This approach to analysis using the EMR opens doors to future research, highlighting the power of routinely captured data. As routinely captured data are more frequently utilized to address clinical questions in everyday practice, the strengths and limitations of such datasets will become more apparent.

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**Anti-carbamylated protein antibodies in patients with ageing associated inflammatory chronic disorders**

**Rheumatology key message**

- Anti-carbamylated protein antibodies are of help to early diagnose elderly-onset RA patients with poly-myalgic clinical onset.

SIR, elderly-onset rheumatoid arthritis (EORA) is one of the most common forms of inflammatory conditions in the elderly [1]. However, clinical characteristics of EORA differ from young-onset rheumatoid arthritis (YORA). Basically, EORA shows a more balanced gender distribution, a higher frequency of acute onset and more...
involvement of large joints than YORA [1]. These patients usually start their clinical manifestations with polymyalgic symptoms affecting principally the shoulders, with an increase in acute-phase reactants [1]. Polymyalgia rheumatica (PMR) is one of the more difficult disorders to distinguish from EORA at the onset and remains a diagnostic challenge since there is a lack of diagnostic laboratory tests [2]. The detection of serum ACPA, but not RF, was previously demonstrated to be useful to differentiate EORA from PMR patients [3]. Indeed, the lack of ACPA and/or RF is a provisional classification criterion for PMR [4]. However, the prevalence of seropositive RF and ACPA is lower in EORA than YORA, and there are still a number of seronegative EORA patients to differentiate from PMR, especially at clinical onset [1, 3].

Anti-carbamylated protein antibodies (anti-CarP Abs) have been proposed as a new autoantibody system in RA, different from ACPA. Carbamylation is a post-translational modification mediated by cyanate that results in the conversion of lysine into homocitrulline [5]. Anti-CarP Abs are present in both seropositive and seronegative ACPA YORA patients and help to predict the development of RA [5]. In addition these Abs help to predict joint damage and disease activity in RA [5, 6]. Since anti-CarP Abs seem to detect otherwise seronegative YORA patients, we aimed to assess whether the presence of anti-CarP Abs could aid in the diagnosis of EORA at clinical onset in inflammatory disorders of elderly subjects.

Serum samples obtained at clinical onset of symptoms from 188 aged (>60 years) individuals were studied, 53 EORA (76.4 ± 6.2 years, 62.3% females) and 135 PMR (73.3 ± 7.8 years, 66.7% females). All the RA patients fulfilled the ACR/EULAR 2010 classification criteria [6]. PMR patients fulfilled the criteria proposed by Chuang et al. [4] and all of them were negative for ACPA and RF as measured with our routine tests. As controls, samples from 67 young onset RA patients (YORA, 43.9 ± 10.8 years, 73.1% females), 50 SLE (43.0 ± 13.2 years, 82% females), 50 patients with infectious diseases (40.3 ± 13.9 years, 40% females) and 61 elderly age-paired healthy subjects (HS, 67.1 ± 7.0 years, 59% females) were analysed. The study was approved by the Ethical Committee of Clinical Trials of Cantabria and informed consent from all subjects was obtained before the samples were collected (serum collection registered at the ISCIII-Biobank Register, reference number C.0001031).

Sera were studied for the presence of ACPA by chemiluminescence (BIO-FLASH, Inova Diagnostics, San Diego, CA, USA), anti-CarP Abs by ELISA (Inova, research use only [10]) and RF by nephelometry (BNII, Siemens Healthcare, Erlangen, Germany).

The frequency of seronegative patients for RF (75.5%) and anti-CCP3 Abs (75.5%) in the EORA group of patients was very high as compared with the frequencies described in other EORA cohorts. These autoantibodies were highly prevalent in the serum of YORA patients.
When looking at the presence of serum anti-CarP Abs at onset of polymyalgic symptoms, their titres were increased in both PMR and EORA patients, to a similar extent to YORA. In contrast, serum anti-CarP Abs were not increased in SLE or infectious disease patients (Fig. 1). When looking at the receiver operating characteristic (ROC) curves, anti-CarP Abs did not add any significant advantage to the diagnosis of RA as compared with RF or ACPA (the whole RA patients in the study versus healthy subjects showed a sensitivity of 55.8% vs. 65%, and specificity of 93.4% vs 98.4%). However, when seronegative patients for RF and ACPA were selected from the different patient groups included in the study, anti-CarP Abs were positive in almost half of the EORA (16/33) and 38.7% (48/124) of the PMR patients. They were only detected in 10.8% and 2.3% of SLE and infectious disorders, respectively.

In conclusion, there are a number of PMR patients who might be seronegative for EORA for the established laboratory markers, whereas the remaining PMR patients might be close to GCA or represent a frustrated form of subclinical vasculitis. Prior evidence from our group points to similar genetic, immunological and environmental factors influencing the development of PMR and EORA that differ from those involved in GCA [7, 8]. One of our limitations is the lack of a GCA group, but we had very few patients with GCA at onset to be included. Results with anti-CarP Abs from our seronegative cohort of aged with inflammatory disorders suggest that these autoantibodies could help in the early diagnosis and treatment of EORA. A prospective study to find out whether positive anti-CarP Abs PMR patients develop a full RA remains to be performed.

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References


Long-term continuation of chloroquine-induced retinal toxicity in rheumatoid arthritis despite drug cessation

SIR, A 45-year-old male diagnosed with rheumatoid arthritis presented with a progressive diminution of vision in both eyes over 12 years. On examination, his best corrected visual acuity was finger counting at a 1-m distance with an accurate projection of rays in the right eye and 6/60 in the left eye. There was sensory exotropia with a relative afferent pupillary defect in the right eye. Fundus

Rheumatology key message

- Chloroquine therapy in patients with RA can result in a variable retinal toxicity.

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