16 are in part responsible for T cell abnormalities in SLE patients.

Objectives To investigate whether increased levels of IL-16 is a characteristic underlying susceptibility to SLE or is a characteristic of the disease itself.

Methods Accumulated organ damage was measured with the SLICC/ACR Damage Index. Twenty-five severe (SLICC/ACR: 4.9 + 2.5) and ten non-severe (SLICC/ACR: 1.0 + 0.8) SLE patients were included in this study. Also 11 first degree relatives and 12 healthy volunteers were included in this study. Plasma IL-16 levels were measured by ELISA.

Results No significant difference in the IL-16 levels of the first degree relatives of patients with SLE (38.3 + 11.1 pg/ml) were observed when compared to controls (31.2 + 10.1 pg/ml). In order to analyse characteristics of the SLE in relation to concentration of IL-16, IL-16 was measured in severe SLE patients (71.3 + 87.4 pg/ml; $P = 0.025$) compared to healthy controls. On the other hand, no significant differences were observed between the non-severe SLE patients (37.8 + 26.1 pg/ml) and controls.

Conclusion No evidence for increased IL-16 levels in first degree relatives of the SLE patients was observed. IL-16 is enhanced in SLE patients with a severe disease, but not in patients with non-severe disease, thereby suggesting that IL-16 is associated with disease severity, and not with susceptibility for SLE.

FRI0084 AUTOPSY REPORTS OF THE CEREBRUM OF 24 PATIENTS WITH SLE IN THE PERIOD 1988–99

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Background Clinical manifestations of neurologic involvement in patients with SLE (Neuropsychiatric SLE or NPSLE) may be either due to secondary causes such as antiphospholipid-syndrome associated infarctions or bleedings or infections, or due to primary causes such as immune-mediated vasculitis or cerebritis. Depending on the probable cause, different therapeutic approaches are chosen.

Objectives Previous reports on histopathologic have suggested that, since it is so seldomly found, cerebral vasculitis cannot be an important cause of neurologic symptoms in SLE.

Methods

Results However, a search in the computer archives of PALGA, the foundation that collects all pathology reports from Dutch PA-laboratories, beginning in 1988 and covering all reports since 1990, revealed vasculitis lesions in no less than 5 of 24 cranial autopsies of patients with SLE. In an additional 4, lesions were described that were compatible with remnants of previous vasculitis.

Abstract FRI0084 Table 1 Conclusions of autopsy reports of 24 consecutive patients with SLE in the medical history and a cranial autopsy report

Primary NPSLE	7
Secondary NPSLE	9 (4 bleeding, 5 infection)
Other causes	6
No abnormalities/insufficient information	1
Insufficient information	1

Conclusion These findings suggest that cerebral vasculitis must be considered as a possible underlying cause of symptoms when it comes to choosing therapy for patients with NPSLE.

FRI0085 ANTI-BETA-2- GLYCOPROTEIN I ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background

Objectives

Methods Anticardiolipin antibodies (aCL) react with negatively charged phospholipids, which may often be complexed with a protein cofactor such as beta-2-glycoprotein I.

Results To obtain information about the prevalence and levels of IgG anti- β 2-GPI, IgG- and IgM-aCL in systemic lupus erythematosus (SLE) patients (pts) these antibodies were measured, by an enzyme linked immunosorbent assay, in sera from 147 pts with SLE (70 men and 77 women). The results were compared with 20 healthy subjects. Anti- β 2-GPI were found positive (more than 3s.d. above the mean in normal controls) in 15 females (19,4%), 14 males (20%) in pts with SLE compared to 1 person (5%) in normal controls. 48,3% of pts with anti- β 2-GPI had the history of thrombosis, compared with 11,02% of pts without anti- β 2-GPI ($p < 0,001$). 35,7% of females with anti- β 2-GPI had the history of fetal loss, in comparison with 6,56% of anti- β 2-GPI negative pts.

APS was diagnosed in 16 (69,56%) anti- β 2-GPI (+)-aCL(+) pts ($n = 23$) and in 15 (37,5%) anti- β 2-GPI (-)-aCL(+) pts ($n = 40$) ($p < 0,01$). Anti- β 2-GPI(+)-aCL(+) pts had a history of thrombosis more frequently ($n = 14$, 60,86%) than anti- β 2-GPI (+)-aCL(-) ($n = 6$) ($n = 0$, 0%, $p < 0,002$).

Our data show that the presence of anti- β 2-GPI simultaneously with aCL is strong associated with APS in SLE.

Conclusion

FRI0086 CHARACTERISATION OF RA33 (HNRNP-A2/B1)-AUTOREACTIVE T CELLS IN SLE-PATIENTS

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Background SLE is a systemic autoimmune disease with distinct immunological characteristics including defective T cell functions, especially concerning IL2 production and proliferation. Furthermore, B-cell hyperactivity is observed leading to the formation of several characteristic autoantibodies (ab), among them ab to the heterogenous nuclear ribonucleoprotein A2/B1 (hnRNP/RA33). These antibodies are known to occur in over 20% of SLE patients.

Objectives In order to elucidate the role of T cells and their influence in antibody production in SLE, we studied proliferation of PBMC to purified hnRNP-A2/B1 in SLE patients and healthy controls.

Methods Stimulation assays with PBMC of 34 SLE patients and 21 healthy controls were performed. We then proceeded to draw RA33-specific T cell clones (TCC) by cultivation and limiting-dilution cloning of T cell lines.

Results While the stimulation indices (SI) in the healthy control group ranged from 0.5 to 3.5 (mean SI: 1.5 ± 0.9), the proliferative response of PBMC of the patient group ranged from 0.7 to 17 with a mean SI of 4.8 ± 4.0 (only 6 of 34 patients had an SI < 2 ; $p < 0.00004$). The generated 30 TCC derived from SLE patients and 19 TCC from healthy controls did not reveal a significant difference in SI and produced either more IFN γ than IL4 or none of these cytokines at all, suggesting that these TCC were of T1 or T0, but not T2 phenotype. Interestingly though, while only 11% of healthy control patients showed a CD4-/CD8 $^{+}$ subtype and 16% displayed a CD4 $^{+}$ /CD8 $^{+}$ phenotype, 37% of TCC derived from SLE patients were CD4-/CD8 $^{+}$ (and 20% expressed CD4 as well as CD8).

Conclusion Our data reveal that more than 80% of SLE-patients have a significant T cell reactivity (SI > 2) to the nuclear protein hnRNP-A2/B1 indicating that the antibody response might be T cell driven. Furthermore, almost 60% of TCC derived from SLE patients were CD8 $^{+}$, which supports the importance of these T cells in SLE. Further studies will have to elucidate the pathogenetic implications of these findings.

FRI0087 ANAEMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Systemic lupus erythematosus (SLE) is accompanied by haematological abnormalities. A very common haematological abnormality observed in SLE is anaemia. It is well known that anaemia in SLE may have many causes, however no correlation has been performed between anaemia and the morphology of red blood cell precursors in the bone marrow in SLE.

Objectives The aim was to investigate the aetiology of anaemia in SLE by analysing blood, bone marrow aspirate and bone marrow biopsy findings.

Methods SLE patients were included in the study, $n = 17$, aged 40.9 ± 3.6 (range 18–36) years. None of the patients were taking any disease modifying agents and 11 were newly diagnosed and had never taken any treatment for SLE, duration of disease of the remaining being 5.7 ± 3.6 (range 1–23) years. In all patients antinuclear antibodies, anti-DNA antibodies and serum rheumatoid factor were measured. Haematocrit, haemoglobin, MCV, MCH, MCHC, serum iron, serum ferritin, serum iron-binding capacity, serum folate and vitamin B12 levels were also measured and indirect and direct Coombs' test was performed. In all patients a bone marrow aspirate was obtained and a bone marrow biopsy was performed.

Results In 17 SLE patients haemoglobin levels were 11.4 ± 0.4 g/dl (mean $\pm$ SEM), haematocrit $35.0 \pm 1.3\%$, MCV 88.9 ± 1.2 fl, MCH 29.0 ± 0.4 pg, MCHC $32.7 \pm 0.1\%$, serum iron levels 83.2 ± 7.2 μ g/dl, serum iron-binding capacity 359.0 ± 11.2 μ g/dl, ferritin levels 123.1 ± 65.3 μ g/dl, folate 6.4 ± 1.1 ng/ml and vitamin B12 levels 534.7 ± 79.4 pg/ml. In 10 of 17 patients with SLE haemoglobin levels were 12 g/dl, hyperplasia of red blood cell precursors was noted in all of them, megaloblastoid alterations in 3 and blasts of the red cell series in 2 patients. No correlation was observed between the presence or absence of anaemia and the dysplastic alterations in the red blood cell precursors in the bone marrow in the SLE patients studied.

Conclusion The aetiology of anaemia in SLE patients seems to be multifactorial. Dysplastic alterations in red blood cell precursors was noted in all the groups of SLE patients, irrespective of the presence of anaemia, indicating either a primary defect of the stem cell in the bone marrow in SLE which is implicated in the pathogenesis of the disease or that inflammatory cytokines may affect the microenvironment of the bone marrow.

FRI0088 POLY(ADP-RIBOSE) POLYMERASE (PARP) POLYMORPHISM IN SPANISH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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Background PARP is a DNA-binding protein that catalyses the covalent addition of ADP-ribose to many nuclear proteins. It is involved in DNA repair and apoptosis, processes that have been implicated as causative factors for SLE. It has been shown that patients suffering SLE have decreased PARP mRNA levels and a low enzyme activity. The PARP gene is located at 1q41-q42 and contains a microsatellite (CA) $_n$ polymorphism in the promoter region that probably affects the transcription and mRNA levels. A recent study found preferential transmission of the allele containing 12 CA repeats to affected offspring in Caucasian SLE families.

Objectives To investigate the association between PARP polymorphism and SLE susceptibility in Spaniards.

Methods 76 unrelated SLE patients from Canary Islands (Spain) fulfilling at least four of the ACR criteria and 79 sex-matched healthy donors were included. A segment of the PARP gene containing the microsatellite was amplified by PCR and the resulting products were electrophoresed in denaturing polyacrilamide gels. Chi-square test was used for statistical analysis.

Results Allelic distributions of PARP polymorphism showed no statistical differences between SLE patients and controls. But considering particular clinical features we found several associations with specific alleles: a) homozygotes for 11rep. allele suffered more lymphopenia ($p = 0.04$) but less hypocomplementemia ($p = 0.03$), b) autoantibodies anti-Ro/La were more frequent ($p = 0.02$) in carriers of 15rep., c) carriers of 16rep. allele presented more malar rash ($p = 0.03$) and seizures ($p = 0.04$), and finally d) carriers of 17rep. allele showed a reduced risk of production of several autoantibodies as anti-Sm ($p = 0.007$) and anti-Ro/La ($p = 0.04$).

Conclusion Although PARP alleles seem not to influence susceptibility to SLE in Spaniards, some of them may be related to the presence of several clinical and analytical manifestations of the disease.

FRI0089 IL10G PROMOTER POLYMORPHISM OF THE INTERLEUKIN 10 (IL10) IN SPANISH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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