

January 01/09: IgA-class antibodies to CCP

The discovery of anti-citrullinated peptide (CCP) antibodies has had a large impact on routine serological testing of rheumatoid arthritis (RA). Besides being highly specific diagnostic markers for RA, anti-CCP tests serve as predictors of disease course and outcome. As most clinically relevant autoantibodies are from the IgG isotype, commercial anti-CCP tests generally work with IgG conjugate. On the other hand, the rheumatoid factor of the IgA isotype is known to be important in RA. Thus, more and more studies are done to investigate the diagnostic and prognostic role of IgA-class anti-CCP such as the following study from Svärd et al:

Svärd A, Kastbom A, Reckner-Olsson A, Skogh T

Presence and utility of IgA-class antibodies to cyclic citrullinated peptides in early rheumatoid arthritis: the Swedish TIRA project

Arthritis Res Ther 2008, 10: R75 (doi: 10.1186/ar2449)

Serum samples were available from 228 patients at the time of diagnosis of RA, and from 72 of these patients at the 3-year follow-up. 66 of the 228 sera (29%) tested positive for IgA anti-CCP, compared with 64% regarding IgG anti-CCP. All sera testing positive for IgA anti-CCP were also positive in the IgG assay. The levels of IgG anti-CCP and IgA anti-CCP showed a high degree of correlation. The IgA-positive sera had significantly higher levels of IgG anti-CCP as compared with the IgG anti-CCP-positive sera without concomitant IgA. IgA-anti-CCP-positive patients tended to have a more severe disease course over 3 years as compared with IgA-negative cases with the same baseline levels of IgG anti-CCP.

The status of IgA anti-CCP positivity remained essentially stable at the 3-year follow-up: 93% of patients were therefore unchanged regarding IgA anti-CCP positivity. 1 patient had changed from negative to positive and 4 had changed from positive to negative.

The authors concluded that measuring anti-CCP antibodies of the IgA class does not offer any diagnostic information in addition to IgG anti-CCP analysis. However, further efforts are justified to investigate the prognostic implications.

Indeed, another Swedish study by Johan Rönnelid and his group was done last year which was published as a poster last autumn:

Mullazehi M, Wick MC, Kristensen B, van Vollenhoven R, Klareskog L, Rönnelid J

Diagnostic and prognostic value of IgG and IgA antibodies against cyclic citrullinated peptides (anti-CCP) among early rheumatoid arthritis patients (RA)

Poster shown at the 6th International Congress on Autoimmunity in Porto in September 2008

They investigated 270 patients with RA and 100 healthy controls for IgG and IgA anti-CCP. 166 of 270 patients (61.5%) showed positive values of IgG anti-CCP and 173 of 270 patients (64%) had increased IgA anti-CCP antibody levels. In contrast to the study by Svärd et al, the authors found 29 patients which were negative for IgG but positive for IgA anti-CCP, resulting in a total sensitivity of 72% for IgA and/or IgG anti-CCP. Thus, here the use of both IgA anti-CCP and IgG anti-CCP yielded a greater sensitivity together with unchanged specificity compared to the IgA anti-CCP test alone. In this study, patients only positive for IgA anti-CCP had a better prognosis compared to patients lacking both IgG and IgA anti-CCP antibodies. According to the authors of this study, the additional diagnostic contribution of IgA anti-CCP in early RA might be clinically important to diagnose more RA patients at an early stage.

Obviously, the diagnostic value of IgA-type anti-CCP antibodies is still discussed controversially as different patient panels might lead to different results. In our eyes, further studies are needed for a final conclusion.

