Prevalence of autoantibodies in patients with pemphigus

Sir,

Pemphigus is an autoimmune blistering skin disease mediated by pathogenic antibodies directed against desmoglein (Dsg). It includes two major forms: pemphigus vulgaris (PV) and pemphigus foliaceus (PF). Several reports suggest an association between pemphigus and other autoimmune disorders. Such data are mainly based on isolated case reports or on serologic surveys using a limited number of autoantibodies.[1-5] Data related to the prevalence of nonorgan-specific autoantibodies in pemphigus are often lacking.

In order to determine the possible association between pemphigus and other autoimmune phenomena, we screened serum samples from 40 Tunisian patients with pemphigus (28 PV and 12 PF) and 40 healthy Tunisian volunteers (control group) for the presence of the following antibodies: anti-desmoglein antibodies (Anti-Dsg); antinuclear antibodies (ANA); anti-cardiolipin antibodies (aCL); anti-smooth muscle antibodies (ASMA); gastric parietal cell antibodies (GPCA); anti-mitochondrial antibodies (AMA); liver kidney microsomal (LKM1); rheumatoid factor (RF).

Anti-Dsg (1 and 3) and aCL were detected using commercial ELISA (MBL, Nagoya, Japan and Binding site, respectively). ANA, ASMA, GPCA, AMA and anti-LKM1 antibodies were determined by indirect immunofluorescence on homemade liver, stomach and kidney cryostat sections from a Wistar rat. Cut-offs were 1:80 for ANA and 1:40 for ASMA, anti-LKM1 antibodies, GPCA and AMA. The RF was detected using human IgG-covered latex particle agglutination.

For statistical analysis, a *P*-value less than 0.05 was considered statistically significant.

Table 1 summarizes major results of this study. Within the pemphigus group, 35% (PV: 10/28, PF: 4/12) were positive for at least one of the following autoantibodies: ANA, ASMA, GPCA and AMA versus only 12.5% of healthy controls with a statistically significant difference (P=0.017). Two patients with PV exhibited antibodies against two different specificities (ASMA with aCL and ANA). In our cohort, ASMA and aCL were the most frequently detected autoantibodies.

Table 1: Autoantibody positivity in the pemphigus patients and the control group

Autoantibodies	Pemphigus (n=40) (PV/PF)	Healthy controls (n=40)	P value
Anti-Dsg 1	23 (12/11)	2	<0.05
Anti-Dsg 3	25 (23/2)	0	<0.05
ANA	4 (3/1)	2	>0.05
aCL	6 (5/1)	1	0.052
ASMA	6 (4/2)	2	>0.05
GPCA	1 (PF)	1	>0.05
AMA	0	0	>0.05
LKM1	0	0	>0.05
RF	0	0	>0.05

Anti-Dsg: Anti-desmoglein antibodies, ANA: Antinuclear antibodies, aCL: Anti-cardiolipin antibodies, ASMA: Anti-smooth muscle antibodies, GPCA: Gastric parietal cell antibodies, AMA: Anti-mitochondrial antibodies, LKM1: Liver kidney microsomal, RF: Rheumatoid factor, N: Number, PV: Pemphigus vulgaris, PF: Pemphigus foliaceus

Concerning aCL, they were found in sera of 15% (6/40) of pemphigus patients, whereas they were detected in only one healthy volunteer (2.5%), the difference was significant (P=0.052). Interestingly, the frequency of aCL was significantly higher in the PV subgroup compared with healthy controls (PV: 5/28, HC: 1/40; P=0.039). Besides, within the pemphigus group, three patients exhibited aCL at a high titer (>40 GPL/ml), whereas for the healthy controls the titer was low (16.67 GPL/ml). None of the patients or the healthy controls showed clinical symptoms of thromboembolism.

For all the others tested for autoantibodies, there was no significant difference between patients and healthy controls. Besides, no significant difference was noted between the untreated and the treated patients or between the PV and PF subgroups [Table 1].

The present study demonstrated that, globally, the occurrence of nonspecific autoantibodies in patients with pemphigus is higher than that observed in healthy controls. There was no clinical evidence of other concomitant autoimmune diseases. However, when we analyze the individual frequency of each tested antibody (except for anti-Dsg), there was no significant difference between the whole pemphigus group (without considering PV and PF subgroups) and healthy controls. Our results corroborate with findings obtained in other series, showing that ASMA, RF, AMA, GPCA and LKM1 positivity is not frequent in pemphigus.[5] Concerning ANA, their prevalence was low in our pemphigus cohort and, in the literature, there are conflicting results concerning its presence in pemphigus patients.[1,2] This may be explained by a variation in the genetic background of the cohorts,

differences in the techniques as well as differences in the number of enrolled patients.

It is worth noticing that corticosteroids and/or immunosuppressive treatment in 57.5% of the patients of our study should be considered as important as it may have interfered with the positivity of circulating autoantibodies.

aCL autoantibodies were higher in the pemphigus group as compared with the healthy controls group, with a tendency to significance. The small number of patients investigated could explain the absence of a clear statistically significant difference in comparison with the control group. Interestingly, within the PV subgroup, aCL antibodies were significantly higher as compared with healthy controls, but without any relevant clinical symptoms. However, we cannot rule out the possibility of the presence of concomitant infections explaining the presence of aCL autoantibodies. Our findings also corroborate the results of a recent study showing an increased prevalence of IgG aCL in patients with autoimmune blistering diseases.[4] But, contrary to our findings, the authors reported thromboembolism in seven of 10 patients. Nevertheless, careful observation and follow-up may be required in this form of pemphigus to prevent symptomatic thrombotic events.

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