PREDICTIVE VALUE OF ANTI-C REACTIVE PROTEIN ANTIBODIES IN LUPUS NEPHRITIS

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Introduction: Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus (SLE). In SLE tissues are damaged by pathogenic autoantibodies and immune complexes. Physiological role of monomeric CRP (mCRP) is opsonization, elimination of immune complexes, and clearance of apoptotic cells. This is achieved by interaction of mCRP with C1q and factor H [1]. Anti-mCRP antibodies (aCRP-Ab) might lead to decreased clearance of apoptotic cells and thus be involved in pathogenesis of LN [2].

A high prevalence of aCRP-Ab in SLE and LN patients was previously described [3-6]. Sjöwall *et al.* [4] proved that levels of aCRP-Ab predicted a poor response to therapy.

Table 1: Baseline characteristics

	aCRP-Ab positive (n=13)	aCRP-Ab negative (n=16)	p
s-creatinine (umol/l)	71 (47-147)	82 (52-253)	NS
C_{Cr} (ml/s)	1.48 (0.64-2.81)	1.4 (0.2-3.06)	NS
Proteinuria (g/day)	1.04 (0.26-6.36)	0.76 (0-1.6.44)	NS
Erythrocyturia	87.5%	82.4%	NS
SLEDAI	17 (9.2-22.6)	16 (4.0-29.2)	NS

Table 2: Therapy

	aCRP-Ab positive (n=13)	aCRP-Ab negative (n=16)
Induction Therapy		
Cyclophosphamide	9	8
Mycophenolate mofetil	2	3
Cyclosporine A	1	2
Azathioprine	1	2
Plasmaferesis+CPH	0	1
Maintenance Therapy		
Azathioprine	5	9
Mycophenolate mofetil	2	4
Cyclosporine A	4	2

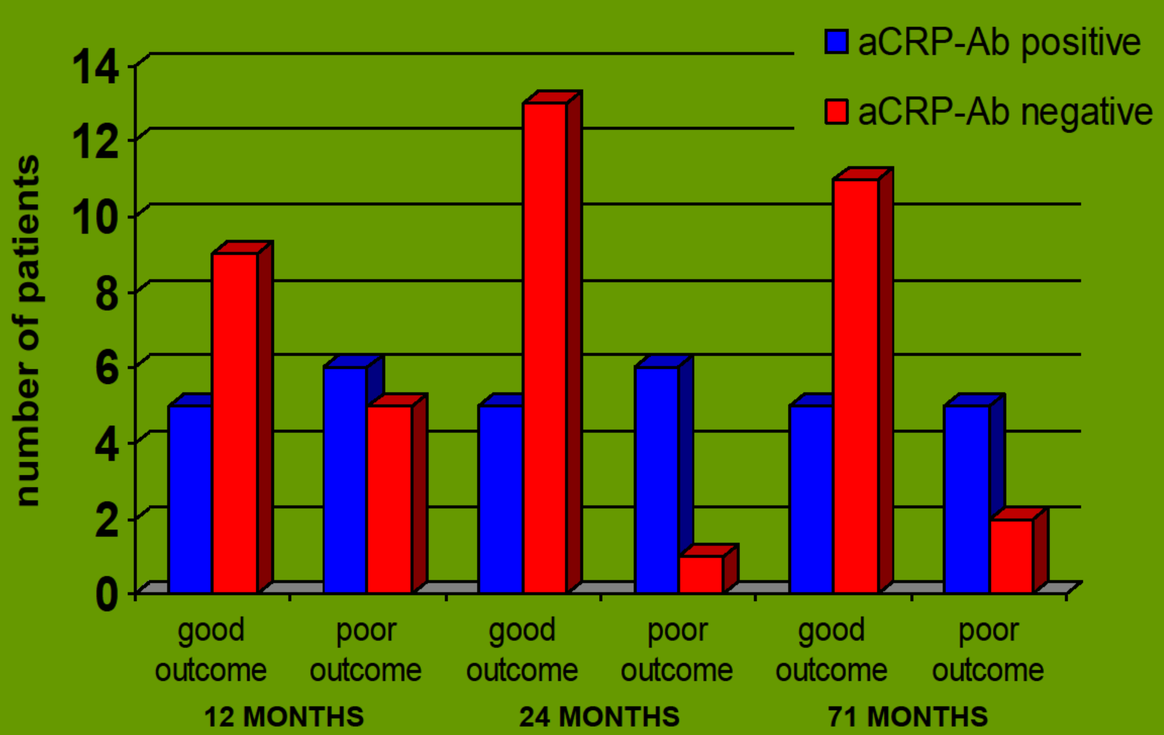
Aim: To assess the possible association between baseline levels of aCRP-Ab at the time of renal biopsy and therapeutic response in long term follow up.

Methods: Patients (n=29;median age 31 years; M/F 3/26) with definite diagnosis of SLE according to American College of Rheumatology criteria and newly diagnosed active proliferative form of LN were enrolled to the study between 2005-2010 and followed up at the Department of Nephrology and/or the Institute of Rheumatology. Basic patient characteristics are described in Table 1. Response to therapy was assessed with the respect to baseline aCRP-Ab positivity after one and two years of treatment; median length of follow up was 5.9 years. Data from total of 23 patients were available for analysis at the end of follow-up (March 2014). Response to therapy was measured according to the European consensus criteria [7]. Overview of induction and maintenance therapy is listed in Table 2. At least partial response after the first year and second year of treatment was considered as a good outcome and no response to treatment, renal flare and end stage renal disease (ESRD) as a poor outcome. Renal flare was defined based on intention-to-treat principles. In the long term follow up we counted renal flares, at least one flare was considered as a poor outcome. Levels of aCRP-Ab were measured by using an in-house ELISA method according to Sjöwall *et al* [8] with slight modifications. All samples were analyzed in quadruplicates. The cut off value for positive test was set as the 95th percentile in 122 healthy individuals.

Statistics

Results are presented as median and 5-95 percentiles or odds ratio (OR) and 95% confidential interval (95% CI). Mann-Whitney rank sum test was calculated using STATISTICA (version 9), logistic regression was calculated using EpiInfo (version 3.5.3).

Figure 1: Clinical outcome in follow up



Results: After first year of therapy aCRP-Ab positivity was not a risk factor for worse response to therapy, (OR; 95%CI=1.8;0.3-11.4, p=0.268).

Patients with **baseline positivity of aCRP-Ab** had a very high risk of renal flare or no response to therapy after two years of therapy compared to aCRP-Ab negative patients **(OR;95%CI =13.7;1.2-770.9, p=0.014).** See figure 1.

Non response to therapy in the first year proved to be a predictor of poor outcome in the second year **(OR; 95% CI=10.8;1-596.6; p=0.027).** These two predictors seemed to be independent and ORs of these risk factors were similar (10.8 and 13.7), we considered them as equipotent risk factors and analyzed using logistic regression.
Each of these risk factors increases the risk of poor outcome **(OR; 95% CI =26.3;2.2-308.7, p=0.009).** The OR in patients **having both risk factors** would be doubled, meaning the patients have to face **more than fifty times higher probability of poor outcome** compared to patients without any risk factor.

In the long-term follow up baseline aCRP-Ab positivity was a not risk factor for higher incidence of renal flares . This difference reached only borderline statistical significance, most likely due to low number of patients involved (OR;95%CI=5.1;0.6-71.1, p=0.092). See figure 1.

Conclusions: **aCRP-Ab seem to predict poor outcome after two years of standard therapy, while its role for long-term risk prediction requires further and larger studies.**

Project was supported by grant of Czech Society of Nephrology, No 2008/01

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DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.