Third Update on Psoriatic Disease Conference: Trainee Session

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ABSTRACT. Trainee sessions have become an established feature of international conferences and were an important part of the proceedings of the Third Update on Psoriatic Disease. Presentations featured a wide range of topics from clinical, etiopathological, and therapeutic aspects of psoriatic disease and spondyloarthropathy. A selection of 7 reports from the sessions is presented here. (J Rheumatol Suppl. 2015 Nov;93:6–9; doi:10.3899/jrheum.150623)

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DIAGNOSIS MEETING REPORT

As part of the Third Update on Psoriatic Disease, held in Naples, Italy, from May 22-23, 2014, the following presentations were delivered by rheumatology trainees at a session on the first morning of the conference.

Trainee sessions have now become an established feature of international conferences in the field of psoriasis and related disorders — including previous Updates held in Naples, and meetings organized by GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis). It is hoped that this type of forum will provide challenging inspiration for junior research workers in the field, and thus a robust body of clinico-scientific rheumatologists for the future.

All presentations were delivered in English using PowerPoint, with 15 min being allowed for each delivery. A period for questions and comments from delegates was allocated at the end of the session.

The 7 presenting trainees had been selected previously on the basis of abstracts approved by members of the Scientific Committee. Six of those selected were from Italian Academic Centers and 1 was from New Orleans, Louisiana, USA.

All presentations dealt with in-depth analysis of topics within the field of psoriatic disease/spondyloarthropathy. And as will be seen from the following reports, a wide spectrum of research endeavors emerged, including studies focusing on clinical, etiopathological, and therapeutic aspects.

PRESENTATIONS

1. Tools for Screening Psoriatic Arthritis in Psoriatic Patients: The Multi-Centric Trial HERACLES *De Marco G. Department of Rheumatology, G. Pini Orthopedic Institute, Milan, Italy*

OBJECTIVE. The early detection of psoriatic arthritis (PsA) requires multidisciplinary cooperation. This trial is designed to set methods useful for dermatologists to identify psoriatic patients who are more likely to have PsA and thus are eligible for rheumatological referral.

PATIENTS AND METHODS. Based on previous experiences[1], the following 8 items seem reliable for rheumatological referral: complaints of (i) arthralgia; (ii) dactylitis; (iii) enthesitis; (iv) spinal pain; presence (recorded by a dermatologist) of (v) dactylitis; (vi) joint swelling; (vii) joint deformity; (viii) limping. According to preliminary analyses, scoring at least 3 of those items would better balance sensitivity and specificity. Since skewing toward sensitivity would disclose more PsA cases, a score of 2 will be considered the threshold in our study. Isolated dactylitis (the strongest variable linked to PsA) will score 2 automatically. All these patients will form the "rheumatological group." Psoriatic patients with a score ≤ 1 and without dactylitis will be the control group. Every subject enrolled will also fill in screening questionnaires (PASE, PEST, EARP, ToPAS), although these will not influence referral. The rheumatologists, blinded to dermatological evaluations, will assess all candidate subjects, regardless of their referral score. For ethical reasons and aiming to reproduce standard clinical care as much as possible, any investigation (blood tests or imaging) will be encouraged only if useful for the patient.

RESULTS. This cross-sectional study was proposed to 13 Italian centers. By now, 5 centers have enrolled 72 subjects. Data are available on a Web-hosted database. Data collection phase will last 18 months.

CONCLUSION. After data collection, the study will follow the standard analysis procedures (data cleaning and validation, statistical analysis, report writing).

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2. Longterm Efficacy of Anti-tumor Necrosis Factor-α Treatment in Psoriatic Arthritis: Extension of Administration Interval

Mariagrazia Lorenzin, Paola Frallonardo, Augusta Ortolan, Leonardo Punzi, Roberta Ramonda, Rheumatology Unit, Department of Medicine DIMED, University of Padua, Padua, Italy

OBJECTIVE. Psoriatic arthritis (PsA) is a progressive chronic inflammatory disease that affects both the axial and peripheral joints and often causes patient impairment. When anti-tumor necrosis factor (TNF) agents are used to treat active spondyloarthritis, several aspects including disease activity, spinal mobility, peripheral arthritis and enthesitis, as well as quality of life are considerably improved[1,2,3]. The aim of this study was to evaluate the longterm efficacy in clinical practice of adalimumab (ADA) and etanercept (ETN) treatment in patients with PsA and to assess the percentage of patients with progressive lengthening of therapy interval administration in the event of optimal treatment response.

PATIENTS AND METHODS. A retrospective study was carried out on 141 PsA outpatients receiving the same anti-TNF-α treatment over a 4-year period (March 2005–June 2013) and attending the Rheumatology Unit, University of Padua. Age, sex, onset age, disease and therapy duration were evaluated. The therapy efficacy was determined using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Health Assessment Questionnaire (HAQ), 28-joint Disease Activity Score 28 (DAS28), patient global assessment, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). The percentage of patients in whom therapy interval administration was prolonged was also evaluated.

RESULTS. One hundred forty-one patients (88 male, 62.4%; median age 51.22 ± 12.34 yrs; mean disease duration 12.1 ± 8.42 yrs) were treated with ETN and ADA (47.5% and 52.5%, respectively). The average baseline and after-treatment values were BASDAI 51.05 ± 22.30 vs 26.70 ± 19.55 ($p < 0.0001$); BASFI 34.25 ± 23.74 vs 16.85 ± 10.51 ($p < 0.0001$); HAQ 0.72 ± 0.60 vs 0.36 ± 0.22 ($p < 0.0001$); DAS28 3.53 ± 1.56 vs 2.17 ± 0.92 ($p < 0.0001$); visual analog scale (VAS) 47.20 ± 23.20 vs 26.11 ± 18.23 ($p < 0.0001$); VAS 41.09 ± 21.44 vs 25.83 ± 18.29 ($p < 0.0001$); ESR 26.90 ± 20.31 vs 13.76 ± 11.71 mm/h ($p < 0.0001$); CRP 10.35 ± 8.36 mg/l vs 2.82 ± 1.82 mg/l ($p < 0.0001$). Sixty-five patients (46.1%) responded to therapy in a satisfactory manner. The interval between injections was extended after a mean treatment of 11.46 ± 5.27 months, in 18.4% and 27.7% of patients, respectively, receiving ADA and ETN. The mean interval was 3.12 weeks for ADA and 2.75 weeks for ETN.

CONCLUSION. A clinical, functional, and biochemical improvement was observed in the patients with PsA treated with both drugs. A satisfactory prolonged clinical response was observed. The interval between injections was extended in a high percentage of the patients.

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3. Is There a Role for Inflammasome Activation in PsA Pathogenesis and Its Comorbidities?

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OBJECTIVE. New data have emerged about the role of inflammasome in psoriasis and psoriatic arthritis (PsA). The assembly of the inflammasome components in innate immune cells (monocytes) results in the rapid activation of caspase-1, which cleaves pro-interleukin-1β (IL-1β) and pro-IL-18 to generate active forms of these cytokines. We hypothesized that "inflammasome activation occurs in monocytes, as a key element on the initiation and amplification of the innate immune response in PsA pathogenesis." The aims of the study were as follows: (1) to determine whether inflammasome activation occurs in monocytes of patients with PsA, and (2) to determine the relationship between inflammasome activation with disease activity and metabolic syndrome in these patients.

PATIENTS AND METHODS. After informed consent, 13 patients with PsA (CASPAR criteria) and 16 age-matched healthy individuals attending the outpatient rheumatology clinic were enrolled. Demographic, laboratory, and clinical data were recorded. Disease activity was determined by DAS28 score. Blood pressure, diabetes history, lipid profile, and waist circumference data were included. Metabolic syndrome (MS) was defined following the International Diabetes Federation criteria. Purified monocytes were plated and stimulated for 18 h with lipopolysaccharide (LPS; 100 ng/ml) in presence or absence of caspase-1 inhibitor. CD14 and Caspase-1 expression was analyzed by flow cytometry. Cell lysates and supernatants were collected for determination of caspase-1 and NLRP3 protein by Western blot and cytokine levels by ELISA, respectively. Student's t test and Mann-Whitney tests were used for statistical analysis.

RESULTS. Sixty-two percent of patients were female, mostly white (77%). The mean age was 45.15 years (SD 9.7) and mean disease duration was 6.7 years (SD 5.5). Ten patients presented with active disease, mean DAS28 3.25 (SD 1.2). Metabolic syndrome was present in 77% of patients.

The percentage of CD14+/caspase1+ was numerically higher in peripheral blood mononuclear cells-monocytes from patients with PsA compared to normal controls (33.5 ± 13 vs 22.5 ± 11.3, respectively), although the difference did not reach statistical significance ($p < 0.1$). Caspase-1 expression was confirmed by Western blot. No differences were found regarding cytokine levels. Purified monocytes from patients with PsA displayed a robust inflammatory response after LPS stimulation where these were highly expressed: caspase-1, NOD-like receptor family, pyrin domain containing 3 (NLRP3) inflammasomes, IL-1β, and IL-18. Neither caspase-1 nor cytokine expression were associated with disease activity. In a subset of PsA patients with MS, there was only a trend of higher IL-1β levels (19.4 ± 24.8 vs. 4.1 ± 6.6; $p = 0.08$).

CONCLUSION. In this pilot study, patients with PsA showed an increased expression of inflammasome activity, although results did not reach statistical significance. Further studies including a larger number of patients are needed to truly establish a role of inflammasome activation in PsA pathogenesis and associated comorbidities.

4. A COBRA-like Therapy: A Possible Alternative in Axial SpA? *Simone D, Nowik M, Ferraccioli GF, Gremese E. Division of Rheumatology, School of Medicine, Catholic University of the Sacred Heart, CIC, Rome, Italy*

OBJECTIVE. We aimed to evaluate the effectiveness of a combination therapy of sulfasalazine (SSZ), methotrexate (MTX), and high doses of oral corticosteroids (COBRA scheme) in patients with axial spondyloarthritis (axSpA) resistant to nonsteroidal antiinflammatory drugs.

PATIENTS AND METHODS. Ten patients with axSpA with active disease [Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥ 4] treated with the COBRA-like scheme (SSZ 2 g/day + MTX 10–20 mg/week + oral corticosteroid 0.5–1 mg/kg/day) were prospectively evaluated. Disease activity was assessed by BASDAI, Ankylosing Spondylitis Disease Activity Score (ASDAS)-erythrocyte sedimentation rate (ESR), ASDAS-C-reactive protein (CRP), ESR, and CRP. Bath Ankylosing Spondylitis Functional Index and requirement for anti-TNF-α therapy were also assessed.

RESULTS. All patients were treated with the combination therapy for at least 3 months. After this time, BASDAI score was not significantly decreased, and no patient reached the low disease activity status (BASDAI < 4). ESR was decreased after 3-month followup (38.7 ± 25.9 at baseline vs 12.7 ± 11.3 mm/h; $p = 0.01$) whereas CRP did not significantly change ($p = 0.24$). The therapeutic regimen was continued for a mean of 5.6 months; 7 patients (70% of the cohort) needed anti-TNF-α.

CONCLUSION. In our cohort of patients with axSpA, the COBRA regimen was not an effective alternative to anti-TNF-α therapy; nor was it able to decrease disease activity or to improve functionality index, in contrast to the evidence in rheumatoid arthritis.

5. Remission in SpA: Only ASDAS or Also BASDAI Scoring?

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OBJECTIVE. In patients with spondyloarthritis (SpA), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) has been historically the most widely used clinical disease activity measure. More recently, the ASDAS was introduced by the Assessment of SpA International Society. While BASDAI is a fully patient-oriented measure, ASDAS includes inflammatory markers among its items. In our study, we looked for an agreement between the definition of low disease activity assessed using ASDAS-C-reactive protein (CRP) and BASDAI and tried to identify a cutoff value indicating remission on the BASDAI scale.

PATIENTS AND METHODS. We evaluated a population of 187 patients meeting ASDAS criteria for SpA receiving followup at our division. For each patient, disease activity was assessed by BASDAI and ASDAS-CRP at the last available followup; also CRP values were analyzed. Receiver-operating characteristic (ROC) curves were drawn to identify the BASDAI cutoff indicating remission. The κ coefficient was computed to evaluate agreement between the definition of remission according to ASDAS and the previously indicated remission cutoff for BASDAI of 1.

RESULTS. In our population of 187 patients, of which 117 were male (62.6%), mean BASDAI was 3.1 ± 2.3, mean ASDAS-CRP was 1.8 ± 1.0 mg/l, and mean CRP was 4.1 ± 6.1. At the last followup visit, 53 patients (28.3%) showed a BASDAI ≤ 1[1], and 59 patients were in remission according to ASDAS (31.6%). This BASDAI cutoff (κ coefficient 0.62) appeared to be more difficult to achieve in comparison to the ASDAS remission ($p < 0.001$). ROC curve analysis showed that a value of 1.8 on the BASDAI scale was the cutoff indicating remission (area under the curve 0.91 ± 0.02, $p = 0.02$). Remission evaluated using BASDAI ≤ 1.8 was achieved in 71 patients (38%), and good agreement was found between said cutoff and the definition of remission using ASDAS (κ coefficient 0.72). In contrast, poor agreement was found between a normal CRP value (considered as ≤ 1.1 mg/l) and BASDAI remission (κ coefficient 0.11).

CONCLUSION. Our results show a good agreement between ASDAS remission and the previously indicated BASDAI remission of ≤ 1. A value of BASDAI ≤ 1.8 was found to

have the strongest agreement with the ASDAS remission of 1.3.

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6. Effectiveness and Safety of Anti-Tumor Necrosis Factor-α in Elderly Patients with Psoriatic Arthritis *Luisa Costa[1], Roberta Ramonda[2], Ennio Lubrano[3], Francesco Caso[1,2], Luca Cantarini[4], Paolo Bottiglieri[1], Darda Md Abud[5], Mariagrazia Lorenzin[2], Antonio Del Puente[1], Ugo Fiocco[2], Leonardo Punzi[2], Raffaele Scarpa[1]; [1]Rheumatology Unit, Department of Clinical Medicine and Surgery, University of Federico II, Naples, Italy; [2]Rheumatology Unit, Department of Medicine DIMED, University of Padua, Padua, Italy; [3]Rheumatology Unit, Department of Medicine and Health Sciences, University of Molise, Campobasso, Italy; [4]Rheumatology Unit, Policlinico Le Scotte, University of Siena, Siena, Italy; [5]Natural Science Academic Group, National University, Gazipur, Bangladesh.*

OBJECTIVE. The management of elderly patients with psoriatic arthritis (PsA) is a peculiar challenge, owing to the frequent comorbidities and the related concomitant use of additional drugs. Further, rheumatologists use with caution tumor necrosis factor (TNF)-α blockers in this group of patients, because the different trials do not take into consideration this kind of population. The aim of our study was to evaluate the efficacy and safety of TNF-α blockers in elderly patients with PsA.

PATIENTS AND METHODS. This is an observational multicenter study carried out in 4 Italian centers specializing in the diagnosis and treatment of PsA. Inclusion criteria were as follows: subjects ≥ 65 years old, PsA classified on the basis of CASPAR criteria, starting therapy with anti-TNF-α, stable medical conditions, no autoimmune diseases other than PsA. Exclusion criterion was the previous use of biologic therapy. At baseline (T0) and after 6 (T6) and 12 (T12) months of therapy, data concerning PsA activity and possible adverse events were collected.

RESULTS. A total of 68 elderly patients (M/F 27/41; mean age 68.51 yrs, range 65-81 yrs) with PsA were included in the study. Thirty patients were taking etanercept, 28 adalimumab, 8 infliximab, and 2 golimumab. During the observation period, all variables concerning PsA activity showed a statistically significant improvement from baseline to T12, except for Health Assessment Questionnaire. An important finding was the evidence of a reduction in disease-modifying antirheumatic drug use from T0 to T12. In addition, at T6 minimal disease activity was achieved by 71% of patients and at T12 by 77% of patients. Moreover, occurrence of adverse events was reported in only 6% of patients (cystitis and tracheitis).

CONCLUSION. Results of this study suggest that TNF-α blockers are effective and safe in elderly patients with PsA. Therefore age should not be considered a limitation to their use.

7. Systemic Inflammation: Psoriasis as a Model

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OBJECTIVE. Inflammation is a defense mechanism that constitutes a protective response following the harmful action of physical, chemical and biological agents, whose ultimate goal is the elimination of the initial cause of cell damage or tissue, as well as the initiation of the repair process. Inflammation consists of a sequence of dynamic phenomena with characteristics relatively constant despite the infinite variety of damaging agents. Among the many exogenous stimuli, the following are of fundamental importance: infection, necrosis, hypoxia, and the immune response. It is through the study of the latter that psoriasis is proposed as a model for the evaluation of systemic inflammation. The aim of our study was to investigate systemic inflammation, using psoriasis as a model; in particular, the involvement of numerous proinflammatory cytokines and chemokines at both cutaneous and circulation levels will be analyzed.

RESULTS. The alarmin IL-33 was found to be increased in psoriatic skin as well as other cutaneous inflammatory disorders, like allergic contact dermatitis and atopic dermatitis. IL-33 was shown to have proinflammatory activity through the activation of keratinocytes and mast cells. TNF-α was able to regulate IL-33 in normal and psoriatic skin.

CONCLUSION. The biology of IL-33 is gaining in complexity, and this molecule is now known to have additional roles beyond its original description. We believe that the production of IL-33 in a very initial phase of damage may lead to the activation of the complex proinflammatory pathway in psoriasis.

In Closing

At the conclusion of the session, chairs J.M. Moll and R. Scarpa noted that all presentations were of an excellent standard, of much valuable research relevance, and had raised considerable interest from the audience during the question period.

The trainees were warmly congratulated, and each was presented with a certificate (endorsed by the conference president, Professor Scarpa) at the gala dinner at the Circolo Canottieri on the evening of 23 May, 2014.

The tutors of the trainees were also presented with certificates on that occasion, after having been thanked for their careful supervision and commitment.