GRAPPA Fellows Symposium Adjacent to the European Academy of Dermatology and Venerology Meeting, Verona, 2012: A Meeting Report

Wolf-Henning Boehncke and Brian Kirby

ABSTRACT. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) organized a Fellows Symposium adjacent to the European Academy of Dermatology and Venerology (EADV) spring meeting in Verona, Italy, in 2012. Wolf-Henning Boehncke from Geneva and Brian Kirby from Dublin formed the faculty. Five papers were presented, followed by extended discussions among participants and faculty. Two contributions were on comorbidities of psoriasis patients and 2 on treatment of non-plaque-type psoriasis; the fifth presentation was a discussion of possible modes of action of vitamin D derivatives in the treatment of psoriasis. Summaries of all 5 papers are included here. (J Rheumatol 2013;40:1410–2; doi:10.3899/jrheum.130451)

Key Indexing Terms:
COMORBIDITIES PALMOPLANTAR PSORIASIS ERYTHRODERMA
PSORIATIC ARTHRITIS METABOLIC SYNDROME

Chronic plaques are the most common manifestation of psoriasis, and plaque-type psoriasis is most often studied in clinical trials. Consequently, all currently approved biologics for the treatment of psoriasis are exclusively licensed for plaque-type psoriasis. This has substantial implications for dermatology practice, since a significant minority of patients present with clinical manifestations other than plaque-type psoriasis. The use of biologics in these patients represents an off-label application, and resulting data are sparse[1].

In the first of 5 papers presented at the GRAPPA symposium, Noori Kim (Department of Dermatology, Tufts Medical Center, Boston, MA, USA) presented results of an investigator-initiated, open-label trial, wherein the group analyzed ustekinumab for the treatment of moderate to severe palmoplantar psoriasis[2]. Twenty subjects were included, half with pustular lesions at baseline; all patients had failed previous therapy with topical glucocorticosteroids. Ustekinumab was administered at Weeks 0, 4, and 16 according to the dosing approved for plaque-type psoriasis (45 mg for patients with < 100 kg body weight, 90 mg for those ≥ 100 kg). No other systemic or phototherapies were used during the treatment period. The primary endpoint was the percentage of patients achieving "clear" or "almost clear" on the Physician Global Assessment at Week 16.

Seven of the 20 patients experienced complete clearance at Week 16 of the trial. Interestingly, 6 of 9 patients receiving the 90 mg dose, but only one of 11 receiving the 45 mg dose, reached the primary endpoint. The patients' quality of life improved substantially at Week 24, with 56% improvement on the Dermatology Quality of Life Index [DLQI; baseline mean 13.9 (SD 7.0); Week 24 mean 6.2 (SD 6.3)].

The authors conclude that ustekinumab can effectively control signs and symptoms of palmoplantar psoriasis, particularly at the 90 mg dose. However, these conclusions must be interpreted carefully, because 5 patients did not complete the study (withdrawal of consent or loss of followup), and there was some uncertainty regarding the definite diagnosis of some patients, who may have had pustulosis palmoplantaris[3].

Erythroderma is another difficult-to-treat manifestation of psoriasis, particularly in childhood. In a case report, presented by Joana Maria Cabete (Department of Dermatology, Hospital de Santo Antonio dos Capuchos, Lisbon, Portugal), the group followed a 5-year-old boy who developed psoriasis at the age of 5 months[4]. Since then, he had had 3 episodes of erythrodermic psoriasis, which was controlled using cyclosporin A, followed by maintenance therapy with topical agents, including vitamin D derivatives and corticosteroids. When he was hospitalized during the last flare, he again developed erythrodermic psoriasis, complicated by hypovolemic shock, despite treatment with cyclosporin A (5 mg/kg body weight). After also taking antidepressants, he exhibited a developmental delay and refused to walk. Doctors decided to initiate etanercept therapy at 0.8 mg/kg body weight. After the first week of

From the Department of Dermatology, Geneva University Hospital, Geneva, Switzerland; and Department of Dermatology, St. Vincent's University Hospital, Dublin, Ireland.

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W-H. Boehncke, MD, Department of Dermatology, Geneva University Hospital; B. Kirby, MD, Department of Dermatology, St. Vincent's University Hospital.

Address correspondence to Dr. W-H. Boehncke, Department of Dermatology, Geneva University Hospital, Rue Gabrielle-Perret-Gentil 4, CH1211, Geneva 14, Switzerland. E-mail: wolf-henning.boehncke@hcuge.ch

treatment, the patient regained his walking capacity. He achieved complete clearance after 14 weeks of treatment, and the therapy was well tolerated. The authors conclude that etanercept may be an effective and well tolerated drug for the treatment of even young children with severe forms of psoriasis. To date, etanercept is the only biologic approved for the treatment of children with psoriasis; however, the label covers only plaque-type psoriasis in children ≥ 4 years old[5].

It is well established that psoriatic arthritis (PsA) is common (6%–40%) among patients with psoriasis and is progressive in about 50% of cases[6]. More recent studies suggest that, as in rheumatoid arthritis, a window of opportunity may exist where patients receiving treatment early in the course of their disease obtain better clinical results than those with a longer history of PsA. Therefore, screening for PsA is an important task for dermatologists seeing patients with psoriasis. Several questionnaires have been validated as screening tools for this purpose[7].

In a study presented by Muhammad Haroon (St. Vincent's University Hospital, Dublin, Ireland), the group assessed the prevalence of PsA among patients with psoriasis attending dermatology clinics, to identify clinical predictors of the development of PsA, and to compare the performance of 3 PsA screening questionnaires: the Psoriatic Arthritis Screening and Evaluation (PASE), Psoriasis Epidemiology Screening Tool (PEST), and the Toronto Psoriatic Arthritis Screening tool (ToPAS)[8].

The study was performed in 2 groups of patients (100 per group) in general dermatology and rheumatology clinics. Group 1 comprised consecutive patients attending dermatology clinics with (skin) psoriasis without known diagnosis of inflammatory arthritis. Group 2 comprised consecutive patients attending rheumatology clinics with a confirmed diagnosis of PsA. All patients in Group 1 were clinically evaluated by a rheumatologist.

In Group 1, 29% of patients were diagnosed with PsA after rheumatologic evaluation, and these patients had significantly less polyarticular disease, compared to Group 2 patients. On uni- and multivariate analyses, the only significantly positive association was noted between high Psoriasis Area and Severity Index scores and the new diagnosis of PsA (OR 1.454, 95% CI 1.0–2.11, p = 0.05; and OR 1.61, 95% CI 1.02–2.44, p = 0.023, respectively). In Group 1, the PEST, PASE and ToPAS had sensitivities of 27.5%, 24%, and 41%, and specificities of 98%, 94% and 90%, respectively. In contrast, sensitivities in Group 2 were 86%, 62%, and 83%. PEST and ToPAS had comparatively better sensitivities to identify polyarticular patterns of PsA (77% and 88%), but very low sensitivities for non-polyarticular disease manifestations (5% and 20%), while the PASE performed poorly on both polyarticular and non-polyarticular disease (22% and 20%).

The low sensitivities of all screening questionnaires, particularly in non-polyarticular PsA, demonstrate a need to develop better screening tools to effectively support dermatologists in their efforts to identify patients with PsA early.

Metabolic syndrome is a well recognized comorbidity of psoriasis. Recent studies documented a strikingly high prevalence of this and other comorbidities in children and adolescents with psoriasis. Investigating this issue, Shiu-Chung Au (Department of Dermatology, Tufts Medical Center, Boston, MA, USA) presented the results of an assessor-blinded study[9]. The group identified 20 patients between 9 and 17 years old with moderate to severe psoriasis (≥ 5% of body surface) or PsA, and compared this cohort with a control group of 1563 subjects from the National Health and Nutrition Examination Survey 2007–2008 database. Six of the 20 psoriasis patients (30%) but only 115 of the 1563 controls (7%) suffered from the metabolic syndrome (p = 0.045). No significant differences were found in body mass index (BMI) between the 2 groups (22.7 and 22.3, respectively; p = 0.74).

While the increased frequency of the metabolic syndrome in pediatric psoriasis might not be surprising, no significant differences in BMI between children with and without psoriasis were found in this study. Psoriasis may represent a state of chronic systemic inflammation where insulin resistance could play a key role in multiple symptoms of the metabolic syndrome, possibly also in the absence of obesity[10].

Finally, a paper by Cheryl Sweeney (St. Vincent's University Hospital, Dublin, Ireland) analyzed the effects of 1,25(OH)2D3 on cytokine production by Langerhans cells (LC), a specialized subset of dendritic cells residing in the epidermis (unpublished data). The group used monocyte-derived LC stimulated with the Toll-like receptor-2/dectin-1 agonist zymosan for their *in vitro* experiments, observing the production of interleukin 23 (IL-23) (supporting the clonal expansion of Th17 cells) and IL-10 (promoting the development of regulatory T cells). It was found that 1,25(OH)2D3 significantly suppressed zymosan-induced IL-23 production, but enhanced IL-10 in LC from healthy donors. Neither effect could be observed when LC from patients with psoriasis were used. However, 1,25(OH)2D3 directly suppressed IL-17 production in activated T cells from both healthy and psoriatic donors. Thus, a direct inhibitory effect on Th17 cells might be part of the anti-psoriatic efficacy of 1,25(OH)2D3.

This first GRAPPA Fellows Symposium adjacent to a major dermatology congress was highly stimulating, and received positive feedback from all participants. GRAPPA will continue to organize similar meetings, the next one to be adjacent to the EADV meeting in Istanbul in 2013.

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