, differential leukocyte count and total platelet count were normal. The comparative analysis between anti-Rib-P positive and anti- Rib-P negative lupus patients are explained in Table 1 and Figure 2.

It seems that ribosomal anti-P antibodies have a positive association with headache, depression, anxiety, and lupus psychosis (Table 2, Figure 3). All of the anti-Rib-P positive lupus patients have a strong history of photosensitivity thus representing100% association with photosensitivity. The data were compiled and univariate analysis was done by using SPSS version 13. Significance was calculated by using chi-square test. The value $p>0.05$ was taken as non-significant and value $p<0.05$ was taken as significant.

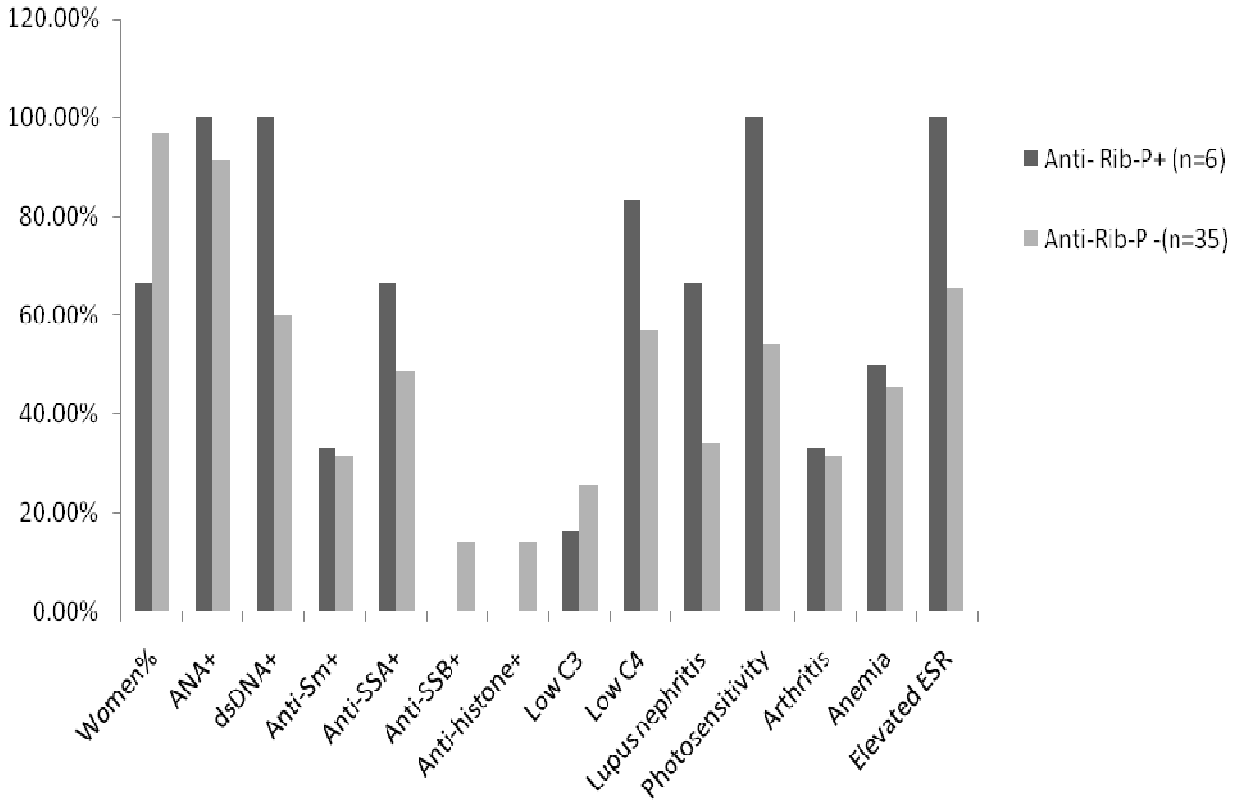

Figure 2. Neuropsychiatric syndromes in anti Rib-P positive patients.

Table 2. Neuropsychiatric syndromes in anti Rib-P positive patients.

Central nervous system	Anti Rib-P positive patients (n=6)
Headache	100%
Depression	100%
Anxiety	66.6%
Psychosis	33.3%
Movement disorder	0%
Mood Disorder	0%
Seizures	0%
Cerebrovascular disease	0%
Aseptic meningitis	0%
Acute confusional state	0%
Myelopathy	0%
Demyelinating syndrome	0%
Peripheral nervous system	
Autonomic disorder	0%
Acute inflammatory polyneuropathy	0%
Mononeuropathy	0%
Plexopathy	0%
Polyneuropathy	0%
Cranial neuropathy	0%
Myasthenia gravis	0%

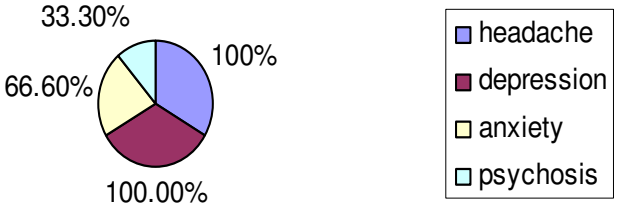

Figure 3. Neuropsychiatric manifestations in anti-Rib-P positive lupus patients.

DISCUSSION

Anti-Rib-P positive patients were evaluated according to the ACR Neuropsychiatric Lupus Nomenclature Committee criteria that include anxiety, cognitive dysfunction, mood disorder, acute confusional state and psychosis (Strous and Shoenfeld, 2007).

This study included 41 lupus patients which were further subdivided into two groups: anti-Rib-P positive and anti-Rib-P negative lupus patients. Serological testing of anti-P antibodies is of high diagnostic value in suspected SLE patients. Of the 41, 14.6% of the lupus patients have positive anti Rib-P antibodies as these were the patients suffering from severe headache, de-

pression, anxiety and psychosis but no other neuropsychiatric manifestations such as organic brain syndrome, peripheral neuropathy, transverse myelitis etc were found. 100% association between lupus psychosis and anti-Rib-P has been reported (Ghirardello et al., 2001) but in our case it is just 33.3%.

Measurement of CRP is important in monitoring the disease activity and response to therapy. CRP was positive in 33.3% of the anti-P positive patients. In humans, polymorphism at CRP locus influences CRP expression and predisposes e SLE (Sjowall et al., 2005).

In Raynaud's phenomenon, there is vasospasm of fingers and toes which is induced by exposure to cold (Caccouo et al., 2004). The prevalence of Raynaud's phenomenon was higher in those SLE patients that were anti-Rib-P positive than the anti- Rib-P negative lupus patients. Moreover, anti Rib-P positive lupus patients showed association with nephritis (66.6%) and to some aspect with rheumatoid arthritis (33.3%). ESR was quite high in those anti-Rib-P positive patients who have positive rheumatoid arthritis factor. One of the most important non-genetic factors responsible for lupus is photosensitivity; anti-Rib-P positive patients showed 100% association with photosensitivity.

In Pakistan, nobody has studied the relationship of anti-Rib-P with other parameters of lupus, so this study may add something informative to the scientific literature. There is need for more work at molecular level in this aspect on Pakistani population.

REFERENCES

Bonfa E, Elkon KB (1986). Clinical and serological associations of ribosomal P protein antibody, Arthritis Rheum, 29: 981-985.

Bonfa E, Gaburo N Jr, Tovares AV, Cossermelli W (1994). Comparison of five methods for the detection of anti-Ribosomal P protein antibodies, Braz. J. Med. Biol. Res. 27: 637-643.

Caccouo D, Del Porto F, Garzia P, Mitterhofer AP, Galluzzo S, Rigon A, Vadacca M, Navajas MF, Amoroso A, Afeltra A (2004). Raynaud's phenomenon and aPL antibodies in SLE: Is there an association", Ann. Rheum. Dis. 62: 20.

Caponi L, Pegoraro S, Di Bartolo V, Rovero P, Revoltella R, Bombardieri S (1995). Autoantibodies directed against ribosomal P proteins: use of a multiple antigen peptide as the coating antigen in ELISA", J. Immunol. Methods, 179: 193-202.

Chu JL, Brot N, Weissabach H, Elkon K (1991). Lupus antisera contain antibodies to a small fragment of 28S rRNA located in the proposed ribosomal GTPase center, J. Exp. Med. 174: 507-514.

Elkon K, Weissbach H, Brot N (1990). Central nervous system function in Systemic lupus erythematosus", Neurochem. Res. 15: 401-406.

Elkon KB, Parnassa AP, Foster CL (1985). Lupus autoantibodies target the ribosomal P proteins, J. Exp. Med. 162: 459-471.

Elkon KB, Skelly S, Parnassa A, Moller W, Danho W, Weissbach H, Brot N (1986). Identification and chemical synthesis of a ribosomal P protein antigenic determinant in systemic lupus erythematosus", Proc. Natl. Acad. Sci. USA, 83: 7419-7423.

Francouer AM, Peebles CL, Heckman KJ, Lee JC, Tan EM (1985). Identification of Ribosomal P protein antigens, J. Immunol. 135: 2378-2384.

Ghirardello A, Doria A, Zampieri S, Gambari F, Todesco S (2001). Autoantibodies to Ribosomal P proteins in SLE, IMAJ, 3: 854-857.

Hay EM, Isenberg DA (1993). Autoantibodies in central nervous system, Br. J. Rheumatol. 32: 329-332.

Khoshbin S, Glanz BI, Schur PH (1999). Neuropsychiatric syndromes in systemic lupus erythematosus, Clin. Exp. Rheumatol. 17: 395-398.

Koren E, Reichlin MW, Koscec M, Fugate RD, Reichlin M (1992). Autoantibodies to the ribosomal P proteins react with plasma membrane-related target on human cells, J. Clin. Invest. 89: 1236-1241.

Nakamura RM (1997). Role of autoantibody test in the diagnostic and evaluation of neuropsychiatric Systemic Lupus Erythematosus", Clin. Lab. Med. 17: 378-393.

Nojima Y, Minota S, Yamada A, Takaku F, Aoutsuka S, Yokohari R (1992). Correlation of antibodies to ribosomal P proteins with psychosis in patients with systemic lupus erythematosus, Ann. Rheum Dis, 51: 1053-1055.

Rayno K, Reichlin M (1995). Evaluation of assays for the detection of autoantibodies to the ribosomal P proteins, Clin. Immunol, 99: 103.

Sato T, Uchiumi T, Kikuchi M, Nakano M, Kominami R, Arakawa M (1991). Autoantibodies to the ribosomal P proteins found with higher frequency in patients with Systemic lupus erythematosus with active disease, J. Rheumatol. 18: 1681-1684.

Schneebaum AB, Singleton JD, West SG, Blodgett JK, Allen LG, Cheronis JC, Kotzin BL (1991). Association of psychiatric manifestations with antibodies to ribosomal P protein in Systemic Lupus Erythematosus, Am. J. Med. 90: 54-62.

Sibely JT, Olszynski WP, Decoteau WE, Sundaram MB (1992). The incidence and prognosis of central nervous system disease in systemic lupus erythematosus", J. Rheumatol. 19: 47-52.

Sjowall C, Bengtsson T, Skogh T (2005). CRP and anti-CRP autoantibodies in SLE, Curr. Rhematol. Rev, 1: 81-89.

Strous RD, Shoenfeld Y (2007). Behavourial changes in SLE are of an autoimmune nature", Nat. Clin. Pract. 3: 592-593.

The LS, Isenberg DA (1994). Antiribosomal P protein antibodies in systemic lupus erythematosus, Arthitis Rheum, 37: 307-315.

West SG (1994). Neuropsychiatric Lupus", Rheum. Dis. Clin. North Am. 20: 129-158.

Zampieri S, Degen W, Ghirardello A, Doria A, Van Venrooij WJ (2001). Dephosphorylation of autoantigenic ribosomal P proteins during Fas-L induced apoptosis: a possible trigger for the development of the autoimmune response in patients with systemic lupus erythematosus, Ann. Rheum Dis. 60: 72-76.