Hierarchical Cluster Analysis of Systemic Lupus Anti-Nuclear Antibody Pattern and Clinical Ischaemic Stroke in Systemic Lupus

Background and aims Systemic lupus erythematosus (SLE) is a heterogeneous disorder with diverse manifestations and serologic features. The purpose is to categorise SLE patients into similar initial characteristics.

Methods Hierarchical cluster analysis approached to 389 SLE patients and 10 laboratory values. Laboratory values were transformed into Z-score for hierarchical clustering. Ward’s method as agglomeration method was a criterion applied with fisher’s exact test. To find each SLE cluster using initial laboratory, linear discriminant analysis was applied.

Results Three clusters were revealed by initial laboratory data; Cluster 1 had higher anti-dsDNA antibody, ANA titer and ESR, and low complements, lymphocyte, haemoglobin and platelet counts, Cluster 2 had lower anti-dsDNA antibody, ANA titer and ESR, and Cluster 3 had lower anti-dsDNA antibody titer, WBC and lymphocyte counts, and higher ANA titer. As a result from analysing cumulative manifestations and treatment, Cluster 1 showed more frequent malar rash, alopecia and renal disease with higher SLEDAI, and more use of cyclophosphamide and azathioprine. Also, oral ulcer was developed frequently in Cluster 2. During disease duration, total and mean corticosteroids and the number of flare were higher in Cluster 1.

Conclusions With initial laboratory values, SLE patients could be divided 3 clusters. Each Cluster showed different characteristics in clinical manifestations and treatment patterns. This predictive model considered disease severity had 84.6% of total predictability.

Ischaemic Stroke in Systemic Lupus Erythematosus, Distribution of Subtypes and a Risk Genotype in the STAT4 Gene

Background and aims We investigated the distribution of ischaemic stroke subtypes, classified according the Trial of Org 10 172 in Acute Stroke Treatment (TOAST) system, among patients with systemic lupus erythematosus (SLE). Genetic susceptibility in the signal transducer and activator of transcription factor 4 (STAT4) gene, defined by the single nucleotide polymorphism (SNP) rs10181656(G) were explored.

Methods We identified 69/665 SLE patients with stroke. Medical charts were retrieved and brain, cardiac and vascular imaging at the time of stroke were examined. Classification was performed according to TOAST: large-artery atherosclerosis (LAA), cardioembolism (CE), small-artery occlusion (SAO), stroke of other determined aetiology (OC) and stroke of undetermined aetiology (UE). Occurrence of the anti-phospholipid syndrome (APS) was documented. Evaluators were blinded to genotypes. General population controls (n=658) and SLE patients free from previous cerebrovascular disease (n=517) were used as comparators.
Results 56/69 patients with ischaemic stroke had charts with sufficient information for TOAST classification. Median age was 52 (17–84) years, 91% were female. All strokes classified as OC were attributed to APS. TOAST classification is presented in Table 1. Stroke of OE/APS and CE origin were associated with the STAT4 risk genotype as presented in Table 2.

Conclusions The majority of ischaemic strokes among SLE patients were of APS or CE origin. These two subtypes were associated with genetic susceptibility in the STAT4 gene. Patients with APS associated strokes were remarkably young. STAT4 genotype could, in addition to antiphospholipid antibodies and echocardiography, add information about stroke risk and help identify patients who will benefit from prophylactic anticoagulation treatment.