Publication of the Month

November 11/09: CCP 2 – Usefulness in Very Early Arthritis Diagnosis

Early diagnosis of rheumatoid arthritis is difficult since patients with very recent arthritis (≤12 weeks of evolution) may have been diagnosed with other diseases, including self-limited arthritis. The classification criteria for RA of the American College of Rheumatology (ACR) are ineffective for patients with recent onset arthritis. Machold et al. suggested that a diagnosis of RA in patients with very recent onset arthritis may be accurate in the very first visit if they are referred to a rheumatologist. In this context, the following study was conducted to identify the factors associated with a diagnosis of RA, including the rheumatologist's predictive ability in a cohort of patients with very recent onset arthritis after 1 year of follow-up:

Rojas-Serrano J, Burgos-Vargas R, Lino Pérez L, García García C, Moctezuma F, Vázquez-Mellado J
Very recent onset arthritis: the value of initial rheumatologist evaluation and anti-cyclic citrullinated peptide antibodies in the diagnosis of rheumatoid arthritis
Clin Rheumatol 2009, 28:1135-1139

78 patients (age 35.5±13.5 years; 69 females) were diagnosed at baseline as very recent onset arthritis (median duration 6 weeks). Of 75 patients completing 1-year follow-up, 51 (66.5%) were classified as RA; 12 (16%) had self-limited arthritis; and 13 (17.5%) had other diagnoses. The characteristics of patients with RA as final diagnosis were polyarthritis, morning stiffness ≥1 h, high counts of swollen joints, and low frequency of systemic symptoms. Rheumatologist prediction of RA and anti-cyclic citrullinated peptide (anti-CCP) antibodies was strongly associated with RA as a final diagnosis in the logistic regression analysis. Sensitivity and specificity of the rheumatologist prediction were 94% and 74%, for anti-CCP antibodies, 56% and 96%; the combination of both variables had a specificity of 100% and a sensitivity of 53%, and a positive predictive value of 98%. The authors concluded that the combination of RA as predicted diagnosis by a rheumatologist and anti-CCP antibodies is highly specific for RA diagnosis in patients with very early arthritis.

In August 2009, anti-CCP testing was also the subject of the Arthritis & Rheumatism editorial. It accompanies a study from van der Linden et al in the same journal comparing different tests using citrullinated proteins or peptides:

Levesque MC, Zhou Z, Moreland LW
Anti–Cyclic Citrullinated Peptide Testing for the Diagnosis of Rheumatoid Arthritis and the Quest for Improved Sensitivity and Predictive Value
Arthritis Rheum 2009, 60: 2211-2215

In the study of van der Linden et al (which is discussed in the editorial) rheumatoid factor (RF), CCP2, CCP3 and mutated citrullinated vimentin (MCV) were performed on serum samples from a cohort of patients with early arthritis.

Van der Linden and colleagues found that anti-CCP2 had the highest positive predictive value (PPV) and specificity for progression from undifferentiated to rheumatoid arthritis. The PPV did not improve significantly when test results from the 4 different tests (RF, anti-CCP2, anti-CCP3 and MCV) were combined in pairs. However, other studies have shown that the addition of RF testing to anti-CCP2 testing lowers the specificity but increases the sensitivity for a diagnosis of RA. Indeed, subjects with positive findings for both RF and anti-CCP have a nearly 100% likelihood of developing or having RA.

The study of van der Linden et al confirms that anti-CCP2 antibodies are also a marker of severe disease. The results suggest that anti-CCP2 remains the single most powerful serological test for predicting the development of RA.