News Release

Title

Autoinflammatory keratinization diseases

Key Points

- Autoinflammatory pathogenic mechanisms have been elucidated one by one in inflammatory keratinization disorders.
- Here we advocate for the new disease category autoinflammatory keratinization diseases, which describes inflammatory keratinization disorders with autoinflammatory mechanisms as their predominant etiology.
- Further understanding of the pathophysiology of autoinflammatory keratinization diseases may contribute to innovation of novel, more effective therapies for autoinflammatory keratinization diseases as autoinflammatory syndromes.

Summary

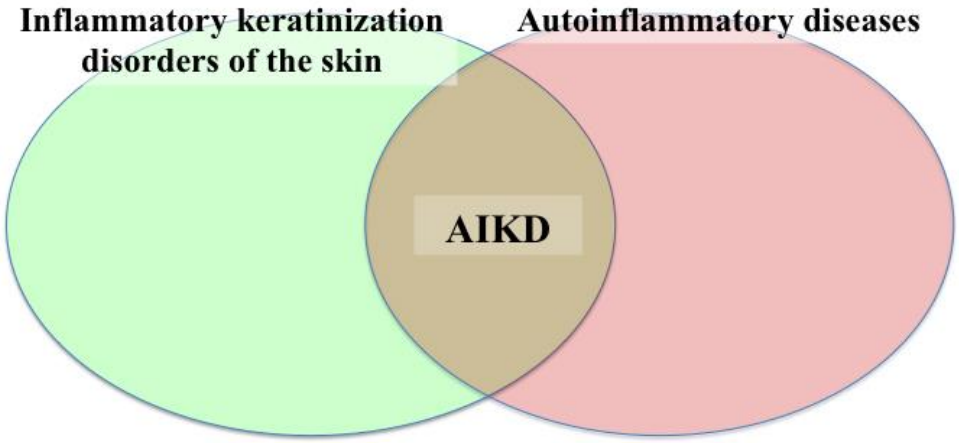
Prof. Masashi Akiyama, Dr. Takuya Takeichi at Department of Dermatology, Nagoya University Graduate School of Medicine (Dean: Kenji Kadomatsu, MD, PhD), Prof. John A. McGrath, MD, FRCP, at St John's Institute of Dermatology, King's College London, Guy's Hospital, and Prof. Kazumitsu Sugiura at Department of Dermatology, Fujita Health University School of Medicine, reviewed inflammatory keratinization disorders with autoinflammatory pathogenic mechanisms and advocate the novel, unique concept of "autoinflammatory keratinization diseases" (AIKD). The authors propose the following definition of AIKD. (1) The primary and main inflammation sites are the epidermis and the upper dermis. (2) The inflammation in the epidermis and the upper dermis leads to hyperkeratosis, which is the main and characteristic phenotype of AIKD. (3) AIKD have primary genetic causative factors associated with the hyperactivation of innate immunity (autoinflammation), mainly in the epidermis and the upper dermis. (4) The concept of AIKD subsumes diseases with mixed pathomechanisms of autoinflammation and autoimmunity. AIKD have genetic abnormalities as causative factors, and hyperactivation of the innate immune system resulting from those genetic defects plays an important role in the pathogenesis. The new disease category AIKD includes minor subsets of psoriasis and related diseases, pityriasis rubra pilaris type V and keratosis lichenoides chronica. Inflammatory hyperkeratotic skin lesions are not common in conventional autoinflammatory diseases. Thus, although AIKD is thought to have autoinflammatory pathogenic mechanisms, unique pathomechanisms with inflammation that involves epidermal keratinocytes and results in hyperkeratosis are assumed in AIKD. As the causes/predisposing factors for inflammatory keratinization disorders come to be successively elucidated, a larger number of disorders will be categorized into AIKD.

Research Background

The pathogenic mechanisms of most inflammatory keratinization disorders are still unknown. Concerning some inflammatory keratinization disorders, genetic causes and predisposing factors have been reported recently. Among the genetic causes/predisposing factors, several factors are associated with autoinflammatory mechanisms. In other words, autoinflammatory pathogenic mechanisms have been elucidated one by one in inflammatory keratinization disorders.

Research Results

The research team reviewed the inflammatory keratinization disorders with autoinflammatory pathogenic mechanisms and advocates the novel, unique concept of "autoinflammatory keratinization diseases" (AIKD). The authors propose the following definition of AIKD. (1) The primary and main inflammation sites are the epidermis and the upper dermis. (2) The inflammation in the epidermis and the upper dermis leads to hyperkeratosis, which is the main and characteristic phenotype of AIKD. (3) AIKD have primary genetic causative factors associated with the hyperactivation of innate immunity (autoinflammation), mainly in the epidermis and the upper dermis. (4) The concept of AIKD subsumes diseases with mixed pathomechanisms of autoinflammation and autoimmunity. AIKD have genetic abnormalities as causative factors, and hyperactivation of the innate immune system resulting from those genetic defects plays an important role in the pathogenesis. Right now, minor subsets of psoriasis and related diseases, pityriasis rubra pilaris type V and keratosis lichenoides chronica are included in the new disease category AIKD.



Research Summary and Future Perspective

The authors advocate the new disease category "autoinflammatory keratinization diseases" (AIKD), which describes inflammatory keratinization disorders with autoinflammatory mechanisms as their predominant etiology, including minor subsets of psoriasis and related diseases, PRP type V and KLC. Inflammatory hyperkeratotic skin lesions are not common in conventional autoinflammatory diseases. Thus, although AIKD is thought to have autoinflammatory pathogenic mechanisms, unique pathomechanisms with inflammation that involves epidermal keratinocytes and

results in hyperkeratosis are assumed in AIKD. As the causes/predisposing factors for inflammatory keratinization disorders come to be successively elucidated, a larger number of disorders will be categorized into AIKD.

The novel identification of genetic causes and disease susceptibility factors and the correct evaluation of their significance to the pathogenesis promise to give clues for further understanding of the pathophysiology of AIKD and for developing novel, more effective therapies for them as autoinflammatory syndromes.

Publication

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