IFN type I score in children with systemic lupus erythematosus: single center experience

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Background

Systemic lupus erythematosus (SLE) is characterized by substantial clinical and genetic heterogeneity. Interferon type I-signaling pathway plays essential role in the pathogenesis of SLE. The associations between IFN-I score and disease activity, clinical manifestations were controversial in previous studies. Genetic nature of SLE is still unknown.

Objectives

to analyze IFN-I score and evaluate association with clinical parameters in SLE children.

Methods

40 SLE patients (33 girls, 7 boys) under 18 years old were enrolled in the study. The data about clinical manifestations, laboratory findings in the onset of the disease and at the time of interferon signature assessment were evaluated. Interferon signature was assessed by RT-PCR quantitation of 5 IFN I-regulated transcripts; median relative expression of ≥2 was considered as a threshold. DNA samples of patients having highest IFN-scores were subjected to clinical exome sequencing.

Results

The mean age of disease onset was 12 (9.5; 14.0) years. The most frequent clinical manifestation were skin involvement (85%), arthritis (67.5%), fever (55%), mucosa (45%), CNS (37.5%) and kidneys (30%) involvement in the disease onset. Anemia, leukopenia and thrombocytopenia were registered in 62.5%, 27.5% and 50% cases. 87,5% and 70% of patients had ANA and RF positivity. The comparison of patients with high IFN-I score (31 patients) and normal IFN-I score (9 patients) at the time of IFN-I score measurement is presented in the Table 1.

Pathogenic or likely pathogenic variants in lupus-associated genes (C1QA, RNASEL, DDX58) were identified in 4 of 10 patients with IFN score of ≥ 10 (Table 2).

Key points:

1. Increased IFN-I score is associated with kidney involvement

2.Patients with increased IFN-I score required more aggressive treatment

3. Children with SLE have rare possible causative variants in lupus-associated genes

4.The prognostic value of IFN-I score required further investigations

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Table 1. Pediatric SLE patients with increased and normal IFN-I score

Parameters	Increased IFN-I score	Normal IFN-I score	p-value
Girls, n (%)	25 (80.7)	8 (88.9)	0.567
The age of onset, years	12.0(10.0; 14.0)	11.0 (9.0; 13.0)	0.353
Time to IFN-I score measurement, months from the onset	18.3 (7.0; 26.5)	0.97 (0.87;1.73)	0.987
Skin involvement, n (%)	12 (38.7)	4 (44.4)	0.837
CNS involvement, n(%)	8 (25.8)	1 (11.1)	0.353
Nephritis, n(%)	12 (38.7)	0 (0.0)	0.026
Arthritis, n(%)	11 (35.5)	2 (22.2)	0.455
Anemia, n(%)	9 (29.0)	2 (22.20	0.687
Leukopenia, n(%)	9 (29.0)	1 (11.1)	0.274
ANA-positivity, n (%)	27 (87.1)	5 (55.6)	0.037
Anti dsDNA antibodies, n(%)	12 (38.7)	2 (22.2)	0.361
RF-positivity, n (%)	11 (35.5)	0 (0.0)	0.036
Hypocomlementemia, n (%)	18/28 (64.3)	2/6 (33.3)	0.162
Ferritin level, mkg/l	112.0 (39.0; 271.0)	21.0 (5.3; 23.7)	0.0008
Hematuria, n (%)	10 (32.3)	0 (0.0)	0.049
Proteinuria, n (%)	11 (35.5)	0 (0.0)	0.036
SELENA-SLEDAI, points	9 (2;15)	1 (0; 4)	0.073
ECLAM, points	3.0 (1.0; 6.0)	1.0 (0.0; 1.5)	0.048
The use of Rituximab and/or Cyclophosphamide, n (%)	22 (71.0)	3 (33.3)	0.040
The dose of CS 0.2mg/kg achievement in 6 months, n (%)	9/21 (42.9)	5/6 (83.3)	0.080

Table 2. Characteristics of patients with mutations

Mutation	Clinical manifestations	IFN-I score	Treatment
C1QA,homo	Skin, mucosa involvement, immunodeficiency	38	CS, RTX, MMF, IVIG
RNASEL	APS, arterial thrombosis	10	CS, anticoagulant
RNASEL	Myositis, APS	11	CS
DDX58	Skin, mucosa, arthrtitis, nephritis, cytopenia, serositis	21	CS, RTX, MMF

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