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LETTER

Response to 'Adipokines, inflammation, insulin resistance, and carotid atherosclerosis in patients with rheumatoid arthritis'

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In a recent report in *Arthritis Research & Therapy*, Kang and colleagues [1] assessed a series of patients with rheumatoid arthritis (RA) to establish whether adipokines could be a link between inflammation, insulin resistance, and atherosclerosis in RA.

We have noticed that Kang and colleagues did not pay attention to our former studies on the same issue. In this regard, in the last decade, we conducted a series of studies on insulin resistance and adipokines in a cohort of Spanish patients with long-standing RA, undergoing anti-tumor necrosis factor-alpha (anti-TNF-α) infliximab therapy because of severe disease, refractory to conventional disease-modifying anti-rheumatic drugs [2-6].

Kang and colleagues described that resistin was associated with erythrocyte sedimentation rate (ESR) ($r = 0.322$, $P < 0.001$), C-reactive protein (CRP) ($r = 0.209$, $P = 0.004$), and increased disease duration ($r = 0.176$, $P = 0.014$) [1]. These data are not new. We previously reported a close association between laboratory markers of inflammation, particularly CRP and resistin levels [3]. In our series, we found a significant association between the mean ESR ($r = 0.405$, $P = 0.03$) and CRP ($r = 0.571$, $P = 0.0005$) from disease diagnosis and ESR ($r = 0.486$, $P = 0.004$), CRP ($r = 0.599$, $P = 0.0005$), and platelet count ($r = 0.559$, $P = 0.0007$) at the time of the study and resistin levels [3]. These findings, along with these new data described by Kang and colleagues, highlight the potential role of resistin in the inflammatory cascade in RA.

Kang and colleagues also found a positive correlation between adiponectin and ESR ($r = 0.162$, $P = 0.025$) [1]. Prior to these results, in our series of patients with severe and active disease despite anti-TNF-α therapy, we observed that high-grade inflammation was independently and negatively correlated with circulating adiponectin concentrations [4]. CRP levels correlated with circulating adiponectin concentrations (partial r (pr) = −0.370, $P = 0.04$), independently of age and gender [4]. In contrast, low adiponectin levels clustered with metabolic syndrome features that contribute to atherogenesis in RA [4]. Adiponectin concentrations correlated with triglycerides/high-density lipoprotein (HDL) cholesterol ratios (pr = −0.396, $P = 0.03$), total cholesterol/HDL cholesterol ratios (pr = −0.444, $P = 0.01$), and high fasting plasma glucose levels (pr = −0.366, $P = 0.04$), independently of CRP levels and the body mass index [4]. These results also suggest an implication of adiponectin in the development of cardiovascular disease in RA.

In the series by Kang and colleagues, leptin was associated with homeostasis model assessment-estimated insulin resistance ($r = 0.369$, $P < 0.001$) [1]. In our series of RA patients with active disease despite anti-TNF-α therapy, there was a positive correlation between body mass index of RA patients and serum leptin levels ($r = 0.665$, $P < 0.001$) [5]. Also, a significant correlation of leptin with biomarkers of endothelial activation (vascular cell adhesion molecule-1; $r = 0.349$, $P = 0.04$) was observed [5]. However, no significant correlations between leptin levels and disease duration, ESR and CRP levels, disease activity score using 28 joint counts, lipids, insulin sensitivity, resistin, adiponectin, or the cumulative prednisone dose at the time of the study were found [5]. Therefore, in Western patients with severe and active RA, leptin levels seem to be related to adiposity [5]. However, in our series, circulating visfatin levels were unrelated to disease activity, adiposity, or metabolic syndrome [6].

Although adipokines have been demonstrated to exert a key role in the interface between obesity, inflammation, insulin resistance, and atherosclerosis in the general

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population, we agree with Kang and colleagues that information on their potential contribution is still limited in RA. In this regard, in Western individuals with RA, adipokines have not been demonstrated to represent a significant risk factor for indirect measures of organic arterial wall atherosclerotic damage, as assessed by carotid intima-media thickness in our cohort of long-standing active RA patients undergoing infliximab treatment [7], or by coronary artery calcification evaluation, as shown in recent work by Rho and colleagues [8].

Abbreviations

anti-TNF-α: Anti-tumor necrosis factor-alpha; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; HDL: High-density lipoprotein; RA: Rheumatoid arthritis.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MAG-G made substantial contributions to conception and design of the manuscript, helped to draft the manuscript, and has given final approval of the version to be published. RL-M, CG-J, and JL helped in the design of the manuscript and drafted the manuscript. All authors have read and approved the final manuscript.

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