Desmoglein Story from Masayuki Amagai Teach us How to Discover the Beauty of Nature

After so many years of learning about the epidemiology, nature, diagnosis and management of the pemphigus group and other bullous dermatoses at University Department of Dermatology and Venereology, Zagreb University Hospital Center and School of Medicine, it was wonderful to discover – from the oral presentation entitled "Bullöse Dermatosen 2007" held by Prof. Michael Hertl in Graz (Austria) at the 3rd Derm Akademie Graz, October 20, 2007 – the beauty of the exact molecular mechanism of the pathogenesis of pemphigus and cell-cell adhesion of keratinocytes, clarifying the question of desmoglein as a transmembrane glycoprotein of the desmosome. The modern history of pemphigus began with the discovery of circulating antibodies against the cell surface of keratinocytes in the sera of patients with pemphigus vulgaris (PV) by Beutner and Jordan in 1964 (1,2). In the late 1970s and early 1980s, it was demonstrated that autoantibodies in pemphigus are pathogenic and induce blister formation in skin organ culture systems, and Anhalt demonstrated IgG passive transfer from patients to neonatal mice (3). In 1982, Stanley *et al*. identified PV antigen in PV sera as glycosylated 130kDa glycoprotein (4); later Hashimoto *et al*. showed epidermal extracts binding to 130-kDa polypeptide (5); and in 1984 Stanley *et al*. first characterized pemphigus foliaceus (PF) antigen as a polypeptide of about 160-kDa and recognized by PF sera as identical to desmoglein 1 (Dsg (1). In 1991, Amagai *et al*. isolated a cDNA clone for the PV antigen from the sera of patients with PV (6). Both Dsg1 and PV antigen are cadherin-type adhesion molecules that occur in desmosomes. PV antigen is termed desmoglein 3 (Dsg3) closely related to Dsg1 (1). IgG autoantibodies against Dsg1 and Dsg3 are pathogenic and induce blister formation in pemphigus, and can cause suprabasilar acantholysis, a typical histologic finding in PV. Thus, pemphigus has been redefined as an antidesmoglein autoimmune disease.

PV can be divided into 2 subgroups: the mucosal dominant type (anti-Dsg3 IgG) with minimal blister skin involvement, and the mucocutaneous type with extensive skin blisters and mucosal involvement with anti-Dsg3 and anti-Dsg1 IgG with distinct intraepithelial expression patterns. Patients with PF have only anti-Dsg1 IgG autoantibodies that are insufficient to induce blisters in neonatal skin, which is rarely absent in pregnant women with pemphigus but neonates of mothers with PV develop blisters. PF shares many features with staphylococcal scaled skin syndrome (SSSS): both diseases involve only the skin, have desmoglein 1 autoantibodies and show superficial epidermal separation (1). Now we known that PV and PF had different autoantigens. We dermatologists see many different skin lesions in a variety of shapes. That is why we could enjoy while listening to Prof. Hertl's lecture. As Prof. Masayuki Amagai said, "the nature shows amazing beauty and logic. If you continue seeing the shape of skin lesions with your own eyes in your daily practice, you will have plenty of chances to discover the beauty of nature".

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References

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