GRAPPA Trainees Symposium 2014: A Report from the GRAPPA 2014 Annual Meeting

Lihi Eder, William Tillett, and Christopher T. Ritchlin

ABSTRACT. The seventh trainees symposium was held at the 2014 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in New York, New York, USA. A total of 26 rheumatology and dermatology trainees engaged in psoriasis or psoriatic arthritis research presented their work to meeting attendees. This article briefly reviews the 4 oral presentations and 22 posters presented at the meeting. (J Rheumatol 2015;42:1016–20; doi:10.3899/jrheum.150122)

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At the 2014 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in New York, New York, USA, 26 rheumatology and dermatology researchers from Europe and from North and South America described their studies in a trainee symposium. The symposium has become an integral part of the annual GRAPPA meeting[1,2,3,4,5], providing an opportunity for trainees who perform research in psoriatic disease to discuss their studies with experts in the field. A total of 42 abstracts were submitted and ranked by a committee of reviewers led by Dr. Christopher Ritchlin (Rochester, New York, USA). The 4 top-ranked abstracts were chosen for oral presentation and 22 additional abstracts were presented as posters. The session was attended by members of GRAPPA and the Spondyloarthritis Research and Treatment Network (SPARTAN), who provided feedback and suggested how to improve and further develop the research projects.

Oral Presentations

Proposal of a novel composite radiographic score for longitudinal observational studies of psoriatic arthritis: Reductive X-ray Score for Psoriatic Arthritis (ReXSPA) (William Tillett, Bath, UK). Dr. Tillett presented results from a study to devise a shortened, more feasible, composite radiographic score for observational studies using a reductive analysis of existing composite scores. Each of the hand and foot radiographs from 50 patients with psoriatic arthritis (PsA) were scored at 2 timepoints with the PsA-Modified Sharp Score, the modified Sharp/van der Heijde score, and the Ratingen score[6]. Data reductions were undertaken to derive a novel score comprising the lowest number of any variables that would account for > 90% of the variance between the 2 timepoints (progression). The reductions identified 6 possible scores of which the best performing one was reported. The score that was finally selected required the assessment of only 16 variables (32 when made symmetrical; area under the curve 0.92).

Dr. Tillett concluded that the ReXSPA score was sensitive to change in this dataset; it includes osteoproliferation, the only radiographic feature specific to PsA, but requires fewer joints to be assessed than the other most commonly used score in observational studies, the PsA-modified Steinbrocker. This reductive score and its dataset can now be discussed, and modifications assessed before testing in a larger study.

HLA risk factors for disease severity are associated with more severe atherosclerosis in patients with psoriasis and psoriatic arthritis (Lihi Eder, Toronto, Ontario, Canada). Dr. Eder presented a study investigating the association between human leukocyte antigen (HLA) markers of severe phenotype and extent of atherosclerosis in psoriatic disease. Consecutive white patients with PsA and psoriasis alone were recruited. An ultrasound (US) of the carotid arteries was performed and the presence, size, and total area of atherosclerotic plaques were recorded. HLA genotyping was performed by sequence-specific oligonucleotide probes. The association between each HLA allele and the severity of atherosclerosis was assessed by ordinal logistic regression models adjusted for age, sex, and traditional cardiovascular risk factors.

In total, 353 patients with psoriatic disease (233 PsA, 120 psoriasis) were analyzed. HLA-B*13 and HLA-C*06 were associated with more severe atherosclerosis (age-adjusted and sex-adjusted OR 2.5, 95% CI 1.24, 5.03; and OR 1.68,

From Toronto Western Hospital, Toronto, Ontario, Canada; Royal National Hospital for Rheumatic Diseases, Bath, UK; and Division of Allergy, Immunology, and Rheumatology, University of Rochester Medical Center, Rochester, New York, USA.

L. Eder, MD, PhD, Toronto Western Hospital; W. Tillett, BSc, MB ChB, PhD, MRCP, Royal National Hospital for Rheumatic Diseases; C.T. Ritchlin, MD, MPH, Professor of Medicine, Division of Allergy, Immunology, and Rheumatology, University of Rochester Medical Center.

Drs. Eder and Tillett contributed equally to this article.

Address correspondence to Dr. L. Eder, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, 399 Bathurst St., 1E-415, Toronto, Ontario M5T 2S8, Canada. E-mail: leder@uhnresearch.ca

95% CI 1.09, 2.61, respectively). The haplotype HLA-C*06-B*13 was also associated with more severe atherosclerosis (OR 2.5, 95% CI 1.24, 5.03). The association between HLA-C*06 and B*13 and atherosclerosis severity remained statistically significant after adjusting for traditional cardiovascular risk factors (OR 1.66, 95% CI 1.07, 2.62; and OR 2.22, 95% CI 1.09, 4.55, respectively). Dr. Eder concluded that HLA-C*06 and B*13 are markers of more severe atherosclerosis in patients with psoriatic disease.

Arthritis mutilans: natural radiographic history and characteristics (Deepak Jadon, Bath, UK). Dr. Jadon presented a retrospective cohort study of the clinical characteristics and natural radiographic history of arthritis mutilans (AM), defined as osteolysis affecting ≥ 50% of the visualized articular surface on both sides of the joint[7,8,9]. All available radiographs were scored by 2 raters using a novel hybrid score, the Bath Radiographic Arthritis Mutilans Score (BRAMS). Of 610 cases screened, AM was evident on the baseline film in 13/35 (37%) cases. AM was most commonly monoarticular (21/35; 60%) at baseline and polyarticular on the most recent film (28/35; 80%). The most frequently affected joints were foot interphalangeal (foot-IP)1, metatarsophalangeal (MTP)4, hand distal interphalangeal (DIP)2, and metacarpophalangeal 1 at baseline; foot-IP1, MTP3, MTP5, and hand proximal IP5 most recently. Median rate of progression of BRAMS was 7.80 (IQR 4.68–12.04), osteolysis 1.16 (IQR 0.54–2.56), each units/year. Nineteen of 29 (65.5%) AM cases had concurrent axial radiographic disease.

Dr. Jadon concluded that AM appears to present as a monoarticular disease, progressing to polyarticular involvement, and most commonly affects the feet. The rate of radiographic damage is pronounced in all domains. The prevalence and severity of concurrent axial radiographic disease in AM is far greater than observed in general PsA cohorts.

Do patients know best? Reliability of electronic patient self-evaluation of swollen and tender joints in psoriatic arthritis: A comparison study with B-mode ultrasonography, and physician and nurse assessments (Agnes Szentpetery, Dublin, Ireland). Dr. Szentpetery presented a study evaluating the reliability of patient self-assessed joint counts versus joint counts obtained by a physician, a nurse, and B-mode US in PsA. Patients assessed 68 of their own joints followed by a blinded examination from a different nurse and rheumatologist. US evaluation was performed by a further consultant rheumatologist on 34 joints.

Forty-three patients (29 female, 14 male) were enrolled in the study. Of the 34 joints assessed by US, the mean tender joint counts (TJC) assessed by the patients, physician, and nurse were 9 (± 8.3), 7 (± 7.4), and 7 (± 6.9), and mean swollen joint counts (SJC) were 4 (± 5.6), 1 (± 1.8), and 3 (± 3.2), respectively. Mean numbers of affected (swollen or tender) joints per patient, physician, nurse, and US evaluation were 10 (± 8.2), 7 (± 7.1), 8 (± 7), and 6 (± 4.4), respectively. Patient- and nurse-assessed SJC were significantly higher than physician counts ($p = 0.0007$; $p = 0.013$, respectively). The number of affected joints as evaluated by patients was higher compared to physicians and US ($p = 0.019$; $p = 0.012$, respectively). TJC and the number of affected joints did not correlate significantly with any of the US measurements irrespective of assessor. Patient SJC significantly correlated with US-assessed joint effusion, and with synovitis [greyscale and power Doppler (PD)]. Physician- and nurse-reported SJC correlated with US-derived synovitis scores only.

Dr. Szentpetery concluded that patients scored their SJC and number of affected joints higher than physicians and US measurements. Patient-reported SJC correlated with both effusion and synovitis as detected by US, suggesting that patients' self-evaluated SJC may be valid in routine clinical practice for monitoring disease activity in PsA.

Poster Presentations

Lisbeth Arancibia (São Paulo, Brazil) assessed the association between sleep quality, depression, fatigue, and quality of life in patients with PsA, using validated questionnaires to assess 29 patients who were classified into 3 groups based on their disease activity. A correlation was found between poor sleep quality, depression, worse quality of life, and high disease activity. These results highlight the need for a multidisciplinary approach in the management of patients with PsA.

Ana Maria Arredondo (San Rafael, Colombia) conducted a cross-sectional study of ultrasonographic nail features in 22 patients with psoriasis without arthritis and 3 healthy controls. The features included thickening of the nail, changes in ventral and dorsal plates, and the presence of PD signal at the nail bed and DIP joint[10]. Patients with psoriasis had higher prevalence of abnormal ultrasonographic nail features (4.3 vs 1). Additionally, patients with psoriasis had higher frequency of PD signal (37 vs 1 nails) and abnormal nail plates (32 vs 0 nails). Dr. Arredondo concluded that US can identify subclinical psoriatic nail disease and suggested further investigations are needed of the prognostic value of US of the nail in predicting psoriatic nail lesions and PsA.

Camila De Gaspari (São Paulo, Brazil) investigated the prevalence and predictors of work disability in patients with PsA. Of a total of 53 patients in the study, 66% of patients were not working (35% disabled because of PsA). Unemployment and work disability from PsA were associated with higher joint score, hypertension, and use of methotrexate (MTX), biologics, and nonsteroidal antiinflammatory drugs. Dr. De Gaspari concluded that work disability is prevalent in patients with PsA and suggested that an early PsA diagnosis and effective treatments may reduce work disability.

Quyen Huynh (San Diego, California, USA) assessed the duration and predictors of clinical benefit among PsA patients discontinuing tumor necrosis factor (TNF) inhibitors while

in a state of low disease activity (LDA). A total of 325 patients with PsA were assessed, using the CORRONA (Consortium of Rheumatology Researchers of North America) database; 146 of those patients lost clinical benefit after a median of 29.2 months. The predictors for loss of benefit at discontinuation of TNF inhibitors were Clinical Disease Activity Index > 3.2, patient's global assessment (PtGA) > 5, moderate Disease Activity Score (DAS), and smoking. These results suggest that patients with PsA who achieve LDA while receiving treatment may maintain clinical benefit after discontinuation of TNF inhibitors. Relapse may be predicted by smoking and by higher disease activity at the time of discontinuation.

Margarita Landi (Buenos Aires, Argentina) presented a study about the effect on quality of life of comorbidities in 76 patients with PsA. The most frequent comorbidities were cardiovascular diseases (57.3%), hypertension (64.5%), and dyslipidemia (27.6%); 36.8% of the patients were smokers, and 44.7% were obese. Obesity was associated with more active disease.

A similar study by Raul Sueldo (Tucuman, Argentina) compared the prevalence of metabolic syndrome (MetS) in 24 patients with psoriasis and 19 patients with PsA. The prevalence of MetS was higher in PsA (42.1%) compared with psoriasis alone (20.8%), although it did not reach statistical significance. Anti-TNF treatment was associated with a lower prevalence of MetS ($p = 0.05$) while sedentary lifestyle was associated with a higher prevalence of the disease ($p = 0.002$).

These 2 studies highlight the high prevalence of comorbidities and their association with disease activity, in particular cardiovascular conditions, in patients with psoriatic disease.

Maria Marino (Bogota, Colombia) compared the levels of leptin between 48 patients with psoriasis and 85 controls. No difference was found in leptin levels across the groups ($p = 0.52$). Higher leptin levels were found in females. Lower levels of leptin were found in patients who were using systemic medications for their psoriasis compared with controls ($p = 0.02$). Dr. Marino suggested that leptin might be considered a biomarker of treatment response, but more studies are needed.

Adrian Levine (Boston, Massachusetts, USA) compared the reasons for discontinuation of biologic and nonbiologic systemic medications in 159 patients with psoriasis who underwent 284 courses of treatment. The proportion of failures was higher in patients who were treated with nonbiologics compared to biologics (75% vs 48%, $p < 0.0001$). The most frequent reasons for discontinuation were lack of efficacy for biologics and side effects for nonbiologics. Adverse events were seen in the highest proportion with infliximab (IFX) and MTX, and golimumab had the highest rates of both loss and lack of efficacy. The study demonstrated the differences in the reasons for discontinuation of treatments for psoriasis between biologic and nonbiologic medications.

Alicia Lieberman (Rochester, New York, USA) assessed the hypothesis that the expression of receptor activator of nuclear factor-κB ligand (RANKL) in the epidermis of patients with PsA is higher compared to those with psoriasis only. Using immunohistochemical staining, Dr. Lieberman found increased cytoplasmic membrane-localized RANKL expression on keratinocytes from PsA samples compared to psoriasis alone. She also observed a differential staining pattern between keratinocytes from psoriasis and PsA plaque samples, with increased perinuclear and cytoplasmic staining of RANKL in PsA. These findings support the pretest hypothesis of the study and point to the potential role of epidermal RANKL in PsA disease pathogenesis.

Janice Lin (Boston, Massachusetts, USA) reported 3 cases [2 rheumatoid arthritis (RA), 1 PsA] of successful use of abatacept (ABA) in treating patients with psoriasiform eruptions induced by anti-TNF therapy. Initiation of ABA resulted in clearance of the rash while maintaining good control of the arthritis. Dr. Lin proposed an algorithm for the management of psoriasiform eruptions induced by anti-TNF therapy. Topical corticosteroids and/or phototherapy was suggested for mild eruptions. The addition of a systemic medication (such as MTX or dapsone), or a switch to another class of biologic therapy was suggested for moderate to severe eruptions. She concluded that ABA can be considered in patients with RA or PsA who experience anti-TNF induced psoriasiform eruptions.

Ana Millan (Barcelona, Spain) presented her group's experience in a combined dermatology-rheumatology clinic for the management of patients with psoriatic disease. Of the 47.5% of their patients who were referred for the confirmation of the diagnosis of PsA, 57.6% had the diagnosis of PsA confirmed on the first visit. Diagnostic or therapeutic resolution was achieved in 81% of cases after a maximum of 2 visits. Nail lesions presented a diagnostic challenge and required several consultations. Significant proportions of the patients had concomitant comorbidities: hypertension (23.4%), dyslipidemia (28.5%), psychiatric disorder (9.5%), and diabetes (7.6%). This study highlights the complexity entailed in the management of patients with PsA and suggests a model to approach these challenges.

Elena Pezzolo (Verona, Italy) investigated cognitive performance in patients with psoriasis in a study where the prevalence of mild cognitive impairment (MCI), as identified by neuropsychological tests, was compared between 41 patients with psoriasis and 37 controls. Structural brain changes, as assessed by high-field magnetic resonance imaging and cortical thickness analysis, were also compared across the groups. MCI was more prevalent in patients with psoriasis than in controls (44% vs 11%, $p = 0.002$). Cortical thickness analysis showed a reduction in brain thickness in parahippocampal, superior temporal, and frontal gyrus of left

hemisphere in psoriasis patients. These findings suggest that MCI affects a significant proportion of patients with psoriasis. Further studies are needed to elucidate the underlying mechanisms of these abnormalities.

Laura Savage (Leeds, UK) conducted a pilot study to assess the prevalence of US entheseal abnormalities in patients with severe psoriasis who did not have clinical arthritis. Twenty-five entheses in the upper and lower extremities in 19 patients were assessed using greyscale and power Doppler US (PDUS). Inflammatory abnormalities, including hypoechogeneity, thickening, tenosynovitis, joint effusion, bursitis, and PD signal, were found in 19 entheses within 6 patients. Five of these also had damage (enthesophytes, calcifications, bony erosions). Most of the abnormalities affected the lower limb entheses. No abnormalities were found in the wrists or small joints of the hands. Based on these results, Dr. Savage suggested that this short, targeted US of the Achilles tendons, plantar aponeurosis, and patellar and quadriceps tendons of the knee may be adequate to detect early PsA and may be performed in dermatology clinics.

Hagit Padova (Tel Aviv, Israel) performed a cross-sectional study that assessed the prevalence of TNF-α immunogenicity in PsA and its correlation to drug levels, disease activity, and the effect of MTX. Ninety-three patients with PsA who were treated with ADA (48), IFX (24), and etanercept (21) for more than 3 months were analyzed. Drug levels and the presence of antidrug antibodies (ADAb) were measured. ADAb were found in 54% of patients treated with ADA, 21% receiving IFX, and 0% receiving etanercept. ADAb correlated with low drug levels, higher 28-joint Disease Activity Score, and higher PtGA. The use of MTX was associated with a lower prevalence of ADAb ($p = 0.049$). This study showed that ADAb develop in a significant proportion of the patients treated with ADA and IFX. MTX may prevent the development of these antibodies and should be considered in combination with anti-TNF agents in the management of PsA.

Suzanne Tintle (Boston, Massachusetts, USA) performed a chart review of 61 patients with lupus erythematosus (LE), including systemic, discoid, or subacute cutaneous LE, who had a concomitant diagnosis of psoriasis or PsA. The safety and efficacy of disease-modifying antirheumatic drugs and biologic medication in these cases were reviewed. Twelve patients received at least 1 biologic agent, and only 1 patient experienced a flare of LE induced by a biologic (IFX). Of patients receiving biologics, the incidence of LE flare was 0.19% per patient-year. The proportion of patients with active LE or psoriatic disease who achieved remission was higher in those who used ustekinumab compared to nonbiologic systemic agents ($p < 0.01$). Four patients (33.3% of patients receiving biologics) remained well-controlled and without significant adverse effects while receiving ustekinumab. This study demonstrates that biologic agents, in particular ustekinumab, can be considered for the management of patients with moderate to severe psoriasis and concomitant LE.

Ingrid Serrato (Bogota, Colombia) assessed the performance of the PsA Screening and Evaluation (PASE) questionnaire as a screening tool in 77 patients with psoriasis attending a dermatology clinic. The diagnosis of PsA was confirmed by a rheumatologist in 22% of the patients. The median PASE score was higher in PsA compared with psoriasis alone (49 vs 23). A cutoff of 36 points identified PsA with a sensitivity of 69% and a specificity of 95%. The study supports the use of screening questionnaires in dermatology clinics to improve the detection of PsA in patients with psoriasis.

Recent literature suggests that epidermal insulin resistance contributes to different skin pathologies such as psoriasis or diabetes-associated skin conditions such as acanthosis nigricans (AN). Bartosz Malisiewicz (Frankfurt, Germany) studied the changes in epidermal insulin signaling caused by undertreatment in a patient with AN and type II diabetes. In this patient, optimized antidiabetic therapy with a glucagon-like peptide-1 analog was associated with an improvement of her AN. Skin biopsies showed signs of epidermal insulin resistance. Signs of epidermal insulin resistance ameliorated during antidiabetic treatment in nonlesional skin, while signs of epidermal insulin resistance remained in lesional skin. These changes were mediated by mammalian target of rapamycin (mTOR). The results of the study highlight the potential role of mTOR signaling and epidermal insulin resistance as an underlying mechanism of psoriasis.

Julio Ramirez (Barcelona, Spain) compared the extent of disease activity as assessed by greyscale and PDUS in patients of the hands and knees in 46 patients with RA and 54 patients with PsA who were in LDA with treatment by TNF inhibitors. Patients with PsA had lower US scores compared with patients with RA (9.5 vs 6.8, $p = 0.046$). Only 1 (1.8%) patient with PsA showed signs of active synovitis by US (positive PD signal and synovial hypertrophy ≥ grade 2) compared with 18 (39.1%) of patients with RA. This study suggests that there is higher concordance between the clinical and ultrasonographic assessment of disease activity in PsA compared with patients with RA.

Laura Maria Acosta Felquer (Buenos Aires, Argentina) assessed the frequency of ultrasonographic abnormalities in the joints, tendons, and entheses in 83 patients with PsA and their correlation with clinical remission. Dr. Acosta Felquer reported that of the 39% of patients who were in minimal disease activity (MDA), 46% in DAS28 remission and 36% in Disease Activity in PsA score remission had at least 1 site with positive PD signal. She concluded that a significant number of patients with PsA fulfilling MDA criteria or in clinical remission show ultrasonographic evidence of active inflammation.

Josefina Marin (Buenos Aires, Argentina) evaluated the proportion of patients who have actively inflamed joints

despite fulfilling the criteria for MDA and assessed the most frequent components of MDA that prevented patients from achieving MDA. Of the 83 patients with PsA who were assessed, 41 (49.3%) met the criteria for MDA. Only 1 patient (2.4%) showed > 2 tender joints, and 2 other patients showed ≥ 2 swollen joints. Altogether, 7.4% of patients in MDA had a clinically significant number of tender/swollen joints. Among patients not achieving MDA, patient pain (100%) and PtGA (76.5%) were the most frequently failed criteria. These results suggest MDA is an appropriate target in patients with PsA because only a minority of patients fulfilling MDA has clinically significant actively inflamed joints.

Tiago Silveira Lima (Rio de Janeiro, Brazil) assessed the frequency of HLA alleles in patients with geographic tongue (GT; n = 26), psoriasis vulgaris (58), and controls (125). He hypothesized that GT may be an oral manifestation of psoriasis. Higher frequency of HLA-A*25 (p = 0.044), HLA-B*57 (p = 0.001), and HLA-C*06 (p = 0.02) was seen in patients with psoriasis compared with GT and controls, while HLA-B*58 was more frequent in patients with GT (p = 0.018). No HLA-class II allele showed any difference across the groups.

Kory Parsi (Sacramento, California, USA) compared the rates of wound complications between patients with psoriasis and controls in a retrospective cohort of 164 patients with cutaneous wounds. The primary outcome was aggregated incidence of wound complications including wound infection, tissue necrosis, hematoma development, and leukocytosis. No significant differences were detected in incidence of wound complications (14.6% vs 13%, RR 1.11, CI 0.34–3.58) between patients with and without psoriasis.

The oral and poster presentations generated lively discussion among GRAPPA and SPARTAN members, and trainees were encouraged to continue their work. The next GRAPPA trainees symposium will be held in July 2015 in Stockholm, Sweden.

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