Fas and Bcl-2 expression on peripheral blood T and B lymphocytes in juvenile-onset systemic lupus erythematosus and the relationship with disease activity

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INTRODUCTION

- Apoptosis is responsible for the deletion of auto-reactive T and B lymphocytes in central and peripheral tolerances.
- During apoptosis lupus specific autoantigens are exposed on the surface of apoptotic cells.

Andrade et al., Rheum Dis Clin North Am. 2000;26:215-27.
Casciola-Rosen et al., J Exp Med. 1994;179:1317-30.
White et al., Curr Opin Rheumatol. 2003;177:557-62.

INTRODUCTION

- Fas and Bcl-2 are the main proteins involved in the control of apoptosis.

- An altered expression of these proteins may:
  - result in the presence of peripheral autoreactive T and B lymphocytes.
  - contribute to the exposure of lupus specific autoantigens to the immune system.

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OBJECTIVES

- To examine the expression of Fas and Bcl-2 proteins on peripheral blood T and B lymphocytes from patients with Juvenile-onset Systemic Lupus Erythematosus (JSLE).
- To correlate the expression of these two proteins with SLE disease activity index score (SLEDAI).

METHODS

- 38 children and adolescents with JSLE
  11 with active disease (SLEDAI score≥8)
- 21 sex-and age-matched healthy controls
- Freshly isolated peripheral blood lymphocytes were stained for CD3, CD4, CD8, CD19 and for Fas and Bcl-2 proteins.
- Expressions of Fas and Bcl-2 proteins were measured by three-color flow cytometry.
- Statistical analysis used Kruskall-Wallis test and Sperman's rank. $p \leq 0.05$ was significant.

RESULTS

Percentage of lymphocytes positively stained for Fas - Mean ± SD

Subjects	N°	CD3+ T cells	CD4+ T cells	CD8+ T cells	CD19+ B cells
JSLE	38	43.7 ± 10.3 *	20.3 ± 6.7 *	21.5 ± 9.6 *	2.1 ± 1.4 *
Healthy controls	21	28.9 ± 9.4	16.2 ± 6.2	12.3 ± 5.8	1.4 ± 0.7

* $p<0.05$ patients vs healthy controls

The density of Fas antigen expressed on cell surface measured by mean fluorescence intensity (MFI) was higher ($p<0.05$) in JSLE patients compared to healthy controls on CD8+ T cells (26.1±5.5 vs 21.5±1.6) and on CD4+ T cells (45.3±10.7 vs 39.4±4.9).

RESULTS

Mean fluorescence intensity (MFI) of Bcl-2 positive lymphocytes - Mean ± SD.

Subjects	N°	CD3+ T cells	CD4+ T cells	CD8+ T cells	CD19+ B cells
JSLE	38	28.8 ± 8.4 *	28.6 ± 8.2 *	29.4 ± 9.3 *	25.5 ± 9.6 *
Healthy controls	21	22.9 ± 4.2	22.9 ± 4.4	22.8 ± 3.6	21.5 ± 3.6

* $p<0.05$ patients vs healthy controls

Percentages of lymphocytes positively stained for Bcl-2 protein did not differ between JSLE patients and healthy controls.

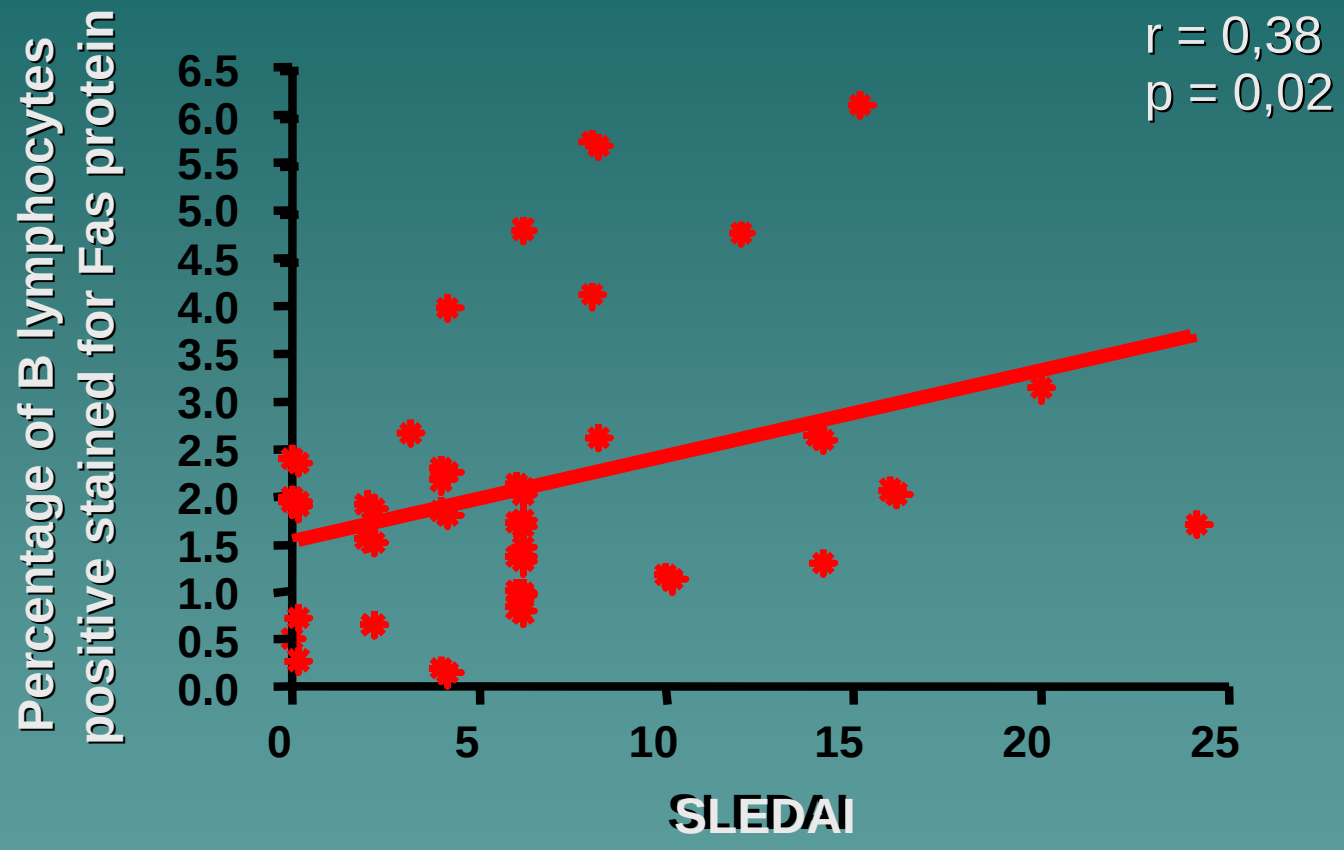
RESULTS

Percentage of lymphocytes positive stained for Fas on active and inactive JSLE patients - Mean ± SD.

Subjects	N°	CD3+ T cells	CD4+ T cells	CD8+ T cells	CD19+ B cells
Active JSLE	11	47.1 ± 10.1 &	23.9 ± 7.8 &	23.4 ± 10.7 &	3.2 ± 1.7 * &
Inactive JSLE	27	42.4 ± 10.2 &	18.8 ± 5.7	20.7 ± 9.3 &	1.7 ± 1.0
Healthy controls	21	28.9 ± 9.4	16.2 ± 6.2	12.3 ± 5.8	1.4 ± 0.7

* $p<0.05$ active JSLE patients vs inactive JSLE patients
& $p<0.05$ JSLE patients vs healthy controls

RESULTS



Correlation between CD19+ B cells positive for Fas and SLEDAI score.

CONCLUSIONS

- The occurrence of circulating T and B lymphocytes with abnormally high Fas and Bcl-2 expression suggest a dysregulation of apoptosis in patients with juvenile-onset systemic lupus erythematosus.

- These data also suggest that JSLE patients with active and inactive disease present different profile of Fas expression.