MATTERS ARISING

Normal values of laboratory tests in elderly onset psoriatic arthritis

I read with interest the article recently published by Punzi et al.1 The results shown in this study demonstrate higher levels of acute phase response markers such as ESR and CRP in elderly onset psoriatic arthritis patients (EOPA) than those displayed by younger onset psoriatic arthritis patients (YOPA). The authors included 16 EOPA (>60 years) and 50 YOPA (<60 years).

I would like to comment that the information regarding normal values was restricted to the following words “CRP, normal values <0.6 mg/dl”, no other information is given. It is not possible to know how and from whom these normal values were obtained. Even if a commercial test that includes their own controls was used, it is clear that you will need to test groups of normal subjects that cover the age spectrum of both groups of patients EOPA and YOPA. This strategy will allow you to estimate the influence of age in the higher levels of ESR and CRP exhibited by EOPA. The inclusion of this control group of normal subjects is also recommended because YOPA does not belong to the same age cohort that EOPA does, and in fact, EOPA represents a group of survivors from their original birth cohort more that YOPA does.

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Authors’ reply

In his comments on our paper,1 Dr Nava regrets that little information was given on the normal values of laboratory markers of acute phase response (APR), in particular ESR and CRP, to support the observation that APR is higher in elderly onset psoriatic arthritis (EOPA) than in younger onset PsA (YOPA). This criticism probably derives from the possibility that the differences in ESR and CRP may simply be attributable to age rather than disease. ESR and CRP are the most widely known and commonly used laboratory indices used to investigate APR and disease activity. ESR is a composite measurement depending on several factors, including in particular red cell and serum protein changes. Physiological changes able to influence one or more of these factors, such as sex and age, may in turn influence ESR. Since the first introduction of Westergen’s technique, the most recommended method for ESR determination,2 many studies have been performed to establish normal values in the elderly: irrespective of sex, upper limits of 20 mm 1st h for subjects under 50 years and 40 mm 1st h for those older than 70 years are considered normal, acceptable values. Thus, the ESR mean values of 64.2 (35.3) mm 1st h found in our EOPA patients must be viewed entirely above suspicion.

The differences between our EOPA and YOPA were even more evident for the CRP, a protein that best reflects the APR and that is only slightly influenced by age and sex. The normal values we reported (<0.6 mg/dl for any age and sexes) are accepted worldwide and, although some rare healthy subject may reach an upper limit of 1.0 mg/dl, these values mainly differ from the mean of 3.9 (2.0) mg/dl found in our patients with EOPA.

In this context, however, another aspect might have seemed surprising: the low values of ESR and CRP found in YOPA, 30.5 (30.0) mm 1st h and 1.33 (1.3) mg/dl respectively, reflecting difficulties in applying these indices to patients with seronegative spondyloarthritides and in assessing disease activity.3 Further considerations, unpublished observation from the Italian Group of Psoriatic Arthritis Study, involving 1306 patients with PsA, CRP values of >1 mg/dl were found in only 52.9% of the patients. As the agents mainly involved for CRP production are pro-inflammatory cytokines, mainly interleukin (IL) 6 but also IL1 and tumour necrosis factor, and as these cytokines are usually found at low levels in the synovial fluid of YOPA,1,4 PsA may be considered a disease characterised by a frequent low synthesis of pro-inflammatory cytokines and usually mild APR. However, factors able to stimulate or deregulate the production of these cytokines, such as aging, trauma, infections or immunogenetic predisposition to severe polyarticular diseases,56 may be responsible for an increased APR and account for a wide spectrum of presentations typical of PsA.

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Table 1 Frequency of HLA B antigens in patients with RS3PE

<table>
<thead>
<tr>
<th>Number of Reference patients</th>
<th>B7%</th>
<th>B27%</th>
</tr>
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<tbody>
<tr>
<td>8§</td>
<td>126 14 (11)</td>
<td>7 9 2 (9)</td>
</tr>
<tr>
<td>7</td>
<td>80 7 (9)</td>
<td>12 2 (17)</td>
</tr>
<tr>
<td>6</td>
<td>126 14 (11)</td>
<td>8§ 12 2 (17)</td>
</tr>
</tbody>
</table>

Leonardo Punzi, Pierfranca Gambari


10 Diederichs TA, Punzi L, Gambardi PF, Rossini P, Mianon M. Normal values of laboratory markers in elderly onset psoriatic arthritis patients (EOPA) than those displayed by younger onset psoriatic arthritis patients (YOPA). The authors included 16 EOPA (>60 years) and 50 YOPA (<60 years).

11 We agree with Dudler et al that RS3PE is one way in which late onset polyarthritis can present. However, we believe it is a more a clinical feature indicating a good prognosis rather than a specific syndrome. As they have admirably summarised its occurrence in a number of other conditions, in which the only linking feature is that the patients tend to be elderly, would support this view. The association with HLA B7 is as yet not proved, the incidence varying with the population screened (table 1).

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Authors’ reply

We are grateful to Drs Pease and Bhakta for their interesting comments on the relation of RS3PE and HLA B7. We agree with them that the association with HLA B7 is not yet proved, and that actually data from diverse groups tend to speak against it. We also found that their prospective study looking at pitting oedema in various subsets of late onset rheumatoid arthritis as a good and independent factor of good prognosis was very interesting.\(^1\) Nevertheless, a syndrome is simply a group of signs and symptoms occurring together and characterising a particular abnormality. We believe that it is still useful to define RS3PE as a specific syndrome particularly regarding its excellent prognosis as compared with the other aetions responsible for pitting oedema in various subsets of late onset rheumatoid arthritis as a good and independent factor of good prognosis.\(^1\)

We are grateful to Drs Pease and Bhakta for their interesting comments on the relation of RS3PE and HLA B7. We agree with them that their prospective study looking at pitting oedema of the hands in various subsets of late onset rheumatoid arthritis as a good and independent factor of good prognosis was very interesting.\(^1\) Nevertheless, a syndrome is simply a group of signs and symptoms occurring together and characterising a particular abnormality. We believe that it is still useful to define RS3PE as a specific syndrome particularly regarding its excellent prognosis as compared with the other aetions responsible for pitting oedema in various subsets of late onset rheumatoid arthritis as a good and independent factor of good prognosis.\(^1\)

Intra-articular corticosteroids in septic arthritis: beneficial or barmy?

We read with interest the paper by Wysenbeek et al about the treatment of staphylococcal septic arthritis in rabbits by intra-articular corticosteroids in addition to antibiotics\(^2\) and would like to share our recent clinical experience that we feel pertinent to this scientific research.

Traditional teaching dictates that intra-articular corticosteroids are contraindicated in the management of septic arthritis, the appropriate treatment being antibiotics and lavage or surgical drainage. The following two cases of septic arthritis illustrate the apparent benefits of the unconventional use of intra-articular corticosteroids. Both patients presented with a septic arthritis of an osteoarthritic knee. The first patient, a 87 year old women, had developed a staphylococcal aureus infection (sensitive to flucloxacillin) while the second, a 62 year old man, had a proteus infection (sensitive to cephalosporins). Surgical management was inappropriate because of frailty and warfarin treatment respectively. Despite treatment of both patients with appropriate intravenous antibiotics for two weeks and joint lavage, pain and synovitis persisted. At this stage, in both cases, knee aspirates and blood cultures on two separate occasions were negative. After a single intra-articular injection of 80 mg depomedrone and lignocaine (lidocaine) their symptoms resolved dramatically. Both were able to return to a full and independent life with no sequelae.

Our decision to use corticosteroids was based on the observation that bacterial antigens can promote cytokine proliferation\(^3\) within the joint and activate chondrocyte proteases.\(^1\) We postulate that despite adequate treatment of infection, cytokine mediated inflammation persists and that intra-articular corticosteroid may limit damage and improve outcome. The use of intra-articular corticosteroids in addition to antibiotics in experimental staphylococcal septic arthritis in rabbits found no adverse effects of the corticosteroids and an improvement in joint histological-histochemical parameters.\(^3\)

We therefore propose that intra-articular corticosteroids may be useful in septic arthritis where: (a) synovitis persists despite adequate intravenous antibiotic treatment and ravage; and (b) repeat synovial fluid and blood cultures are found to be sterile.

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RS3PE syndrome. The relation with HLA B7

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