Pemphigus vulgaris in Two MHC-Haploidentical Brothers

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Key Words

Pemphigus vulgaris
Major histocompatibility complex
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Pemphigus vulgaris (PV) is an autoimmune bullous dermatosis caused by antibodies to desmoglein 3, a keratinocyte membrane protein [1]. Although PV etiology remains elusive, it is well known that some alleles of the major histocompatibility complex (MHC) confer a stronger susceptibility to this condition [2]. Nevertheless PV affects members of the same family with a low frequency [3]. We report two brothers with PV who shared identical MHC haplotypes.

A 43-year-old white Spanish male presented with bullae and erosions of his mouth, trunk and members. A skin biopsy showed suprabasal acantholysis, and direct immunofluorescence (DIF) of per-ilesional skin revealed IgG and C3 deposition in epithelial intercellular spaces. Circulating epithelial intercellular substance antibodies (EICSA) were detected at a titer of 1/160 by indirect immunofluorescence (IIF) with monkey esophagus as substrate. Three months later, a 40-year-old brother of this patient was seen in another department of dermatology for widespread bullae and erosions. A skin biopsy and DIF confirmed the diagnosis of PV. IIF on monkey esophagus revealed EICSA at a titer of 1/160.

MHC typing of both brothers and the rest of their living relatives (mother, sister, brother, sons, daughters, nieces and nephews) was done (fig. 1). Using monkey esophagus as substrate, we examined the presence of EICSA in the whole family and only found it in the two members clinically affected by PV.

PV is an autoimmune disease with a strong association with some MHC alleles. In Jewish patients, the alleles more commonly found are DR4 and DQ8, and in non-Jewish the former as well as DR6 and DQ5 are found [4, 5].

The relation of PV to the MHC has been well demonstrated but only a few cases of familial PV have been reported. Beutner and Chorzelski [6] found only one case of familial PV in their series of 234 cases. Reohr et al. [3] studied the MHC of two siblings with PV by restriction fragment polymorphism methods and found that they shared the DR4 and DQw 3.2 alleles.

Although familial occurrence of PV is rare, some authors have found the presence of antibodies to PV antigen at a low level in almost 50% of healthy relatives of PV patients [7, 8]. They studied sera by immunoblot, which has a better sensitivity than IIF. Ahmed et al. [7] found that the inheritance of these low antibody levels in asymptomatic relatives of PV patients was linked

to DR4 or DR6 haplotypes. He postulated that some MHC alleles would confer a predisposition to PV and that a second trigger would be necessary to develop this disease. Bhol et al. [9] demonstrated that sera from patients with active PV contained antibodies to pemphigus antigen of the IgG1 and IgG4 subclasses, while sera from healthy relatives and patients in remission only had antibodies of the IgG1 subclass. Brenner et al. [10] also suggested that some drugs could act as trigger factors in some cases of familial PV.

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A3 Cw7 B7 Bw6 DR4 DR53 DQ3 A2 Cw5 B44 Bw4 DR11 DR52 DQ7

PATIENT M

A3 Cw7 B7 Bw6 DR4 DR53 DQ3 A11 C- B14 Bw6 DR4 DR53 CQ3

M

A11 C- B14 Bw6 DR4 DR53 DQ3 A32 Cw4 B35 Bw6 DR4 DR53 DQ3

A3 Cw7 B7 Bw6 DR4 DR53 DQ3 A33 C- B14 Bw6 DR1 DQ1

M

A2 Cw5 B44 Bw4 DR11 DR52 DQ7 A1 Cw7 B8 Bw6 DR3 DR52 DQ2

A1 Cw7 B8 Bw6 DR3 DR52 DQ2 A23 Cw5 B50 Bw6 DR4 DR53 DQ3

A2 Cw5 B44 Bw4 DR11 DR52 DQ7 A23 Cw5 B50 Bw6 DR4 DR53 DQ3

Fig. 1. MHC of both patients and their family. M = Male; F = female.

PV was diagnosed in our two patients based on clinical, histo-pathological and immunofluorescence data. They were MHC-haplo-identical and homozygous for DR4 and DQ3. MHC typing was done in their nearest living relatives and, surprisingly, we found that a sister was MHC-haploidentical to the patients. She did not have any skin disease or cutaneous fragility and IIF was negative as in the other healthy relatives.

Our data confirm the hypothesis that PV is an autoimmune disease related to the MHC and that other factors are needed for its full development.

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Adenocarcinoma of the Mouth in a Patient with Psoriasis under Short-Term Cyclosporine Therapy

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Key Words

Psoriasis ■ Cyclosporine · Side effect · Carcinoma

Cyclosporine (CsA) can be effective in the treatment of several diseases, however, an increased risk of developing malignant neoplasms including lymphomas and solid tumors has also been reported. We describe a case of adenocarcinoma of the mouth of minor salivary gland origin which developed during the course of oral CsA therapy in a patient with psoriasis.