Complement in Pemphigus Vulgaris and other Bullous Dermatoses

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Received February 10, 1975

Summary. The behaviour of the complement and of its components C4 and C3 has been studied in serum and in blister fluid both in patients with pemphigus vulgaris and other bullous dermatoses and in healthy subjects with experimentally induced blisters.

The results are suggestive of local activation of the complement, in the blister fluid of patients with pemphigus vulgaris, pemphigus erythematosus and bullous pemphigoid according to the classical enzymatic sequence.


Die Ergebnisse sprechen für eine lokale Aktivierung von Komplement im Sinne der klassischen Enzymsequenz bei Patienten mit Pemphigus vulgaris, Pemphigus erythematosus und beim bullösen Pemphigoid.

Introduction

It is possible that the complement plays an important role in autoimmunobullous dermatoses. In some of them, e.g. in bullous pemphigoid, specific autoantibodies that are capable of binding the complement are present in the sera of most patients [3]. Instead in pemphigus vulgaris it is not yet verified whether or not the autoantibodies to the intercellular substance (ICS) of epidermis and mucosa are capable of binding complement. In fact, in pemphigus vulgaris even if the fixed complement in intercellular areas of epidermis has been shown by direct immunofluorescent staining in some skin lesions [1,2,5,13], such a phenomenon has not been confirmed by indirect immunofluorescent assays [4]. However, recent research carried out with haemolytic assays would suggest that also in pemphigus vulgaris [6], as well as in bullous pemphigoid [7,11], the complement is activated in the blister fluid, both according to the classical enzymatic sequence, that is by formation of C3 convertase, and according to the properdinic pathway or “C3 shunt”, in which the early three complement components (C1, C4 and C2) are not utilized.

Since the hypothesis of the complement activation in blister fluid, particularly via the classical pathway, is of considerable immunologic interest in pemphigus vulgaris, as well as in other autoimmune bullous dermatoses, we undertook the present study to determine if such a hypothesis could be confirmed by evaluation
of the total complement and immunochemical dosage of its components C4 and C3 in serum and in blister fluid both of patients with pemphigus vulgaris and other bullous dermatoses and of healthy subjects with experimentally induced blisters.

**Materials and Methods**

**Patients**

Eight patients were studied: four with pemphigus vulgaris one with pemphigus erythematosus, two with bullous pemphigoid and one with blisters which appeared on scars of relatively recent burns. Diagnosis of patients suffering from pemphigus and pemphigoid was supported by cytological and histological examinations. Indirect immunofluorescence, using rabbit oesophagus as a substrate, demonstrated ICS antibodies in the sera of the four with pemphigus vulgaris (titres ranged between 1:16 and 1:240) and antibodies directed against the basement membrane (BM) in the sera of the two with bullous pemphigoid (titres 1:64 and 1:320). Both the ICS (titre 1:128) and BM (titre 1:32) antibodies were detected in the serum of the patient with pemphigus erythematosus. No circulating ICS and BM antibodies were detectable in the patient with blisters on burn scars.

**Controls**

The control group comprised of four healthy voluntary subjects, on whom blisters were provoked by cantharidin or solid carbon dioxide, and of one with second degree burns.

**Methods**

Paired specimens of serum and blister fluid were collected from each examined subject under sterile conditions. A part of each specimen was utilized within the first eight hours after collection, for the dosage of the total complement activity by method of 50% haemolysis [10]. The rest was stored at −25°C until it was used for the quantitative determination of the complement components C4 and C3 and of the immunoglobulins (Ig) with the single radial immunodiffusion method [9]. Partigen® immunodiffusion plates (Behringwerke) were used containing the following antisera: goat anti-human Ig (γG + γA + γM), rabbit anti-human C4 B1E and rabbit anti-human C3 fragment B1A.

For each sample of serum and blister fluid, the total haemolytic complement was expressed in CH50 units per 10 mg of Ig and the two components C4 and C3 were expressed in mg per 10 mg of Ig.

**Results**

The results of this study are presented in Tables 1—4.

**Total Complement**

In the patients with pemphigus vulgaris, pemphigus erythematosus and bullous pemphigoid, the complement levels in the blister fluid, expressed in CH50 units/10 mg of Ig, were found to be not ably reduced when compared to the serum levels. Instead, in the control subjects and in the patient with blisters on burn scars the complement titres were found to be practically equivalent in the serum and in the blister fluid.

**Complement Components C4 and C3**

In the blister fluid of the patients with pemphigus vulgaris, pemphigus erythematosus and bullous pemphigoid, the concentration of the complement component C4 and C3, expressed in mg/10 mg of Ig, when compared to the serum levels, was reduced. In 1 of the 2 patients with bullous pemphigoid (case 7) the level of these