ANTIBODIES TO EARLY EBV ANTIGEN ASSOCIATE WITH THE GENERATION OF ANTI-DOUBLE STRANDED DNA ANTIBODIES AND ACTIVITY OF LUPUS NEPHRITIS

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INTRODUCTION

Epstein-Barr virus (EBV) has long been suggested to be one of the potential triggers of systemic lupus erythematosus (SLE) [1, 2]. Recent results performed on cohorts of patients disclosing a low/intermediate disease activity point to an aberrant control of EBV reactivation in SLE. In this respect, of particular value seems to be the serological response to early EBV antigen [3-5].

AIM

Our aim was to compare the antibody levels against early and late EBV antigens between healthy controls (C) and patients with lupus nephritis (LN) that is the condition having one of the worst prognoses among SLE manifestations.

MATERIAL AND METHODS

The study involved 51 C subjects and 39 patients with LN (mostly with class III and IV of LN) at median age 32 (25-45) years. The median time from SLE diagnosis was 24 (6-60) months. The median total SLE activity calculated by scoring the SLE disease activity index (SLEDAI) was 16 (8-20) points. The activity of LN, assessed by calculating kidney SLEDAI (K-SLEDAI), was eight (4-16) points. Levels of anti-dsDNA antibodies, C3 and C4 were, respectively, 392 (135-672) IU/mL, 0.6 (0.42-0.84) g/L, and 0.09 (0.06-0.16) g/L, thus reflecting a relatively high immunological activity of the disease. Serum levels of antibodies to EBV early antigen (EA), EBV viral capsid antigen (VCA), and EBV nuclear antigen-1 (EBNA1) were determined in IgG (EA-G, VCA-G, EBNA1-G) IgA (EA-A, VCA-A, EBNA1-A), and IgM (EA-M, VCA-M, EBNA1-M) classes using the specified enzyme-linked immunosorbent assays.

RESULTS

Ninety-five percent of LN patients and 80.4 % subjects from the C group were seropositive for EBNA1-G, thus revealing previous EBV infection. This was confirmed by seropositivity for VCA-G in 99.4 % of LN patients and 94% of C. The frequencies of EA-G, EA-A and EA-M detection differed highly significantly between C and LN (***Fig. 1***). The serum levels of these antibodies followed the pattern observed for their frequency of detection (***Fig. 2A, 2B, 2C***). Furthermore, although it did not reach a statistical significance, EBNA1-G reactivity was lower in LN than in C. In addition, significant correlations between serum levels of EA-A and anti-dsDNA (***Fig. 3***) as well as EA-M and anti-dsDNA (***Fig.4***) were observed.

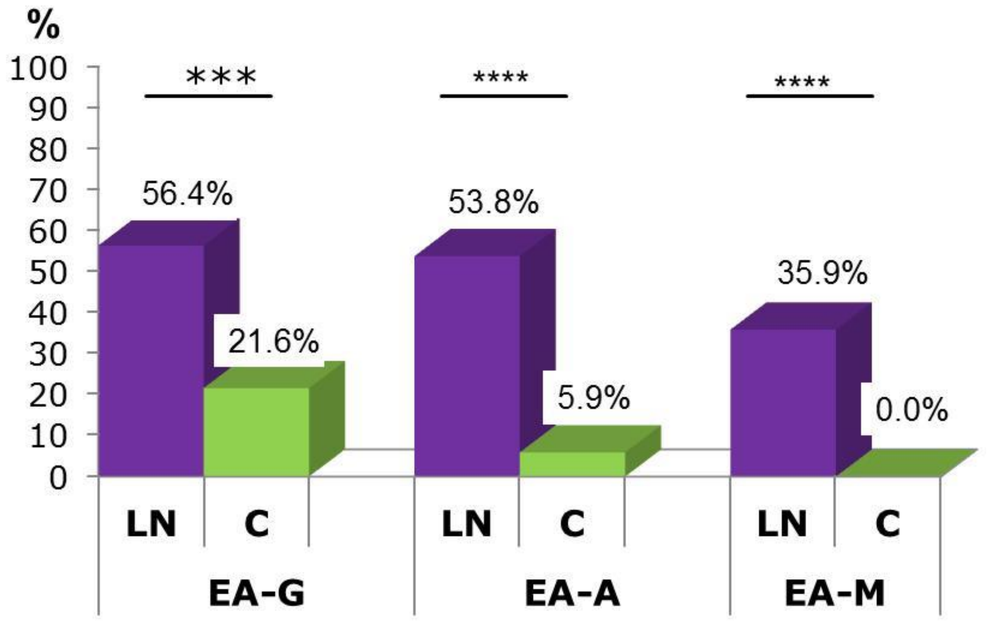

Fig. 1. **Frequency of EA-G, EA-A, and EA-M detection in patients with LN and in the C group.**

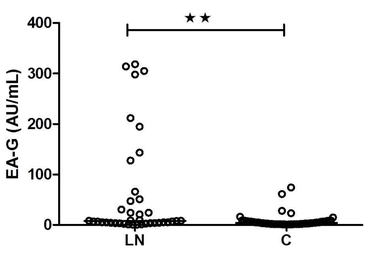

Fig. 2A. Serum levels of EA-G in patients with LN and in C.

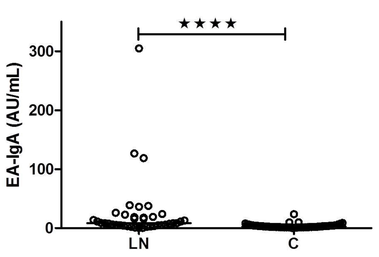

Fig. 2B. Serum levels of EA-A in patients with LN and in C.

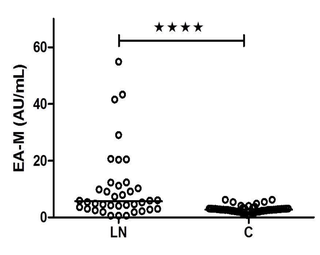

Fig. 2C. Serum levels of EA-M in patients with LN and in C.

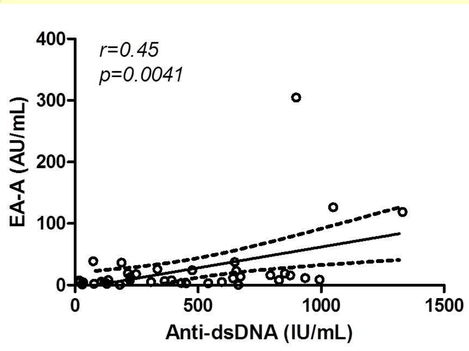

Fig. 3. Correlation between levels of anti-dsDNA and EA-A in LN.

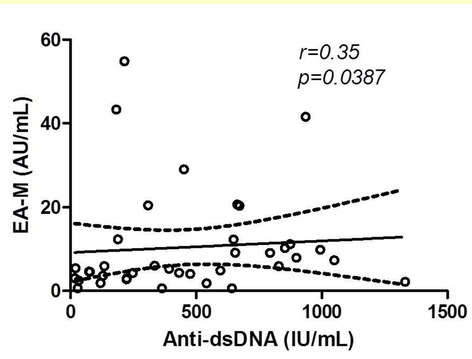

Fig. 4. Correlation between levels of anti-dsDNA and EA-M in LN.

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Compared to EA-A (-) and EA-M (-) subjects, levels of anti-dsDNA were significantly higher in EA-A (+) (p=0.0013) and EA-M (+) (p=0.0199) patients. Moreover, concentrations of C3 and C4 were significantly lower in the latter group of patients (p=0.0439 and p=0.0026, respectively) with significant correlations between levels of EA-M and C3 (***Fig. 5***), and particularly C4 (***Fig. 6***).

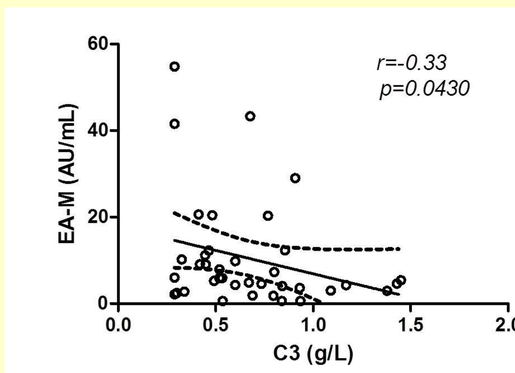

Fig. 5. Correlation between levels of C3 and EA-M in LN.

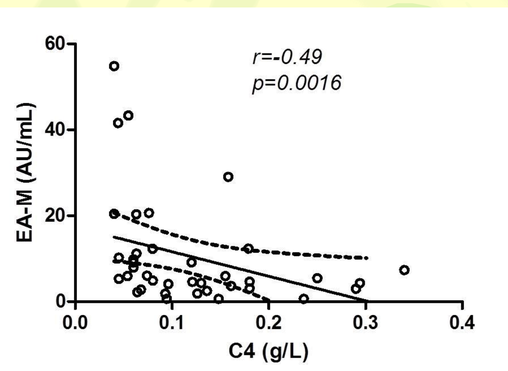

Fig. 6. Correlation between levels of C4 and EA-M in LN.

In relation to the clinical activity of LN, a significant correlation between the levels of EA-G and K-SLEDAI was noted (***Fig. 7***). Taking into account time from SLE diagnosis, it was shorter in EA-M (+) subjects (***Fig. 8***).

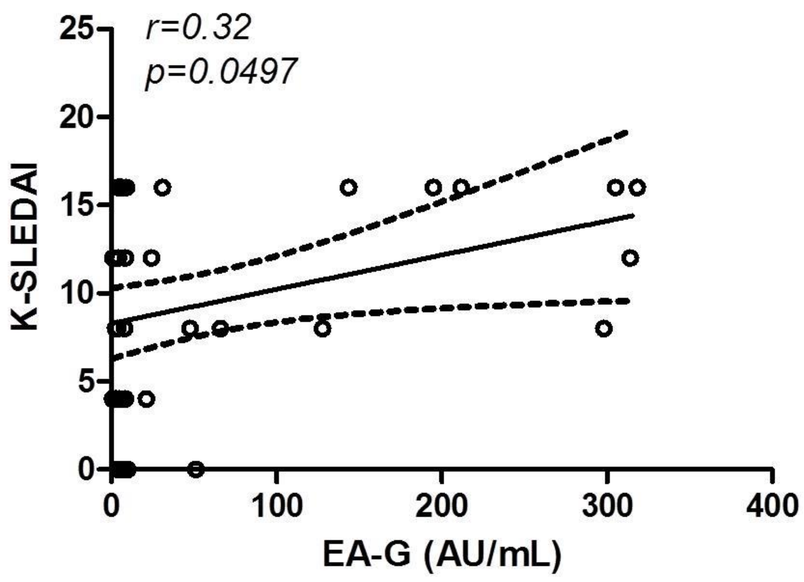

Fig. 7. **Correlation between levels of EA-G and K-SLEDAI in LN.**

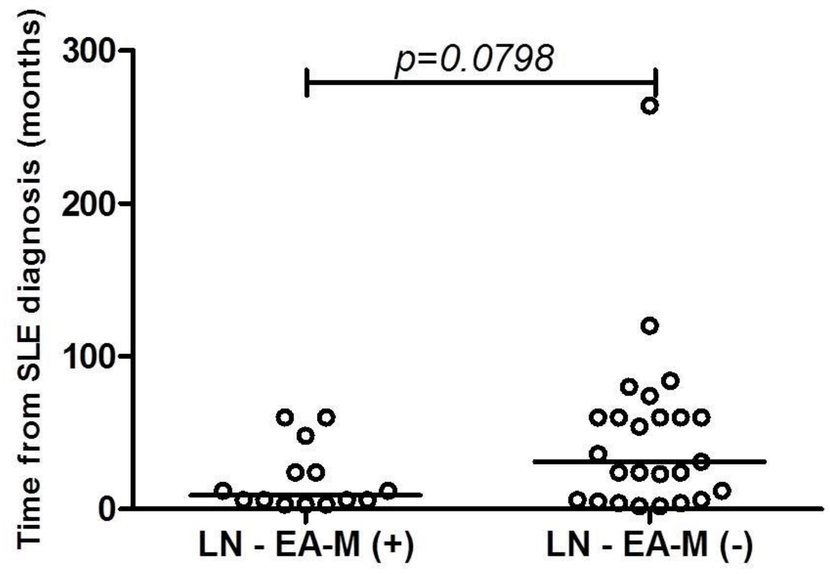

Fig. 8. **Time from SLE diagnosis in EA-M (+) and EA-M (-) LN patients.**

CONCLUSIONS

- Our results confirm the previous suggestions that the control of EBV reactivation is lost in SLE.
- Moreover, responses to the lytic EBV antigen associate with the formation of anti-dsDNA antibodies and low complement activity, thus contributing to LN activity.
- Further studies, particularly those including patients with primary glomerulonephritides are required in this field.

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