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Editorial

Genetics and ultrasound in rheumatoid arthritis

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Received on December 30, 2011; accepted in revised form on May 14, 2012.

Clin Exp Rheumatol 2012; 30: 815-816.

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Key words: genetics, ultrasound, rheumatoid arthritis

Several evidences have demonstrated the role of genetic factors in the pathogenesis of rheumatoid arthritis (RA) (1).

Genetic variants of candidate genes encoding for several cytokines (such as IL-1, IL-6, IL-10 and TGF-β), proteases (such as protein tyrosine phosphatase non-receptor type 22) and other immune/inflammatory genes (such as macrophage protein 1) have been investigated with contrasting results (1, 2). Published data on the effects of polymorphisms on bone-erosive damage in RA have been mainly obtained using conventional radiography (2). However, this technique is characterised by a lack of sensitivity in detecting the presence of erosions in early stages of disease (3).

Musculoskeletal ultrasound (MSUS) is an easily available, quick-to-perform and relatively low-cost technique that has gained an increasing role in the evaluation of both inflammation and structural damage lesions in RA patients (4-8). Particularly, MSUS demonstrated a higher sensitivity in the evaluation of bone erosive damage, compared to radiographic assessment.

The association between genetic factors and bone erosive damage assessed by MSUS has recently been analysed in RA patients. After evaluating sonographically the number of erosions present at the level of metacarpophalangeal (MCP), proximal interphalangeal (PIP), and metatarsophalangeal (MTP) joints, a semiquantitative score (ranging from 0 to 3) has been developed at each joint site. By the sum of single joint scores, at each anatomic district a MCP-total erosion score (TES), PIP-TES and MTP-TES (ranging from 0 to 30) were then calculated. In addition, a global erosive score was obtained by the sum of these scores (range 0–90) (9, 10).

The association between the single nucleotide polymorphism (SNP) -308 A/G of tumour necrosis factor (TNF) and the severity of bone erosive damage using MSUS was analysed in a recent study performed in 52 consecutive RA patients (9). More specifically, in patients carrying the genotype AG or AA a significantly higher global TES, MCP-TES and MTP-TES were identified compared with patients carrying the GG genotype (28.5±23.7 *vs*. 38.1±17.1, $p<0.05$; 11.2±8.2 *vs*. 18±8.4, $p=0.027$; 8.2±8 *vs*. 11.2±6, $p<0.05$, respectively) (9).

Moreover, the role of SNPs of transforming growth factor beta (TGF-β) and interleukin (IL)-6 genes was evaluated and correlated to MSUS-detected erosive damage (10). The results of this study showed that the TGF-b 869TT genotype showed a statistically significant lower MTP-TES than those with the CC or CT genotype (mean MTP-TES±SD for 869TT 6.3±5.7 *vs*. 869CC/CT 11.7±7.8; $p=0.011$). Interestingly, patients with the TT genotype showed dichotomous behaviour that seems dependent on autoantibody status. In presence of anti-citrullinated protein antibodies (ACPA) and/or rheumatoid factor (RF), the TT genotype was associated with lower erosion scores at all anatomical sites compared with the CC and CT genotypes. Conversely, the same 869TT patients showed higher erosion scores in the absence of ACPA or RF (10). No significant association was found when considering the IL-6 SNP. The authors concluded that the TGF-β 869C/T SNP seems involved in determining the severity of bone damage in RA, with dichotomous roles according to the patient's autoantibody (ACPA and RF) status (10).

In conclusion, recent exploratory studies suggest that the use of a sensitive technique such as MSUS can help to identify the association between genetic factors and bone erosive damage. This

Competing interests: none declared.

issue has a relevant importance considering the possibility to identify the marker of severity of disease and the subset of patients requiring a more aggressive treatment. Further studies conducted in larger populations and prospective designs are needed to better clarify these complex aspects of RA.

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