FRI0114 DIAGNOSTIC VALUE OF NUCLEOSOME-SPECIFIC ANTIBODIES IN RECENT ACTIVE NON TREATED SLE

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Background The nucleosome is considered as a major antigen in SLE and nucleosome-specific antibodies (Ab) seem to be the most specific and the earliest markers of SLE.

Objectives To evaluate different methods of detecting anti-nucleosome Abs and determine the diagnostic value of these Abs in recently active SLE.

Methods A 2 year (1998–99) prospective multicenter study in 13 European Immunopathology Centres (Groupe d'Etude de l'Auto-Immune).

Patients: (i) 55 cases of recently active SLE (evolution < 1 year), (ii) 50 other autoimmune diseases: 31 RA, 15 primary SJÖGREN'S syndrome, 2 scleroderma, 2 unclassified connective tissue disease.

IgG anti-nucleosome Abs were detected by ELISA or immunodot using different nucleosome preparations.

IgG anti-ds DNA Abs were detected by ELISA (calf thymus and human recombinant plasmid DNA).

Results

- 34/55 SLE patients had anti-nucleosome Abs reacting with 4 kits.
- 16/55 SLE patients had anti-nucleosome Abs reacting with 1 to 3 kits.
- 5/55 SLE patients were negative for anti-nucleosome Abs.
- 5/50 patients with other autoimmune diseases had anti-nucleosome Abs.

Abstract FRI0114 Table 1

	1-ELISA (IgG)	2-ELISA (IgG)	3-ELISA (IgG)	4-Immunodot (IgG)
Nuclear extract	Mouse erythroleukemia cell line	Calf thymus	Calf thymus	Calf thymus
Antigen	Native nucleosomes	Native nucleosomes	Nucleohistones without H1	Nucleohistones without H1
Sensitivity	0.84	0.76	0.84	0.67
Specificity	0.92	0.96	0.94	0.98

Conclusion 50/55 (91%) of patients with recently active SLE had anti-nucleosome Abs (by at least 1 method), 46/55 (84%) also had anti-ds DNA Abs (by ELISA). The sensitivity and the specificity of the anti-nucleosome Abs for SLE depend on the method and the nucleosome preparation.

FRI0115 SYSTEMIC LUPUS ERYTHEMATOSUS IN MEN

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Background

Objectives To evaluate whether gender influences the clinical course and outcome in systemic lupus erythematosus (SLE).

Methods Four hundred eighty-nine SLE patients were followed up at the University Hospital of Ioannina, Greece between 1981 and December 2000. These patients were reevaluated and the demographic, clinical, serological, radiological and therapeutic information were entered in a database. We divided our patients in two groups according to the gender. The disease activity and outcome were measured using the European Lupus Activity Score (ECLAM).

Results There were 421 women and 68 men, ratio 7:1. There were no differences between men and women concerning age, disease duration, age at disease onset and disease follow up. Except for serositis in men, which was significantly more frequent ($p = 0.01$), organ involvement was not statistically different between the two groups. Laboratory evaluation showed that women had significantly higher levels of erythrocyte sedimentation rate compared to men ($p = 0.001$), while positive anti-nuclear antibodies and raised complement levels were more frequent in women ($p = 0.08$). There were no significant differences in ECLAM scores between the two groups as well as in the disease outcome for SLE patients.

Conclusion SLE in men is a rare disease and the clinical expression and disease outcome seem to be similar to those described in women.

FRI0116 HYPERMOBILITY IN SISTEMIC LUPUS ERYTHEMATOSUS

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Background

Objectives To investigate hypermobility in patients in systemic lupus erythematosus (SLE).

Methods Setting: University Hospital; 80 patients with SLE (1999 ACR criteria), 90% females and 10% males, mean age 44 ± 16 , who regularly attended a specialist SLE clinic were examined. Control group was composed of 280 patients attending a general practitioner office, 70% females and 30% males, mean age 46 ± 19 . Joint laxity was measured according to Carter and Beighton criteria (total score 4 or more). A regression analysis was performed (SAS statistical package).

Results Forty-eight% or patients with SLE and 12% of the control group were hypermobile. Regression analysis showed that after adjustment for the age and sex, patients with SLE were more hypermobile (Odds Ratio:5). Neither the clinical and analytical profile nor the use of corticosteroids was related to hypermobility.

Conclusion Patients with SLE are more hypermobile than control group. No clinical or analytical profile is related. Steroids are not related to the presence of hypermobility in patients with SLE.

FRI0117 NEUROPSYCHIATRIC DISORDERS IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Neuropsychiatric symptoms of systemic lupus erythematosus (SLE) are one of the more common features and are the least understood.

Objectives To clarify the association of clinical manifestations and instrumental investigation findings in children with neurolupus.

Methods 20 children (aged 5–15 years) that met 4 or more ARA criteria of SLE were examined. Investigations included immune system changes indicating increased lupus activity, lupus anticoagulant, anticardiolipin antibodies by ELISA, electroencephalogram (EEG), in 10 patients magnetic resonance imaging (MRI).

Results The clinical manifestations of neurolupus were transient ischaemic attack (2), epilepsy (3), chorea (1), coordination disturbance (4), low extremity paresis (1). Eighteen children demonstrated psychiatric disturbances (psychosis, hysteria, fobia, anorexia, behavioural abnormalities). In all 20 children intensity of neuropsychiatric symptoms correlated with lupus activity. The most severe neuropsychiatric clinical manifestations were associated with the presence antiphospholipid antibodies. Instrumental assessment revealed pathologic abnormalities in both: children with subtle clinical symptoms and children with severe brain damage. EEG demonstrated diffuse abnormalities in 12 patients, epilepsy in 3, but not sensitive enough for diagnosis. MRI visualised diffuse and focal changes in 10 children: widening subarachnoid space and cortex atrophy.

Conclusion MRI can visualise diffuse and focal changes even in children with no history of overt symptoms of neurolupus and seems to be of real help in diagnosis. Antiphospholipid antibodies appeared to be the laboratory parameter most frequently relied upon in the diagnosis of neuropsychiatric SLE and in decision regarding treatment.

FRI0118 A CLINICOPATHOLOGICAL STUDY OF TUBULOINTERSTITIAL CHANGES IN PATIENTS WITH LUPUS NEPHRITIS

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Background The prognostic importance of renal involvement in Systemic Lupus Erythematosus (SLE) is well known. Predominant interstitial nephritis is a rare manifestation of SLE. The prognostic importance of histopathological tubulointerstitial (TIC) changes in renal tissue in patients with lupus nephritis (LN) is very little known.

Objectives Our objectives were to more precisely determine TIC in the renal tissue and correlate these data with clinical features, daily proteinuria and 24-hour creatinine clearance in pts with LN. Our long-term goal is to identify pts during clinical quiescence who may be at high risk of developing progression to renal failure from LN.

Methods Renal biopsies from 26 pts were analysed with emphasis on TIC. At the time of biopsy all pts had defined clinical evidence of active LN. Presence and intensity of oedema, inflammatory mononuclear infiltrate, fibrosis, hyaline casts and tubular atrophy were determined. TIC were graded from 0 to 3 (absent, mild, moderate and severe). We correlated these results with clinical data of 24-hour creatinine clearance (CC) and 24-hour urine total protein excretion (TP) at pre-treatment and post-treatment period.

Results Patients were divided into 4 groups: first group with absent TIC (0 score) 6 pts with TP mean 2.17 gr/24 h, CC mean 1.32 ml/s; second group with mild TIC (1–5 score), 12 pts with TP mean 2.61 gr/24 h, CC mean 0.76 ml/s; third group with moderate TIC (6 to 10 score) 5 pts with TP mean 2.67 gr/24 h, CC 0.95 ml/s; fourth group with severe TIC (11 to 15 score) 3 pts with TP mean 1.52, CC mean 0.37 ml/s. These analyses were repeated after treatment with corticosteroids and cytotoxic drugs at period of 3 to 6 months and correlated with previous data. Significant results occurred for TP in first group ($p < 0.05$) and in second group ($p < 0.01$), as well as in second group for CC ($p < 0.05$).

Significant improvement for both parameters occurred in group of 12 pts with mild TIC. (TP $p < 0.01$; CC $p < 0.05$). In group of pts with severe TIC, TP has decreased as well as CC.

Conclusion TP decrease as well as increase of CC correlated well with mild degree of TIC. TIC could be prognostic predictors in LN. This has to be proved with a greater number of pts.

FRI0119 HLA-DM POLYMORPHISM IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background HLA-DR (DRB1*15 and DRB1*03) component is weakly associated to SLE and other genes and genetic regions are investigated in order to better characterise the genetic predisposition to the disease. DMA and DMB genes are located within the HLA class II region. The alpha beta heterodimer encoded by these genes is directly involved in the HLA class II-restricted antigen presentation pathway. Limited nucleotide polymorphism has been described in the 3rd exon of the DMA and DMB genes.

Objectives To look for an association between DM polymorphism and SLE, the DMA and DMB allele distribution was compared between patients and controls from the same geographic area.

Methods 73 SLE patients were selected according to the 1997 ACR criteria. 147 unrelated control individuals were randomly selected (random controls: RC). A second group of 88 unrelated controls who were closely matched for DRB1 genotypes with patients was defined (matched controls: MC) in order to determine whether the association between SLE and certain DM alleles resulted from direct influence of the DM genes or indirect influence through linkage disequilibrium with alleles at the DRB1 locus. All the individuals were typed for DR and DM by SSOs after genomic DNA extraction of peripheral mononuclear cells and PCR. The significance of differences in phenotype frequencies was determined by Fischer's exact tests with Bonferroni correction.

Results 49.3% of the patients carry either DRB1*15/16 (21.9%) or DRB1*03 alleles (27.4%), or both. DMA*0103, DMA*0104 and DMB*0102 were found to be more frequent in SLE patients compared to RC ($p = 0.0012$, $p = 0.0012$, $p = 0.0097$, respectively). Similarly the frequency of these alleles was increased in patients compared to MC ($p = 0.0058$, $p = 0.0013$, $p = 0.017$, respectively) suggesting a direct influence of DM genes on SLE susceptibility. This direct influence was confirmed by showing no significant difference of DM allele frequencies between RC and MC. Finally, after stratification of the patients and the MC