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FOREWORD

Foreword

Peter C. M. van de Kerkhof[1]

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In a disease as heterogeneous as psoriasis, we need stratification to predict the course of the disease in the individual patient and to provide the most optimal treatment to patients with the various subtypes. Generalized pustular psoriasis (GPP) has been shown to be associated with enhanced interleukin (IL)-36 signaling, partly based on loss-of-function mutations of *IL36RN*.

In this supplement, the different chapters provide a comprehensive understanding of GPP, which, in turn, provides a step towards a successful targeted treatment.

The variation of the prevalence of GPP across the world suggests that GPP has an important genetic trait. Min Zheng, Denis Jullien, and Kilian Eyerich provide us with an insight into the genetics related to the phenotype [1].

Understanding the inflammatory pathways and associated risk factors in the development of GPP is required before pathogenesis-based treatments can be developed. The IL-36 pathway appears central to GPP pathogenesis, and early phase data indicate that treatments targeting various components of this pathway represent promising treatments for GPP. In the second article, Slaheddine Marrakchi and Lluís Puig summarize the current understanding of GPP, describe novel therapeutic options, and detail how the unique pathophysiology of the disease may guide future treatment strategies [2].

The clinical course and characteristics of GPP have been described by Siew Eng Choon, Alexander A. Navarini, and Andreas Pinter [3]. The course with flares and remissions may be highly variable and various triggering factors may be important.

Diagnosis of GPP can be complicated. A relationship with plaque psoriasis may exist or may be entirely missing. Generalized and localized forms of pustular psoriasis may present. Biomarkers such as loss-of-function mutations of *IL36RN*, amongst other genetic mutations, may be of help to define pustular psoriasis at the genetic level. In their article, Hideki Fujita, Melinda Gooderham, and Ricardo Romiti provide an integrated description of current diagnostic methods, differential diagnosis strategies, and future advances in the diagnosis of GPP [4].

For more effective and accurate monitoring of patients, disease assessment tools are needed such as the Generalized Pustular Psoriasis Physician Global Assessment and the Generalized Pustular Psoriasis Area and Severity Index, as well as tools to measure patient-reported outcomes. A critical presentation and review of assessment tools is provided by A. David Burden, Siew Eng Choon, Alice B. Gottlieb, Alexander Navarini, and Richard B. Warren [5].

An overview of treatment options and goals is provided by James Krueger, Lluís Puig, and Diamant Thaçi [6]. Based on case reports and small, open-label, single-arm studies, we have evidence that some of the classical systemic treatments and biologics are effective in GPP. We have, however, no GPP-specific therapies approved in the USA or Europe. Based on the discovery of *IL36RN* mutations and the central role of IL-36 receptor ligands in the pathogenesis of GPP, biologics that target the IL-36 pathway have demonstrated promising efficacy in patients with GPP.

Finally, Dale R. Reisner, Frida Dunger Johnsson, Nirali Kotowsky, Steven Brunette, Wendell Valdecantos, and Kilian Eyerich report on the outcomes of a survey on the burden of GPP in people with the condition, and highlight the substantial emotional burden of GPP and its impact on daily life of patients [7].

Generalized pustular psoriasis is a showcase of successful research on disease stratification. Genetic associations have been discovered, IL-36 signaling proved to be a crucial pathway in the immune-pathogenesis of GPP, and finally, a treatment targeted at the IL-36 receptor proved to be highly effective in pustular psoriasis.

✉ Peter C. M. van de Kerkhof
Peter.vandeKerkhof@radboudumc.nl

[1] Department of Dermatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Declarations

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