Two Different Isoforms of Desmocollin Are Recognized by Autoantibodies in Various Types of Pemphigus

T.		Hashimoto
T.		Ebihara
T.		Nishikawa

Department of Dermatology, Keio University School of Medicine, Tokyo, Japan

Key Words

Cadherin
Desmocollin
Desmosome
Intercellular IgA vesiculopustular dermatosis
Pemphigus

Abstract

We have previously reported that, in addition to [well-known](#) pemphigus antigens (desmoglein and pemphigus vulgaris antigen), desmocollin (Dsc), another desmosomal cadherin, is recognized by certain pemphigus sera. Furthermore, we noticed that two Dsc species with a slightly different relative molecular weight were recognized by various pemphigus sera. This difference may contribute to the different clinicopathological features between the subcorneal pustular dermatosis type and the intraepidermal neutrophilic IgA dermatosis type of intercellular IgA vesiculopustular dermatosis.

Takashi Hashimoto, MD, Department of Dermatology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo 160 (Japan)

Buxton et al. [1 and the references therein] have recently proposed a new nomenclature for desmosomal cadherins. According to their paper, desmosomal cadherins are divided into two groups, desmoglein (Dsg) and desmocollin (Dsc), both of which consist of multiple isoforms derived from different genes. Pemphigus is divided into two major subtypes, pemphigus vulgaris (PV) and pemphigus folia-ceus (PF). Brazilian pemphigus foliaceus (BPF) is seen endemically in certain areas of South America.

A number of cases with anti-cell-surface antibodies of IgA class showing various clinical features have recently been reported, and we previously proposed the term intercellular IgA vesiculopustular dermatosis (IAVPD) for these cases [2, 3 and the references therein]. Like PV and PF, IAVPD also seems to be divided into two subtypes, an intraepidermal neutrophilic IgA dermatosis (IEN) type showing pustule formation and IgA deposition in the entire epidermis [4] and a subcorneal pustular dermatosis (SPD) type showing pustules and IgA deposition in the upper epidermis [5].

Autoantigen for PF was identified as Dsg [6], and various evidences indicate that PF sera seem to react with Dsgl [1,7]. Later, by molecular cloning using PV sera as a probe, Amagai et al. [8] revealed that PV antigen is a highly homologous protein to Dsgl. PV antigen is actually Dsg3 according to the new nomenclature [1]. Moreover, we have recently reported that another desmosomal cadherin, Dsc, is also recognized by certain pemphigus sera, particularly IAVPD [2] and BPF [9].

In the present study, to further study the anti-Dsc autoantibodies, we examined sera from 15 PV patients, 15 sporadic PF patients, 10 BPF patients, 7 IAVPD patients (4 cases of SPD type and 3

of IEN type) and 2 cases with anti-keratinocyte cell surface antibodies of both IgG and IgA classes (referred to as a G/A case).

We first surveyed sera from various types of pemphigus for the presence of anti-Dsc autoantibodies of either IgG or IgA class by immunoblot analyses using a bovine snout desmosome preparation, by comparing the reactivity with those of anti-Dsc antibodies. As we have previously

© 1994 S.KargerAG. Basel 1018-8665/94/1897-0124 \$ 5.00/0

reported [2, 9], with immunoblot of a desmosome preparation, some sera from all types of pemphigus, particularly BPF, G/A and IAVPD, reacted with a doublet of proteins showing similar migrations as proteins recognized by anti-Dsc antibodies. These antibodies included IgG antibodies from 3 out of 15 PV, 1 of 15 PF and 5 of 10 BPF, both IgG and IgA antibodies from one G/A, only IgA antibodies from another G/A and IgA antibodies from 4 of 7 IAVPD.

However, closer inspection revealed that most patients' sera reacted with a doublet of proteins with a slightly lower molecular weight (Dsc-L), while fewer sera reacted with a doublet of proteins with a slightly higher molecular weight (Dsc-H). All of these data are summarized in table 1.

In order to confirm this heterogeneous reactivity with Dsc, we next produced recombinant Dsc1 protein as reported previously [9] and examined the reactivity of the patients' sera with the recombinant protein by immunoblot (table 1). Almost all sera containing anti-Dsc-L autoantibodies reacted specifically with this protein, although BPF sera reacted with Dsc-H were negative for this protein. Although IgA antibodies in both G/A patients weakly but clearly reacted with this protein, none of IAVPD sera showed apparent reactivity with this protein. It is at present unknown which isoform of bovine Dsc the Dsc-H belongs to. Sequence comparison analysis for various species of Dsc will answer this question in the future.

The most interesting speculation drawn from above results is that the distinct antigen profile may be responsible for the clinicopathological difference between IEN and SPD types of IAVPD.

Only sera of the IEN type reacted with Dsc-H, and only sera of the SPD type reacted with Dsc-L (Dsc1). Therefore, there may be a possibility that

Table 1. Summary of reactivity of sera from various types of pemphigus with immunoblot analyses of bovine desmosome preparation and Dsc1 recombinant protein

anti-Dsc-H antibodies in IEN type sera bind their antigen expressed in the whole epidermis and produce the lesions in the whole epidermis, whereas anti-Dsc1 antibodies in SPD type sera bind to and produce lesions in the upper epidermis. To clarify whether the anti-Dsc autoantibodies actually play a role in the pathogenesis of pemphigus, further studies on more cases with anti-Dsc autoantibodies should be needed.

Acknowledgment

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan (04454289), a Collaboration Research Project of the British Council, Tokyo, Japan, and a grant from the Ministry of Health and Welfare of Japan.

References

Buxton RS, Cowin P, Franke WW, Garrod DR, Green KJ, King IA, Koch PJ, Magee At, Rees DA, Stanley JR, Steinberg MS: Nomenclature of the desmosomal cadherins. *J Cell Biol* 1993;121:481-483.

Ebihara T, Hashimoto T, Iwatsuki K, Takigawa M, Ando M, Ohkawara A, Nishikawa T: Auto-antigens for IgA anti-intercellular antibodies of intercellular IgA vesiculopustular dermatosis. *J Invest Dermatol* 1991;97:742-745. Iwatsuki K, Hashimoto T, Ebihara T, Teraki Y, Nishikawa T, Kaneko F: Intercellular IgA ve-siculo-pustular dermatosis and related disorders: Diversity of IgA anti-intercellular autoantibodies. *Eur J Dermatol* 1993;3:7-11.

Teraki Y, Amagai N, Hashimoto T, Kusunoki T, Nishikawa T: Intercellular IgA dermatosis of childhood: Selective deposition of monomer IgA1 in the intercellular space of the epidermis. *Arch Dermatol* 1991;127:221-224. Hashimoto T, Inamoto N, Nakamura K, Nishikawa T: Intercellular IgA dermatosis with clinical features of subcorneal pustular dermatosis. *Arch Dermatol* 1987; 123:1062. Stanley JR, Koulu L, Klaus-Kovtun V, Steinberg MS: A monoclonal antibody to the desmosomal glycoprotein desmoglein I binds the same polypeptide as human autoantibodies in pemphigus foliaceus. *J Immunol* 1986; 136: 1227-1230.

Koch PJ, Walsh MJ, Schmelz M, Goldschmidt MD, Zimbelmann R, Franke WW: Identification of desmoglein, a constitutive desmosomal glycoprotein, as a member of the cadherin family of cell adhesion molecules. *Eur J Cell Biol* 1990;53:1-12.

Amagai M, Klaus-Kovtun V, Stanley JR: Autoantibodies against a novel epithelial cadherin in pemphigus vulgaris, a disease of cell adhesion. *Cell* 1991;67:869-877. Dmochowski M, Hashimoto T, Garrod DR, Nishikawa T: Desmocollins I and II are recognized by certain sera from patients with various types of pemphigus, particularly Brazilian pemphigus foliaceus. *J Invest Dermatol* 1993; 100:380-384.